

Hyperaldosteronism - First Line Investigation of Suspected Hyperaldosteronism - Full Clinical Guideline

Reference No: CHISCG6

1. Introduction

Primary aldosteronism (PA) involves about 5% of the hypertensives seen by general practitioners, more than 11% of those referred to specialized hypertension centres and up to 20% of those with difficult to treat hypertension. Moreover, unilateral adrenal-vein sampling (AVS)-guided adrenalectomy has been shown to resolve resistant hypertension in practically all patients.

The main causes of primary hyperaldosteronism are: bilateral idiopathic adrenal hyperplasia (incidence ~65%), unilateral aldosterone-producing adenoma (Conn's Syndrome) (incidence ~30%,), unilateral primary adrenal hyperplasia (incidence ~3%), Glucocorticoid-suppressible hyperaldosteronism (incidence ~1%), Adrenocortical carcinoma (incidence <1%).

The use of single simultaneous samples for aldosterone and renin measurement, with derivation of the "aldosterone/renin ratio" has been advocated as the first line in the investigation of suspected hyperaldosteronism. Low or undetectable renin levels along with inappropriately raised plasma aldosterone concentration (PAC) are the biochemical hallmarks of PA.

Since the renin-aldosterone axis is primarily regulated by renal blood flow, subjects under investigation should not be taking any drugs that interfere with fluid balance or potassium. Subjects should also be adequately hydrated and have an adequate oral intake of sodium. Hypokalaemia should be avoided since it suppresses aldosterone secretion.

2. Guideline for measurement of plasma renin and aldosterone

INDICATIONS

This test is indicated in the differential diagnosis of secondary hypertension.

- Hypertension and hypokalaemia (spontaneous or diuretic induced)
- Resistant hypertension (≥150mm Hg resistant to 3 conventional antihypertensive drugs)
- Adrenal "incidentaloma" ≥10mm and hypertension
- Hypertension with a Family history of primary hyperaldosteronism
- Hypertension onset or Stroke before 40 years of age

PREPARATION

Patient

- Give potassium replacement (Slow K or Sando-K tabs) sufficient to raise serum potassium into reference range (3.5 5.3 mmol/L)
- Patients should be normally hydrated and have an adequate oral intake of sodium

• Patients should be ambulatory for at least 120 minutes before the test (performing usual activities), however samples are best taken between 08:00 and 10:00 during the diurnal peak of aldosterone secretion and after 5-15 mins of sitting.

Stopping medications: The table below indicates drugs which can interfere with renin and/or aldosterone measurements. Most antihypertensives are implicated but α -adrenoceptor blockers (eg Doxazosin), slow release Verapamil and Hydralazine are thought to have minimal effects. Ideally all drug therapy should be stopped at least 2-3 weeks before testing, but this is not generally practical. The test does not give useful results in patients treated with spironolactone or eplerenone.

A pragmatic approach is to stop spironolactone and eplerenone in order to send an initial aldosterone:renin ratio sample. Then if necessary stop or switch all other medication in order to perform the test under ideal test conditions. If the initial results are suggestive of primary hyperaldosteronism, then secondary confirmatory tests for primary hyperaldosteronism can be carried out at the same time as repeating the renin:aldosterone ratio under ideal conditions.

When stopping antihypertensives for testing, replacement with Doxazosin and then calcium channel blockers are often appropriate.

Drug	Physiological effect	Potential effect on interpretation	Time to remove interference	
Spironolactone Increases renin, variable effect on aldosterone		Uninterpretable	6 weeks	
Eplerenone / Amiloride	Increases renin, variable effect on aldosterone	Uninterpretable	2 weeks	
Oestrogens	Increase renin substrate	False negative	2 weeks	
ACE / AR2B inhibitors	Increase renin and reduce aldosterone	False negative	2 weeks	
Beta-blockers	Reduce renin more than aldosterone	False positive	2 weeks	
Diuretics	Increase renin and aldosterone	Variable	2 weeks	
Hypokalaemia	Inhibits aldosterone secretion	False negative	1 week	
NSAIDs	Retain sodium and reduce renin, ?effect on aldosterone	False positive	2 weeks	

Please be sure to include details of all current drug therapy on the request form.

<u>Equipment</u>

Blood collection tubes:

1x yellow top tube: for U&E

1x 4ml EDTA (purple top): for renin and aldosterone

PROCEDURE

- 1. Samples for renin are stable for 6 hours at room temperature.
- 2. Take blood samples and place in RED BAG and transfer immediately to the lab.

INTERPRETATION

Plasma Renin reference ranges (mIU/L)

Supine – <59.7 Ambulant – 5.3 – 99.1

Plasma Aldosterone reference ranges (pmol/L)

 Supine
 –
 103 - 859

 Ambulant
 –
 103 - 1197

Aldosterone / Renin Ratio (ARR)

Raised ARR (>30 pmol/mIU) suggests possible primary hyperaldosteronism.

Interpretative comments are included on reports.

The aldosterone:renin ratio is <u>only</u> an additional indicator of the state of the aldosterone:renin axis, and <u>must</u> be considered in the light of the actual aldosterone and renin levels. A high aldosterone together with a suppressed renin and elevated aldosterone:renin ratio indicates primary hyperaldosteronism.

Note that:

- 1. Some patients with significant renal disease may give similar results.
- 2. For patients taking ACE inhibitors at the time of assessment:
 - detectable renin does not exclude primary hyperaldosteronism
 - undetectable renin would strongly suggest primary hyperaldosteronism

Higher aldosterone values are seen in children and very high renin values are seen in neonates.

The differential diagnosis of mineralocorticoid excess

Low Renin (primary mineralocorticoid excess)				
Aldosterone producing adenoma (Conn's)	34%			
Bilateral adrenal hyperplasia	60%			
Glucocorticoid suppressible hyperaldosteronism	<1%			
Primary adrenal hyperplasia				
Adrenal carcinoma	Rare			

High Renin (secondary mineralocorticoid excess)

Renovascular hypertension Renin secreting tumor Malignant hypertension

Low renin, low aldosterone (pseudohyperaldosteronism)

Deoxycorticosterone secreting tumor Ectopic ACTH secreting tumor Hypertensive forms of CAH Syndrome of apparent mineralocorticoid excess Liquorice Liddle's syndrome Further investigations may include "aldosterone suppression tests" (e.g. saline loading, captopril challenge test), adrenal imaging with venous mapping and adrenal venous sampling.

ASSAYING LABORATORY

Royal Victoria Infirmary, Newcastle-upon-Tyne

TURNAROUND TIME

Results will normally be available within 3 weeks.

3. References

AACE Hypertension guidelines, Endocr Pract. 2006;12(No 2): 193 - 222

Valloton MB. Primary hyperaldosteronism. Part 1 Diagnosis of primary hyperaldosteronism. Clin Endocrinol 1996; **45:** 47-52

Lim PO, Dow E, Brennan G, Jung RT, MacDonald TM. High prevalence of primary aldosteronism in the Tayside hypertension clinic population. J of Human Hypertension 2000; **14:** 311-315

Cartledge S, Lawson N. Aldosterone and renin measurements. Ann Clin Biochem 2000, **37:** 262-278

4. Documentation Controls

Reference Number CHISCG6	Version: 11.0.0		Status Final	Practiti Consu	ors: list Healthcare Science oner (Helen Seddon) ltant Endocrinologist ia Ugur)	
Version /	Version	Date	Authors		Reason	
Amendment History	11.0.0	Feb 2024	Helen Seddo Antonia Ugur		Update to stability of renin (page 2)	
Intended Recipients: Endocrinology (medics and nurse specialists) and Biochemistry staff						
Training and Dissemination: Guideline reviewed and agreed at the monthly Biochemistry/Endocrine MDT meeting. All relevant staff are aware of this guideline.						
Linked Documents: None						
Keywords: Renin, Aldosterone, Hyperaldosteronism						
Business Unit Sign Off		Group: Biochemistry/Endocrinology MDT meeting Date: 22/11/2023				
Divisional Sign Off		Group: Division of Cancer, Diagnostics & Clinical Support Date: Dec 2023				
Date of Upload			23/02/2024			
Review Date			Dec 2026			

Suitable for printing to guide individual patient management but not for storage Review Due: Dec 2026 Page **4** of **5**

Contact for Review	Consultant Healthcare Scientist (Julia
	Forsyth)
	Specialist Healthcare Science Practitioner
	(Helen Seddon)