Difficult Hypertension

Cardiologists:

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WDHB

June 2015
Disclosures

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

COLIN EDWARDS
Meetings - Pfizer
Introduction
history, important trials, current guidelines and treatment algorithms
Renal denervation update

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
INTRODUCTION

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

- **Normotensive**
- **Hypertension**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Men</th>
<th>Women</th>
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</thead>
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<tr>
<td>CAD</td>
<td>22.7</td>
<td>9.5</td>
</tr>
<tr>
<td>Stroke</td>
<td>45.4</td>
<td>21.3</td>
</tr>
<tr>
<td>PAD</td>
<td>3.3</td>
<td>2.4</td>
</tr>
<tr>
<td>CHF</td>
<td>12.4</td>
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</tr>
<tr>
<td>Risk ratio</td>
<td>2.0</td>
<td>2.2</td>
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</tbody>
</table>

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

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<th>Should we treat HBP?</th>
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</table>

**VA Cooperative Studies**
- HDFP
- EWPHE
- MRC-1
- ANHBP-1
- SHEP
- Syst-Eur
- Syst-China

**HAPPHY**
- MAPHY
- MRC-Elderly
- STOP-1
- TOMHS
- VA MONOTHERAPY

**VA MONOTHERAPY**

Adapted from Black H, 2003.

BUILD SEQUENCE
Question: At what level of DBP should patients be treated.

Patients: 143 patients with DBP > 115 - 129 (mean age 50yrs)

Method: double blind placebo controlled.

Drugs: HCTZ, RESERPINE, HYDRALAZINE
Question: How low should the DBP be lowered to?

Patients: 380 pts DBP 90-114

Method: placebo controlled

Drugs – HCTZ, RESERPINE, HYDRALAZINE

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### Key Clinical Trials in Hypertension

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<td>VALUE</td>
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<td>TROPHY</td>
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<td>ACCORD BP</td>
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Adapted from Black H, 2003.

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<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo n=194</th>
<th>Active Rx* n=186</th>
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</thead>
<tbody>
<tr>
<td>Accelerated hypertension</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Total coronary event</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Fatal coronary event</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Renal damage</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Deaths</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>TOTAL</td>
<td>81</td>
<td>30</td>
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</tbody>
</table>
Q: Harm in lowering SBP in elderly patients

Patients: 4736 pts, >60yrs, SBP>160, DBP <90mmHg

Method: double blind placebo controlled

Drugs: chlorthalidone, atenolol
Key Clinical Trials in Hypertension

Target BP Groups
- 90 vs 85 mm Hg
- 85 vs 80 mm Hg
- 90 vs 80 mm Hg

Patients With Diabetes
- 90 vs 85 mm Hg
- 85 vs 80 mm Hg
- 90 vs 80 mm Hg

Favors Higher BP  Favors Lower BP
Question: How low should BP be lowered in diabetics?

Patients: >55 years, NIDDM, Microalbumin +, 2 CV risk factors

Intensive arm – SBP <120mmHG

Standard arm – SBP <140mmHg

SBP 133 vs 119mmHg

Nonfatal Stroke or CVD Death

HR = 0.88
95% CI (0.73-1.06)
Key Clinical Trials in Hypertension

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<td>CONVINCE</td>
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<td>ALLHAT ANBP2</td>
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<td>LIFE</td>
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No significant differences among the 3 treatment groups

- Chlorothalidone
- Amlodipine besylate
- Lisinopril

Cumulative event rate (%) vs. Time to event (y)
LIFE: Effects of a Losartan-based vs Atenolol-based Regimen on Primary Outcome and Its Components

Adjusted RR: 13.0% \( P=0.021 \)
(Losartan vs Atenolol)

- CV Death: Risk reduction \( P=0.206 \)
- Stroke: Risk increase \( P=0.491 \)
- MI: Risk increase \( P=0.001 \)
Hypertension in 2015

Still lots of questions

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

What’s more important Systolic hypertension or Diastolic hypertension?

What level of BP constitutes hypertension and why
– CONFUSION
– 4 NEW GUIDELINES – AND STILL NO CONSENSUS!!

Hypertensive 80 year old versus an Hypertensive 18 year old

Renal Denervation?

Inaccurate BP Measurement Common

“The measurement of BP is likely the clinical procedure of greatest importance that is performed in the sloppiest manner.”

—Norman Kaplan, MD
Lancet. 2007;370:591
Renal Denervation......update
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.
Externally Delivered Focused Ultrasound for Renal Denervation

• Safety and efficacy study completed in 69 patients
• 1 year after procedure – SBP reduction is 21mmHg.
• No major adverse events
• Set a platform for a Randomised Sham controlled study to confirm efficacy

ACKNOWLEDGE: Dr J Ormiston
Stages of Hypertension and Guidelines

<table>
<thead>
<tr>
<th>Stage</th>
<th>SBP</th>
<th>DBP</th>
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<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>
<tr>
<td>IS</td>
<td>&gt;160</td>
<td>&lt;90</td>
</tr>
<tr>
<td>Diastolic IS</td>
<td>&lt;140</td>
<td>&gt;90</td>
</tr>
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Distribution of Hypertension Subtypes by Age

- ISH (SBP ≥140 and DBP <90)
- SDH (SBP ≥140 and DBP ≥90)
- IDH (SBP <140 and DBP ≥90)

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>
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<tbody>
<tr>
<td>Age ≥ 60 years</td>
<td>≥ 150/90</td>
<td>&gt; 140/90</td>
<td>N.A.</td>
<td>N.A.</td>
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<tr>
<td>* ≥ 80</td>
<td>&gt; 150*/90</td>
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<td></td>
<td></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>
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<tr>
<td>Diabetics</td>
<td>&gt; 140/90</td>
<td>&gt; 140/90</td>
<td>&gt;140/80</td>
<td>N.A.</td>
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<tr>
<td>With CKD</td>
<td>&gt; 140/90</td>
<td>&gt; 140/90</td>
<td>N.A.</td>
<td>&gt; 140/90</td>
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<tr>
<td>With CVD</td>
<td>&gt; 140/90</td>
<td>&gt; 140/90</td>
<td>N.A.</td>
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**BP Targets for the USA—2014**

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<td>Age ≥ 60 years</td>
<td>&lt; 150/90</td>
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<td>N.A.</td>
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<td>Diabetics</td>
<td>&lt; 140/90</td>
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<td>&lt;140/80</td>
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<tr>
<td>With CKD</td>
<td>&lt; 140/90</td>
<td>&lt; 140/90</td>
<td>&lt;130/80 for some</td>
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<tr>
<td>With CVD</td>
<td>&lt; 140/90</td>
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**BP targets (recent BPAC guidelines)**

<table>
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<th>Normal &lt;80yrs</th>
<th>Diabetic CKD Vascular Disease</th>
<th>Elderly &gt;80 yrs</th>
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</thead>
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<tr>
<td>Blood Pressure</td>
<td>&lt;140/90</td>
<td>&lt;130/80</td>
<td>&lt;150/90</td>
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Reference:
JNC 8: Initial Medications For The Management of Hypertension

Lifestyle Modification—Especially Diet and Exercise

Diuretics

ADD B-BLOCKER IF THERE IS A COMPELLING INDICATION

4th line
SPIRONOLACTONE

ACE inhibitors or ARBs

Calcium antagonists

CBPM ≥140/90 mmHg & ABPM/HBPM ≥ 135/85 mmHg
Stage 1 hypertension

CBPM ≥160/100 mmHg & ABPM/HBPM ≥ 150/95 mmHg
Stage 2 hypertension

If target organ damage present or 10-year cardiovascular risk > 20%

Offer antihypertensive drug treatment

If younger than 40 years
Consider specialist referral

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**

- **Age <55 yrs**
  - Step 1: A
  - Step 2: A + C†
  - Step 3: A + C + D
  - Step 4: A + C + D + further diuretic‡
    - Consider resistant hypertension
    - Consider specialist advice

- **Age ≥55 yrs or black**
  - C†

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
Need 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’
Uncontrolled Hypertension
Caring Does Matter
Study Aim and Design

• To estimate the prevalence of uncontrolled and RHT in NZ primary care populations

• Electronic medical records (EMR):
  – 29,740 patients aged ≥ 20 years, enrolled with 14 general practices from 2009 to 2012
  – *Uncontrolled HT*: ≥ 2 SBP readings ≥ 160mmHg (or ≥150mmHg for patients with diabetes, CVD or CKD)
  – *RHT*: ≥ 3 classes of BP-lowering drugs (including a diuretic) prescribed in the 90 days prior to SBP readings

Prof R Doughty et al.
NHC/HRC partnership grant
Results

• 12,900 (43%) did not have a BP recorded in the EMR during the 12 month study period
• More likely to have BP recorded with increasing age
• 966 (3.2%) had Uncontrolled HT
  – or 5.7% of those with recorded BP
• 81 had RH (8.4% of Uncontrolled HT group)
• More than 60% of the Uncontrolled HT group lived in disadvantaged areas (quintile index 4 or 5)
Results: Uncontrolled HT Prevalence by Age & Ethnicity

% of HT patients in the population of each age group

- Maori
- Pacific
- non-Maori/non-Pacific

Age group:
- 20-34
- 35-39
- 40-44
- 45-49
- 50-54
- 55-59
- 60-64
- 65-69
- 70+
Results: BP-lowering Medication

For Uncontrolled HT Group:

• 507 patients (52%) had no BP-lowering medication prescribed in the 90 days prior to the first SBP

• 906 patients (94%) had ≥ 1 BP-lowering medications prescribed in the quarter following the recording of the high SBP

• But, by 12 months, 277 (29%) did not have BP-lowering medications prescribed
Hypertension

Fiona Stewart
Auckland Heart Group
Auckland City Hospital

GP Conference
Rotorua
June 2015
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
Resistant Hypertension

Colin Edwards
Cardiologist
WDHB
Auckland Heart Group

JUNE 2015
1/3 of patients with RESISTANT HYPERTENSION have WHITE COAT HYPERTENSION emphasizing the importance of AMBULATORY BP MONITORING

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.
History

52 year old Indian female

GP referral – poorly controlled hypertension and breathlessness

Diagnosed with hypertension 6 years previously – presumed essential

Medication:

- Bendrofluazide 2.5mg/d
- Atacand 16mg/d
- Amlodipine 5mg/d

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

INTERMEDIATE CV RISK
EXAMINATION

EXAMINATION:

Raised BMI

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

Fundoscopy –mild A-V nipping

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

END ORGAN DAMAGE
Normal ECG and CXR
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
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*
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 – left ventricular hypertrophy
- ETT – rule out CAD
- 24 hr holter – rule out AF

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<tr>
<th>Intervention</th>
<th>Targeted change</th>
<th>Expected BP change</th>
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<tr>
<td>Sodium reduction</td>
<td>&lt; 1500 mg/day</td>
<td>-5 / -3</td>
</tr>
<tr>
<td>Weight loss</td>
<td>BMI &lt; 25 kg/m²</td>
<td>-7 / -6</td>
</tr>
<tr>
<td>Alcohol reduction</td>
<td>&lt; 2 drinks/day</td>
<td>-5 / -2</td>
</tr>
<tr>
<td>Exercise</td>
<td>4+ times/week</td>
<td>-5 / -4</td>
</tr>
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Results

ABPM – average 24-hour 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.
no ischaemia
Hypertensive response - Peak SBP – 220mmHg
Treatment

**STEP 1:**
Amlodipine 5mg/d – 10mg/d  
Atacand 16mg/d  
Continue Bendrofluazide 2.5mg/d

**STEP 2: 2 weeks later still hypertensive**
Amlodipine 10mg/d  
Atacand 16 - 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  
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

RENNAL FUNCTION:

Normal renal US

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tr>
<td>Sodium</td>
<td>139 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.4 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>62 umol/L</td>
</tr>
<tr>
<td>eGFR</td>
<td>87 mL/min/1.73m²</td>
</tr>
</tbody>
</table>

24 hour urine catecholamines

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>24 h</td>
</tr>
<tr>
<td>Volume</td>
<td>1.69 L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>9.0 mmol/d</td>
</tr>
<tr>
<td>Adrenalin/Creatinine Ratio</td>
<td>2.1 nmol/mmol creat</td>
</tr>
<tr>
<td>Urine Adrenalin</td>
<td>19 nmol/d</td>
</tr>
<tr>
<td>Noradrenalin/Creatinine Ratio</td>
<td>23 nmol/mmol creat</td>
</tr>
<tr>
<td>Urine Noradrenaline</td>
<td>200 nmol/d</td>
</tr>
<tr>
<td>Dopamine/Creatinine Ratio</td>
<td>0.15 umol/mmol creat</td>
</tr>
<tr>
<td>Urine dopamine</td>
<td>1.4 umol/d</td>
</tr>
</tbody>
</table>

24 hr urine Cortisol

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>24 h</td>
</tr>
<tr>
<td>Volume</td>
<td>1.48 L</td>
</tr>
<tr>
<td>Cortisol (free) Urine</td>
<td>110 nmol/d</td>
</tr>
<tr>
<td>Creatinine</td>
<td>11.0 mmol/d</td>
</tr>
</tbody>
</table>

*Patients with Cushing's syndrome usually have levels >180 nmol/d. This test is not indicated in the diagnosis of cortisol deficiency.*
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
Factors affecting plasma renin concentration

1) Sodium intake – renin is suppressed by a high salt diet
2) Age – Renin levels gradually fall as renal function declines.
3) Menstrual phase, and pregnancy – Renin levels drop during pregnancy and menstruation.
4) Time of day – highest early mornings.
5) Posture- higher standing
6) Medication – ↑ renin levels: diuretics and spironolactone, calcium blockers(DHP),ACE,ARB
   ↓ Renin levels: B-Blockers, NSAIDS, α-methyl dopa

Stop these agents for 2 weeks prior to measuring RAAS.
Alpha blockers and Verapamil can be substituted for BP control.

Low salt diet, avoid licorice and caffeine for 24 hours before testing.
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

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

<table>
<thead>
<tr>
<th>Plasma Aldosterone</th>
<th>399 pmol/L</th>
<th>60-1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Renin</td>
<td>4 mU/L</td>
<td>4-46</td>
</tr>
<tr>
<td>Aldosterone/Renin ratio</td>
<td>100</td>
<td>H See below</td>
</tr>
</tbody>
</table>

Please note the new reference range(s)

Aldosterone/Renin ratio

New Hyperaldo Cases in Germany

Clues:
- very suppressed active renin level
- Up to 50% can have normal K+
Prevalence of Primary Aldosteronism in Subjects With Resistant Hypertension

<table>
<thead>
<tr>
<th>Location</th>
<th>Prevalence of PA (%)</th>
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<tbody>
<tr>
<td>Seattle¹</td>
<td>17</td>
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<tr>
<td>Birmingham²</td>
<td>20</td>
</tr>
<tr>
<td>Oslo³</td>
<td>22</td>
</tr>
<tr>
<td>Prague⁴</td>
<td>19</td>
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</tbody>
</table>
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
68 years, obese, post CABG, severe RESISTANT hypertension

Work-up for 2° causes

Na142 K5.4 SCR 157umol/l RAISED serum renin levels 1368mUI/L (N 4-46)

?  

Work-up for 2° causes

Na 139, K 4.4, Scr 62umol/l SUPPRESSED serum renin level 4mUI/L (N 4-46) N Aldo level Aldo:renin raised >100

Bilateral adrenal adenomas on CT Confirmed by adrenal vein sampling
Raised serum renin

Causes:
1) Renin producing tumour – very rare
2) **Severe renal artery stenosis – underperfusion of JGA.**
3) Heart failure, liver failure, nephrotic syndrome – oedema is associated with relative intravascular hypovolemia.
4) Pseudo hypoaldosteronism – aldosterone receptor problem
5) Bartter and Gitelman syndromes – renal tubular abnormalities ➔ salt wasting.
# Secondary causes

<table>
<thead>
<tr>
<th>Date</th>
<th>Sodium</th>
<th>Potassium</th>
<th>Creatinine</th>
<th>eGFR</th>
<th>Serum Cortisol</th>
<th>Comment</th>
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</thead>
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<tr>
<td>22/04/14</td>
<td>142</td>
<td>5.2</td>
<td>157</td>
<td>29</td>
<td>224 nmol/L</td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>20/12/13</td>
<td>141</td>
<td>4.7</td>
<td>97</td>
<td>52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15/11/13</td>
<td>140</td>
<td>4.3</td>
<td>104</td>
<td>48</td>
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</tr>
<tr>
<td>24/08/13</td>
<td>141</td>
<td>4.4</td>
<td>106</td>
<td>47</td>
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<td></td>
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<tr>
<td>24/04/13</td>
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<td>4.8</td>
<td>102</td>
<td>49</td>
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<tr>
<td>20/12/12</td>
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<td>5.2</td>
<td>100</td>
<td>48</td>
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<td>23/08/11</td>
<td>141</td>
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</tbody>
</table>

| Normetanephrine | 799 pmol/L | <900 |
| Metanephrine    | 86 pmol/L  | <500 |
| Plasma Aldosterone | 273 pmol/L | 60-1000 |
| Active Renin    | 1368 mU/L  | 4-46 |
| Aldosterone/Renin ratio | <1 | See below |
Investigations

Renal U/S - mild moderate L renal artery stenosis
- poor quality and limited accuracy due to obesity
- Suspect RAS in an obese patient- CT or MRA renal arteries
RESISTANT HYPERTENSION

Secondary ALDOSTERONISM

Work-up for 2° causes

Na 142 K 5.4 SCR 157umol/l
RAISED serum renin levels 1368mUl/L (N 4-46)

Primary ALDOSTERONISM

Work-up for 2° causes

Na 139, K 4.4, Scr 62umol/l
SUPPRESSED serum renin level 4mUl/L (N 4-46)
N Aldo level
Aldo:renin raised >100

Bilateral adrenal adenomas on CT
Confirmed by adrenal vein sampling
Hypertension in the Elderly

Fiona Stewart
Auckland Heart Group
Auckland City Hospital

GP Conference
Rotorua
June 2015
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

Follow-up (years)

Blood Pressure (mmHg)

Placebo

Indapamide SR +/- perindopril
All stroke (30% reduction)

\[ P = 0.055 \]

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>IndapamideSR ± perindopril</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at Risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>1912</td>
<td>1484</td>
</tr>
<tr>
<td>IndapamideSR ±</td>
<td>1933</td>
<td>1557</td>
</tr>
<tr>
<td>perindopril</td>
<td>807</td>
<td>873</td>
</tr>
<tr>
<td></td>
<td>374</td>
<td>417</td>
</tr>
<tr>
<td></td>
<td>194</td>
<td>229</td>
</tr>
</tbody>
</table>
Fatal Stroke (39% reduction)

**No. of Events per 100 Patients**

- **Placebo**
  - Follow-up (yr): 0, 1, 2, 3, 4
  - Events: 0, 1, 2, 3, 4
  - Patients: 1912, 1492, 814, 379, 202

- **Indapamide SR ± perindopril**
  - Follow-up (yr): 0, 1, 2, 3, 4
  - Events: 0, 1, 2, 3, 4
  - Patients: 1933, 1565, 877, 420, 231

**P = 0.046**
Total Mortality (21% reduction)

Placebo
Indapamide SR ± perindopril

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

P = 0.019
Heart Failure
(64% reduction)

Placebo

Indapamide SR ± perindopril

No. at Risk
Placebo
Indapamide SR ± perindopril

1912  1480  794  367  188
1933  1559  872  416  228

P < 0.0001
**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 2nd 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

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

EXAMINATION:

Tall and thin

Bp 150/90mmHg and PR 70 bpm       Fundoscopy – no hypertensive retinopathy
CV – No murmurs to suggest aortic coarctation and no radiofemoral delay

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
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
Fibromuscular Dysplasia

FMD is a non-inflammatory, non-atherosclerotic 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 - flash pulmonary oedema, 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
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
SUMMARY

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
Thank You

Cardiologists:

Fiona Stewart – Auckland Heart Group ADHB
Colin Edwards - Auckland Heart Group WDHB