



Primary Aldosteronism

The commonest secondary hypertension · Screen, confirm, lateralize, treat

SCREEN ALL
hypertensives, 2025

WHAT CHANGED IN THE 2025 ENDOCRINE SOCIETY GUIDELINE

Screen every patient with hypertension, not just the classic high-risk groups. PA affects **5 to 14%** of hypertensives in primary care and up to **30%** in referral centers, and it was being detected in almost nobody. **Confirmatory testing is now selective**, reserved for an intermediate screen in someone who actually wants surgery. **Spironolactone is preferred over other MRAs** on cost and availability, and **MRAs are preferred over ENaC inhibitors** (amiloride, triamterene). **Add a dexamethasone suppression test whenever an adenoma is found**, to catch co-secreted cortisol.

WHY IT MATTERS MORE THAN THE BLOOD PRESSURE *aldosterone injures the heart and kidney directly*

NOT JUST A BP PROBLEM

At the **same blood pressure**, PA carries higher rates of **stroke, myocardial infarction, atrial fibrillation and heart failure** than essential hypertension, because aldosterone drives **myocardial and vascular fibrosis** directly. **That is why the diagnosis matters even when the BP is controlled on drugs.**

MOST PATIENTS ARE NOT HYPOKALEMIC

The textbook triad is hypertension, hypokalemia and metabolic alkalosis, but **only 30 to 50% have a low potassium**. **Waiting for hypokalemia before screening is the single commonest reason PA is missed.** Normokalemia does not exclude it.

TWO SUBTYPES, TWO PATHS

Bilateral adrenal hyperplasia (~60%) is treated medically. **Aldosterone-producing adenoma, Conn syndrome (~35%)** is potentially **surgically curable**. Separating them is the whole point of the workup.

THE FOUR STEPS *screen, confirm, lateralize, treat*

- 1 SCREEN** with a paired aldosterone and renin. **ARR > 30 with a plasma aldosterone of at least 10 to 15 ng/dL is a positive screen.** Draw it **mid-morning, seated for 15 minutes, with the potassium repleted**, because hypokalemia suppresses aldosterone and produces false negatives. **Stop the MRA for 4 weeks**; spironolactone and eplerenone invalidate the result entirely.
- 2 CONFIRM**, but only when it changes management. Skip confirmation altogether when there is **spontaneous hypokalemia plus undetectable renin plus an aldosterone above 20 ng/dL**, which is diagnostic by itself. Otherwise use a **saline infusion test** (2 L over 4 h; aldosterone above 10 ng/dL afterwards confirms) or **oral salt loading** with a 24 hour urine aldosterone. **If the patient will be treated medically whatever the result, the test is not needed.**
- 3 LATERALIZE** before offering surgery. **CT alone is wrong in a substantial minority**: a non-functioning incidentaloma gets blamed, or a small adenoma is missed. **Adrenal vein sampling is the gold standard**, with a **lateralization ratio of 4:1 or more** indicating a unilateral source. The one reasonable exception is a patient **under 35 with a clear unilateral adenoma over 1 cm and a normal contralateral gland**. **Add a dexamethasone suppression test when there is an adenoma.**
- 4 TREAT** by subtype. Unilateral disease: laparoscopic adrenalectomy. Bilateral disease: a **mineralocorticoid receptor antagonist for life**, with the dose titrated until **renin becomes detectable**, which is the marker of adequate blockade. **Specific therapy beats generic antihypertensives**, because it treats the fibrosis as well as the pressure.

SURGERY CURES THE HORMONE MORE RELIABLY THAN THE BLOOD PRESSURE *counsel this before the operation*

WHAT ADRENALECTOMY ACTUALLY ACHIEVES

Complete biochemical success in 94%, but **only 37% become normotensive off all antihypertensives**; a further **47% improve PASO, 2017**. **Younger patients and women do better**. A patient told they will be cured of hypertension and who still needs two drugs afterwards will feel the operation failed, so set the expectation up front.

THE POST-OPERATIVE TRAP

Stop or halve the MRA and any potassium supplement on the day of surgery. The contralateral zona glomerulosa has been chronically suppressed, so **transient hypoaldosteronism with hyperkalemia** is common in the first weeks. **Check potassium within the first week.** Continuing the MRA into that window is the classic error.

MEDICAL THERAPY *titrate to renin, not just to blood pressure*

Drug	Dose	Where it fits, and what to watch
Spironolactone <i>first line, 2025</i>	25 to 100 mg daily	Preferred MRA on cost and availability, and the most effective. Anti-androgenic effects limit it : gynecomastia in up to half of men, plus menstrual irregularity and reduced libido. Also the best fourth-line drug in resistant hypertension generally PATHWAY-2, 2015 .
Eplerenone	25 to 50 mg BID	Selective MRA with far fewer hormonal side effects , so it is the switch when gynecomastia appears. Roughly half as potent per mg and needs twice-daily dosing because of its shorter half-life.
Amiloride	5 to 10 mg daily	An ENaC inhibitor, now second choice behind the MRAs . Useful when both MRAs are not tolerated, but it blocks the channel without blocking the receptor, so it does not address the fibrotic effects of aldosterone .
Monitoring	K and Cr at 1 and 4 weeks	Then every 3 to 6 months. Hyperkalemia risk rises sharply with CKD or a concurrent ACE inhibitor or ARB . A creatinine rise up to 30% is expected. Aim for a detectable renin : if renin stays suppressed the dose is too low and the cardiovascular risk persists despite a normal BP.

DRUGS THAT WRECK THE SCREEN *know which way each one biases the ratio*

Drug	Effect on the ARR	What to do
MRAs (spironolactone, eplerenone), amiloride, triamterene, potassium-wasting diuretics	False negative renin rises	Stop for 4 weeks . These invalidate the result completely; a normal ARR on spironolactone tells you nothing at all.
ACE inhibitors, ARBs, dihydropyridine calcium blockers	False negative renin rises	Hold for 2 weeks where it is safe to do so. A suppressed renin despite an ACE inhibitor is strongly suggestive of PA , so a positive result on treatment is still meaningful.
Beta-blockers, clonidine, methyldopa, NSAIDs	False positive renin suppressed	Hold for 2 weeks if possible, or interpret a borderline positive with caution before committing the patient to confirmatory testing.
Safe to continue	Minimal effect	Verapamil slow-release, hydralazine, and alpha-blockers such as doxazosin . Use these to hold the BP while the interfering drugs wash out.

PEARLS & PITFALLS

- Normal potassium does not exclude PA.** Only 30 to 50% are hypokalemic, and waiting for it is why the diagnosis is missed.
- Replete potassium before drawing the ARR.** Hypokalemia suppresses aldosterone and gives a false negative.
- Never send a patient to surgery on CT alone** unless they are under 35 with a clear unilateral adenoma.
- Titrate the MRA until renin is detectable**, not just until the blood pressure looks acceptable.

References: Primary Aldosteronism: an Endocrine Society Clinical Practice Guideline, J Clin Endocrinol Metab 2025 (complete update of the 2016 guideline) · Williams et al, PASO, Lancet Diabetes Endocrinol 2017 · Williams et al, PATHWAY-2, Lancet 2015.

Educational aid; verify against local endocrine protocol, renal function and patient factors.

