

What is Primary Aldosteronism?

Primary aldosteronism (PA) is a disease where the adrenal glands produce too much of the hormone aldosterone.

The two adrenal glands sit on top of each kidney and produce a number of hormones, including aldosterone. Aldosterone is important for survival as it helps the body absorb salt through the kidneys. This helps the body maintain a normal blood pressure. In healthy people, the adrenal glands respond to a person's blood pressure and salt intake, and regulate how much aldosterone is produced. For example, if no salt is eaten for many days, the adrenal glands will produce more aldosterone so that the body retains salt.

However, in primary aldosteronism, either one or both adrenal glands are overactive and produce aldosterone even when the body does not need it. This leads to too much salt and water being retained in the body, which causes high blood pressure.

Aldosterone also causes direct damage to the heart, brain, kidney and blood vessels. As a result, patients with primary aldosteronism are more likely to have heart disease, stroke and kidney failure than other forms of high blood pressure¹.

What causes Primary Aldosteronism?

Primary aldosteronism occurs for two main reasons:

- **When both adrenal glands are affected and produce aldosterone in excess.** This is called bilateral adrenal hyperplasia (BAH), also known as idiopathic hyperaldosteronism (IHA) and accounts for around 60% of cases of primary aldosteronism. The exact reason for the development of bilateral adrenal hyperplasia is unclear.
- **When a benign (non-cancerous) tumour or overgrowth in one adrenal gland produces too much aldosterone.** This is known as aldosterone producing adrenal adenoma, or Conn's syndrome and accounts for around 30% of cases of primary aldosteronism. Research over the past ten years has shown that these tumours contain genetic mutations which lead to uncontrolled aldosterone production.

It is very rare for primary aldosteronism to be caused by a cancer of the adrenal gland (adrenocortical carcinoma).

Hereditary types of primary aldosteronism are less common, and still being studied. One type deserves a special mention due to the specific treatments available. This is glucocorticoid remediable aldosteronism (GRA). GRA is caused by a genetic abnormality in the gene that controls aldosterone production. It is most often seen in people younger than 20 years and in people with a family history of stroke and hypertension at a young age.

Symptoms of primary aldosteronism

Much of the time, primary aldosteronism does not cause any symptoms other than high blood pressure. The high blood pressure may be difficult to control using conventional antihypertensive medicines.

In around 2-3 in 10 patients (20 – 30%), blood potassium levels will be low and require potassium tablets to normalise. In some, the potassium level may drop after taking diuretic medicines. Low potassium may cause a person to feel weak and tired, and in severe cases cause muscle paralysis and/or abnormal heart beats.

In the longer term, high blood pressure can lead to strokes, heart arrhythmias, heart disease and kidney disease. Primary aldosteronism is more likely to cause these health problems than high blood pressure alone, due to the harmful effects of too much aldosterone.

Other symptoms sometimes reported by patients with primary aldosteronism include tiredness, easy fatigue, difficulty concentrating, having to get up frequently overnight to pass urine, anxiety, having a short temper and heavy snoring (in some cases leading to obstructive sleep apnoea).



For more information visit: <http://www.hormones-australia.org.au>
To Find an Endocrinologist near you visit: <http://www.hormones-australia.org.au/find-an-endocrinologist/>

How is primary aldosteronism diagnosed?

A series of tests are required to properly diagnose primary aldosteronism².

1. Blood test to measure aldosterone and renin levels

This test involves taking a small amount of blood in the morning, at least 2 hours after getting out of bed, and sending it to pathology for lab tests. This may need to be repeated several times. The ratio of aldosterone to renin is used to screen for primary aldosteronism.

What do the results mean?

Normal to high aldosterone levels, with a very low renin level, suggests primary aldosteronism. Your doctor may recommend other tests to confirm the diagnosis.

Note that results can vary a little due to different techniques being used by different pathology labs. This can mean different cut-offs are used between labs to suggest the presence of primary aldosteronism.

2. A saltwater (saline) infusion test

This test is used to confirm that the adrenal glands are abnormal and making too much aldosterone despite increased salt. This procedure is usually done in hospital and takes around 4 – 5 hours. A blood test is done before and after the saline infusion to measure the level of aldosterone. Some hospitals may offer a different type of confirmatory test, but the saline infusion test is the most common in Australia.

What do the results mean?

If your aldosterone does not lower sufficiently following saline, you will be diagnosed with primary aldosteronism.

3. An adrenal CT scan and adrenal vein sampling (AVS)

Your doctor may want to look at the size and shape of your adrenal glands using an imaging method called computerised tomography (CT scan). A CT scan uses X-ray and computer

technology to create pictures of the body. These images can help identify the cause of your high aldosterone levels in combination with the results of adrenal vein sampling, and are used to guide treatment decisions.

For a CT scan, your doctor will send you to an imaging specialist called a radiologist. Before having a CT scan, you will change into a gown and remove any watches or other metallic objects. For the scan, you will lie on a platform that slides into the scanning machine. Inside the machine, a scanner moves around your body as it takes the X-ray pictures. You will need to lie very still, as movement can blur the images. Usually X-ray contrast is injected to help the radiologist interpret the pictures. This contains iodine – some people may be allergic to this and furthermore in some people it can trigger an overactive thyroid. The scan takes around 30 minutes.

Adrenal vein sampling is a procedure that takes blood samples from the main blood vessels that drain blood from the adrenal glands. The amount of aldosterone is compared in each sample to work out if the aldosterone comes from one adrenal gland or both glands.

This procedure is done in a specialist centre and normally takes 1 – 3 hours (plus additional waiting/rest time). Under local anaesthetic, a fine needle and very thin tube (catheter) will be inserted into a vein and guided through the main blood vessels in your body until they reach the adrenal glands. Once in place, blood samples are collected from veins draining each adrenal gland. You won't be able to feel the catheters or samples being collected. After the procedure, the catheter is removed, and you will need to rest for between 2-4 hours.

Adrenal vein sampling is only done if you are happy to undergo adrenal surgery should you have disease involving only one adrenal gland.

For more information visit: <http://www.hormones-australia.org.au>
To Find an Endocrinologist near you visit: <http://www.hormones-australia.org.au/find-an-endocrinologist/>

How is primary aldosteronism treated?

The goal of treatment is to prevent the harmful effects of high aldosterone by returning your aldosterone levels to normal or blocking the actions of aldosterone.

Medication

For patients whose disease is caused by aldosterone production from both adrenal glands, medication is the best form of treatment².

In Australia, the most common medication (tablet) for treating primary aldosteronism is spironolactone which can be taken once a day. Spironolactone blocks the effects of aldosterone, not only in the kidneys but in all the organs where aldosterone may be causing harm. The main side effects are breast growth and pain (in both men and women), reduced libido or sex drive (in men and women) and irregular periods (in pre-menopausal women). These side effects are usually seen

at higher doses, and are reversible once the dose is reduced or you switch to another medication.

Another medication that does not have these side effects is **eplerenone**. This also blocks the effects of aldosterone, however, eplerenone is not subsidised by the government and is therefore more expensive. It usually needs to be taken twice a day.

Another option is **amiloride**, which blocks the effect of aldosterone in the kidneys.

Your doctor will discuss these options with you, and monitor your progress over time to ensure that your blood pressure is improving and to monitor for side effects. Sometimes more than one tablet is required to keep the blood pressure under control, especially if you have had high blood pressure for many years.

It is important to keep taking the medication as instructed by your doctor. If you stop taking this medication suddenly, it can cause high blood pressure which increases the risk for heart attack, stroke and kidney disease.

Surgery

For patients who have primary aldosteronism caused by aldosterone overproduction from only one adrenal gland, the best treatment is key-hole surgery to remove the affected gland².

Medication is given before surgery to get your blood pressure and potassium in the normal range ahead of surgery.

Keyhole surgery to remove an adrenal gland is performed in hospital under general anaesthetic, so you are completely asleep during the procedure. You will have four small incisions made in the side of your back. These allow the surgeons to view the adrenal gland using a tiny camera (called a laparoscope) through one incision, and then access and remove the adrenal gland through the other incisions. The procedure generally lasts for 2-4 hours and will require an overnight stay in hospital.

The response to surgery depends on your age and how long you have had primary aldosteronism. The earlier the diagnosis, the less injury caused by aldosterone and therefore surgery is likely to have the greatest blood-pressure lowering effect. Blood tests of aldosterone and renin around three months after surgery will indicate if you have had a cure of the disease. Blood pressure may take longer to return to normal, although you may still need blood pressure lowering tablets (usually much less than before) even after a cure of primary aldosteronism.



For more information visit: <http://www.hormones-australia.org.au>
To Find an Endocrinologist near you visit: <http://www.hormones-australia.org.au/find-an-endocrinologist/>

FAQs about primary aldosteronism

How long before my blood pressure returns to normal after I start taking medication?

Medications that block the effects of aldosterone (spironolactone, eplerenone and amiloride) generally start to reduce blood pressure within a few weeks after taking them but the full effect may not be obvious for 6 – 12 months.

Is my condition temporary? Or will I always have it?

Primary aldosteronism can be cured if you have surgery to remove an affected adrenal gland that has been confirmed to be the source of excessive aldosterone production. However, some people require ongoing medication even after surgery has cured primary aldosteronism, to reduce high blood pressure caused by stiff blood vessels or other factors. There is also a small chance of the disease returning after the initial curative surgery.

For patients who have primary aldosteronism caused by both adrenal glands, the condition will always be present, however the harmful effects of excess aldosterone will be blocked by lifelong medication, either with spironolactone or eplerenone.

Will I always need medication?

Medication to treat primary aldosteronism caused by bilateral adrenal disease (that is, when both adrenal glands are affected) is generally required lifelong.

When a single affected adrenal gland is surgically removed, the aldosterone-blocking medication can be stopped and may no longer be necessary if your aldosterone levels return to normal. However, other blood-pressure lowering medications may still be needed. Regular check-ups with your doctor are the best way to monitor your blood pressure and your need for medication.

Questions to ask your doctor

Seeing your doctor or having a medical problem can be stressful. It often takes time for information to sink in and it is very common to feel overwhelmed by what is happening.

Sometimes it is helpful to write down questions for your doctor before you go. Some questions that might be useful for you are:

- Do I need new medication?

- Do I still take my old blood pressure medication?
- How quickly should the medicine work?
- For how long do I need to take my medication?
- Does my medication have any side effects?
- Do I need another appointment?

Common Terms & Definitions

Antihypertensive medication – A group of medications used to treat high blood pressure

Benign – Not cancerous

Bilateral – Having or affecting two sides

Diuretic – A substance that causes increased production of urine (therefore removing salt and water from the body)

Infusion – The administration of a liquid medication into the vein through a needle or catheter (very thin tube)

Tumour – An abnormal growth in the body. Tumours can be benign or malignant

References

1. Monticone, S., et al., Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis. *The Lancet Diabetes & Endocrinology*, 2018. 6(1): p. 41-50.
2. Funder, J.W., et al., The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, 2016. 101(5): p. 1889-916.
3. Yang, J., P.J. Fuller, and M. Stowasser, Is it time to screen all patients with hypertension for primary aldosteronism? *Med J Aust*, 2018. 209(2): p. 57-59.

About this Fact Sheet

The content on this page was prepared by Dr Jun Yang; and medically reviewed by Professor Peter Fuller and Professor Michael Stowasser.

We are extremely grateful to our volunteers for reviewing this information.

For more information visit: <http://www.hormones-australia.org.au>
To Find an Endocrinologist near you visit: <http://www.hormones-australia.org.au/find-an-endocrinologist/>