2009 Shattuck Lecture

The Hypertension Paradox: Remarkable Advances in Therapy but Continued Increase in Prevalence of Uncontrolled Hypertension

Disclosures: Dr. Chobanian has no conflicts to disclose

George Cheyne Shattuck, M.D.

From Burrage WL, A History of the Massachusetts Medical Society, 1781-1922.
Objectives

• Discuss treatment advances in hypertension and current approach to management

• Identify factors responsible for rising prevalence and poor control rates of hypertension

• Propose strategies for dealing with the growing problem


Walter Kempner, M.D.

Reginald H. Smithwick, M.D.

“No case of hypertension with normal renal function is accepted as impossible to treat medically until so proved”

Robert W. Wilkins, M.D.

Edward D. Freis, M.D.


Lasker Awards for Clinical Research

Robert W. Wilkins 1958
Edward D. Freis 1971
Advances in Treatment of Hypertension

1940's
Potassium thiocyanate
Kempner diet
Lumbo-dorsal sympathectomy

1950's
Rauwolfia/reserpine
Ganglionic blockers
Veratrum alkaloids
Hydralazine
Guanethidine
Thiazide diuretics

1960's
Methyldopa
Spironolactone
Beta-adrenergic blockers

1970's
Alpha-1 adrenergic receptor antagonists
ACE inhibitors

1980's
Calcium antagonists

1990's
Angiotensin receptor blockers
Endothelin receptor antagonists*

2000's
Renin Inhibitors

Landmark Treatment Trials


• Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension. Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. JAMA 1967;202:1028-1034.

• Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. JAMA 1970;213:1143-1152.
Landmark Treatment Trials (cont’d)


Summary of Clinical Trial Data on Effects of Antihypertensive Drugs on Cardiovascular Disease Incidence

Effect of Treatment vs. Placebo

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke Incidence</td>
<td>↓ 35-40%</td>
</tr>
<tr>
<td>Coronary Disease Events</td>
<td>↓ 20-25%</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>↓ 50-60%</td>
</tr>
</tbody>
</table>
Benefits of Controlling Stage 1 Hypertension

• Sustained reduction of SBP by 12 mm Hg for 10 years estimated to prevent 1 death for every 11 patients treated

• In presence of CHD or other target organ disease, only 9 patients would require such sustained BP reduction to prevent 1 death

from Ogden et al., Hypertension 2000;35:539

Comparative Drug Trials in Hypertension

<table>
<thead>
<tr>
<th>Trial</th>
<th>Drug Comparisons</th>
<th>Primary Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>STOP-2</td>
<td>D/BB vs ACEI/CCB</td>
<td>NSD</td>
</tr>
<tr>
<td>ALLHAT</td>
<td>D vs ACEI vs CCB</td>
<td>NSD</td>
</tr>
<tr>
<td>INVEST</td>
<td>D/BB vs CCB/ACEI</td>
<td>NSD</td>
</tr>
<tr>
<td>ASCOT</td>
<td>D/BB vs CCB/ACEI</td>
<td>NSD</td>
</tr>
<tr>
<td>LIFE</td>
<td>ARB vs BB</td>
<td>ARB superior</td>
</tr>
<tr>
<td>ANBP2</td>
<td>D vs ACEI</td>
<td>ACEI superior in males only</td>
</tr>
<tr>
<td>ACCOMPLISH</td>
<td>ACEI/D vs ACEI/CCB</td>
<td>ACEI/CCB superior</td>
</tr>
</tbody>
</table>
Stage 1 Hypertension
(BP 140-159/90-99 mm Hg)

- Assess adherence
- Add 3rd DRUG OF DIFFERENT CLASS
- Optimize dosages

Diuretic                   BB                     CCB
ADD 2nd DRUG OF DIFFERENT CLASS
ACE I                     ARB

Diuretic                              CCB
ADD 2nd DRUG OF DIFFERENT CLASS
ACE I                     ARB

Control Other CVD Risk Factors

LIFESTYLE MODIFICATION
- Weight Control
- Alcohol Restriction
- Exercise
- DASH Diet
- Salt Reduction

Stage 2 Hypertension
(BP ≥ 160/100 mm Hg)

- Evaluate for SECONDARY HYPERTENSION
- Add 4th DRUG OF DIFFERENT CLASS
- Assess alcoholic excess, and salt retention

Diuretic                   BB                     CCB
TWO-DRUG REGIMEN FOR MOST and healthy lifestyle
ACE inhibitor
ARB

Assess adherence
Add 3rd DRUG OF DIFFERENT CLASS
Optimize dosages

DASH denotes Dietary Approaches to Stop Hypertension; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; BB, beta blocker; CVD, cardiovascular disease; CHD, coronary heart disease
Treatment and Control of High Blood Pressure in Adults Ages 18-74 (140/90 mm Hg)

Adapted from Cutler JA, et al., Hypertension 2008;52:818, and Chobanian et al., JAMA 2003;289:2560.

Relationship of Race/Ethnicity to Hypertension Control -- NHANES

Control (<140/90 mm Hg)

- Whites: 33.4%
- Non-Hispanic Blacks: 28.1%
- Mexican-Americans: 17.7%

Clinical Conditions in Which Blood Pressure Goal of < 130/80 mm Hg Is Recommended

- Chronic kidney disease
- Diabetes
- High coronary heart disease risk*
- Stable angina
- Acute coronary syndromes
- Left ventricular dysfunction (goal < 120/80)

* known coronary carotid or peripheral arterial disease, abdominal aortic aneurysmal or Framingham risk score > 10 percent

Adapted from Chobanian et al., JAMA 2003, 289:2560 and Rosendorff et al., Circulation 2007, 116:2761

Changes in Prevalence and Control Numbers of Hypertensives Between 1988 and 2004

1988-1994 Total

<table>
<thead>
<tr>
<th>Controlled</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 million</td>
<td>37 million</td>
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</table>

1999-2004 Total

<table>
<thead>
<tr>
<th>Controlled</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 million</td>
<td>42 million</td>
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Adapted from Cutler JA, et al., Hypertension 2008;52:818, and Chobanian et al., JAMA 2003,289:2560
Risk Factors for Hypertension

- Genetics/family history
- Black race
- Increasing age
- Prehypertension
- Obesity
- High sodium/low potassium intake
- Excessive alcohol intake
- Low socioeconomic status
- Sleep apnea
- Certain illicit drugs and over-the-counter medications

Adapted from JNC-7 Report

1976-98 Cumulative Incidence of Hypertension in Women and Men Aged 65 Years

Risk of Hypertension %

Women

Men

Years of Follow-up

Blood Pressure Classification

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP mmHg</th>
<th>DBP mmHg</th>
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</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120-139</td>
<td>80-89</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>≥ 160</td>
<td>≥100</td>
</tr>
</tbody>
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Benefits of lower BP on MI and stroke mortality from middle to old age
Prospective Studies Collaboration, 1 million adults, 61 prospective studies

Salt Intake and Hypertension

- Hypertension and age-associated increase in BP uncommon in societies with NaCl intake < 50 mmol/d (< 3 gm NaCl or 1.2 g Na)

- INTERSALT Study: 50 mmol/d lower NaCl intake associated with 4.0/2.5 mm Hg lower BP

Sodium and Potassium Intake in the US

<table>
<thead>
<tr>
<th></th>
<th>Current (mmol/day)</th>
<th>IOM Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>150-170</td>
<td>50-65</td>
</tr>
<tr>
<td>Potassium</td>
<td>55-60</td>
<td>120</td>
</tr>
</tbody>
</table>

From National Academies Press, 2005
“I was at first at a great loss for salt, but custom soon reconciled me to the want of it; and I am confident that the frequent use of salt among us is an effect of luxury, and was first introduced only as a provocative to drink, except where it is necessary for preserving flesh in long voyages. . . and as to myself, when I left this country, it was a great while before I could endure the taste of it in anything that I ate.”

Gulliver’s Travels by Jonathan Swift (1762)

Prevalence in Children and Adolescents of Being Overweight

<table>
<thead>
<tr>
<th></th>
<th>2-5 (%)</th>
<th>6-11 (%)</th>
<th>12-19 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic Whites</td>
<td>11.5</td>
<td>17.7</td>
<td>17.3</td>
</tr>
<tr>
<td>Non-Hispanic Blacks</td>
<td>13.0</td>
<td>22.0</td>
<td>21.8</td>
</tr>
<tr>
<td>Mexican Americans</td>
<td>19.2</td>
<td>22.5</td>
<td>16.3</td>
</tr>
</tbody>
</table>

Adapted from Heart Disease and Stroke Statistics—2007 Update, American Heart Association. Circulation 2007;115:e69-e171
Larger Portion Size Introductions

From Young and Nestle, Am J Public Health 2002;92:246

Advertising Budgets for Selected Foods & Beverages

In $millions

- McDonald’s: 572
- Burger King: 408
- Breakfast cereals: 792
- Candies and gum: 765
- Carbonated soft drinks: 549
- Fruits and vegetables: 105
- Milk: 30

National Strategy to Combat Obesity
Necessary Involvement

- Federal, state and local governments
- Public health departments and organizations
- Community organizations
- Schools
- Families and individuals
- Healthcare system
- Insurers
- Food and beverage industries
- Agribusiness

Ounces of Prevention – The Public Policy Case for Taxes on Sugared Beverages.

Brownell KD, Frieden TM.
NEJM 2009;360:1805-8

“Sugar, rum and tobacco are commodities which are nowhere necessaries of life, which are become objects of almost universal consumption, and which are therefore extremely proper subjects of taxation.”

Adam Smith, The Wealth of Nations, 1776