Hypertension: Who and How (and Why) to Investigate

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Andy Levy
What I'm not going to talk about
Most Common: Renal Disease

Renal USS

• Likely to be normal if bloods and urine normal

Renal artery stenosis, Retroperitoneal fibrosis, PCKD
Less common: Cardiac Disease

Echocardiogram

- Most helpful for signs of end organ damage
  - LVH, LVF

Coarctation
Further Investigations If:

- Severe or malignant hypertension (>180/110)
- Acute rise in a patient with previously stable values.
- Resistant hypertension despite 3 antihypertensive agents
- Age <40 years (+ non-obese, non-black)
- Family history hypertension or stroke aged <50 years
- Suggestive clinical history

Not everyone with hypertension!
Red Flags: Case #1

~5% of all cases of hypertension
Increased cardiovascular mortality
(50% versus 34% in hypertensive controls)

• 38 year old children’s entertainer
• Hypertensive for 4 years; 162/95 mmHg (today)
• Ramipril 10mg, Amlodipine 5mg, Bendroflumethiazide 2.5mg
• Bloods normal before Bendroflumethiazide,
  now K+ fallen from 4.2 to 3.1 mmol/L; Na 147 mmol/L
• Father had a stroke aged 45
• BMI 32, smokes 10-15/day, 3-4 pints on a Friday night
• No peripheral oedema
Primary Hyperaldosteronism

- Liver → Angiotensinogen
  - Acts on Renin
- Angiotensinogen → Angiotensin I → Angiotensin II
  - Lungs
    - Angiotensin converting Enzyme (ACE)
  - Adrenals
- Aldosterone → Heart
- Kidney
  - Sodium & Water Retention
  - Increased BP
  - Vasoconstriction
- ↓BP
# Primary Hyperaldosteronism: Screening pitfalls of ARR

## False POSITIVES
- Uncorrected hypokalaemia
- Renal impairment
- Ageing
- Obesity + OSA
- Females (higher ratio than males)
- Volume depletion, NSAIDs

## False NEGATIVES
- Diuretics, CCBs, ACEi’s, ARB’s, SSRI
- Dietary salt restriction
- Malignancy
- Renovascular hypertension
- Pregnancy

### Don’t send if:
- mild hypertension,
- It wont change management, or
- not a surgical candidate...

### Ideally morning sample
- Ratio >30 is suggestive of primary aldosteronism.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Stop for:</th>
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<tbody>
<tr>
<td><strong>Spironolactone</strong> and Oestrogens</td>
<td>6 weeks</td>
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<tr>
<td>Diuretics</td>
<td>4 weeks</td>
</tr>
<tr>
<td>ACE Inhibitors and NSAIDs</td>
<td>2 weeks</td>
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<tr>
<td>Calcium antagonists</td>
<td>2 weeks</td>
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<tr>
<td>Sympathomimetics</td>
<td>2 weeks</td>
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<tr>
<td>Beta blockers</td>
<td>2 weeks</td>
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Subtype evaluation of primary aldosteronism

Subtype testing

Adrenal CT scan

- Normal, micronodularity, bilateral masses, or atypical unilateral mass (eg, >2 cm)
  - Surgery not desired
  - IHA or GRA: Pharmacologic therapy
  - No lateralization with AVS

- Unilateral hypodense nodule >1 cm and <2 cm
  - Surgery desired
    - >40 y consider
    - APA or PAH: Unilateral laparoscopic adrenalectomy
    - Lateralization with AVS
  - <40 y consider
    - Pharmacologic therapy
Primary Hyperaldosteronism: Management

1. **Lifestyle advice**

2. **Spironolactone;** Eplerenone, Amiloride, Thiazides

3. **Surgery only if unilateral disease**
   - Cure in possibly 33-60% (case series of 21-93 pts)
   - **Complete resolution less likely if:**
     - FHx >1 first degree relative with hypertension
     - Preoperative use of 2+ antihypertensives
     - (lack of preoperative response to Spironolactone)
     - Age >44 years
     - Duration of hypertension >5 years
     - Lower ARR
Summary

- High level of suspicion even if K⁺ normal
- Screening test ARR, but beware limitations
  - Don’t send if not a surgical candidate
  - If positive, or possible false negative, send for further investigation
- Treatment with Spironolactone (or Eplerenone, or Amiloride)
• Julie, 44 year old medical secretary
• Concerned about stress at work
• Long term frontal headaches, now pounding headaches at end of day (enjoys red wine and stilton)
• Feels her heart racing, particularly when carrying notes & colleagues tell her she goes pale, and she feels sweaty, and she used a colleagues CBG monitor (8.5mmol/L)
• Her mother had menopause aged 48
• Blood pressure 150/90 mmHg
Pheochromocytoma

- Paroxysms of elevated blood pressure (~50%)
- Stable chronic hypertension / Normotensive (~50%)
- Glucose impairment (catecholamine induced)

- Asymptomatic? ~5% of adrenal incidentalomas
Hereditary forms:

Average age at diagnosis 25 years

- MEN2, VHL, NF1, Carney triad (screening)

Genetic testing often recommended if:

- Personal or family history of clinical features suggestive of a hereditary syndrome.
- Bilateral or multifocal tumours.
- Malignant extra-adrenal paragangliomas.
- Diagnosis under age of 40 years.
  - Hereditary forms <2% of people aged >50
Phaeochromocytoma:
Screening Pitfalls

- **Standard screening test:** Urinary catecholamines /metanephrines
- Sensitivity & specificity 98%, but higher false positives
- 24 hour collections, non-consecutive days

- **Special cases:** Plasma catecholamines /metanephrines
- Higher negative predictive value, sensitivity 96-100%; specificity 85-89%
- **Measure if can’t do urine collections, borderline urinary results, or high clinical suspicion** (genetic syndrome, characteristic adrenal mass)

<table>
<thead>
<tr>
<th>INTERFERING MEDICATIONS</th>
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<tr>
<td>Paracetamol</td>
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<tr>
<td>TCAs / SSRIs/ MAOis</td>
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<tr>
<td>Diuretics</td>
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<tr>
<td>Steroids</td>
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<tr>
<td>Lithium</td>
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Phaeochromocytoma: Management

Medication:
• Calcium Channel blocker (e.g. Amlodipine 5-10mg), can add α-1 receptor blockers (e.g. Doxazosin) later if needed.
• Phenoxybenxamine: Preoperative management, causes significant postural hypotension and reflex tachycardia, nasal stuffiness. Careful titration.
• β-blockers: combined with Phenoxybenxamine to prevent tachycardia.

Surgery
Follow up:
• Who has benign disease?
• Up to 16% develop recurrence (usually 5-15 years later)
  o 50% of these have distant metastasis (5 year survival <50%)
• All patients: post-operative and annual biochemical testing
Summary

• Ensure urinary collections performed after symptoms and ideally without interfering medications

• If concerned, Amlodipine is safe to commence as first line treatment.

• If young, or family history, need genetic screening

• All need follow up post-operatively
Cushing’s syndrome

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<tr>
<th>SYMPTOMS</th>
<th>SIGNS</th>
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<tbody>
<tr>
<td>No symptoms with high sensitivity and specificity</td>
<td>Easy bruising</td>
</tr>
<tr>
<td></td>
<td>Facial plethora</td>
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<tr>
<td></td>
<td>Proximal myopathy</td>
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<td></td>
<td>Striae</td>
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- Exclusion criteria
  - Ability for weight loss almost impossible
  - Must have changes in appearance, not simply weight gain
Cushing’s Screening: Pitfalls

• For non-specialists, stick with 24 hr UFC & ONDST

• Difficulty: many conditions associated with hypercortisolism
  • Depression and Alcohol dependence
  • Morbid obesity
  • Poorly controlled diabetes
  • Physical stress (hospitalisation, surgery, pain)
  • Malnutrition, anorexia nervosa
  • Intense chronic exercise
  • Hypothalamic amenorrhea
  • Pregnancy
# Cushing’s Screening: Pitfalls

<table>
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<tr>
<th>UFC</th>
<th>ONDST</th>
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<tr>
<td>• Must be done accurately</td>
<td>Not helpful if:</td>
</tr>
<tr>
<td>• Avoid excessive fluid intake</td>
<td>• OCP/HRT (false + in 50%)</td>
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<tr>
<td>• Avoid exogenous steroids</td>
<td>• Liver/renal failure</td>
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<tr>
<td>• 2+ collections (more if creatinine excretion varies by &gt;10% between tests)</td>
<td>• Drugs: antiepileptics, rifampicin, alcohol</td>
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<tr>
<td>False positives</td>
<td>• malnutrition</td>
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<td>• Pregnancy, exercise, psychosis, alcohol (+ withdrawal), anorexia</td>
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- Avoid excessive fluid intake
- Avoid exogenous steroids
- 2+ collections (more if creatinine excretion varies by >10% between tests)

False positives:
- Pregnancy, exercise, psychosis, alcohol (+ withdrawal), anorexia
Summary

• Do you *really* think it’s Cushing’s?
• 24 hour UFC – at least 2
• Refer for second opinion and further screening (not “confirmation”)
Questions?