Atherosclerosis

• A build up of fats & cholesterol on arterial walls that can lead to Stroke and Heart disease. This is generally considered a problem of modern times, a result of fatty diets and inactive lifestyles.
CT Scans on 137 Mummies

- 25 of 76 Egyptians 38%, Dated: 4000 B.C.
- 13 of 51 Peruvians 29% dated: 200 to 1500 A.D.
- 3 of 5 Aleutian Islanders dated: 19th & early 20th century, and
- 2 of 5 Pueblo people of the American Southwest, dated: 1500 B.C. to 500 A.D.
WHY?

• Diet and Climate varied among these four groups.
  • Egyptians: Diet high in saturated fat.
  • Peruvians: Farmed corn, potatoes, & Beans and kept domestic animals.
  • Pueblans: Grew corn & Hunted rabbits, deer, and sheep
  • Aleutian Islander: Fish, shellfish, seals, seaotters and whale
Over All results:

• Egyptians 38% vs 29% other Mummies had definite or probable evidence of Atherosclerosis.
• All Mummies age 40 and older showed 50% had Atherosclerosis
its part of the aging process!

- Do we have control over the variables of the aging process?
- Hypertension
- Hyperlipidemia
- Diabetes
- Industrial exposures
- Genetics
JNC-8 HYPERTENSION GUIDELINES

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EAST VIRGINIA MEDICAL SCHOOL
Objectives

• History of Hypertension
• Review of Historic Recommendations
• JNC History
• JNC 8 – Current Guidelines
• Resistant Hypertension-Etiologies
Statistics

• HTN affects approximately 50 million individuals in the US and 1 billion people worldwide.

• HTN is the most common primary diagnosis in the USA with 35 million office visits per year.

• Framingham Heart Study—Individuals who are normotensive at 55 years of age have a 90% lifetime risk of developing HTN.

• Relationship between BP and risk of CVD is continuous, consistent, and independent of other risk factors.

• Only 35% of hypertensive patients on treatment are under control.

• For those age 40-70, each increased increment of 20 mmHg in systolic BP or 10 mmHg in diastolic BP doubles the risk of CVD across the entire BP range.
Benefits of Lowering BP

- Anti-HTN Therapy associated with:
  - 35 – 40% mean decrease in stroke
  - 20 – 25% decrease in MI
  - More than 50% decrease in HF

- Patients with Stage 1 HTN/Additional Risk Factors:
  - Achieving a sustained 12 mmHg decrease in systolic BP for 10 years will prevent 1 death for every 11 pts treated

- The majority of Patients will require 2 or more anti-HTN drugs.
Number of Visits to PAs in 2004
(millions)

- Congestive heart failure
- COPD
- Diabetes
- Dyslipidemia
- Hypertension
- Respiratory/ ENT infections

Source: AAPA 2004 Annual Conference Survey

17,575,573 visits
Stephen Hales 1733, First Blood Pressure Measurement.
A Direct Sphygmograph, 1881.
1881
Sphygmomanometer
Average blood pressure: 220/160
HYPERTENSION
FIRST TREATMENTS

- **1900**: Mayo Clinic-Sodium Thyocyanate; First Chemical Treatment of Hypertension
- **1904**: Sodium Reduction.
- **1905**: Korokoff enabled research to grow from anecdotal to objective approaches.
- **1923**: First Sympathectomy Operation.
- **1947**: First Chemical Sympathectomy.
- **1949**: Hydralazine
- **1957**: Chlorothiazide
- **1960’s**: Beta-Blockers
- **1980’s**: Ace Inhibitors and Calcium Channel Blockers
JNC: The Past

• First JNC report published in 1977 by NIH (NHLBI). Since that time, JNC has repeatedly recommended the use of diuretics.

• In JNC 5, ACE-I and beta-blockers were added as first-line therapy.

• In JNC 6, these two classes were removed, and diuretics remained as the sole first-line agent.
JNC: The Present

- What was new in JNC-7?
  - 1. New disease classification of ‘Pre-Hypertension’
  - 2. Start with 2 drug combo therapy for BP ≥ 160/100, i.e. Stage 2.
  - 3. Simpler approach to risk stratification - deletion of Stage 3 HTN
  - 4. Committee’s fine print comment on choosing first line agent: choice can be based on patient’s co-morbid conditions, i.e. ‘compelling indication’
## Applying Classification of Recommendations and Level of Evidence

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class Ila</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit &gt;&gt;&gt; Risk</td>
<td>Benefit &gt;&gt; Risk Additional studies with focused objectives needed</td>
<td>Benefit ≥ Risk Additional studies with broad objectives needed; Additional registry data would be helpful</td>
<td>Risk ≥ Benefit No additional studies needed</td>
</tr>
<tr>
<td>Procedure/Treatment SHOULD be performed/administered</td>
<td>IT IS REASONABLE to perform procedure/administer treatment</td>
<td>Procedure/Treatment MAY BE CONSIDERED</td>
<td>Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL</td>
</tr>
</tbody>
</table>

### Level of Evidence

<table>
<thead>
<tr>
<th>Level A: Multiple populations evaluated; Data derived from multiple randomized clinical trials or meta-analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level B: Limited populations evaluated. Data derived from a single randomized trial or non-randomized studies</td>
</tr>
<tr>
<td>Level C: Very limited populations evaluated: Only consensus opinion of experts, case studies, or standard-of-care.</td>
</tr>
</tbody>
</table>

ACC/AHA 2009 Joint STEMI/PCI Guidelines Focused Update
9 CURRENT JNC-8 RECOMMENDATIONS

In patients aged >60 years, initiate pharmacologic treatment in systolic BP >150mmHg or diastolic BP >90mmHg and treat to a goal systolic BP <150mmHg and goal diastolic BP <90mmHg.

(strong recommendation grade A)
In Patients aged <60 years, initiate pharmacologic treatment at diastolic BP ≥90mmHg and treat to a goal <90mmHg.

(For ages 30–59 years, Strong Recommendation–Grade A; For ages 18–29 years, Expert Opinion–Grade C)
In Patients aged <60 years, initiate pharmacologic treatment at systolic BP ≥140mmHg and treat to a goal <140mmHg.

(Expert Opinion–Grade C)
In Patients Aged $\geq 18$ years with Chronic Kidney Disease, Initiate Pharmacologic Treatment at systolic BP $\geq 140\text{mmHg}$ or diastolic BP $\geq 90\text{mmHg}$ and treat to goal systolic BP $<140\text{mmHg}$ and goal diastolic BP $<90\text{mmHg}$.

(Expert Opinion–Grade C)
In Patients Aged ≥18 years with Diabetes, Initiate Pharmacologic Treatment at systolic BP ≥140mmHg or diastolic BP ≥90mmHg and treat to a goal systolic BP <140mmHg and goal diastolic BP <90mmHg.

(Expert Opinion—Grade C)
In the general nonblack population, including those with Diabetes, Initial Antihypertensive Treatment should include a Thiazide-Type Diuretic, CCB, ACE inhibitor, or ARB. This recommendation is different from the JNC 7 in which the panel recommended Thiazide-Type Diuretics as initial therapy for most patients.

(Moderate Recommendation–Grade B)
In the general black population, including those with Diabetes, Initial Antihypertensive Treatment should include a Thiazide-type Diuretic or CCB.

(For general black population: Moderate Recommendation - Grade B; for black patients with diabetes: Weak Recommendation—Grade C)
In the population aged ≥18 years with Chronic Kidney Disease, initial (or add-on) antihypertensive Treatment should include an ACE inhibitor or ARB to improve kidney outcomes.

(Moderate Recommendation–Grade B)
If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in Recommendation 6. If goal BP cannot be reached with two drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using only the drugs in Recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be used.
<table>
<thead>
<tr>
<th>Anti hypertensive Medication</th>
<th>Initial Daily Dose, mg</th>
<th>Target Dose in RCTs Reviewed, mg</th>
<th>No. of Doses per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>50</td>
<td>150-200</td>
<td>2</td>
</tr>
<tr>
<td>Enalapril</td>
<td>5</td>
<td>20</td>
<td>1-2</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>10</td>
<td>40</td>
<td>1</td>
</tr>
<tr>
<td>Angiotensin receptor blockers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eprosartan</td>
<td>400</td>
<td>600-800</td>
<td>1-2</td>
</tr>
<tr>
<td>Candesartan</td>
<td>4</td>
<td>12-32</td>
<td>1</td>
</tr>
<tr>
<td>Losartan</td>
<td>50</td>
<td>100</td>
<td>1-2</td>
</tr>
<tr>
<td>Valsartan</td>
<td>40-80</td>
<td>160-320</td>
<td>1</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>75</td>
<td>300</td>
<td>1</td>
</tr>
<tr>
<td>(\beta)-Blockers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atenolol</td>
<td>25-50</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>50</td>
<td>100-200</td>
<td>1-2</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2.5</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Diltiazem extended release</td>
<td>120-180</td>
<td>360</td>
<td>1</td>
</tr>
<tr>
<td>Nitrendipine</td>
<td>10</td>
<td>20</td>
<td>1-2</td>
</tr>
<tr>
<td>Thiazide-type diuretics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bendroflumethiazide</td>
<td>5</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>12.5</td>
<td>12.5-25</td>
<td>1</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>12.5-25</td>
<td>25-100(^a)</td>
<td>1-2</td>
</tr>
<tr>
<td>Indapamide</td>
<td>1.25</td>
<td>1.25-2.5</td>
<td>1</td>
</tr>
</tbody>
</table>
Hypertension in the Very Elderly Trial (HYVET)

- Trial showed favorable outcomes for patients 80 and older, with systolic BP greater than 160, but targeted to less than 150.
British Guild lines

• Based on 24 Hour Ambulatory BP Monitoring vs. Clinic Measurement.
• If over 55: Ca++ Blocker- Based on event reduction & Cost.
• Thiazide Diuretics for CHF or the very elderly who are intolerant to Ca++ Blockers.
European Guild lines

- Uncomplicated HTN: Thiazide diuretics.
- Beta Blockers, Ca++ Blockers, ACE & ARB’s if second agent needed or Co-morbidities of: CHF, Diabetes, Renal Failure.
Japanese Guild lines

- Similar as European with flexibility in Octogenarians for Higher systolic numbers
AUSTRALIAN GUILDLINES

• START WITH: THIAZIDES, ACE/ARB, or CALCIUM BLOCKERS FOR MONOTHERAPY, OR COMBINATION THERAPY OF DIURETICS: ACE’S or BETA-BLOCKERS. TITRATE AS NEEDED.  WAIT 3 MONTHS TO ADD SECOND DRUG, TITRATE, THIRD DRUG AT 6 MONTHS.
Causes of Resistant HTN

Improper Measurement
Volume Overload and Pseudotolerance
  Excess Sodium
  Volume retention from Renal Disease
Inadequate Diuretic Therapy

Drug-Induced/Other Causes
Noncompliance
Inadequate Doses
Inappropriate Combos
NSAIDS; COX 2 inhibitors
Cocaine, amphetamines, other illicits
Sympathomimetics (decongestants etc.)
ETOH
OCPs
Steroids
Erythropoietin
Sleep Apnea
Licorice, Bitter Orange
Ephedra, Obesity
ma haung
Steroids
Erythropoietin
Sleep Apnea
### Lifestyle Modifications to Manage HTN

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate SBP Reduction, Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Reduction</td>
<td>Maintain normal body wt (BMI 18.5 – 24.9)</td>
<td>5-20 mmHg/10 kg wt loss</td>
</tr>
<tr>
<td>Adopt DASH eating Plan</td>
<td>Consume a balanced diet with reduced content of saturated and total fat</td>
<td>8 – 14 mm Hg</td>
</tr>
<tr>
<td>Dietary sodium Restriction</td>
<td>Reduce dietary sodium intake to no more than 100 mEq/L (2.4 sodium or 6 sodium chloride)</td>
<td>2 – 8 mmHg</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>Regular aerobic activity such as brisk walking at least 30 min/day most days a week</td>
<td>4 – 9 mm Hg</td>
</tr>
<tr>
<td>EtOH in Moderation</td>
<td>Limit consumption to no more than 2 drinks per day in men and 1 drink per day in women and smaller people</td>
<td>2 – 4 mmHg</td>
</tr>
</tbody>
</table>
The Eyes

- Retinopathy, retinal hemorrhages and impaired vision.
- Vitreous hemorrhage, retinal detachment
- Neuropathy of the nerves leading to extraocular muscle paralysis and dysfunction
Retina Normal and Hypertensive Retinopathy

Normal Retina

Hypertensive Retinopathy

A: Hemorrhages
B: Exudates (Fatty Deposits)
C: Cotton Wool Spots (Micro Strokes)
Stage I - Arteriolar Narrowing
Stage II- AV Nicking
Stage III- Hemorrhages (H), Cotton Wool Spots and Exudats
Stage IV - Stage III+Papilledema
Renal Artery Stenosis
Renal Artery Angioplasty
Renal Artery Post Stent
Coarctation of Aorta
Adrenal Glands with Cushings Syndrome

- The pair of adrenals in the center are normal.
- Those at the top come from a patient with adrenal atrophy (with either Addison’s disease or long-term corticosteroid therapy).
- The adrenals at the bottom represent bilateral cortical hyperplasia. This could be due to a pituitary adenoma secreting ACTH (Cushing’s disease), or Cushing’s syndrome from ectopic ACTH production, or idiopathic adrenal hyperplasia.
Cushing’s Syndrome

• Urine Free Cortisol Measurement X 2 or Late Night Salivary Cortisol X 2. Rx: Excision of Pituitary Microadenoma or Bilateral adrenalectomy with Pituitary Radiation.
Medical Rx: ACE Inhibitor until surgery & Radiation complete.
This pheochromocytoma demonstrates the chromaffin reaction. This neoplasm of the adrenal medulla contains catecholamines (epinephrine and norepinephrine). The section of tumor at the bottom has been placed into a dichromate fixative which turns the tissue brown as the catecholamines are oxidized. Compare to the section of pink to yellow tumor at the top which has not been placed in dichromate fixative.
Pheochromocytoma

- **Sx:** HeadAche secondary to labile High BP, Palpatations, Diaphoresis.
- **Dx:** 24 Hour Urine collection to look for Metanephrines & CT Scan to look for Adrenal tumors.
Noncompliance

- Estimates of noncompliance with medical treatment in general:
  - Noncompliance causes 125,000 deaths a year - twice the mortality rate from MVAs
  - 30% of hospital admissions for people over the age of 65 are directly caused by noncompliance.
  - Half of all prescriptions are taken incorrectly, contributing to prolonged or additional illnesses.
  - Noncompliance increases with the number of meds and doses per day; at 4 times a day, only 40% get it right.
Improving Hypertension Control

- Models suggest that even the most effective therapy will only control HTN if the patient is motivated to take meds and to establish and maintain a healthy lifestyle.
- Motivation improves when patients have positive experiences with their physicians and develop a trusting relationship.

- HTN treatment must be patient centered.
- Drug selection to take into account patient’s age, race and special circumstances.
- Physicians must be willing to try different drugs and aim for monotherapy before adding on a second agent.
Renal Denervation

Energy is transmitted through the artery wall, disabling the renal nerves
Summary

• New guidelines are less conservative - new category of ‘prehypertension’ was not addressed

• Require less aggressive treatment tailored to particular medical condition - encourages starting with 2 drug therapy for BPs over 160/100

• Effective therapy combines lifestyle modifications, exercise, and drug therapy

• Must maintain an open relationship with the patient in order to provide effective therapy