**Question 6**

A 35 year old man is found to be hypertensive with a blood pressure of 180/110 mmHg. At presentation, on no treatment, the following results are obtained.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum potassium</td>
<td>3.3 mmol/L</td>
<td>(3.5 – 5.0)</td>
</tr>
<tr>
<td>Urinary potassium</td>
<td>40 mmol/L</td>
<td>(&lt;30)</td>
</tr>
<tr>
<td>Plasma aldosterone</td>
<td>620 pmol/L</td>
<td>(supine 50-450)</td>
</tr>
<tr>
<td>Plasma renin</td>
<td>4 mU/L</td>
<td>(ambulatory 5-75)</td>
</tr>
</tbody>
</table>

The most appropriate next investigation is measurement of:

A. 24 hour urinary aldosterone  
B. Plasma aldosterone after 4 hours of saline infusion  
C. Plasma aldosterone after 5 days of dexamethasone administration  
D. Plasma aldosterone after synthetic ACTH administration  
E. Adrenal venous aldosterone concentration during bilateral venous catheterisation

Answer:

Important facts provided:
- Severe hypertension in a young person - look for secondary causes  
- Hypokalaemia with increased urinary potassium losses  
- Inappropriately high plasma aldosterone: renin ratio, suggesting autonomous aldosterone secretion

**Secondary causes of Hypertension**
- Check: if young (<50), severe or refractory hypertension, no family history of hypertension, acute rise over previously stable blood pressure values  
- Also check for end organ damage (retinopathy and papilloedema, nephropathy and cardiomyopathy) and other cardiovascular risk factors

<table>
<thead>
<tr>
<th>Obesity</th>
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| Drugs   |Steroids  
|         |OCP       
|         |Alcohol   |

<table>
<thead>
<tr>
<th>Endocrine</th>
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</table>
| ↑ steroids (Cushing's)  
| - Primary eg adrenal tumour  
| - Secondary eg ↑ ACTH  
| - Exogenous steroids  
| ↑ renin  
| - Primary eg renin secreting tumour (rare)  
| - Secondary eg renal artery stenosis  
| ↑ mineralocorticoid (aldosterone)  
| - Primary eg adrenal tumour/ hyperplasia  
| - Secondary eg high renin or high ACTH (glucocorticoid remediiable aldosteronism GRA) |

<table>
<thead>
<tr>
<th>Hypothyroidism</th>
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<tbody>
<tr>
<td>Hypercalcaemia eg primary parathyroidism</td>
</tr>
<tr>
<td>Renal</td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Vascular</td>
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<td></td>
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<td></td>
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<tr>
<td>Sleep apnoea</td>
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</tbody>
</table>

When triad of **hypertension, hypokalaemia and metabolic alkalosis** present
- Suggests ↑ mineralocorticoid levels (mainly hyperaldosteronism and to lesser extent, deoxycortisone)
- Leads to sodium and water retention, urinary potassium loss and thus hypokalaemia, loss of urinary hydrogen ions thus alkalosis
- Note: normokalaemia often more common in primary hyperaldosteronism (>50%) and always the case in GRA

- **Ddx:**
  1) **Primary hyperaldosteronism** ($\uparrow$ **plasma aldosterone**, $\downarrow$ **plasma renin**)
     - Aldosterone secreting adrenal adenoma (unilateral/ bilateral)
     - Ectopic adrenal adenoma
     - Adrenal hyperplasia (idiopathic ?increased sensitivity to angiotensin)
     - Familial hyperaldosteronism (autosomal dominant)
       - Type 1: GRA
       - Type 2: Non- GRA
  2) **Apparent mineralocorticoid excess** ($\downarrow$ **plasma aldosterone**, $\uparrow$ **plasma renin**)
     - Genetic disorder: mutation in 11-beta-hydroxysteroid dehydrogenase Type 2 enzyme
     - Chronic liquorice ingestion: deactivation of this enzyme
  3) **Renovascular disease** ($\uparrow$ **plasma aldosterone**, $\downarrow$ **plasma renin**)
  4) **Diuretics**
     - Pre-existent hypertension, diuretics cause urinary potassium losses eg frusemide
  5) **Cushing’s** ($\downarrow$ or normal aldosterone, $\downarrow$ or normal renin)
     - Aldosterone and cortisol bind to mineralocorticoid receptors with equal affinity
     - Normally, even though plasma glucocorticoid levels are >100x than aldosterone, enzyme 11B- HSD Type 2 inactivates cortisol
     - In Cushing’s, this mechanism is overwhelmed by the vast excess of cortisol
  6) **Liddle’s syndrome** ($\downarrow$ **plasma aldosterone**, $\uparrow$ **plasma renin**)
     - Rare autosomal dominant disease: primary increased sodium reabsorption and potassium loss in proximal tubules
  7) **Renin secreting tumours** ($\uparrow$ **plasma aldosterone**, $\downarrow$ **plasma renin**)

**Approach to this patient**
1) Plasma aldosterone: renin ratio
2) Urinary potassium (spot value also acceptable)
3) To confirm primary hyperaldosteronism either:
   - 3 days oral sodium chloride then retesting of plasma aldosterone
   - 4 hour 2L saline infusion IV then retesting of plasma aldosterone
   (Principle is that in normal subject, aldosterone will be suppressed)
4) To confirm source
   - Imaging (either CT or MRI are reasonable)
   - Bilateral adrenal vein testing (gold standard) if no adrenal masses seen on imaging, or if both adrenals are asymmetrical/abnormal

Back to the question
A. Not helpful
B. Correct
C. This is assuming the hyperaldosteronism is GRA, so that when dexamethasone is administered -> suppresses ACTH which is stimulating aldosterone secretion. In any case there is hypokalaemia in this patient, which is unusual for GRA
D. Synthetic ACTH (or Synacthen test) usually used to test for cortisol deficiency. Under normal circumstances, aldosterone secretion is NOT ACTH-dependant.
E. As above