QUESTION 96

A 32yo woman if found to have high blood pressure (180/105mmHg) at an insurance medical examination. She is asymptomatic. Clinical examination is normal. Similar blood pressure readings are recorded on 2 follow-up examinations.

Serum biochemistry shows:

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Reference (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>146</td>
<td>[134-146]</td>
</tr>
<tr>
<td>Potassium</td>
<td>2.5</td>
<td>[3.4-5.0]</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.08</td>
<td>[0.06-0.12]</td>
</tr>
</tbody>
</table>

Which of the following investigations is the most appropriate next step?

A. 24 hour urinary electrolytes  
B. Upright plasma aldosterone to renin ratio  
C. Captopril renogram  
D. Adrenal CT scanning  
E. 24 hour urinary aldosterone

PRIMARY HYPERALDOSTERONISM

- **Causes**
  - Adrenal adenoma
  - Bilateral idiopathic adrenal hyperplasia
  - Familial forms of primary hyperaldosteronism
  - Adrenal carcinoma

- **Conn’s syndrome** refers specifically to an adrenal adenoma producing excess aldosterone  
- More common in women, usually occurs between 30 and 50yrs

**Presentation**

- Spontaneous hypokalaemia, especially if associated with hypertension  
- Severe and/or persistent hypokalaemia when taking low to moderate doses of K-wasting diuretics  
- Refractory HT

**Symptoms**

- HT and associated complications  
- Muscle weakness  
- Abdominal distension  
- Ileus from hypokalaemia  
- Oedema is NOT a feature and if present suggests an alternative diagnosis

**Investigations**

- Plasma rennin activity (PRA) is very low in patients with primary mineralocorticoid excess  
- Raised PRA (in associating with HT and hypokalaemia) is seen with diuretic therapy, renovascular or malignant hypertension and rarely rennin-secreting tumours  
- When PRA is suppressed and plasma aldosterone concentration (PAC) is raised, this suggests primary hyperaldosteronism
- Secondary hyperaldosteronism (eg: renovascular disease) should be considered when both PRA and PAC are increased
- An alternate source of mineralocorticoid receptor stimulation (eg: hypercortisolism, licorice ingestion) should be considered when PRA and PAC are both suppressed
- Test should be performed at 0800
- Most anti-hypertensives can be continued and postural stimulation is not required
- Cannot interpret test if patient on spironolactone or eplerenone
- ACE-I/s may falsely elevate PRA so a low PAC/PRA ratio does not exclude primary hyperaldosteronism but if PRA is very low/undetectable this makes PH very likely

24 hour urine no longer used to diagnose PH
Used if above blood tests do not show the expected results or if there is suspicion of surreptitious vomiting or laxative abuse
Inappropriate K wasting is defined as urinary K >30meq/day in a pt with hypokalaemia
An appropriately low rate of K excretion in the urine suggests extrarenal losses (eg: vomiting, diarrhoea) or diuretic treatment with the urine being collected after the diuretic effect has worn off
- Aldosterone excretion can be measured with high values being consistent with primary hyperaldosteronism if the PRA is low

- Elevate PAC/PRA ratio indicates either
  - PH (high PAC, low PRA)
  - Non-aldosterone mineralocorticoid excess (low PAC, low PRA)

- To confirm the diagnosis, need to do aldosterone suppression testing
  - Sodium loading (orally or IV) to suppress aldosterone
  - Then collect 24 hour urine for aldosterone, sodium and Cr

APA: aldosterone-producing adenoma; AVS: adrenal venous sampling; CT: computed tomography; GRA: glucocorticoid-remediable aldosteronism; IHA: idiopathic hyperaldosteronism; PAH: primary adrenal hyperplasia.

- Once diagnosis of PH is confirmed, need to differentiate adrenal adenoma (or rarely carcinoma) from bilateral idiopathic hyperplasia as treatment is different
- Adenomas (30-60%) should be surgically removed if possible
Adrenal hyperplasia is generally milder and should be treated with an aldosterone receptor antagonist.
CT or MRI are ok for initial investigation.
>4 cm unilateral mass suggests carcinoma.
Can be difficult to differentiate adenomas and hyperplasia on imaging.
Adrenal vein sampling – measuring aldosterone in samples of adrenal venous blood is gold standard to distinguish between adenomas and hyperplasia.

Correct answer is B – aldosterone:renin ratio.
A – 24 hour urine no longer used to diagnose hyperaldosteronism. May be useful if blood tests inconsistent with diagnosis other cause.
C – Captopril renogram is used in the diagnosis of renal artery stenosis.
D – CT scan may be useful once diagnosis of primary hyperaldosteronism is made on bloods/urine. Will help to determine cause – adrenal adenoma/carcinoma/hyperplasia.
E – Aldosterone suppression test, using 24 hour urinary aldosterone levels, is used to confirm the diagnosis of PH but is not the initial test.

SECONDARY HYPERTENSION
Consider secondary HT when pts develop HT under age 35 or over age 55.
Causes are primarily:
⇒ Renal
⇒ Endocrine
Coarctation of the aorta is a further cause.
Renal
⇒ Renovascular – stenosis of renal vessels leads to reduced flow and activation of rennin-angiotensin system → angiotensin II elevates blood pressure by vasoconstriction and by stimulation aldosterone which results in sodium retention.
⇒ Renal parenchymal - likely multiple mechanisms including rennin-angiotensin system and sodium retention.
⇒ Renin secretion by juxtaglomerular cell tumours or nephroblastomas (rare).
Endocrine
⇒ Adrenal hypertension
  * Primary hyperaldosteronism – sodium retention (in exchange for potassium loss in the renal tubule).
  * Cushing’s syndrome - due to corticosteroids causing sodium retention.
  * Phaeochromocytoma – increased secretion of adrenaline and noradrenaline by tumour → excessive stimulation of adrenergic receptors → vasoconstriction.
⇒ Acromegaly.
⇒ Hypercalcaemia
  * May be associated with HT due to direct vasoconstrictive effect.
* Hyperparathyroidism can also lead to renal parenchymal disease with nephrolithiasis and nephrocalcinosis

LABORATORY TESTS FOR EVALUATION OF HYPERTENSION
- Urine for protein, blood and glucose and M/C/S
- Haematocrit
- Serum potassium
- Serum Cr and urea
- Fasting glucose
- Cholesterol
- TFT
- Calcium and phosphate
- ECG
- CXR

ADRENAL CORTEX
- Produces 3 major classes of steroids:
  ⇒ Glucocorticoids
  ⇒ Mineralocorticoids
  ⇒ Adrenal androgens

Aldosterone
- Main effect is to regulate extracellular fluid volume and potassium balance
- Aldosterone stimulates
  ⇒ Na-K ATPase pump which reabsorbs Na and excretes K into the urine
  ⇒ Na channels which passively reabsorb Na
- Aldosterone secretion is controlled by
  ⇒ Renin-angiotensin system
  ⇒ ACTH
  ⇒ Potassium
- Via feedback from the macula densa, juxtaglomerular cells release renin in response to low ECF volume ⇒ angiotensin ⇒ aldosterone ⇒ Na and water retention
- Potassium directly stimulates aldosterone secretion
- Physiological amounts of ACTH stimulate aldosterone acutely but this is not maintained unless ACTH is administered in a pulsatile fashion