# SCREENING FOR CONN'S SYNDROME (PRIMARY ALDOSTERONISM)

| | |
|---|---|
| **TARGET AUDIENCE** | Secondary care |
| **PATIENT GROUP** | All adult patients in NHS Lanarkshire |

## Clinical Guidelines Summary

- **Indications**
  - Resistant hypertension
  - With/without hypernatraemia/hypokalaemia
  - With/without adrenal incidentaloma
- **Patient preparation**
  - Discontinue spironolactone and amiloride for, ideally, 2 weeks prior to test.
  - Correct low potassium.
  - Ensure normal diet with adequate sodium intake in the few days prior to sampling.
- **Procedure**
  - Patient should be seated for 15-30 minutes prior to sampling.
  - Sample type: one 4 mL potassium EDTA Vacutainer (367869), lilac top.
  - Transport sample to laboratory immediately (<4 h). **DO NOT USE ICE OR REFRIGERATE**.
- **Interpretation**
  - Samples are sent for analysis to Glasgow Royal Infirmary.
  - Aldosterone/renin ratio >30 where aldosterone is >300 pmol indicates further investigation (repeat, saline suppression test etc)

***Screening for Conn's syndrome (primary hyperaldosteronism)***

## Contents


1. Background ..... 2
2. Indications ..... 2
3. Patient Preparation ..... 2
4. Procedure ..... 2
5. Interpretation ..... 3
6. Effect of medication on renin and aldosterone ..... 3
7. Appendices ..... 4


## 1. Background

Primary aldosteronism is characterised biochemically by a low plasma renin with a raised plasma aldosterone. This guideline describes recommended initial testing procedures when primary aldosteronism is suspected. Abnormal results do not necessarily confirm a diagnosis and should be referred for specialist opinion.

## 2. Indications

Consider testing for primary aldosteronism when:

- Hypertension and hypokalaemia (not diuretic-induced)
- Resistant hypertension
- Adrenal incidentaloma and hypertension
- Severe hypertension (SBP >160, DBP >100)

## 3. Patient Preparation

It is best to take samples for renin and aldosterone measurement under standard conditions. The hormone measurements may be misleading or give false positive or negative results if the following conditions are not met.

Discontinue spironolactone and amiloride at least 2 weeks before measurement. Other antihypertensive drugs can make interpretation difficult and ideally should also be discontinued. Some useful information may be derived from testing in patients taking ACE inhibitors, diuretics, beta-blockers and ARBs (see section 6)

Low serum potassium levels can inhibit aldosterone secretion, and ideally serum potassium should be not less than 3.5 mmol/L at the time of analysis. Potassium supplements may be used to achieve this level, but should be discontinued 12 hours before blood sampling.

Ensure a normal diet with adequate sodium intake in the few days prior to sampling.

## 4. Procedure

The patient should be seated for 15-30 minutes prior to blood sampling. A change in posture may cause a rise in aldosterone levels (false positive result), or a rise in renin levels (false negative).

Specimen tubes are:
RENIN & ALDOSTERONE: 4 mL Potassium EDTA Vacutainer (367869) (Lilac top)

***Screening for Conn's syndrome (primary hyperaldosteronism)***

Venous blood specimens are taken and transported IMMEDIATELY to the Biochemistry Department. Samples must be received within 4 hours of collection. **Do not use ice** for transportation as this may cause cryoactivation of renin. **It may help to phone the lab to say the specimens are arriving.**

## 5. Interpretation

Aldosterone (pmol/L) to renin (mIU/L) ratio (ARR) of greater than 24 where the aldosterone is greater than 210 pmol/L suggests primary aldosteronism (97% sensitivity, 92% specificity). This cut-off is based on current methods at Glasgow Royal Infirmary (August 2024). Patients with a positive screening test first require a repeat to confirm, ensuring the patient is not receiving beta-blockers. If the repeat test is positive, then further investigation is required (e.g. salt loading test) to confirm the presence of primary hyperaldosteronism.

## 6. Effect of medication on renin and aldosterone

ACE inhibitors, ARBs and diuretics may "falsely elevate" plasma renin activity; therefore the finding of a normal ARR would not exclude the diagnosis of primary aldosteronism. However, a low plasma renin activity in such circumstances means primary aldosteronism is highly suspect.

Adrenergic inhibitors (eg beta-blockers and central alpha 2 agonists) suppress renin more than aldosterone, and may cause a falsely elevated ratio. An elevated aldosterone, with an elevated ratio means primary aldosteronism remains suspect in such patients.

| Drug | Renin | Aldosterone | Effect on ratio |
|---|---|---|---|
| Nifedipine/verapamil | Minimal | Minimal | No effect |
| Amlodipine | Minimal | Decreased/minimal | Nil/false negative |
| Alpha blockers | Nil | Nil | No effect |
| Hydralazine | Minimal | Minimal | No effect |
| ACE inhibitors | Increased | Decreased | False negative |
| Diuretics | Increased ++ | Increased | False negative |
| Minoxidil | Increased | Minimal | False negative |
| AR blockers | Increased | Decreased | False negative |
| Beta blockers | Decreased | Minimal | False positive |
| Alpha-methyl dopa | Decreased | Minimal | False positive |

# References/Evidence


1. Gordon RD, Klemm SA, Tunny TJ, Stowasser M. Primary aldosteronism: hypertension with a genetic basis. *Lancet* 1992; 340:159-61
2. Lim PO, Dow E, Brennan G, Jung RT, MacDonald TM. High prevalence of primary aldosteronism in the Tayside hypertension clinic population. *J Hum Hypertension* 2000; 14:311-5
3. Lim PO, Jung RT, MacDonald TM. Raised aldosterone to renin ratio predicts anti-hypertensive efficacy of spironolactone: a prospective cohort follow-up study. *Br J Clin Pharmacol* 1999; 48:756-60
4. Primary aldosteronism: renaissance of a syndrome. *Clin Endocrinol* 2007:66;607-18
5. Doi, SR et al Optimal use and interpretation of the aldosterone renin ratio to detect aldosterone excess in hypertension. *J Hum Hypertension* 2006: 20; 482-9
6. Manolopoulou J, Fischer E, Dietz A *et al*. Clinical validation for the aldosterone-to-renin ratio and aldosterone suppression testing using simultaneous fully automated chemiluminescence immunoassays. *J Hypertens* 2015; 33: 2500-11
7. Dorrian CA, Toole BJ, Alvarez-Madrazo S, Kelly A, Connell JMC, and Wallace AM. A screening procedure for primary aldosteronism based on the Diasorin Liaison automated chemiluminescent assay for direct renin. *Ann Clin Biochem* 2010;47:195-9

# 7. Appendices

**1. Governance information for Guidance document**

| | |
|---|---|
| **Lead Author(s):** | Jacqueline McGuire |
| **Endorsing Body:** | Endocrinology |
| **Version Number:** | 1.5 |
| **Approval date** | |
| **Review Date:** | |
| **Responsible Person (if different from lead author)** | |

| **CONSULTATION AND DISTRIBUTION RECORD** | |
|---|---|
| **Contributing Author / Authors** | Jacqueline McGuire – Clinical Lead Biochemistry, University Hospital Hairmyres<br>Neil Syme – Consultant Clinical Biochemist, University Hospital Monklands |
| **Consultation Process / Stakeholders:** | Sarah Cleary – Consultant Clinical Biochemist, University Hospital Wishaw<br>Babu Mukhopadhyay – Consultant Physician & Endocrinologist |
| **Distribution** | |

| CHANGE RECORD | | | |
|---|---|---|---|
| **Date** | **Lead Author** | **Change** | **Version No.** |
| August 2024 | Jacqueline McGuire | Review, no major changes. | 1.5 |
| | | | |
| | | | |
| | | . | |
| | | | |
| | | | |
| | | | |
| | | | |