HYPERTENSION

Introduction

Colin Edwards
Cardiologist
AHG and WDHB

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Disclosures

FIONA STEWART
Advisory Board – Pfizer, AstraZeneca
Meetings - AstraZeneca, MSD

COLIN EDWARDS
Meetings - AstraZeneca
OUTLINE

Introduction
history, important trials, renal denervation, current guidelines and treatment algorithms

CASES:
Diagnosis of hypertension – Clinic BP vs home BP monitoring vs 24 hr ABPM
Resistant Hypertension
Hypertension and the elderly
Hypertension in the adolescent patient
History

Hypertension has challenged famous physicians for centuries.

1733 - Clergyman Stephen Hales made the 1st published measurement of blood pressure

1896 – Invention of the sphygomanometer.

1905 - Nikolai Korotkoff described the Korotkoff sounds

1925 - Otto Frank introduced the concept of essential hypertension.

1928- Mayo clinic published the concept of malignant hypertension.

Classification of hypertension - benign or malignant. Importance of severe hypertension was appreciated but the importance of mild and moderate hypertension was questioned.

1931 – John Hay - Prof of Medicine in Liverpool “the greatest danger to man with a high BP lies in its discovery, because then some fool is certain to try and reduce it”.
1937 - Paul White (Harvard Cardiologist) suggested that "hypertension may be an important compensatory mechanism which should not be tampered with, even if we were certain that we could control it"

1949 - Charles Friedberg's classic textbook "Diseases of the Heart", stated that "people with 'mild benign' hypertension ... (defined as blood pressures up to levels of 210/100 mm Hg) ... need not be treated".

From the **1950’s** – tide was turning – longitudinal studies such as Framingham Heart Study and other actuarial reports – demonstrated that benign hypertension increased death and cardiovascular disease.
HYPERTENSION ‘SILENT ASSASIN’

Hypertension is a Risk Factor for Cardiovascular Disease

- **Men**
  - CAD: 22.7 vs. 45.4
  - Stroke: 3.3 vs. 12.4
  - PAD: 5.0 vs. 9.9
  - CHF: 3.5 vs. 13.9

- **Women**
  - CAD: 9.5 vs. 21.3
  - Stroke: 2.4 vs. 6.2
  - PAD: 2.0 vs. 7.3
  - CHF: 2.1 vs. 6.3

Biennial age-adjusted rate per 1000 patients at risk

Risk ratio:
- CAD: 2.0 vs. 2.2
- Stroke: 3.8 vs. 2.6
- PAD: 2.0 vs. 3.7
- CHF: 4.0 vs. 3.0

Adapted from Kannel WB. JAMA. 1998;275:1571-1576.
## Key Clinical Trials in Hypertension

<table>
<thead>
<tr>
<th>Should we treat HBP?</th>
<th>What is the goal of treatment?</th>
<th>Should we treat DBP in older persons?</th>
<th>What is the best drug for HBP?</th>
<th>Should we treat ISH?</th>
<th>What are the best combinations?</th>
</tr>
</thead>
</table>

### ACCORD Primary Outcome: Nonfatal MI, Nonfatal Stroke or CVD Death

<table>
<thead>
<tr>
<th>Patients with events, %</th>
<th>Years post-randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active F (n=2,36)</td>
<td></td>
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<tr>
<td></td>
<td>0</td>
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<td>19</td>
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<td></td>
<td>20</td>
</tr>
</tbody>
</table>

- SBP <133 vs 119mmHg
- HR = 0.88
- 95% CI (0.73-1.06)
Hypertension in 2014

Still lots of questions

What’s the best way to
- Clinic measurements
- Home BP monitoring
- Ambulatory BP monitoring

What’s more important

What level of BP constitutes hypertension and what are the BP targets?

Then........if we decide a patient has hypertension

- what is the best drug or drug combination to use ( >125 drugs available)

What’s the best way to document blood pressure
- Clinic measurements – how many measurements, how many clinic visits?
- Home BP monitoring
- Ambulatory BP monitoring

Renal Denervation – thought we had eventually found a cure for hypertension

Hypertensive 80 year old versus an hypotensive 18 year old

What’s more important

Systolic hypertension or Diastolic hypertension?
Renal Denervation

**SYMPLICITY HTN-1: Significant, Sustained BP Reduction to 3 Years**

<table>
<thead>
<tr>
<th>Time</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Months (N = 144)</td>
<td>-22</td>
<td>-10</td>
</tr>
<tr>
<td>1 Year (N = 132)</td>
<td>-27</td>
<td>-14</td>
</tr>
<tr>
<td>2 Years (N = 105)</td>
<td>-29</td>
<td>-14</td>
</tr>
<tr>
<td>3 Years (N = 88)</td>
<td>-32</td>
<td>-14</td>
</tr>
</tbody>
</table>

- **Systolic**
- **Diastolic**

Data is reported only on the patients available at each time point. $p < 0.01$ for $\Delta$ from baseline for all time points.

**Primary endpoint**

- **RDN**
  - (n = 364)
  - [www.cardiosource.org](http://www.cardiosource.org)

- **Sham procedure**
  - (n = 171)
Reasons for failure

3 variables that may have affected the efficacy of the trial:

Drug changes - 40% had additional drug up titrations
‘SHAM ARM’ were advantaged by intensive drug Rx

Patient population – 1/3 were African-Americans
notoriously don’t respond to RDN for unknown reasons
Disadvantaged RDN group

Procedure related – too many inexperienced operators
– too few burns
Disadvantaged RDN

<table>
<thead>
<tr>
<th></th>
<th>HTN-1</th>
<th>HTN-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of operators</td>
<td>20</td>
<td>112</td>
</tr>
<tr>
<td>No. of procedures per operator</td>
<td>6.0</td>
<td>3.3</td>
</tr>
</tbody>
</table>
RDN is here to stay:
- Selected patients (there are non-responders)
- Eligible patients enrolled in trials
- Better standardisation of equipment and technique
Non-Invasive Renal Denervation
(ULTRA SOUND)

External delivery of focused ultrasound energy to specific target tissue. Imaging and tracking of target

**Less trauma** to renal arteries - energy is delivered to sympathetic nerve on the outside of the vessel.

Currently enrolling patients with resistant hypertension in a randomized trial – US RDN versus SHAM
(Principal Investigator: Prof J Ormiston)
### Stages of Hypertension and Guidelines

<table>
<thead>
<tr>
<th>Stage</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&gt;140</td>
<td>&gt;90</td>
</tr>
<tr>
<td>II</td>
<td>&gt;160</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;180</td>
<td>&gt;110</td>
</tr>
</tbody>
</table>

#### Isolated Systolic Hypertension
- SBP >160
- <90

#### Isolated Diastolic Hypertension
- <140
- DBP >90

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**Distribution of Hypertension Subtypes by Age**

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>ISH (SBP ≥140 and DBP &lt;90)</th>
<th>SDH (SBP ≥140 and DBP ≥90)</th>
<th>IDH (SBP &lt;140 and DBP ≥90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>17%*</td>
<td></td>
<td>17%*</td>
</tr>
<tr>
<td>40–9</td>
<td>16%*</td>
<td>16%*</td>
<td></td>
</tr>
<tr>
<td>50–9</td>
<td>16%*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–9</td>
<td>20%*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–9</td>
<td>20%*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80+</td>
<td>11%*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Numbers at top represent the overall % distribution of untreated HTN by age. Adapted from Franklin SS et al. Hypertension. 2001;37(3):869–874.
New Guidelines – JNC 8 plus others

BP Thresholds for the USA-2014

<table>
<thead>
<tr>
<th>Population</th>
<th>JNC 8</th>
<th>ASH/ISH*</th>
<th>ADA</th>
<th>NKF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 60 years (*) ≥ 80</td>
<td>≥ 150/90</td>
<td>&gt; 140/90</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
<tr>
<td>Age &lt; 60 years</td>
<td>&gt; 140/90</td>
<td>&gt; 140/90</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
<tr>
<td>Diabetics</td>
<td>&gt; 140/90</td>
<td>&gt; 140/90</td>
<td>&gt;140/80</td>
<td>N.A.</td>
</tr>
<tr>
<td>With CKD</td>
<td>&gt; 140/90</td>
<td>&gt; 140/90</td>
<td>N.A.</td>
<td>&gt; 140/90</td>
</tr>
<tr>
<td>With CVD</td>
<td>&gt; 140/90</td>
<td>&gt; 140/90</td>
<td>N.A.</td>
<td>N.A.</td>
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BP Targets for the USA—2014

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<tr>
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<td>&lt; 150/90</td>
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<td>N.A.</td>
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<td>N.A.</td>
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<td>&lt; 140/80</td>
<td>N.A.</td>
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<tr>
<td>With CKD</td>
<td>&lt; 140/90</td>
<td>&lt; 140/90</td>
<td>N.A.</td>
<td>&lt; 140/90</td>
</tr>
<tr>
<td>With CVD</td>
<td>&lt; 140/90</td>
<td>&lt; 140/90</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
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</table>

BP targets (recent BPAC guidelines)

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Normal &lt;80 yrs</th>
<th>Diabetic CKD Vascular Disease</th>
<th>Elderly &gt;80 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;140/90</td>
<td>&lt;130/80</td>
<td>&lt;150/90</td>
</tr>
</tbody>
</table>
ADD B-BLOCKER IF THERE IS A COMPELLING INDICATION

4th line
SPIRONOLACTONE
EPLERENONE
**Care pathway**

**Stage 1 hypertension**
- CBPM $\geq$140/90 mmHg & ABPM/HBPM $\geq$ 135/85 mmHg

**Stage 2 hypertension**
- CBPM $\geq$160/100 mmHg & ABPM/HBPM $\geq$ 150/95 mmHg

- If target organ damage present or 10-year cardiovascular risk $> 20%$
- Offer antihypertensive drug treatment
- Consider specialist referral
- If younger than 40 years
- Offer lifestyle interventions
- Offer patient education and interventions to support adherence to treatment
- Offer annual review of care to monitor blood pressure, provide support and discuss lifestyle, symptoms and medication
Antihypertensive Drug Treatment Algorithm
NICE 2011

Step 1
- Age <55 yrs: A
- Age ≥55 yrs or black*: C↑

Step 2
- A + C↑

Step 3
- A + C + D

Step 4
- Resist. Hypertension: A + C + D + further diuretic‡
  - Consider specialist advice

A = angiotensin-converting-enzyme inhibitor or angiotensin receptor blocker
C = calcium channel blocker
D = thiazide-like diuretic

*Of African or Caribbean family origin
†CCB preferred but D is an alternative in people intolerant of C or at high risk of heart failure
‡Consider low-dose spironolactone or higher-dose thiazide

ALLHAT Trial

• Target BP < 140/90
• 67% achieved target
• 2/3 were taking 2+ agents
• 1/4 were taking 3+ agents

• Expect to need multiple medications to control BP
Hypertension is Silent Disease Process Neet to Achieve Patient and Doctor Buy In

Trials → 35-40% mean reduction in stroke
20-25% reduction in MI
50% reduction in heart failure

Pt with BP 159/95 mmHg (stage 1)
on treatment for 10 yrs
12mmHg ↓
prevent 1 death for every 11 pts treated

Helps Achieve Patient ‘Buy In’
Debated for 25 years—lots of confusing observational studies

HOT study—Hypertension Optimal Treatment
Prospective randomised study
>18000 pts → DBP ≤ 90mmHg, ≤ 85mmHg, ≤ 80mmHg
Lowering DBP<80mmHg in pts with normal coronary arteries
→ not harmful.
Lowering DBP<80mmHg in pts with obstructive CAD
→ ↑ MI but no ↑ CVA
THANK YOU
Hypertension

Fiona Stewart
Auckland Heart Group
Auckland City Hospital

GP Conference
Rotorua
June 2014
Blood Pressure Measurement

• Correct cuff size
• Sitting x2 at 2 minute intervals
• Standing

Consider
  Repeat visit
  Nurse check ("white coat hypertension")
  Home BP monitoring
  Ambulatory 24hr BP monitoring
Mrs A aged 65

• Background Hypertension
• Otherwise well
• Very anxious about stroke risk
• Medication
  – Candesartan 16mg
  – Bendrofluazide 2.5mg
  – Metoprolol 95mg
  – Felodipine 2.5mg prn
Home BP Measurements
Ambulatory Blood Pressure Monitoring
Future Monitoring

- Blood pressure rises with increasing age
- White coat hypertension – marker of increased risk of sustained hypertension in the future
Labile (White Coat) Hypertension

- A significant risk for future hypertension
- Consider ABU every 2 years
Case

Resistant Hypertension

Colin Edwards
Cardiologist
WDHB and AHG

JUNE 2014
Definition

- Resistant hypertension is defined as blood pressure that remains above goal in spite of concurrent use of 3 antihypertensive agents of different classes.
- Ideally, one of the 3 agents should be a diuretic and all agents should be prescribed at optimal dose amounts.

1/3 of patients with RESISTANT HYPERTENSION have WHITE COAT HYPERTENSION, emphasizing the importance of ABPM.
History

52 year old Indian female

GP referral because of palpitations and breathlessness x 3 months

Palpitations → likely atrial or ventricular premature beats.

Diagnosed with hypertension 6 years previously – presumed essential

No past cardiac history – no hx of atrial fibrillation

No diabetes
Raised BMI – 30kg/m2
TC 5.2 HDL 2.2 LDL 2.6
Non-smoker
Father had CABG @ 69yrs

No thyroid disease

Medication:

Bendrofluazide 2.5mg/d
Atacand 8mg/d
Amlodipine 2.5mg/d
EXAMINATION:

Raised BMI

PR 70 bpm all pulses present, no radio-femoral delay. **BP 170/80mmHg** right arm sitting – 2 readings 5 min apart

Head and neck: JVP-normal; no carotid bruits; no goitre

Fundoscopy –mild A-V nipping

CVS-normal heart sounds, no murmurs, no aortic coarctation
Chest – normal
Abdomen- no bruits
Lab

Renal and electrolytes:
Na – 137
K – 4.2
Cr- 76
Ca- 2.17
HbA1c-normal

Urine:
Urine microalbumin 36mg/l (0-30)
Albumin:Creat 4.1 (0-2.5)

Renal US - normal

Microalbuminuria/Proteinuria Associated With Increased Risk for CV Mortality in Type 2 Diabetics
Figure 2: Assessing 5-year cardiovascular risk and treatment benefit

How to use the Table:
1. Identify the table relating to the person’s sex, diabetic status, smoking history and age.
2. Within the table choose the cell nearest to the person’s age, blood pressure and TC/HDL ratio.
3. When the systolic and diastolic values fall in different risk levels, the higher category applies.
4. For example, the lower left cell contains all non-smokers without diabetes who are under 45 years and have a TC/HDL ratio less than 4.5 and a blood pressure less than 130/80 mmHg. People who fall exactly on a threshold between cells are placed in the cell indicating higher risk.

Risk Level
5-year CVD risk (non-fatal and fatal)
- Very High >30%
- High 25-30%
- Moderate 20-25%
- Low 10-15%
- Very Low 5-10%
- Minimal 2.5-5%
- Negligible <2.5%
Important Questions in Hypertensive Non-responders

Stress – work, family, financial

Exercise

Diet – salt, alcohol

Meds - NSAID, COX-2, OCP, decongestants

Sleep - OSA – Epworth Sleepiness Scale

Compliance

---

When to Suspect OSA (Obstructive Sleep Apnea)

- Loud snoring
- Snore arousals (waking with snorting, gasping)
- Apnea or crescendo breathing witnessed by bed partner or family member
- Complaints of daytime sleepiness
- All patients with resistant hypertension

If OSA is suspected, patient should be referred to sleep specialist for consideration of overnight polysomnography
Assessment

Intermediate CV risk 13.7%

Important and likely essential hypertension with microalbuminuria

Breathlessness – hypertensive heart disease and diastolic dysfunction need to rule out CAD

Palpitations – likely due to VPB’s/APB’s
Always need rule out atrial fibrillation if pt is hypertensive
Management

TARGET BP ≤ 140/90

Lifestyle Intervention
Aerobic exercise program-30 min /d
Weight loss-10% body weight
Diet – low salt, low CHO

Medication:
Optimise Atacand dose
Optimise Amlodipine dose

Investigations:
- Ambulatory BP
- Echo - breathless
- ETT – rule out CAD
- 24 hr holter – rule out AF
Results

ABPM – average over 24-hour period was 158/87mmHg,
daytime average 161/90mmHg,
nocturnal average 146/79mmHg

Echo – normal LV size and function – LVEF 60%
borderline LV hypertrophy and mild diastolic dysfunction
mild left atrial dilatation

Exercise tolerance test – normal to 9 min of Bruce Protocol.
optimal
Peak SBP – 220mmHg
Treatment

**STEP 1:**
Amlodipine 5mg/d  
Atacand 16mg/d  
Continue Bendrofluazide 2.5mg/d

**STEP 2: 2 weeks later still hypertensive**
Amlodipine 10mg/d  
Atacand 32mg/d  
Increased to top dose over 1 month period

**STEP 3: 1 month later**
Average of 2 seated BP’s 5 min apart 154/85mmHg  
Still c/o palpitations – Bisoprolol 2.5mg/d added

**STEP 4: 3 months later**
Atacand 32mg/d  
Felodipine 10mg/d  
Bendro 2.5mg/d  
Bisoprolol 5 mg/d  
Average of 2 seated BP’s 5 min apart 155/80mmHg

Patient admitted to good compliance

**RESISTANT HYPERTENSION**
Exclude secondary causes of hypertension

**RENAL FUNCTION:**

Normal renal US

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<tbody>
<tr>
<td>Sodium</td>
<td>139 mmol/L</td>
<td>135 - 145</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.4 mmol/L</td>
<td>3.5 - 5.2</td>
</tr>
<tr>
<td>Creatinine</td>
<td>62 umol/L</td>
<td>45 - 90</td>
</tr>
<tr>
<td>eGFR</td>
<td>87 mL/min/1.73m²</td>
<td>&gt; 80</td>
</tr>
</tbody>
</table>

**24 hour urine catecholamines**

<p>| | | |</p>
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>24 h</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>1.69 L</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>9.0 mmol/d</td>
<td>4.0-17.0</td>
</tr>
<tr>
<td>Adrenalin/Creatinine Ratio</td>
<td>2.1 mmol/mmol creat</td>
<td>0-9.5</td>
</tr>
<tr>
<td>Urine Adrenalin</td>
<td>19 nmol/d</td>
<td>0-100</td>
</tr>
<tr>
<td>Noradrenalin/Creatinine Ratio</td>
<td>23 nmol/mmol creat</td>
<td>0-69</td>
</tr>
<tr>
<td>Urine Noradrenaline</td>
<td>200 nmol/d</td>
<td>0-760</td>
</tr>
<tr>
<td>Dopamine/Creatinine Ratio</td>
<td>0.15 umol/mmol creat</td>
<td>0-0.28</td>
</tr>
<tr>
<td>Urine dopamine</td>
<td>1.4 umol/d</td>
<td>0-4.0</td>
</tr>
</tbody>
</table>

**24 hr urine Cortisol**

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>24 h</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>1.48 L</td>
<td></td>
</tr>
<tr>
<td>Cortisol (free) Urine</td>
<td>110 nmol/d</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>11.0 mmol/d</td>
<td>4.0-17.0</td>
</tr>
</tbody>
</table>

*Cortisol (free) Urine

Patients with Cushing's syndrome usually have levels >180 nmol/d. This test is not indicated in the diagnosis of cortisol deficiency.*
### ALDOSTERONE/RENIN RATIO

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Aldosterone</td>
<td>399 pmol/L</td>
</tr>
<tr>
<td>Active Renin</td>
<td>4 mU/L</td>
</tr>
<tr>
<td>Aldosterone/Renin ratio</td>
<td>100</td>
</tr>
</tbody>
</table>

Plasma Aldosterone
Please note the new reference range(s)

**Aldosterone/Renin ratio**

- **Aldosterone/Renin ratio:**
  - **Screening test for primary aldosteronism**
  - >55: primary aldosteronism possible, if aldosterone >400 pmol/L.
  - <25: primary aldosteronism unlikely.

Information on interpretation of renin and aldosterone results can be found in the LabPlus online Test Guide at [www.labplus.co.nz](http://www.labplus.co.nz)
Testing Laboratory LabPlus - Auckland

Elevated aldosterone renin ratio but aldosterone not >400
Also serum K+ normal

**Conns Syndrome Unlikely??**

Decided to repeat it – with patient off medication for a few days – pt wasn’t keen to stop meds
Progress

Struggled on for months with elevated BP’s and palpitations and breathlessness

Coronary angiogram as breathless- normal

Added Spironolactone as a 5th drug- nasty side effects- dizzy, flushing – therefore stopped.
Blood Pressure Response to Spironolactone in Subjects With Resistant Hypertension

Renal Denervation

CT renal angiogram – normal renal arteries- anatomically suitable for renal denervation.

BUT…….. 2 possible adenomas of her right adrenal gland – likely Conns Syndrome
Conns Syndrome

Clues:
- very suppressed active renin level
- Up to 50% can have normal K+
<table>
<thead>
<tr>
<th>Location</th>
<th>Prevalence of PA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seattle¹</td>
<td>17</td>
</tr>
<tr>
<td>Birmingham²</td>
<td>20</td>
</tr>
<tr>
<td>Oslo³</td>
<td>22</td>
</tr>
<tr>
<td>Prague⁴</td>
<td>19</td>
</tr>
</tbody>
</table>
# Adrenal Vein Sampling

## Aldosterone/Renin Group

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
<th>Unit</th>
<th>Abnormality</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Aldosterone</td>
<td>141300</td>
<td>pmol/L</td>
<td>H</td>
<td>60-1000</td>
</tr>
<tr>
<td>Active Renin</td>
<td>3</td>
<td>mU/L</td>
<td>L</td>
<td>4-46</td>
</tr>
<tr>
<td>Aldosterone/Renin ratio</td>
<td>47100</td>
<td></td>
<td>H</td>
<td>See below</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
<th>Unit</th>
<th>Abnormality</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Aldosterone</td>
<td>35800</td>
<td>pmol/L</td>
<td>H</td>
<td>60-1000</td>
</tr>
<tr>
<td>Aldosterone/Renin ratio</td>
<td>Not avail.</td>
<td></td>
<td></td>
<td>See below</td>
</tr>
</tbody>
</table>
Both adrenal glands implicated

Bilateral adrenal hyperplasia

Surgery is not an option
Both adrenals would need to be removed to cure the patient

Medical management
Medical Therapies

• Mineralocorticoid receptor antagonists are recommended for patients with bilateral disease
  – They help to control BP and maintain eukalemia
  – Spironolactone has the most data, and is usually quite effective
    • Gynecomastia is dose-related (6-month incidence of 7% at ≤50 mg/d, 52% at ≥150 mg/d)
    • Many women blame it for vaginal bleeding (incidence unknown)
  – Eplerenone is newer, more expensive, but has fewer antiandrogenic or progestinogenetic adverse effects
  – Amiloride is an alternative, but often requires large doses (and many pills/day, as it is available only as 5 mg tablets)
Conclusion

Subtypes of Primary Hyperaldosteronism
- Unilateral adrenal adenoma – Conns Syndrome
- Idiopathic primary aldosteronism – Bilateral adrenal hyperplasia
- Adrenal carcinoma – autonomous secretion of aldosterone

Hyperaldosteronism
- Resistant hypertension – characteristically no response to RAAS blockers
- Often have more LVH
- Raised plasma aldosterone levels
- SUPPRESSED RENIN
Hypertension in the Elderly

Fiona Stewart
Auckland Heart Group
Auckland City Hospital

GP Conference
Rotorua
June 2014
Mrs B aged 84

- Lives independently in retirement village
- Keen member of local U3A
- Enjoys village “Never Too Old” exercise programme
- Well with no history of coronary disease or diabetes
- BP on 2 visits 162/84
Treatment of Hypertension in the Very Elderly ≥ 80

HYVET trial

• Patients aged ≥ 80
• SBP >160mmHg, DBP < 110mmHg
• Indapamide 1.5mg + Perindopril 2-4mg vs placebo
• Target BP 150/80
Blood pressure separation

Median follow-up 1.8 years

15 mmHg

6 mmHg
All stroke (30% reduction)

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>IndapamideSR ±perindopril</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1912</td>
<td>1933</td>
</tr>
<tr>
<td>1</td>
<td>1484</td>
<td>1557</td>
</tr>
<tr>
<td>2</td>
<td>807</td>
<td>873</td>
</tr>
<tr>
<td>3</td>
<td>374</td>
<td>417</td>
</tr>
<tr>
<td>4</td>
<td>194</td>
<td>229</td>
</tr>
</tbody>
</table>
Fatal Stroke
(39% reduction)

P=0.046

No. at Risk
Placebo 1912 1492 814 379 202
Indapamide SR ±perindopril 1933 1565 877 420 231
**Total Mortality**

(21% reduction)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. at Risk</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>1912</td>
<td>1492</td>
<td>814</td>
<td>379</td>
<td>202</td>
<td></td>
</tr>
<tr>
<td>Indapamide SR ±perindopril</td>
<td>1933</td>
<td>1565</td>
<td>877</td>
<td>420</td>
<td>231</td>
<td></td>
</tr>
</tbody>
</table>

P=0.019
Heart Failure (64% reduction)

Placebo

IndapamideSR ± perindopril

P<0.0001

No. at Risk

Placebo

IndapamideSR ± perindopril

1912 1480 794 367 188

1933 1559 872 416 228
### ITT – Summary

<table>
<thead>
<tr>
<th>Event</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Stroke</td>
<td>0.70</td>
<td>(0.49, 1.01)</td>
</tr>
<tr>
<td>Stroke Death</td>
<td>0.61</td>
<td>(0.38, 0.99)</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>0.79</td>
<td>(0.65, 0.95)</td>
</tr>
<tr>
<td>NCV/Unknown death</td>
<td>0.81</td>
<td>(0.62, 1.06)</td>
</tr>
<tr>
<td>CV Death</td>
<td>0.77</td>
<td>(0.60, 1.01)</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0.71</td>
<td>(0.42, 1.19)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>0.36</td>
<td>(0.22, 0.58)</td>
</tr>
<tr>
<td>CV events</td>
<td>0.66</td>
<td>(0.53, 0.82)</td>
</tr>
</tbody>
</table>
Initiating Antihypertensive Therapy in the Elderly

• Always record sitting and standing BP
• Start slowly with low dose single agent
  - 1.25mg bendrofluazide
  - 1.25mg cilazapril
• Titrate medication slowly
• Consider 2\textsuperscript{nd} antihypertensive before high dose single agent
• Watch electrolytes and renal function
Hypertension in the Adolescent Patient

2 cases

Colin Edwards
Cardiologist
WDHB and AHG
CASE 1

20 year old female patient

Seen on numerous occasions – average BP is 152/90mmHg

Father (70 years) has hypertension and is on medication

EXAMINATION:
Tall and thin

CV – No murmurs to suggest aortic coarctation and no radiofemoral delay

Bp 150/90 and PR 70 bpm

Fundoscopy – no hypertensive retinopathy

Enjoys going to gym and playing tennis; no recreational drugs or steroids

Abdomen – soft

peripheral bruit –? Flow – patient very thin.

Arteriolar narrowing
Silver wiring

A-V nipping
What next for this Patient

1. Have the patient return for a repeat BP measurement in 6 months

2. Lifestyle counseling to increase physical activity, low salt and repeat BP in 6 months

3. Begin diagnostic evaluation

4. Admit to hospital for immediate BP reduction
Initial Hypertensive Evaluation

24 hour Ambulatory BP monitor
- Hypertensive while awake and asleep, moderately low dipper 7% SBP (normal 10-20%)

Blood chemistry – normal renal fx, normal Na, K, Ca, normal TFT’s
Urinalysis – normal, no proteinuria
Lipids and HbA1c -normal

ECG:
ECHO:
Normal
No left ventricular hypertrophy
Normal aortic valve and ascending aorta – flow murmur
No aortic coarctation

Renal Ultrasound and Doppler:
- Normal R kidney size right renal artery stenosis by doppler
- Normal L kidney size and doppler profile

Fibromuscular Dysplasia of the right renal artery
## Series of PTRA in FMD
**Slovut and Olin, NEJM, 2004**

Results of Percutaneous Transluminal Angioplasty of the Renal Arteries with Fibromuscular Renovascular Disease and Hypertension*

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>No of Patients</th>
<th>Technical Success Rate</th>
<th>Effect on Blood Pressure</th>
<th>Months of Follow-up</th>
<th>Complication Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sos et al</td>
<td>1983</td>
<td>31</td>
<td>87</td>
<td>59</td>
<td>16 (4-40)</td>
<td>6</td>
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<tr>
<td>Baert et al</td>
<td>1990</td>
<td>22</td>
<td>83</td>
<td>58</td>
<td>26 (6-72)</td>
<td>NR</td>
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<tr>
<td>Tegtmeyer et al</td>
<td>1991</td>
<td>66</td>
<td>100</td>
<td>39</td>
<td>39 (1-121)</td>
<td>13</td>
</tr>
<tr>
<td>Bonelli et al</td>
<td>1995</td>
<td>105</td>
<td>89</td>
<td>22</td>
<td>43 (0-168)</td>
<td>11 (major)</td>
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<tr>
<td>Jensen et al</td>
<td>1995</td>
<td>30</td>
<td>97</td>
<td>39</td>
<td>12 (NR)</td>
<td>3 (major) 12 (minor)</td>
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<tr>
<td>Davidson et al</td>
<td>1996</td>
<td>23</td>
<td>100</td>
<td>52</td>
<td>NR</td>
<td>13</td>
</tr>
<tr>
<td>Klow et al</td>
<td>1998</td>
<td>49</td>
<td>98</td>
<td>26</td>
<td>9 (1-96)</td>
<td>0</td>
</tr>
<tr>
<td>Birrer et al</td>
<td>2002</td>
<td>27</td>
<td>100</td>
<td>74†</td>
<td>26</td>
<td>10 (NR)</td>
</tr>
<tr>
<td>Surowiec et al</td>
<td>2003</td>
<td>14</td>
<td>95</td>
<td>79†</td>
<td>21</td>
<td>NR</td>
</tr>
<tr>
<td>De Fraissinette et al</td>
<td>2003</td>
<td>70</td>
<td>94</td>
<td>14</td>
<td>39 (1-204)</td>
<td>11</td>
</tr>
</tbody>
</table>

* NR denotes not reported.
† The percentage shown is the total for cured and improved.

Fibromuscular Dysplasia

FMD is a non-inflammatory, nonatherosclerotic disorder that leads to arterial stenosis, aneurysm, or dissection. It is more common among women and, while initially thought to only occur in the young, may occur at any age.

The most often involved arteries are the renal (70 percent) and internal carotid and vertebral arteries (approximately 65 percent), and less often are the iliac, subclavian, and visceral arteries.

Pathogenesis is uncertain, but genetic factors, hormonal influence, and ischemia may contribute.

Common presentations - hypertension, headache, dizziness, tinnitus, transient ischemic attack, and stroke.

Treatment:
- revascularization by PTA. Surgical revascularization is indicated if PTA not possible or fails.
- Following PTA-pts need to be followed for restenosis after 6 months, 12 months and then yearly thereafter.
Case 2

18 year old Maori female – competitive netball player

Found to be hypertensive by GP when presented with URTI and headache
BP 137 to 149/ 75-80mmHg
Mildly overweight

No recreational drugs or steroids, non smoker

Both parents are hypertensive – father had a stroke aged 55 years
NEXT STEP

1. Start treatment with thiazide or ACE

2. Refer cardiology for an echo

3. Perform 24 hr ambulatory BP monitoring ✓

4. Check BP daily for next 10 days
Further Evaluation

24 hr ABPM – sustained daytime hypertension (mean 150/85 mmHg) with normal nocturnal dipping

Urinalysis, electrolytes (normal Na, K+, Ca; creat-normal)
TC 4.8, LDL 2.5, HDL 1.3
Glucose-normal

ECG-generous voltages, otherwise normal

Echo – definite mild concentric LVH. Normal aortic dimensions.

Renal U/S - normal
Most likely explanation for hypertension

1. Dietary-excess Na intake

2. Essential hypertension – based on a parent with hypertension ✓

3. Metabolic Syndrome

3. Renal artery stenosis
Initial Therapy

Weight loss, diet and Exercise  ✓

Amlodipine 5mg/d  ✓

Metoprolol 47.5mg/d

ACE inhibitor-Lisinopril 10mg/d

DISCUSSION:

She has got LVH – so probably want to more than lifestyle alone

Always stress the importance of exercise and low salt diet
Avoid B-Blockers in sportsman
She is in child bearing age – so want to avoid ACE – numerous fetogenic effects
Discussion

The younger the patient and the higher the BP – more likely the hypertension is secondary.

**Converse is also true**
The older the patient and lower the BP – more likely to be essential hypertension
DIAGNOSIS:
ABPM and Home BP monitoring are important in confirming the diagnosis of hypertension.

TARGETS: Reduce BP to <140/90mmHg and <130/80mmHg in diabetic, CKD, PVD
BP thresholds and targets still remain uncertain. Very low targets do not appear to be beneficial.

Treatment: ACE/ARB, Ca antagonist and thiazide diuretic (chlorthalidone) – ‘HOLY TRINITY’ of anti-hypertensive Rx.
Spironolactone (12.5-25mg/d – useful 4th line agent)

Antihypertensive Rx reduces morbid events
- In all adult age groups including the very elderly (>80 year olds)
- In patients with ↑SBP and/or ↑DBP
Resistant Hypertension
1/3 have white coat hypertension - emphasizing the importance of 24 hr ABPM
Primary hyperaldosteronism is a relatively common secondary cause of hypertension (20%)
- often have normal K+
- suppressed renin levels

Young hypertensives <40 years – consider referral to a specialist to exclude secondary causes of ht.
Thank You