William J. Elliott, M.D., Ph.D.

“Hypertension 4.0: Secondary Hypertension”

DISCLOSURE INFORMATION:
Dr. Elliott has received research funding, honoraria, and/or travel expenses from essentially every pharmaceutical company that makes, markets, or distributes antihypertensive drugs in the United States. A former full-time employee of RUSH Medical College, he was prohibited from (and still does not) own individual stocks or financial instruments related to healthcare.
DISCLOSURE OF RELATIONSHIPS

For William J. Elliott over the past 12 months,

Grant/Research Support: None.

Consultant: Novartis Pharmaceuticals Corp.

Speakers Bureau: None.

Stock shareholder: None! I once worked at RUSH!!

Other Support, Tangible or Intangible: Elsevier (Division of Harcourt); UpToDate®, Springer
Affidavit of Originality

- The following material is based exclusively on the speaker’s own opinion, knowledge and expertise.
- There is no organization, company, or entity that has exercised any control or influence over the content of this presentation, nor has any other person or organization had any part in drafting, scripting or designing its content.
- The information presented is based on the principles of “Evidence-Based Medicine,” and is intended to avoid promotion of any specific commercial interest, product, or company.
“Off-Label Use” Disclaimer

WARNING!
During this lecture, attempts will be made to avoid discussion of “off-label” or investigational use of drugs, but very few antihypertensive drugs have been specifically approved by the US FDA to prevent cardiovascular events or end-stage renal disease, which we all agree is the major reason to diagnose and treat hypertension.

DISCLAIMER:
The audience member should interpret each example and every statement in the context of the “local standard of care” regarding medical practice, and judge each allegation regarding drug therapy within the standards approved by the most current product information for each marketed agent, as reflected in the most recent FDA-approved package insert. The speaker assumes no liability for any erroneous interpretation of the information contained herein, stated or implied.
Disclaimers

• The speaker has participated (with known experts in the field) in writing a recent “Scientific Statement” from the American Heart Association on the topic of “Treatment of Hypertension in Patients with Coronary Heart Disease.”
  – This topic is not part of today’s discussion; today’s presentation does not reflect opinion, consensus, or recommendations from the American Heart Association.

• The speaker currently serves as the Chair of the Continuing Education Committee and on the Education Committee of the American Society of Hypertension, which may be involved in reconciling or revising current US hypertension guidelines in the next few months.
  – This process is embargoed, and will not be discussed.
Learning Objectives

At the conclusion of this fifty (50)-minute presentation, the awake participant should be able to:
Compare and contrast the prevalence, risk factors, most commonly recommended screening test, diagnostic evaluation, and appropriate management (including suitable consultations) for patients with elevated blood pressure related to:
Learning Objectives

a. Chronic kidney disease.
b. Renovascular hypertension.
c. Pheochromocytoma.
d. Primary hyperaldosteronism (including that related to sleep-disordered breathing).
e. Hypercortisolism (Cushing’s syndrome) and variants.
f. Thyroid illness.
g. Coarctation of the aorta.
h. Acromegaly.
i. Hypercalcemic states.
5 (of 10) Key Points

• There is no specific treatment for hypertension due to intrinsic renal disease, except lowering the BP to target with appropriately reduced doses of renally-excreted drugs.

• The probability of renovascular hypertension can be assessed WITHOUT SPECIFIC DIAGNOSTIC TESTING, using a clinical prediction rule.

• Renal angiography (followed by angioplasty) should usually be reserved for patients whose renal function declines or whose BP does not respond to intensive pharmacological treatment.

• Renal angioplasty followed by stenting is typically useful for ostial stenoses, but unnecessary for fibromuscular disease.

• Collections of urinary catecholamine metabolites are generally less expensive and less technically demanding than plasma levels in testing for pheochromocytoma.
• $T_2$-weighted MRI is the most specific imaging technique for pheochromocytoma.

• Important types of primary hyperaldosteronism include: adrenal adenomas, bilateral adrenal hyperplasia, and glucocorticoid-suppressible hyperaldosteronism (for which a specific genetic mutation has been found).

• The source of hypersecretion in most cases of hypercortisolism can be elicited with one or both (i.e., low- or high-dose) dexamethasone suppression tests.

• Both hyper- and hypo-thyroidism can cause hypertension; propranolol is the preferred initial treatment for the former.

• Screening for coarctation of the aorta can be accomplished by physical examination (leg BP measurement, "Hill’s sign," and radiofemoral delay), followed, if necessary, by an echocardiogram.
Causes of Secondary Hypertension

- Chronic kidney disease
- Renovascular hypertension
- Primary aldosteronism
  - Obstructive sleep apnea (sleep-disordered breathing)
  - Bilateral adrenal hyperplasia
  - Aldosterone-secreting adrenal adenoma (Conn’s syndrome)
- Hypercortisolism (Cushing’s Syndrome) & variants
- Pheochromocytoma
- Hypothyroidism
- Hyperthyroidism
- Acromegaly
- Coarctation of the aorta
- Hyperparathyroidism & variants
Why Think About 2° Hypertension?

• Many patients with secondary hypertension can be cured!

• Young people are at higher risk for having it (except for atherosclerotic renovascular disease).

• The cost of diagnosis and treatment/cure is frequently less than the cost of chronic medical therapy, especially in the young.

• It is intellectually appealing (and even fun!) to think of “curing” an occasional patient with hypertension, which keeps us mentally awake.
Patient Populations with High Prevalence of Non-Primary Hypertension

- Higher levels of untreated BP (except primary aldosteronism)
- Those with characteristic physical signs (caveat the postage-stamp sized picture!)
- “Refractory” (“resistant”) hypertension
- Referred hypertension
Evaluation for 2° Hypertension

- Depends on the individual patient and his/her presentation
  - Initial serum creatinine: r/o intrinsic renal disease
  - TSH: r/o or R/I hyperthyroidism, hypothyroidism

- Depends on the demographic and clinical features of the patient
  - Fibromuscular hyperplasia in young white women
  - Atherosclerotic renovascular hypertension in older smokers

- Depends on patient’s symptoms
  - Paroxysmal symptoms are common in pheochromocytoma
  - Hypokalemic symptoms (cramps, etc.) in primary hyperaldosteronism
Hypertension

Due to

Intrinsic

Renal Disease
CKD: Screening & Diagnosis

- Initial tests for new hypertensive patient include:
  - Serum creatinine (eGFR < 60 = Stage 3 or worse CKD)
  - Urinalysis (dipstick for protein, albumin?)

- Follow-up test(s):
  - Former recommendation: get 24-hour creatinine clearance and protein determination as a second step (simultaneous Na⁺, K⁺ costs only a few dollars more!).
  - Now: spot (first AM) albumin/creatinine ratio.
    - < 30 mg/gm = “normal-mildly increased albuminuria”
    - 30-299 mg/gm = “moderately increased albuminuria”
    - ≥ 300 mg/gm = “severely increased albuminuria” ~ proteinuria

- Signs of impaired kidney function must be present for ≥ 3 months to diagnose CKD

Mgmt: HTN 2° CKD

- Identical to 1° HTN, except:
  - BP target < 140/90 mm Hg (yet KDIGO “suggests” < 130/80 mm Hg, especially if ACR > 300 mg/gm)
  - Reduce doses or frequency of renally-excreted or secreted drugs
  - Consider dietary protein excretion
    - Worked well in Australia, not in USA (MDRD)
  - Dietary sodium restriction is VERY important
    - Low-sodium diets lower BP in everybody, but are even more effective for patients taking diuretics.
    - Sodium restriction has an independent, beneficial effect to reduce albuminuria, as well as cardiovascular risk.
Renovascular Hypertension
How Common is RVH?

- It depends on where you look:
  - In the primary care experience, it’s only about 2.5% of hypertensives.
  - In tertiary referral centers, it’s about 5-16% of hypertensives.

- It depends on the patient population being screened:
  - In young, “Stage 3” hypertensive African American men, it’s low (~0.2%).
  - In young, “Stage 3” hypertensive Caucasian women, fibromuscular dysplasia is quite common (as high as 20% in some series).
A priori Probability Estimate of RVH?

• A “decision-rule” has been promulgated by Dutch investigators (a version of which is now used by some MCOs to determine whether a renal angiogram should be prior authorized!).

• Most of us just look for patients with ≥ 2 “clinical clues:”
  • Abdominal bruit (especially with a diastolic component)
  • Appropriate age (> 50 for atherosclerotic disease, ≤ 20 for fibromuscular dysplasia)
  • Occlusive disease in another arterial bed
  • Recent worsening of hypertension
  • White race (I don’t agree, but it’s in the literature!)
  • Past history of “accelerated/malignant hypertension”
  • Keith-Wagener-Barker Grade III or IV fundi (i.e., hemorrhages/exudates or papilledema)
  • Unilateral small kidney (by ultrasound or other radiological test)
  • Hypertension unresponsive to an “appropriate” 3-drug regimen
  • “Bump” of serum creatinine after starting an ACE-Inhibitor or ARB
RVH vs. RAS?

• RVH is a **retrospective** diagnosis:
  - BP should be lower 6-12 weeks after the intervention.
  - Typically, renal artery stenosis is noted first, and then an intervention is performed, followed by a BP measurement.

• Renal artery stenosis is an **ANATOMICAL** diagnosis, **not** a functional one!
  - There are emerging data (from “drive-by angiograms”) suggesting that many patients have a significant stenosis **WITHOUT** an elevated BP!
  - Just because a stenosis is **present** does **not** mean that the patient needs an intervention. This disturbs the “oculostenotic reflex” of many interventional radiologists/cardiologists.
Diagnostic Criteria: RVH vs. RAS

• RENAL ARTERY STENOSIS
  – > 75% luminal narrowing of a main renal artery
  – > 50% luminal narrowing with post-stenotic dilatation

• RENOVASCULAR HYPERTENSION
  – “Cure:” if the diastolic BP is < 90 mm Hg without medication, 6-12 weeks after intervention (angioplasty [±stent], or surgery)
  – “Improvement:” if the diastolic BP is < 90 mm Hg with less medication then before the intervention, OR there has been a lowering of diastolic BP by ≥ 15% on the same or fewer medications vs. before the intervention
# Screening Tests for RVH

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT Angio</td>
<td>0.64</td>
<td>0.92</td>
<td>2100</td>
</tr>
<tr>
<td>Doppler U/S</td>
<td>0.84</td>
<td>0.90</td>
<td>250</td>
</tr>
<tr>
<td>IV DSA</td>
<td>0.80</td>
<td>0.88</td>
<td>1200</td>
</tr>
<tr>
<td>MRA</td>
<td>0.63</td>
<td>0.84</td>
<td>2900</td>
</tr>
<tr>
<td>RS-IVP</td>
<td>0.74</td>
<td>0.86</td>
<td>250</td>
</tr>
<tr>
<td>Captopril</td>
<td>0.86</td>
<td>0.81</td>
<td>300</td>
</tr>
</tbody>
</table>

*Scan*

Pros/Cons of RVH Screening

• **Doppler US**: Operator-dependent, bowel prep often necessary; can predict results of revascularization

• **MRA**: **NO gadolinium** for those with eGFR < 60 mL/min/1.73 m² (risk of nephrogenic fibrosing dermopathy); computer-intensive; good pictures

• **CTA**: Good pictures, contrast load

• **DTPA scan with ACE-inhibitor**: not as good in patients with CKD, may predict results of revascularization
Angioplasty

• **FMD:** Technically successful in 98%; Excellent long-term reductions in BP, especially in the young; may need to be repeated (sometimes > 10 years)

• Atherosclerotic RAS:
  - Technically poor results with:
    • Ostial lesions
    • Lesions in separated/multiple arteries
    • Multiple (sequential) lesions in the same artery
  - Restenosis rates are lower if one places a stent or stents after angioplasty.
Angioplasty±Stents vs. Medical Therapy

• Four recent, large studies show no significant difference in outcomes (BP, rate of decline of renal function, cardiovascular outcomes)
  – Each study has its major flaws, especially “crossovers.”

• The largest, longest-term, NIH-funded CORAL study gave the “final answer.”
  – It is now very difficult to obtain prior authorization for renal angiography from most payors and MCOs.
When to Consider Angioplasty±Stenting?

• Poor control of BP despite maximal medical therapy
  – Often without ACE-inhibitor/ARB/DRI (risk of acute kidney injury); Angioplasty±stent may make RAAS inhibitor therapy possible

• Increasing serum creatinine, despite good BP control
  – ?Ischemic nephropathy (NOT evidence-based!)

• Patient **must** be willing to have surgery, if misadventure occurs…
Primary Aldosteronism
Subtypes: Primary Hyperaldosteronism

- “Conn’s syndrome” (unilateral adrenal adenoma that secretes aldosterone)
- Bilateral adrenal hyperplasia (“idiopathic primary hyperaldosteronism”)
- Adrenal carcinoma (~25 cases in world’s literature)
- Glucocorticoid-suppressible Hyperaldosteronism (~20 families so far)
- Obstructive sleep apnea and/or sleep-disordered breathing
Epidemic of IHA at TWFMC?

1957-1985

- APA: 57%
- Probable APA: 24%
- IPA: 9%
- Probable IPA: 11%

248 Patients

1999

- APA: 20%
- Probable APA: 8%
- IPA: 18%
- Probable IPA: 54%

120 Patients

*Endocrinol., 2003;144:2209*
Aldosterone Synthase/11-OHase Chimera

Normal Chromosomes #8

5' 3'

11β-Hydroxylase

95% identical, closely associated

5' 3'

Aldosterone Synthase

Chimeric Chromosome #8

5' 3'

5' regulatory sequence for ACTH responsiveness of 11β-hydroxylase, fused to enzyme coding sequences for aldosterone synthase (!)

Nature. 1992;355:262
Hyperaldo & Sleep Apnea

- First: high aldosterone plasma levels found in cohorts of resistant hypertensives with sleep apnea
  - This has now been seen in 6 different centers!
  - Some estimate the prevalence of hyperaldo in sleep apnea at 25-30% of such patients, which would make it the **MOST** common form of secondary hypertension!

- Second: BP drops with low-dose spironolactone
  - This has been seen in 4 different centers!

- Third: Low-dose spironolactone for all resistant hypertensive patients!
  - **ASCOT**: Evidence-based with outcomes!
Licorice and Hypertension

• Since about 1980, glycyrrhizic acid (a triterpene) was believed to be an aldosterone agonist.

• Since 1992 or so, elegant studies have shown that both glycyrrhizic acid and its hydrolysis product, glycyrrhetinic acid, inhibit peripheral (i.e., intrarenal) 11-β-hydroxysteroid dehydrogenase, the enzyme responsible for conversion of cortisol to cortisone.

• This leads to an "apparent mineralocorticoid excess state," that has clinical manifestations similar to primary hyperaldosteronism.
Patient Populations with High Prevalence of Primary Hyperaldosteronism

- Hypertensives with low serum potassium at presentation (prior to diuretic!)
- Hypertensives with symptoms of hypokalemia (muscle cramps, etc.)
- Familial 11-hydroxylase deficiency syndrome (call R. Lipton at Yale for genetic testing!)
- Primary hyperaldosteronism is RARE among
  - Patients with BP > 180/110 mm Hg
  - Patients with high-grade retinopathy
Hyperaldosteronism: Screening

• Plasma aldosterone/renin ratio
  – Different labs use different assays:
  – > 20 ng/mL per mg A II/mL/hr in the “classical assays (Quest® Laboratories)
  – Best discrimination when plasma [aldosterone] > 20 ng/mL
  – Easily confused with “low-renin hypertension”

• A few authorities still advocate 24-hour urinary K+ and aldo levels
Controversies in 1° Hyperaldo

• Next test?
  – 2 L saline infusion over 4 hr
  – High-resolution CT of adrenals
  – Other steroid levels
  – Levels after ACE-inhibitor
  – Stop all antihypertensive drugs except CCBs, alpha-blockers

• Pre-operative medications
  – Potassium repletion, aldo blocker, CCB

• Prognosis after (laparoscopic) surgery
  – Hypokalemia usually improves, but normotension is rare!
Workup: Primary Hyperaldosteronism?

Adrenal CT Scan

- Normal or Micronodularity or Bilateral masses
- High Prob. for APA
- Unilateral hypodense nodule > 1 cm diameter

Adrenal Venous Sampling

- Low Prob. for APA
- No lateralization
- 40 y.o.
- Lateralizes!

APA or APC: Laparoscopic Adrenalectomy

IHA: Drugs

*Endocrinol.*, 2003;144:2209
Pheochromocytoma
Populations with High Prevalence of Pheochromocytoma

- BP > 180/110 mm Hg
- Paroxysms of hypertension, headache, sweating ("spells")
- Episodic hypertension with wide swings of BP
- Hypertension with 3-5 "H’s"
  - Hypertension
  - Headache
  - Hyperhydrosis
  - Hyperglycemia
  - "Hypermetabolism"
- Familial syndromes (MEN syndromes)
- Phakomatoses

French experience: 95% sensitivity
Pheo & Multiple Endocrine Neoplasia Syndromes

- **MEN IIa (Sipple’s):**
  - Pheo (usually bilateral),
  - Medullary carcinoma of the thyroid,
  - Parathyroid tumors/adenomas (50% have hyperparathyroidism)

- **MEN IIb:**
  - Pheo (usually bilateral),
  - Medullary carcinoma of the thyroid,
  - Submucosal neuromas,
  - Hyperplastic corneal nerves (sometimes with Marfanoid habitus, and/or adrenomedullary disease)
Pheo & Phakomatoses

- Sturge-Weber Syndrome (choroidal and leptomeningeal angiomas, port wine stain in the trigeminal distribution)
- von Recklinghausen’s Syndrome (neurofibromatosis)
- Tuberous Sclerosis (de Bourneville’s/Pringle’s disease: adenoma subaceum, subungual fibromas, ?mental retardation)
- von Hippel-Lindau Disease (retinal and cerebellar hemangioblastomas, other malignancies)
The “Rule of 10 (%)”

- Approximately 10% of pheochromocytomas are:
  - Bilateral
  - Found in children
  - Extra-adrenal
  - Malignant (at diagnosis)
  - Familial
Screening for Pheo

- Since catecholamines have short serum half-lives, most authorities recommend urine tests (which integrate production and metabolism over many hours).

- Measurements of metabolic products of catecholamines are useful:
  - Vanillylmandelic acid (VMA): perhaps less useful as a single test
  - Metanephrine and normetanephrine ("total metanephrines")
Pheo & 24-Hour Urines

• Some authorities recommend ratios of catecholamine metabolite to creatinine in random urine specimen, but most of us still prefer 24-hour urine results
• Many recommend “split” urines, beginning a collection immediately after a “spell” and another directly following, but this has not been formally evaluated
• There is a lot of literature promoting different ways to collect and analyze urinary data, but little consensus (given the rarity of the disease)
• Falsely negative 24-hour urine collections are common in:
  – Familial pheochromocytoma syndromes
  – Normotensive pheochromocytomas
  – Dopamine beta-hydroxylase deficient pheochromocytomas
  – Intermittently-secreting pheochromocytomas
Pheo: Plasma Screening?

- Some investigators have recommended plasma catecholamine determinations.
- This is expensive, and technically troublesome (difficult collection, quick centrifuge, store/ship over granular NaHSO$_3$).
- **Plasma metanephrines** are becoming more popular in the research literature, but not in large (especially managed care) hospitals!
Pheo: Pharmacological Tests?

- Typically used after other tests are equivocal.
- **Clonidine testing** (usually preferred because of safety), better in patients with elevated plasma levels of catecholamines at baseline.
- **Glucagon testing** (can be done under cover of alpha-blockade, to block the sudden and extreme elevation in BP, which can occur in both patient and testing physician!).
Localizing Pheos

- MRI (better than CT, because of improved specificity of $T_2$-weighted images).
- CT (more widely available, but high-resolution and thin cuts are needed).
- MIBG (mono-$^{123}$I-benzylguanidine): taken up by chromaffin tissue; usually scanned on 3rd post-injection day.
- Octreotide scan (still being investigated, wider availability than MIBG).
T1-weighted image
T2-weighted image
T1-weighted image (after gadolinium)
## Pheo Imaging

<table>
<thead>
<tr>
<th>Scan</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>CT</td>
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<td>~70-75%</td>
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<tr>
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<td>~85-90%</td>
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<tr>
<td>$T_1$-w MRI</td>
<td>~90-95%</td>
<td>~85-90%</td>
</tr>
<tr>
<td>$T_2$-w MRI</td>
<td>~90-95%</td>
<td>~95-99%</td>
</tr>
<tr>
<td>MIBG</td>
<td>~95-99%?</td>
<td>~90-95% (?)</td>
</tr>
</tbody>
</table>

*Arch Intern Med*, 2000;160:2521;  
Pre-Op Pharmacological Preparation for Pheo

• Remember that prior to surgery:

• **Alpha-blockade** is routinely recommended
  – Phentolamine (iv only)
  – Phenoxybenzamine (po only)

• Beta-blockers are necessary only **infrequently**, and may cause unopposed alpha-constriction if used **without** alpha-blockade

• Lesson: follow the alphabet!
Hypercortisolism
Causes of Hypercortisolism

• “Classic Cushing’s disease”
• Ectopic secretion of ACTH (most commonly by lung cancers).
• Adrenal carcinoma (about 100 cases in the world’s literature)
• Congenital adrenal hyperplasia (more common in pediatrics)
  – Bongiovanni’s Syndrome (11β-hydroxylase deficiency): overvirilized little boys
  – Biglieri’s Syndrome (17α-hydroxylase deficiency): delayed sexual development in girls
Causes of Hypercortisolism: Adults

- Cushing's Disease: 68%
- Ectopic ACTH: 12%
- Ectopic CRH: 10%
- Adrenal Adenomas: 8%
- Depression: 8%
- Alcoholism: 12%

### Cushing’s Syndrome: Test Results

<table>
<thead>
<tr>
<th>Pathology</th>
<th>[Cortisol]</th>
<th>[ACTH]</th>
<th>LD-DST</th>
<th>HD-DST</th>
<th>Suppression?</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. Disease</td>
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<td>↑</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Ectopic ACTH</td>
<td>↑</td>
<td>↑ or</td>
<td>No</td>
<td>No*</td>
<td></td>
</tr>
<tr>
<td>Ectopic CRH</td>
<td>↑</td>
<td>↑</td>
<td>No</td>
<td>Usually</td>
<td></td>
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<tr>
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<td>↑</td>
<td>↓</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Pseudo-C</td>
<td>±</td>
<td>↑</td>
<td>often</td>
<td>Usually</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Hypertension & Thyroid Illness
Hyperthyroidism

• Can be a cause of hypertension, but is seldom missed
  – Most are young patients with wide pulse pressures, high pulse rates, and other findings characteristic of hyperthyroidism.
  – Nowadays, most authorities rely on ultrasensitive TSH as the screening test of choice.

• Propranolol may be the drug of choice here, as it treats the tachycardia, hypertension, and inhibits peripheral conversion of $T_4$ to $T_3$ (although some authorities are now questioning this “classic” clinical pharmacological literature).
Hypothyroidism

• Is a less frequently diagnosed cause of hypertension, but one report suggests that it’s present in 3% of hypertensives in upstate New York.
  – Even more important is the observation that BP falls when thyroid hormonal replacement becomes therapeutic.
  – Most authorities still recommend screening with the ultrasensitive TSH, but to select patients judiciously for screening (i.e., TSH is not recommended by JNC 7 as a routine test for evaluation of every hypertensive patient).
Coarctation of the Aorta
Aortic Coarctation

• Although rare, this potentially remediable cause of hypertension should be screened for in every young person who is diagnosed with hypertension, by taking a blood pressure **IN THE LEG**.
  – Remember, 20/10 mm Hg **HIGHER** than the arm pressure is normal!
  – Hill’s sign (of aortic insufficiency): leg BP lower by > 20/10 mm Hg than the arm.

• Radiofemoral delay is the screening test of second choice: the examiner has a built-in “control” observation in him/herself!
Aortic Coarctation

• If the leg BP is lower, remember to measure BP in the other arm, too, to discern Type of coarctation.
• Don’t forget “rib notching” on chest x-ray!
• The cheapest imaging study is probably the echocardiogram, which can identify about 95% of coarcts (down to about 8 cm of the descending aorta).
• Controversy still exists about optimal therapy (surgery vs. angioplasty) and prognosis (most remain hypertensive, despite a beta-blocker).
Hypertension & Acromegaly

- Acromegliacs often have elevated BPs, but usually not out of proportion to their hearts, fasting cortisol levels, and weight.
- Few would argue that acromegliacs ought to have their BP lowered with the usual drug therapies; some would suggest beta-blockers as first-line, to prevent aortic dissection.
- BP usually stays up, despite octreotide.
- Finding an effective antihypertensive should not be a “tall order.”
Hypertension & Hypercalcemia

- Hypertension associated with hyperparathyroidism often disappears after removal of the adenoma.
- Some people believe this is a primary effect of hypercalcemia, but others believe that it’s “parathyroid hypertensive factor,” which has been well characterized in rats.
- There is no specific therapy yet available for this problem in humans.
  - This softly contradicts one popular theory that LACK of calcium intake is associated with essential hypertension; many intervention studies funded by the National Dairy Council have failed to convince most of us about BP-lowering effects of dietary calcium.
Conclusions

• Although uncommon, secondary hypertension is important, particularly in young people.

• Specific screening tests and subsequent diagnostic evaluations can lead to better outcomes, and occasionally, cures!

• Consideration of secondary causes for the #1 reason Americans see a healthcare provider (for a chronic condition) keeps us mentally alert, and can be fun!
A 56-year old man visits the physician’s office for follow-up of hypertension, diagnosed 2 months earlier. Two and 4-months ago, blood tests estimated his glomerular filtration rates (based on the updated Modification of Diet in Renal Disease equation) at 55 and 48 mL/min/1.73 m² (respectively). Two months ago, his first-voided urine of the morning contained 295 mg of albumin per gram of creatinine. According to current US national guidelines (from JNC 8 and the National Kidney Foundation), his office blood pressure should be, at minimum:

a. < 160/95 mm Hg.
b. < 140/90 mm Hg.
c. < 130/85 mm Hg.
d. < 130/80 mm Hg.
e. < 120/80 mm Hg.
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a. 1.
b. 2.
c. 3a.
d. 3b.
e. 4.
f. 5.
Question 2

A 56-year old man visits the physician’s office for follow-up of hypertension, diagnosed 2 months earlier. Two and 4-months ago, blood tests estimated his glomerular filtration rates (based on the updated Modification of Diet in Renal Disease equation) at 55 and 48 mL/min/1.73 m² (respectively). Two months ago, his first-voided urine of the morning contained 295 mg of albumin per gram of creatinine. According to current US national guidelines (from the National Kidney Foundation), he has which Stage of chronic kidney disease?

a. 1.
b. 2.
c. 3a.
d. 3b.
e. 4.
f. 5.
Hypertension due to CKD

Elevated blood pressure due to intrinsic renal disease is most effectively lowered by:

a. Cyclosporine
b. Erythropoeitin
c. Antihypertensive drugs that are appropriately reduced in dose or frequency of administration if the specific drug is renally-excreted.
d. Severe reduction in dietary protein (e.g., < 1 gm/kg/day)
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