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Hypertension from a nephrologist's point of view

W.A. Wilmer, MD
Kidney Specialists, Inc.
Board of Advisors, NKF of Central Ohio
Medical Advisory Board, NKF of Central Ohio

** No financial disclosures*

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Case #1 – When to treat and how to treat

- A 52 year old male presents to your office with concerns of fatigue. He is a smoker of 25 years, is treated for hyperlipidemia (total chol 240, LDL 190). His only medication is a statin.
- Blood pressures:
  - 138/88 mm Hg left arm sitting
  - 140/90 mm Hg right arm sitting
  - Pulse 78 bpm, no orthostatic changes to BP.
  - Followup evaluation in the office one week later confirms similar BP readings.
  - Out-of-office BPs are the same: SBPs 138 – 140 / DBP 88-90 mm Hg.
- **Should you treat his elevated blood pressures?**

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What Hypertension Guideline to Use?

- JNC 8
- ACC/ AHA
- International Hypertension Guidelines
- European Hypertension Guidelines
- Canadian Hypertension Guidelines
- KDIGO guidelines, etc.

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What Hypertension Guideline to Use?

JNC 8

60 years or older without DM or CKD the BP goal is <150/90 mm Hg.

18 to 59 years of age without major comorbidities, 60 years or older with DM, CKD, or both conditions, BP <140/90 mm Hg.

2017 ACC/AHA

Normal BP is defined as <120/80 mmHg

Elevated BP as systolic pressure 120 to 129 mmHg and diastolic pressure as <80 mmHg,

Stage 1 hypertension as systolic pressure 130 to 139 mmHg or diastolic pressure 80 to 89 mmHg,

Stage 2 hypertension as systolic pressure ≥140 mmHg or diastolic pressure ≥90 mmHg.

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ACC/ AHA philosophy:

Risk for CVD increases in a log-linear fashion from SBP levels <115 mm Hg to >180 mm Hg, and from DBP levels <75 mm Hg to >105 mm Hg.

A 20 mm Hg higher SBP and 10 mm Hg higher DBP are each associated with a doubling in the risk of death from stroke, heart disease, or other vascular disease.

SBP has consistently been associated with increased CVD risk. This is not true for DBP.

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ACC/AHA Guideline: Assessment of CVD risks:

Use the cvdrisk.com risk evaluator

- **Using this strategy, this patient has a CVD risk of > 10% in ten years and BP goals should be < 130/80 mm Hg.**
- Earlier initiation of pharmacologic therapy is indicated for patients with hypertension and preexisting CVD, chronic kidney disease (CKD) or diabetes mellitus (DM), or high estimated 10-year CV risk.
- Lifestyle modifications always should be used.

Other risk factors that suggest a BP goal of < 130/80 mm Hg:
CKD, especially if proteinuria.
DM
Patients with mild cognitive impairment.
(SPRINT MIND study: Williamson, JD et al. SPRINT MIND Investigators for the SPRINT Research G: Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial, JAMA 321:553-561, 2019)

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The Emphasis on Out-of-office BP Measurements in addition to Office BP Measurements

Office BP measurements

"White coat effect"

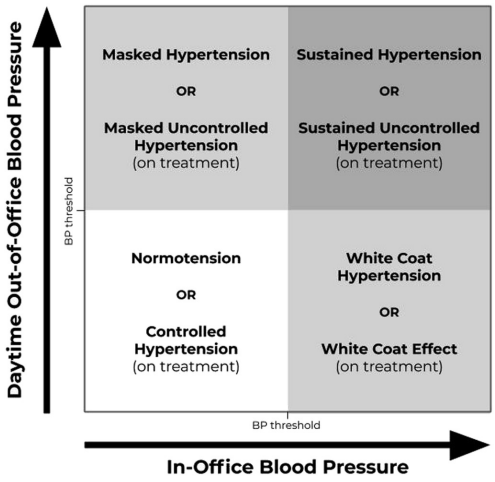
Treatment not as imperative.

>70% will become sustained HTN.

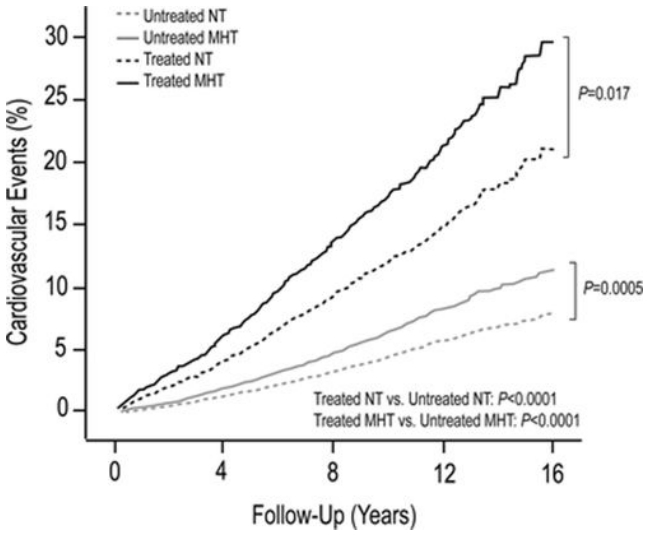
Out-of-office measurements

"Masked HTN"

- *ABPM: 24 hr. monitor*
- *SMBP: self measured BPs – ideally twice in AM and twice PM x 7 days*
- *Kiosk BPs – not as reliable*
- *Wrist / finger BPS – not as reliable.*



End-organ risks of Masked Hypertension



Stanley S. Franklin. Hypertension. Masked Hypertension, 2015, Hypertension-AHA, Volume: 65, Issue: 1, Pages: 16-20,

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You encourage lifestyle modifications (low salt diet, weight loss, exercise) and decide to also start pharmacotherapy. Which of the following is not an appropriate initial choice ?

A. Lisinopril
B. A thiazide diuretic with a potassium sparing diuretic.
C. Amlodipine.
D. Losartan.
E. Atenolol.

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JNC and ACC/AHA:

First tier medications: ACEi, ARB, CCB, thiazide diuretic.

Guidelines eliminate use of beta-blockers (including nebivolol), alpha-blockers, loop diuretics, alpha 1/beta-blockers, central alpha2/adrenergic agonists, direct vasodilators, aldosterone antagonists, and peripherally acting adrenergic antagonists in patients with newly diagnosed hypertension.

There is an increased risk of cerebrovascular events with beta-blockade monotherapy.

Lifestyle management should always be emphasized, but pharmacotherapy strongly considered initially ….due to slow responses to escalate HTN therapy in many practices.

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LEGEND-HTN Study: Large-Scale Evidence Generation and Evaluation Across a Network of Databases for Hypertension.
(Suchard, MA, et al. *Lancet* 394: 1816-1826, 2019.)

- EHR records across four countries, 1 year of data pre-HTN, pharmacy fill rates monitored.
- 4,893,591 patients
  - 48% ACEi
  - 17% thiazide
  - 16% dihydropyridine CCB
  - 15% ARB
  - 3% non-dihydropyridine CCB

Take home message: **MI, hospitalization for heart failure, CVA risks reduced more in the thiazide group. Hyponatremia and hypokalemia more often with thiazides though. (Thiazide potency: indapamide < HCTZ < chlorthalidone.)**

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Case #2 – Stage 2 HTN

- The same patient's older brother – 56 years old - presents to your office with concerns of elevated BP. He is also treated for hyperlipidemia with a statin, BMI 38, he is a smoker.
- Blood pressures:
  - 164/98 mm Hg left arm sitting
  - 166/96 mm Hg right arm sitting
  - Out-of-office BPs are the same: SBPs 165-168 / upper 90s
- **How should you treat this elevated BP?**

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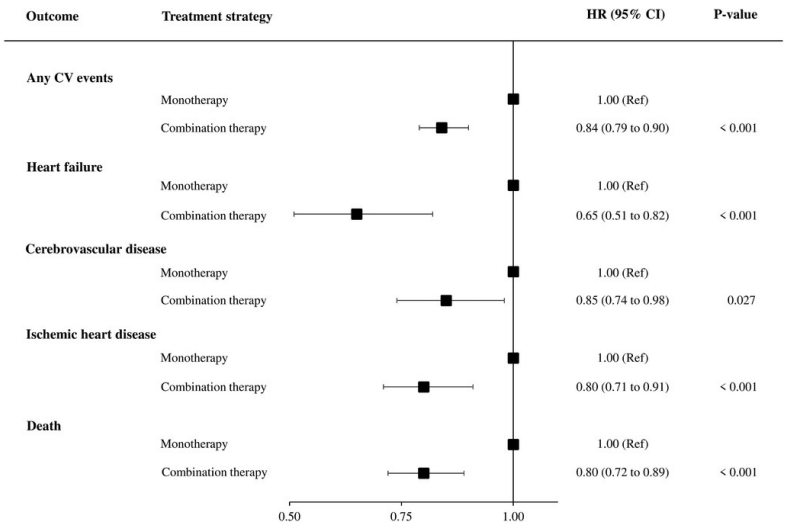
Combination therapy if BPs are 20 / 10 above BP goals

Consider combination therapy from the start



Protective effect of combination therapy over monotherapy in reducing cardiovascular outcomes. A study of 125,635 patients in Italy.

(Rea F, Corrao G, Merlino L, et al.: Initial Antihypertensive Treatment Strategies and Therapeutic Inertia. *Hypertension* 72: 846–853, 2018.)

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Case #3 – Resistant HTN

- A 45 year old female treated for 2 years for HTN reports home BPs of 154 / 92, never with SBP < 140 / DBP < 85. She reports headaches.
- She takes: Lisinopril 40 mg daily, HCTZ 25 mg daily, Nifedipine XL 90 mg daily. She follows a low salt diet and exercises daily. BMI is 25.
- **What is the appropriate NEXT agent to add to her therapy?"**
  - A beta blocker (bisopropol)
  - An alpha blocker (doxazocin)
  - A loop diuretic (furosemide)
  - A mineralocorticoid blocker (spironolactone) ?

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  - An alpha blocker (doxazocin)
  - A loop diuretic (furosemide)
  - **A mineralocorticoid blocker (spironolactone)**

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Resistant Hypertension:

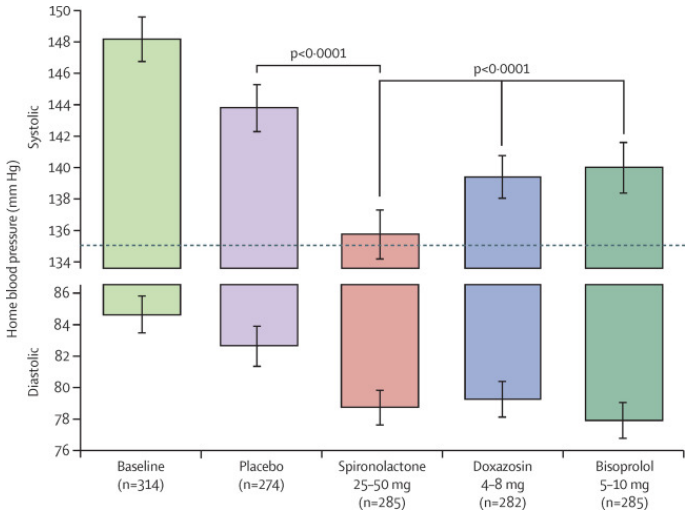
Uncontrolled hypertension while using moderate – high doses of **three** medications one of which is a diuretic

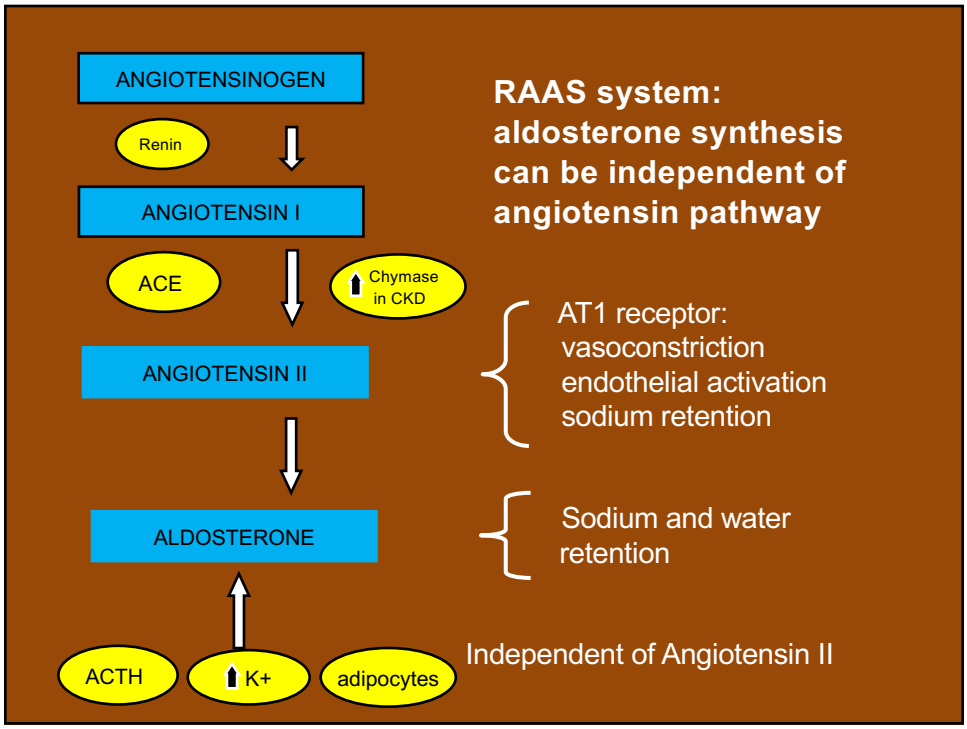
Refractory Hypertension:

Uncontrolled hypertension using moderate-high doses of **five** medications one of which is a diuretic.

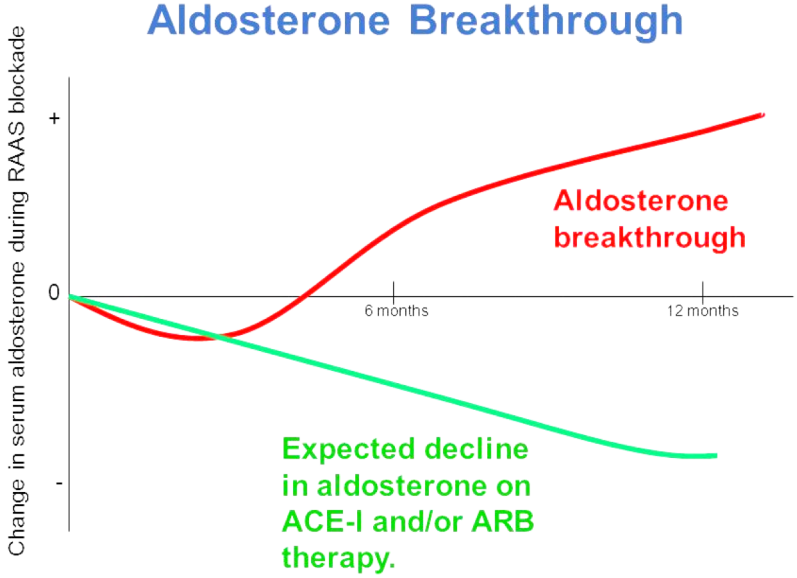
Spironolactone as fourth choice therapy for resistant HTN: The PATHWAY-2 TRIAL

Williams, B. et al, *Lancet.* 386:10008, P2059-2068, 2015





Aldosterone Breakthrough



Slide from University of North Carolina Medical Center presentation at ASN Renal Week. Referencing: Schjoedt, KJ, et al. Aldosterone escape during blockade of the renin-angiotensin-aldosterone system in diabetic nephropathy is associated with enhanced decline in glomerular filtration rate, Diabetologia 2004: 47(11):1936-9.

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Secondary Causes of Hypertension –

Consider when treating resistant HTN

OSA
CKD
Primary hyperaldosteronism
Renal artery strenosis
Medications (NSAIDs, sympathomimetics, cyclosporine, erythropoietin,stimulants)
Alcohol Excess

Other Endocrine:
- Cushings
- Hyperparathyroidism
- Thyroid disease
- Pheochromocytoma

Coarctation of the Aorta

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Hyperaldosteronism

- More prevalent than originally thought.
- Should be considered in cases of resistant hypertension.
- Estimated 20-25% resistant HTN due to aldosterone excess.
- In one study, of 4660 patients with resistant HTN, 2% had hyperaldosteronism workup. (Jaffe,G et al.: Screening rates for primary aldosteronism in resistant hypertension: A cohort study. Hypertension 75:650-659, 2020.)

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Hyperaldosteronism

Does not require hypokalemia to make the dx (!) – *usually* hypokalemia with diuretics, but not always.

High serum bicarbonate (due H+ wasting with K+ wasting).

Primary: adrenal hyperplasia, adrenal adenoma, adrenal carcinoma (CT or MRI adrenal view protocol needed to visualize)

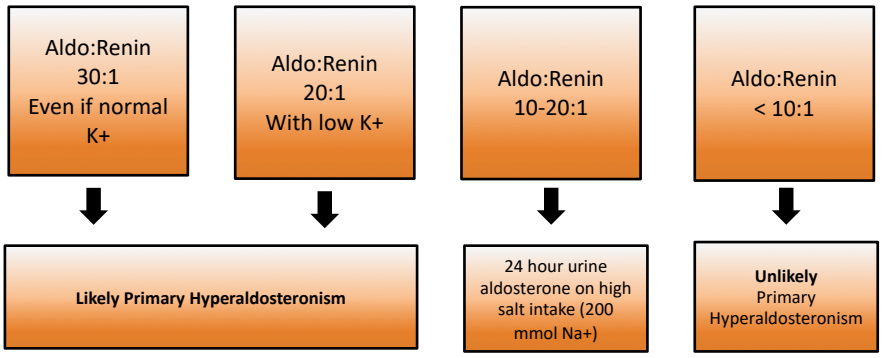
Secondary – atherosclerotic renal vascular disease, FMD (RA duplex, CT angiogram – use when FMD considered)

Evaluation is not that complicated

HOLD: ACEi/ARB/mineralocorticoid blockers
Early AM sitting: renin activity (test result is rate of conversion) and serum aldosterone:

- Plasma renin activity – low in primary (<1 ng/ml/hr), high in secondary (well > 1 ng/ml/hr). Sometimes reported as 'not measurable' – so for use in ratio= 0.5 ng/ml/hr).
- Serum aldosterone levels: usually > 10 ng/dL.

Primary Hyperaldosteronism Evaluation



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Match the renin and aldosterone levels with the following clinical scenarios:

(normal renin 1-4, aldosterone 5-10)

Labs:

1. Renin <1, aldosterone 5.
2. Renin 8, aldosterone 22
3. Renin 30, aldosterone 4
4. Renin 0.5, aldosterone 25

Scenarios:

A. Renal artery stenosis
B. Primary hyperaldosteronism
C. Volume expanded / fluid overload state (Liddle syndrome)
D. ACEi therapy

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Labs:

1. Renin <1, aldosterone 5.
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4. Renin 0.5, aldosterone 25

Scenarios:

A. Renal artery stenosis 2
B. Primary hyperaldosteronism 4
C. Volume expanded / fluid overload state (Liddle syndrome) 1
D. ACEi therapy 3

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Summary

A nephrologist's point of view:

- Emphasis on home / out-of-office BP monitoring
- At risk of CVD / CKD – aggressive control to < 130/80
- Diuretic (thiazide) therapy early
- Diuretic emphasis, monotherapy early, combination therapy with higher BPs
- Resistant HTN – use spironolactone / eplerenone
- Look for secondary forms of HTN if resistant HTN
- Hyperaldosteronism is more common than previously thought.

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Thank you!