THE PATHCARE NEWS

PRIMARY ALDOSTERONISM
AN UNDER-RECOGNISED PROBLEM

Primary aldosteronism (PA), also known as Conn's syndrome, is common and has a significantly higher cardiovascular risk profile than sex-, age-, and BP-matched patients with essential hypertension. PA is now considered a major public health issue, which requires a concerted effort at case detection through screening, followed by targeted care.

What is PA?

PA is a group of disorders characterised by the inappropriately high production of aldosterone, leading to hypertension, cardiovascular damage, sodium retention and increased potassium excretion. It is commonly caused by an adrenal adenoma, unilateral or bilateral adrenal hyperplasia, or rarely by adrenal carcinoma or familial hyperaldosteronism. Studies indicate that 5-15% of patients with hypertension have Conn's syndrome. This high prevalence, the higher cardiovascular morbidity and mortality than patients with essential hypertension, and the specific treatments available make case detection crucial.

Who should be screened?

- Some argue that all hypertensive patients should be screened
- Sustained BP >150/100
- Hypertension (>140/90) resistant to three anti-hypertensives (including a diuretic)
- Controlled hypertension (<140/90) on ≥4 anti-hypertensives
- Hypertension plus hypokalaemia (including diuretic-induced)
- Hypertension plus adrenal incidentaloma
- Hypertension plus sleep apnoea
- Early onset hypertension
- Hypertensive first-degree relatives of patients with PA.

How is screening for PA done?

Request aldosterone and renin

The following are important considerations:

- If hypokalaemic the potassium should first be corrected into the normal range (although >80% with PA are normokalaemic)
- Encourage liberal salt intake prior to the test
- Withdraw agents that affect the test for at least 4 weeks:
    - Spironolactone, eplerenone, amiloride, triamterene, potassium-wasting diuretics, products derived from liquorice root (e.g., found in certain sweets).
    - The following substitute anti-hypertensives can be used if required: verapamil (slow release), hydralazine (with verapamil SR to prevent reflex tachycardia), prazocin, doxazosin, terazosin.
    - If results, after discontinuation of these medications, are not diagnostic, discontinue other medication: β-adrenergic blockers, α-2-agonsts (e.g., clonidine, methyl-dopa), ACE inhibitors, NSAIDS, AR blockers, renin inhibitors and dihydropyridine calcium channel blockers.
- Sample collection:
    - Collect samples in the morning: the patient should be out of bed for at least 2 hrs, and seated for 5-15 min prior to sample collection.
    - Maintain samples at room temperature (do NOT put on ice): aldosterone - serum (yellow top) tube; renin - purple top EDTA tube.
- Aid to interpretation:
    - Females in the luteal phase of the menstrual cycle may have false positive results so, if possible, perform the test during the follicular phase.
    - Oestrogen-containing medication may cause a false positive result.
    - Renal failure can lead to false positive results.

- **Reference intervals:**

	Upright	Supine
Aldosterone (pmol/L)	**70-1086**	**49-643**
Renin (ng/L)	**2.7-27.7**	**1.7-23.9**
AR Ratio (pmol/ng)	**>95**	**>95**

The test is most sensitive when a combination of an AR ratio of >95 pmol/ng and an aldosterone value of >350 pmol/L is used. However, some cases may present with an aldosterone as low as 170 pmol/L with suppressed renin, so interpretation in clinical context and the degree of index of suspicion are important. Some experts only assess the degree of aldosterone elevation and renin suppression, without consideration of the ratio.

Confirmation testing

Confirmation testing can be omitted if the presentation is pathognomonic of PA, e.g., hypertension, hypokalaemia, elevated aldosterone and suppressed renin.

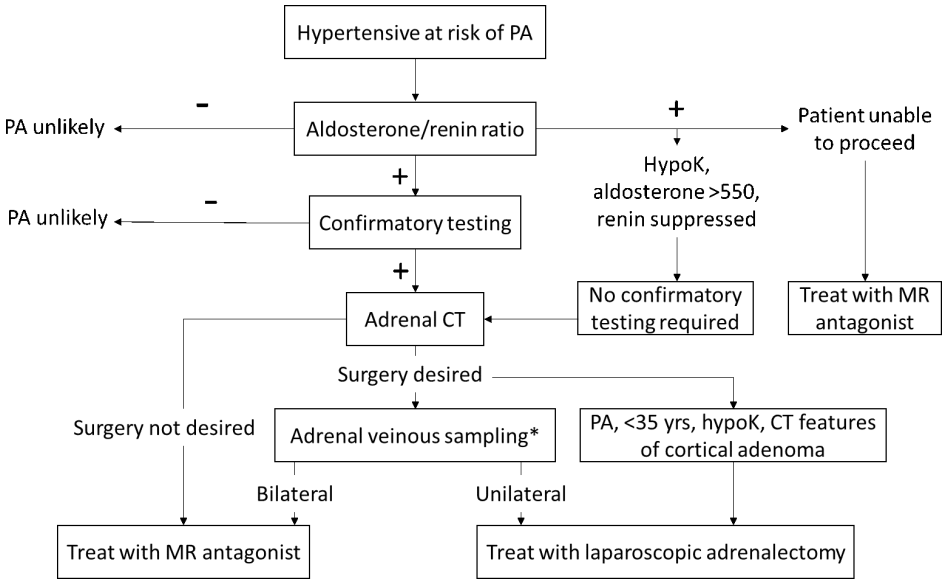
A number of confirmatory testing strategies are available but there is insufficient evidence to support one over the other. The most convenient is saline infusion, but is contra-indicated in patients with uncontrolled hypertension, congestive cardiac failure, cardiac arrhythmia, renal insufficiency or hypokalaemia. Please contact a chemical pathologist for further advice. Patient precautions, as for the screening test above, must be followed.

Saline Infusion Test

- Patient seated for at least 30 min before and during the infusion
- Infuse 2 L of 0.9% saline over 4 h starting at 8-9.30 am with BP and heart rate monitoring
- Blood drawn at 0 h and after 4 h for: aldosterone (serum tube), renin (EDTA tube), cortisol and potassium
- Interpretation:
  - Post-infusion aldosterone >170 pmol/L: PA confirmed
  - Post-infusion cortisol must be lower than basal

Subtype Classification

All patients with PA should undergo adrenal CT (MRI has no advantage) to exclude adreno-cortical carcinoma, and to help discriminate unilateral disease (potential for surgical management) from bilateral disease (medical management). CT, however, misdiagnoses the cause of PA in about 40% of patients, so if a surgical cure is sought, adrenal venous sampling is advised to lateralise disease *(this is complex, difficult and not widely offered. It should only be undertaken after multi-disciplinary consultation with an endocrinologist, interventional radiologist and chemical pathologist).



ECS Clinical Practice Guidelines (2016)
Rossi et *al.* (2016) Clin Chem Lab Med 54(9)