Not Too High, Not Too Low: Keeping Blood Pressure in Check

or

Back to the Future

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Community Medical School

November 4, 2014
Global Burden of Hypertension

• High blood pressure is a major public health burden
  – Astonishing prevalence; about 1 billion people have hypertension (HTN)
  – More pervasive in the Western world
  – Single largest contributor to death and disability worldwide
  – Dramatically increases the risk of stroke, heart attack, heart failure, and chronic kidney disease
  – Starting at 115/75, cardiovascular mortality doubles for every 20 mmHg increase in systolic pressure, and for every 10 mmHg increase in diastolic pressure
Stroke and IHD Mortality vs Systolic BP by Age

Age at risk:
- 80-89 years
- 70-79 years
- 60-69 years
- 50-59 years
- 40-49 years

Mortality (Floating absolute risk and 95% CI)
- 256
- 128
- 64
- 32
- 16
- 8
- 4
- 2
- 1

Usual Systolic BP (mm Hg)
- 120
- 140
- 160
- 180

Lancet. 2002;360:1903-1913
Hypertension in the United States

• Most commonly diagnosed condition in the U.S.
  – About 74 million Americans have HTN (1 in 3-4 adults)
  – Most common reason for a physician visit in the U.S.
  – 82% aware they have HTN (improved from 66%)
  – 75% receiving treatment for their HTN (improved from 50%)
  – But, only 53% have their HTN controlled
  – Estimated economic burden this year: $73.4 billion
Brief History of High Blood Pressure

First noted in China ~2600 BC via a ‘hard pulse’

Once treated with bleeding and leeches

First well tolerated medication, 1958
Brief History of Blood Pressure

• Blood pressure existed for millions of years before it was measured.
• The first recorded instance of the measurement of blood pressure was performed on a horse in 1733 by the Reverend Stephen Hales. He performed it in an invasive intra-arterial manner, using an upright-held tube.
• Human blood pressure was not recorded until 1847.

Hales used a brass tube to cannulate the carotid artery of a horse.

Now I’m going to show you this once, you’ll do one, and then teach the others...OK?

I knew I should have gone to medical school!
The Sphygmomanometer

- 1881: Samuel Siegfried Karl Ritter von Basch from Vienna designs the first “sphyg” to measure systolic blood pressure
- 1896: Scipione Riva-Rocci and Leonard Hill independently improve on von Basch’s design
- 1905: Nikolai Korotkoff combined the ‘sphyg’ and the stethoscope to discover the “Korotkoff sounds” that denote the systolic and diastolic blood pressures
Blood Pressure vs Age for Insured Individuals in 1925

In a 1912 address before the Glasgow Southern Medical Society, Sir William Osler\textsuperscript{21} made the following statement about high blood pressure associated with atherosclerosis: “In this group of cases it is well to recognize that the extra pressure is a necessity—as purely a mechanical affair as in any great irrigation system with old encrusted mains and weedy channels. Get it out of your heads, if possible, that the high pressure is the primary feature, and particularly the feature to treat.” This misinterpretation discouraged early attempts to develop drugs to lower the blood pressure.

Primary (Essential) Hypertension

• What is Essential Hypertension?
  – The upper end of the continuous distribution of blood pressure (among the population) associated with an increased risk of cardiovascular disease (CVD)
  – Any quantitative definition is arbitrary because the risk of CVD increases steadily with BP
  – Based on a meta-analysis of studies correlating BP with vascular events, the optimal BP has been defined as less than 115/75 (MAP < 88.3 mmHg)
  – If so, than people with resting BPs greater than 115/75 have higher than optimal blood pressure
## Prevalence of high blood pressure

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 to 34</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>35 to 44</td>
<td>25%</td>
<td>19%</td>
</tr>
<tr>
<td>45 to 54</td>
<td>37%</td>
<td>35%</td>
</tr>
<tr>
<td>55 to 64</td>
<td>54%</td>
<td>53%</td>
</tr>
<tr>
<td>65 to 74</td>
<td>64%</td>
<td>69%</td>
</tr>
<tr>
<td>&gt;75</td>
<td>67%</td>
<td>79%</td>
</tr>
</tbody>
</table>

**Factors associated with an increased prevalence of hypertension**

- Higher dietary sodium intake
- Lower dietary potassium intake
- Higher body mass index (BMI)
- Lower socioeconomic status
- Higher habitual alcohol use
- Higher after move from rural to urban, non-industrialized to industrialized
- Higher in African Americans and non-black Hispanics than in whites
Hypertension Prevalence (USA) Rises with Age

Chart 9-1. Prevalence of high blood pressure in adults ≥20 years of age by age and sex (National Health and Nutrition Examination Survey: 2007–2010). Hypertension is defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, if the subject said “yes” to taking antihypertensive medication, or if the subject was told on 2 occasions that he or she had hypertension. Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.
### TABLE 3. Classification of Blood Pressure for Adults

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP mm Hg</th>
<th>DBP mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>and &lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>or 80–89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140–159</td>
<td>or 90–99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥160</td>
<td>or ≥100</td>
</tr>
</tbody>
</table>

Table 3 provides a classification of BP for adults aged 18 and older. The classification is based on the average of 2 or more properly measured, seated BP readings on each of 2 or more office visits.
Trends in the awareness, treatment and control of hypertension in U.S. adults

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness</td>
<td>51</td>
<td>73</td>
<td>68</td>
<td>70</td>
<td>81</td>
</tr>
<tr>
<td>Treatment</td>
<td>31</td>
<td>55</td>
<td>54</td>
<td>59</td>
<td>72</td>
</tr>
<tr>
<td>Control</td>
<td>10</td>
<td>29</td>
<td>27</td>
<td>34</td>
<td>50</td>
</tr>
</tbody>
</table>
What is the AHA recommendation for healthy blood pressure?

This chart reflects blood pressure categories defined by the American Heart Association.

<table>
<thead>
<tr>
<th>Blood Pressure Category</th>
<th>Systolic mm Hg (upper #)</th>
<th>and</th>
<th>Diastolic mm Hg (lower #)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>less than 120</td>
<td></td>
<td>less than 80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120 – 139</td>
<td>or</td>
<td>80 – 89</td>
</tr>
<tr>
<td>High Blood Pressure (Hypertension) Stage 1</td>
<td>140 – 159</td>
<td>or</td>
<td>90 – 99</td>
</tr>
<tr>
<td>High Blood Pressure (Hypertension) Stage 2</td>
<td>160 or higher</td>
<td>or</td>
<td>100 or higher</td>
</tr>
<tr>
<td>Hypertensive Crisis (Emergency care needed)</td>
<td>Higher than 180</td>
<td>or</td>
<td>Higher than 110</td>
</tr>
</tbody>
</table>

http://www.heart.org/HEARTORG/Conditions/HighBloodPressure/AboutHighBloodPressure/Understanding-Blood-Pressure-Readings_UCM_301764_Article.jsp
Main complications of persistent high blood pressure

**Brain:**
- Cerebrovascular accident (strokes)
- Hypertensive encephalopathy:
  - confusion
  - headache
  - convulsion

**Retina of eye:**
- Hypertensive retinopathy

**Heart and Blood Vessels:**
- Myocardial infarction (heart attack)
- Hypertensive cardiomyopathy:
  - heart failure

**Blood:**
- Elevated sugar levels

**Kidneys:**
- Hypertensive nephropathy:
  - chronic renal failure

*From: en.wikipedia.org/wiki/Hypertension*
Benefits of Treating Hypertension: RCT

- Heart failure: ↓50%
- Stroke: ↓40%
- Cardiovascular death: ↓20%

Hebert, Archives Int Med 1993; Moser, Am Coll Cardiol 1996
The DASH Diet

Exercise about 150 minutes per week

From: www.webmd.com/hypertension-high-blood-pressure/ss/slideshow-hypertension-overview
### BLOOD PRESSURE LEVEL (mmHg)

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>SYSTOLIC</th>
<th>DIASTOLIC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NORMAL</strong></td>
<td>less than 120</td>
<td>less than 80</td>
</tr>
<tr>
<td><strong>PREHYPERTENSION</strong></td>
<td>120-139</td>
<td>80-89</td>
</tr>
<tr>
<td><strong>STAGE 1 HYPERTENSION</strong></td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td><strong>STAGE 2 HYPERTENSION</strong></td>
<td>160 or higher</td>
<td>100 or higher</td>
</tr>
</tbody>
</table>

### CONSUME LESS THAN 1 TEASPOON (2,300 MG) OF SODIUM A DAY, INCLUDING SODIUM FOUND IN PACKAGED OR PREPARED FOODS.

*From: www.nhlbi.nih.gov/health/health-topics/topics/hbp/
## Blood pressure treatment goals*

<table>
<thead>
<tr>
<th>Blood Pressure Goal</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 150/90 mm Hg</td>
<td>If you're a healthy adult age 60 or older</td>
</tr>
<tr>
<td>Less than 140/90 mm Hg</td>
<td>If you're a healthy adult younger than age 60</td>
</tr>
<tr>
<td>Less than 140/90 mm Hg</td>
<td>If you have chronic kidney disease, diabetes or coronary artery disease or are at high risk of coronary artery disease</td>
</tr>
</tbody>
</table>

*Although 120/80 mm Hg or lower is the ideal blood pressure goal, doctors are unsure if you need treatment (medications) to reach that level.*
Treatment Goals: According to JNC 8

The Bottom Line

- **Age < 60:** Initiate treatment at **SBP ≥ 140 mmHg** or **DBP ≥ 90 mmHg**
- **Age ≥ 60:** Initiate treatment at **SBP ≥ 150 mmHg** or **DBP ≥ 90 mmHg**
- For adults (≥ 18) with diabetes or CKD: Initiate treatment at **SBP ≥ 140 mmHg** or **DBP ≥ 90 mmHg**
Pathophysiology of Hypertension: Genetic and Environmental Factors
Hypothesis

Blood Pressure is Controlled by the Kidney

The cornerstone of the treatment of hypertension is thiazide diuretics, which ↑Na⁺ excretion by the kidney
**Figure 1.** Target-Organ Damage Due to High Intake of Sodium Chloride.

In addition to increasing arterial pressure, a prolonged high intake of sodium chloride has a direct effect on target-organ damage.

**Figure 2.** Average Daily Sodium Consumption in the United States, 1999–2010.

Data are from the National Health and Nutrition Examination Survey. Current recommendations of the U.S. Department of Health and Human Services for the general population and various subgroups are shown.

“Pass the salt please”

Hypertension “follows” a transplanted kidney

REFERENCES
Lifton et al., Cell 104: 545-556, 2001
Case

- **Hx:** In 1962, a 16 year old girl complained of a headache at school and was found to have severe hypertension.
- **PE:** BP 180/110, HR 72, euvoletic, clear lungs, no edema.
- **Data:** Electrolytes (mM): [Na] 143, [K] 2.8, [Cl] 100, [tCO₂] = 30 (with pCO₂ > 40 mmHg)
- **Other tests:** plasma renin activity (PRA) negligible; aldosterone level negligible
- **Family Hx:** Younger brother has BP 200/110, [K] 2.7 mM, and [tCO₂] = 29 mM
The Original Liddle Kindred

18 members hypertensive before the age of 20
C. Liddle Syndrome

- Negligible Aldosterone Levels
- Blood delivery of Sodium

**Principal Cell**
- ENaC
- Na^+ Delivery
- MR
- Liddle

**ENaC**
- K^+
- Na^+
- ATPase

**ROMK**
- H^+
- HCO_3^-
- ATPase

**AE1**
- Cl^-

**α-IC**
- Lumen
Control of Blood Pressure

BLOOD PRESSURE = CARDIAC OUTPUT X PERIPHERAL RESISTANCE

Hypertension = Increased CO and/or Increased PR

Autoregulation
Nephron Number in Patients with Primary Hypertension

Gunhild Keller, M.D., Gisela Zimmer, M.D., Gerhard Mall, M.D.,
Eberhard Ritz, M.D., and Kerstin Amann, M.D.
Table 2. US/Australian autopsy series: Characteristics of the right kidney, in subjects age ≥18 yr, by birth weight tertiles, adjusted mean (95% CI), n = 87a

<table>
<thead>
<tr>
<th>Birth Weight (kg)</th>
<th>n</th>
<th>No. of Glomerulib</th>
<th>Mean Glomerular Tuft Volume ((\mu m^3 \times 10^6)c)</th>
<th>Total Glomerular Tuft Volume ((cm^3)c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range 1.81 to 3.121</td>
<td>29</td>
<td>770,860</td>
<td>9.2</td>
<td>6.7</td>
</tr>
<tr>
<td>Mean (SD) 2.65 (0.29)</td>
<td></td>
<td>(658,757 to 882,963)</td>
<td>(8.3 to 10.1)</td>
<td>(5.9 to 7.5)</td>
</tr>
<tr>
<td>Range 3.18 to 3.38</td>
<td>28</td>
<td>965,729</td>
<td>7.2</td>
<td>6.8</td>
</tr>
<tr>
<td>Mean (SD) 3.27 (0.07)</td>
<td></td>
<td>(885,714 to 1,075,744)</td>
<td>(6.3 to 8.2)</td>
<td>(6.1 to 7.7)</td>
</tr>
<tr>
<td>Range 3.41 to 4.94</td>
<td>30</td>
<td>1,005,356</td>
<td>6.9</td>
<td>6.6</td>
</tr>
<tr>
<td>Mean (SD) 3.93 (0.35)</td>
<td></td>
<td>(900,094 to 1,110,599)</td>
<td>(6.1 to 7.8)</td>
<td>(5.9 to 7.4)</td>
</tr>
<tr>
<td>Pd</td>
<td>0.0126</td>
<td>0.0022</td>
<td>0.920</td>
<td></td>
</tr>
</tbody>
</table>

a CI indicates confidence interval.
b Adjusted for age, gender, and race.
c Adjusted for age, gender, race, and body surface area.
d Test for the difference of three means.

Table 3. Characteristics of right kidney, by documented presence of hypertension (US participants only)a

<table>
<thead>
<tr>
<th></th>
<th>No. of Glomeruli(b)</th>
<th>Mean Glomerular Tuft Volume ((\mu m^3 \times 10^6)c)</th>
<th>Total Glomerular Tuft Volume ((cm^3)c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No hypertension (n = 30)</td>
<td>1,010,622 (915,997 to 1,105,277)</td>
<td>6.9 (6.0 to 7.9)</td>
<td>7.0 (6.0 to 7.9)</td>
</tr>
<tr>
<td>Hypertension (n = 50)</td>
<td>743,531 (670,759 to 816,304)</td>
<td>9.6 (8.8 to 10.4)</td>
<td>6.8 (6.0 to 7.5)</td>
</tr>
<tr>
<td>Pd</td>
<td>&lt;0.0001</td>
<td>0.00022</td>
<td>0.743</td>
</tr>
</tbody>
</table>

a Blacks = 44, whites = 36, men = 51, women = 29, mean age 44 (9.0) yr.
b Adjusted for age, gender, and race.
c Adjusted for age, gender, race, and body surface area.
d Test for the difference of three means.

High nephron endowment protects against salt-induced hypertension

Kenneth A. Walker,¹,³ Xiaochu Cai,² Georgina Caruana,¹ Merlin C. Thomas,⁴ John F. Bertram,¹ and Michelle M. Kett²

¹Department of Anatomy and Developmental Biology, Monash University, Clayton, Victoria, Australia; ²Department of Physiology, Monash University, Clayton, Victoria, Australia; ³Prince Henry’s Institute of Medical Research, Clayton, Victoria, Australia; and ⁴Baker IDI Heart and Diabetes Institute, Prahran, Victoria, Australia
Pathophysiology of Hypertension: Genetic and Environmental Factors
Question

Why do we measure blood pressure?

A. Because people with hypertension are at risk for cardiovascular disease
B. Because hypertension is a disease
C. Because we can
D. A and C
E. A, B, and C
Hypertension Prevalence (USA) Rises with Age

Why?? (and should we let it?)

Chart 9-1. Prevalence of high blood pressure in adults ≥20 years of age by age and sex (National Health and Nutrition Examination Survey: 2007–2010). Hypertension is defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, if the subject said “yes” to taking antihypertensive medication, or if the subject was told on 2 occasions that he or she had hypertension. Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.
It’s All About FLOW

• We measure Pressure, but “it’s all about FLOW”

• Tissues care most about blood FLOW, not blood pressure
  – Optimum: Increase flow by lowering Total Peripheral Resistance (TPR) rather than increasing BP
  – The idea is to keep FLOW optimized WITHOUT excessive pressure (i.e., without developing hypertension)
  – Children: High flow with low BP because of wide open vessels
  – Adults: Maintaining flow takes higher BP as vessels narrow (atherosclerosis) \( \rightarrow \) LV hypertrophy \( \rightarrow \) CHF
  – Older: Hypertension, vascular disease, CHF (viscous cycle)

• Autoregulation of FLOW
  – What’s the difference between a piece of ziti and an arteriole?
The Primacy of FLOW: Autoregulation

**Figure 19-7** Autoregulation of glomerular filtration rate
The Primacy of FLOW

- FLOW is usually what is useful and regulated, so we pay for FLOW (e.g., transport)
- Everyday examples: electrical current, travel by car, train, plane, or boat
- Disease examples:
  - We all pay to treat constipation
  - Asthmatics pay for good airflow
  - Patients with heart disease pay for re-establishing coronary blood flow or flow through valves
  - Older men pay for medications that increase the flow of urine and blood in the pelvis
How Did It All Begin?
Hypothetical Evolution of the Cardiovascular System

• **Primordial Life**: Single-celled and small organisms that usually live in sea water do not have a circulatory system
  – They meet their metabolic needs by diffusion and convection of solutes to and from their environment
  – And everyone pee’d in the pool

• **Early Life**: Organisms became bigger and required a new system
  – A rudimentary circulatory system developed
  – Body movements caused fluids to circulate

• **Later Life**: A two-chamber pump (the first heart) developed in which the circulations mixed, and eventually a four-chamber heart with no mixing developed
Good Flows without Bad Pressures: Is Hypertension Essential?

Alan Segal, M.D.
University of Vermont
Department of Medicine (Nephrology)
Department of Pharmacology
Department of Molecular Physiology & Biophysics
Hypothetical Protovertebrate

Figure 4. (Center): The Hypothetical Protovertebrate (any resemblance to Amphioxus is purely coincidental). (Top): Three Types of Armored Fishes or Ostracoderms from the Devonian. (Bottom): Three Types of Eurypterids from the Silurian. The eurypterids were co-inhabitants of fresh water with the early armored fishes. (Not drawn to scale.)
Water becomes the predator

- Marine animals develop a waterproof covering
  - The waterproof armor will eventually become fins, legs, and wings
- Waterproof covering not a permanent solution - excretory pores must become internalized
  - The open circulation becomes closed; the heart acts as a water pump
- THE KIDNEY IS BORN!
  - The water must be pumped out
  - The kidney tubule agrees to accommodate the glomerulus
The Pre-Nuptial Agreement

- Allow a high-pressure arterial system to evolve in order to “pump out all the water”
- Kidney agrees to accommodate the cardiovascular system and the glomerulus is born
- The glomerulus was evolved independently of, and long after the evolution of the kidney tubule
- Blood pressure is invented; it’s the beginning of the end but no one knows it
- Trusting the cardiovascular system proves to be an immediate disaster because now the heart is not only pumping out the water, it is pumping out everything (solute, amino acids, glucose)
The Marriage in Mammals Today

- At one end, the heart is working hard to pump a huge amount of water out of the body
- At the other end, the kidney tubules are working hard to defeat the heart by keeping 99% of this fluid from being lost from the warm-blooded body
- Nature frequently pits two forces against each other in order to maintain steady state
- The heart and kidney are literally pitched in constant battle against each other
- Our lives depend on neither one of them ever winning out!
A Brief History of Essential Hypertension

• Sir Thomas Clifford Allbutt (1836-1925)
  – Inventor of the clinical thermometer; introduced the ophthalmoscope, weighing scale, and microscope to the clinical wards
  – First one to formally state that people could develop elevated blood pressure in the absence of cardiovascular or kidney disease
  – In 1896, he described ‘Hyperpiesis’ as “high blood pressure without evident cause”
  – Often credited as coining the term “essential hypertension”
The blood pressure varies greatly in different individuals, and in the same individual under varying conditions. The normal blood pressure is from 120 to 130 mm. of mercury, but in persons over 50 it is very often from 140 to 160 mm. A permanent pressure above the latter figure may be called high, but there are great regional variations. Permanently low blood pressure may be met with in asthenia from any cause, in the various toxæmias of the infectious diseases, and there are persons in apparently good health with chronic hypotension.

High tension is met with in many chronic diseases, in various forms of cardiac and renal disease, in lead poisoning, and, above all, in connection with general arterio-sclerosis. The relation to arterio-sclerosis has been much discussed. Briefly, there are three groups of cases: (1) First, the simple high tension without signs of arterial or renal disease—what Clifford Allbutt calls hyperpyësis. In this well recognized condition, met with in individuals otherwise healthy, the blood pressure is permanently high—above 180—but, so far as can be ascertained, there are no arterial, cardiac, or renal changes. It is difficult, of course, to exclude internal, not
What did Sir William Osler think?

Osler’s The Principles and Practice of Medicine (11th edition), 1916

(d) Syphilis, one of the most important single causes, will be spoken of under morbid anatomy.

(e) Overeating.—I am more and more impressed with the part played by overeating in inducing arterio-sclerosis. There are many cases in which there is no other factor. George Cheyne’s advice, quoted at page 451, was never more needed than by the present generation.

(f) The stress and strain of modern life.—There are men in the fifth decade who have not had syphilis or gout, who have eaten and drunk with discretion, and in whom none of the ordinary factors are present—men in whom the arterio-sclerosis seems to come on as a direct result of a high pressure life.

(g) Overwork of the muscles, which acts by increasing the peripheral resistance and by raising the blood pressure.

(h) Renal disease.—The relation between the arterial and kidney lesions has been much discussed, some regarding the arterial degeneration as secondary, others as primary. There are two groups of cases, one in which the arterio-sclerosis is the first change, and the other in which it is secondary to a primary affection of the kidneys.

Transient hemiplegia, monoplegia, or aphasia may occur in advanced arterio-sclerosis. The attacks are very characteristic, often brief, lasting twenty four hours or less. Recovery may be perfect. Recurrence is the rule, and a patient may have a score or more attacks of aphasia, or in the course of a couple of years there may be half a dozen transient hemiplegic attacks or one or two monoplegias, or paraplegia for a day or two. Much attention has of
ESSENTIAL HYPERTENSION.

By O. L. V. de Wesselow, D.M., F.R.C.P.

(Professor of Medicine, University of London).

I do not propose in the following pages to deal with the symptoms or course of the disease which we call essential hypertension—the condition is so common that we are all familiar with it in that aspect—but rather with the problem of its aetiology.

A raised blood pressure, like a raised body temperature or a raised metabolic rate is in itself merely a symptom. An increase in the bodily temperature was recognized at a very early stage of clinical medicine, and the diseases of which it may be a symptom have been gradually distinguished from each other. The measurement of the blood pressure is a relatively recent development in medical science, and our understanding of its significance is therefore less complete. If

Conclusion.

Our conclusions are thus essentially negative; we are at present completely in the dark as to the cause of this common and disastrous disease. The ground is being slowly cleared; certain suggestive analogies can be recognized: there is no reason for pessimism. We must, however, clearly realize that we do not even know as yet whether we are dealing with a single entity or with a pathological state produced by various underlying causes; and that until this problem has been solved, a rational concept of its aetiology is impossible.

Interesting History of Hypertension

• “The greatest danger to a man with high blood pressure lies in its **discovery**, because then **some fool** is certain to try and reduce it.” - J.H. Hay, 1931.

• “Hypertension may be an important **compensatory mechanism** which **should not be tampered with**, even were it certain that we could control it.” Paul Dudley White, 1937.
A Stroke Due to Severe Hypertension Killed FDR

- FDR’s last words on April 12, 1945: “I have a terrific headache.”
- He lost consciousness and 15 minutes later Dr. Bruenn recorded a blood pressure of >300/190. The President was pronounced dead at 3:35 pm.
- The fact that as late as 1945, hypertension was not considered a disease of major clinical consequence should not come as a surprise because the majority of physicians thought it was “essential” to force blood through sclerotic arteries.
- Indeed, Dr. Paul White’s famous 1931 textbook on heart disease said, “The treatment of hypertension itself is a difficult and almost hopeless task in the present state of our knowledge, and in fact for aught we know..the hypertension may be an important compensatory mechanism which should not be tampered with, even were it certain that we could control it.”

Homer W. Smith on Essential Hypertension (1951)

- “Various disorders of the cardiovascular system lead to an increased diastolic or systolic pressure, or both, but the most frequent and the most mysterious is the condition known as essential hypertension, the etiology of which is unknown.” (page 694)
- “The upper limits of ‘normal’ blood pressure are difficult to define, but as an arbitrary basis these limits are widely taken as 90 mmHg diastolic and 140 mmHg systolic pressure.” (page 694)
- “The psychiatrist has reported from investigation of a few hypertensive individuals that such persons tend to display exaggerated dependent strivings, submissiveness coupled with stubbornness, feelings of weakness and defenselessness, suppression of hostility, fear of injury, and emotional detachment that may lead to acute emotional disorders; that essential hypertension may be a somatic manifestation of a psychoneurotic condition based on excessive and inhibited hostile impulses; that protracted resentment may be a specific leit motif running through the anxiety and insecurity of the emotional pattern.” (page 749)

JNC 1!

All Adults
- Diastolic 120 or higher
  - Prompt evaluation and treatment

All Adults
- 160/95 or higher
  - Confirm blood pressure elevation within one month

Younger than 50
- 140/90 to 160/95
  - Blood pressure check within 2-3 months

Age 50 or older
- 140/90 to 160/95
  - Check within 6 to 9 months

Goal DBP < 90 mmHg
Treatment According to JNC 1

Goal DBP < 90 mmHg
What is Hypertension in the 21st Century?

• JNC 7

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP mm Hg</th>
<th>DBP mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>and &lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>or 80–89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140–159</td>
<td>or 90–99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥160</td>
<td>or ≥100</td>
</tr>
</tbody>
</table>
Treatment Goals: According to JNC 8
The Bottom Line

• **Age < 60**: Initiate treatment at **SBP ≥ 140 mmHg** or **DBP ≥ 90 mmHg**

• **Age ≥ 60**: Initiate treatment at **SBP ≥ 150 mmHg** or **DBP ≥ 90 mmHg**

• For adults (≥ 18) with diabetes or CKD: Initiate treatment at **SBP ≥ 140 mmHg** or **DBP ≥ 90 mmHg**
Comparison of Target BP and Initial Drug Treatment (Multiple Societies)

Table 6. Guideline Comparisons of Goal BP and Initial Drug Therapy for Adults With Hypertension

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Population</th>
<th>Goal BP, mm Hg</th>
<th>Initial Drug Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014 Hypertension guideline</td>
<td>General ≥60 y</td>
<td>&lt;150/90</td>
<td>Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB; black: thiazide-type diuretic or CCB</td>
</tr>
<tr>
<td></td>
<td>General &lt;60 y</td>
<td>&lt;140/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;140/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CKD</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>ESH/ESC 2013&lt;sup&gt;37&lt;/sup&gt;</td>
<td>General nonelderly</td>
<td>&lt;140/90</td>
<td>Diuretic, β-blocker, CCB, ACEI, or ARB</td>
</tr>
<tr>
<td></td>
<td>General elderly &lt;80 y</td>
<td>&lt;150/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;140/85</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD no proteinuria</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD + proteinuria</td>
<td>&lt;130/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>CHEP 2013&lt;sup&gt;38&lt;/sup&gt;</td>
<td>General &lt;80 y</td>
<td>&lt;140/90</td>
<td>Thiazide, β-blocker (age &lt;60 y), ACEI (nonblack), or ARB</td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;130/80</td>
<td>ACEI or ARB with additional CVD risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ACEI, ARB, thiazide, or DHPCCB without additional CVD risk</td>
</tr>
<tr>
<td>ADA 2013&lt;sup&gt;39&lt;/sup&gt;</td>
<td>Diabetes</td>
<td>&lt;140/80</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>KDIGO 2012&lt;sup&gt;40&lt;/sup&gt;</td>
<td>CKD no proteinuria</td>
<td>≤140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD + proteinuria</td>
<td>≤130/80</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>NICE 2011&lt;sup&gt;41&lt;/sup&gt;</td>
<td>General &lt;80 y</td>
<td>&lt;140/90</td>
<td>&lt;55 y: ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td></td>
</tr>
<tr>
<td>ISHIB 2010&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Black, lower risk</td>
<td>&lt;135/85</td>
<td>Diuretic or CCB</td>
</tr>
<tr>
<td></td>
<td>Target organ damage or CVD risk</td>
<td>≤130/80</td>
<td></td>
</tr>
</tbody>
</table>

<sup>Abbreviations: ADA, American Diabetes Association; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CHEP, Canadian Hypertension Education Program; CKD, chronic kidney disease; CVD, cardiovascular disease; DHPCCB, dihydropyridine calcium channel blocker; ESC, European Society of Cardiology; ESH, European Society of Hypertension; ISHIB, International Society for Hypertension in Blacks; JNC, Joint National Committee; KDIGO, Kidney Disease: Improving Global Outcome; NICE, National Institute for Health and Clinical Excellence.\</sup>
# Antihypertensive Dosing Strategies

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Start one drug, titrate to maximum dose, and then add a second drug</td>
<td>If goal BP is not achieved with the initial drug, titrate the dose of the initial drug up to the maximum recommended dose to achieve goal BP. If goal BP is not achieved with the use of one drug despite titration to the maximum recommended dose, add a second drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB) and titrate up to the maximum recommended dose of the second drug to achieve goal BP. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP.</td>
</tr>
<tr>
<td>B</td>
<td>Start one drug and then add a second drug before achieving maximum dose of the initial drug</td>
<td>Start with one drug then add a second drug before achieving the maximum recommended dose of the initial drug, then titrate both drugs up to the maximum recommended doses of both to achieve goal BP. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP.</td>
</tr>
<tr>
<td>C</td>
<td>Begin with 2 drugs at the same time, either as 2 separate pills or as a single pill combination</td>
<td>Initiate therapy with 2 drugs simultaneously, either as 2 separate drugs or as a single pill combination. Some committee members recommend starting therapy with ≥2 drugs when SBP is &gt;160 mm Hg and/or DBP is &gt;100 mm Hg, or if SBP is &gt;20 mm Hg above goal and/or DBP is &gt;10 mm Hg above goal. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose.</td>
</tr>
</tbody>
</table>

Abbreviations: ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; SBP, systolic blood pressure.

*This table is not meant to exclude other agents within the classes of antihypertensive medications that have been recommended but reflects those agents and dosing used in randomized controlled trials that demonstrated improved outcomes.

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# Prevalent and Personal

Two years ago, my blood pressure increased to 165/105. Now, using chlorthalidone and lisinopril, it is under control at 130/75. The same blood pressure I had at my college physical.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 to 34</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>35 to 44</td>
<td>25%</td>
<td>19%</td>
</tr>
<tr>
<td>45 to 54</td>
<td>37%</td>
<td>35%</td>
</tr>
<tr>
<td>55 to 64</td>
<td>54%</td>
<td>53%</td>
</tr>
<tr>
<td>65 to 74</td>
<td>64%</td>
<td>69%</td>
</tr>
<tr>
<td>&gt;75</td>
<td>67%</td>
<td>79%</td>
</tr>
</tbody>
</table>
The 2014 Guidelines are Controversial

The question of high blood pressure today is such a common-place clinical entity among laymen, that patients ask about their blood pressure as they do about the condition of their heart and lungs. It is obvious that as medical men, we should know more about the condition other than that the pressure is too high or too low. I want to present a form of high pressure described by Sir Clifford Allbutt many years ago. He called it hyperpiesia, the name implying the presence of high blood pressure without any apparent cause.

Conclusions

1. Routine blood pressure readings should be done on all patients, in order that help if needed may come at a time when it will do the most good.

2. The wholesale relegation of patients to distasteful and unbalanced diets which seem to do little, only adds further to their mental anxiety.

3. Attention to the business and social life of these patients, may give leads toward helpful suggestions.

4. The use of drugs has its place in selected cases. The nitrites seem the most helpful when indicated.

5. Continued high pressure will, if allowed to go on, affect other vital organs, especially the heart. Care should be exercised to watch and protect these organs as far as is possible.
Hyperpiesis: High Blood-pressure without Evident Cause: Essential Hypertension*

Sir GEORGE PICKERING,† M.D., D.SC., F.R.C.P., F.R.S.

Summary and Conclusions

It seems quite extraordinary that I have to emphasize the basic platitude that arterial pressure is a quantity, and should be treated as such. The current practice of treating it as a quality, good or bad, is responsible for a whole series of artifacts which only confuse. Raised arterial pressure seems to have, in man, a series of consequences that are related quantitatively to the degree of elevation of arterial pressure. Because arterial

September 1968

Sir George Pickering
(1904 – 1980)

Over the past 30 years the following has become abundantly clear [1]:

(1) There is no agreement as to what is the dividing line between so-called normotension and so-called hypertension, although WHO, that great propagator of science by committee, has made a recommendation. The dividing line that an authority chooses is based not on fact but on a whim.

(2) Arterial pressure is not a fixed quantity. It varies enormously through the day. In most persons the lowest pressure is about half the highest recorded during the day [2].

(3) In any population arterial pressure is distributed as a continuous variable, the curves being Gaussian in shape when converted to the logarithmic scale as is usual in the case of quantities [3] like arterial pressure and serum cholesterol.

(4) In the Western world, arterial pressure tends to increase with age, but it increases more in some subjects than in others.

(5) The various complications, like myocardial infarction and stroke, are also quantitatively related to the arterial pressure. In fact when high arterial pressure is looked at through nondistorting spectacles, the disease emerges as a quantitative one.

DINNER SPEECH BY SIR GEORGE PICKERING

TO TREAT OR NOT TO TREAT

To treat, or not to treat: that is the question.
Whether tis nobler in the mind to suffer
The risks and complications of hypertension,
Or to take a potion against these ravages,
And by opposing end them? To awake; to live;
For sure; and by some drugs to say we end
The strokes and heart attacks
That flesh is heir to, tis a consummation
Devoutly to be wished. To awake; to live;
To live? perchance to love. Ay, there’s the rub;
For in that living, and loving, what fate may come
When we take our pills, must give us pause.
There’s the impotence that makes calamity
of a long life;
For who would bear the whips and scorns of
that;
The limp response, the lovers pity,
The pangs of lost esteem, the end of “macho”;
The insensitivity of healers and the spurns

That the patient suffers when he himself
Might his therapy adjust? Who would these
afflictions bear,
This dysfunction and depression,
But that the dread of disability and death,
Whose consequences are so certain
and so hopeless
That we rather take those pills we have
Than fly to others we know not of;
Or none at all.
Thus conscience does make cowards of us all;
And thus the certain risk of hypertension,
Is sicklied o’er with the pale cast
of doubt,

That benefit exceeds the risk and inconvenience,
And trials of great cost and moment
Must be mounted,
Or miss the time for action. —Soft you now!
The great Sir George! Lord, in thy remarks
Be all these thots remembered.

William McFate Smith

14-16: Pickering lecturing
16: Nurse sticks resident
23-24: Intimate with wife
1-8: Sleeping

Figure 2. A direct recording from the brachial artery in a doctor aged 31 who was then my resident. (Bevan, Honour, and Stott.)

The Blood Pressure to Goal Project*

*Dr. Virginia Hood and Sue Lapointe
Is Hypertension a Disease?

• Not really, it is more a risk factor for disease, and may even be a natural process (involving diet, genetics, environment, etc) that develops in the setting of:
  1. Sub-optimal Nitric Oxide (NO) signaling in endothelia
  2. A defect in sodium (Na⁺) handling by the kidney
  3. Now obsolete excessive sympathetic nervous system activity
  4. An over-exhuberant renin-angiotensin-aldosterone system

• That has been exacerbated by:
  1. Previous acceptance of non-optimal pressures thought to be “essential”
  2. Insufficient inhibition of the neuro-humoral systems originally designed for pre-historic hunter-gatherers living on a diet very low in sodium (and very high in potassium)

*What was functional for pre-historic humans may be maladaptive for modern life*
Take Home Messages

• Common Sense Healthy Lifestyle
  – Diet: Balanced, with < 2300 mg sodium daily
    • About 1500-mg sodium daily if age > 50, black, diabetic, or CKD
    • And high in potassium, like the DASH diet
  – Exercise at least 150 minutes per week
    • Proven benefit of avoiding obesity and losing weight

• Blood pressure goal
  – Target blood pressure in consultation with your doctor, using either JNC 7 or JNC 8 guidelines
  – When in doubt, try for 130s/70s, especially for those with diabetes or chronic kidney disease