The Challenge of Isolated Systolic Hypertension

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Risk Factors for HTN

- Genetic predisposition or FH.
- Black Race.
- Increasing age.
- High sodium intake.
- Excessive alcohol intake.
- Low socioeconomic status.
- Sleep apnea.
- Illegal drugs or OTC medications.
The estimated total number of people with HTN in 2000 was 972 million and this is projected to increase to 1.56 billion by 2025 i.e 29% of the worldwide adult population.
Elevated systolic BP is more important than elevated DBP as a risk factor for both CV and renal disease.
## Rates of Awareness, treatment & control of high BP in the US 1976-2004

<table>
<thead>
<tr>
<th>Year</th>
<th>Awareness</th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976-1980</td>
<td>51%</td>
<td>31%</td>
<td>10%</td>
</tr>
<tr>
<td>1988-1991</td>
<td>73%</td>
<td>55%</td>
<td>29%</td>
</tr>
<tr>
<td>1991-1994</td>
<td>68%</td>
<td>54%</td>
<td>27%</td>
</tr>
<tr>
<td>1999-2004</td>
<td>72%</td>
<td>61%</td>
<td>35%</td>
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</tbody>
</table>
**Definition of Isolated Systolic Hypertension:**

- ISH has been generally defined as SBP above 160 mm Hg with a DBP that is below 90 mm Hg.
- However, as used in the JNC VII the SBP level of 140 is the upper limit of normal at all ages.
- The ESH and ESC definition $\geq 140 \& < 90$.
- Is the single most frequent subtype of hypertension and overwhelmingly form of hypertension after the age of 60.
**Isolated Systolic Hypertension:**

- Is seen primarily in older patients.
- Accounts for 65 to 75% of cases of HTN in the elderly.
- Is associated with 2-4 fold increase in the risk of MI, LVH, renal dysfunction, stroke and CV mortality.
Systolic vs Diastolic Blood Pressure as Predictors of Cardiovascular Outcomes

- Systolic blood pressure (SBP) is a stronger predictor of future cardiovascular events than diastolic blood pressure (DBP).

- In addition, pulse pressure (PP = SBP minus DBP) is increasingly seen as an independent predictor of risk for coronary artery disease.


The Effects of Age on Blood Pressure

- Systolic BP rises continuously with age.
- Diastolic BP rises continuously until age 60 years.
- It falls thereafter as a consequence of increased arterial stiffness.
- Pulse pressure increases continuously with age.
Pathophysiology

- **Increase in systolic BP:**
  1) Progressive stiffening of the arterial tree due to increasing collagen and fibrin and decreasing elastic fibers.
  2) The reflective wave from the peripheral arteries return to the central arterial circulation during diastole.
  3) The reduction in arterial compliance with age causes the reflective wave to return centrally more quickly thus augmenting the SBP and lowers diastole.
Pathophysiology

- **Decrease in the diastolic BP:**
  Stiffening of the aorta reduces the elastic reservoir capacity & hence more blood runs from each SV during diastole resulting in a reduced blood volume within the aorta at the onset of diastole.
Pulse Pressure & Age

a) The increase in pulse pressure with age places greater stress on arteries resulting in diseased elastic component of the vessel wall & hence the intima becomes prone to atherosclerosis.

b) The increased pulse pressure with age provides an estimate of the overall cardiovascular risk.

c) No clinical data are available on the benefits of reducing PP.
Characteristics of Hypertension in the Elderly

- Increased arterial stiffness.
- Altered renal function.
- Frequent diabetes and hyperlipidemia.
- Frequent association with CV disease & heart failure.
- Frequent occurrence with other complications & disease states (polypharmacy & non-compliance are common issues).
Hypertension in Older Persons

- More than two-thirds of people over 65 have HTN.
- This population has the lowest rates of BP control.
- Treatment, including those who with isolated systolic HTN, should follow same principles outlined for general care of HTN.
- Lower initial drug doses may be indicated to avoid symptoms; standard doses and multiple drugs will be needed to reach BP targets.
The paradigm has shifted to systolic blood pressure:

1. Since the middle of the 20th century most physicians assessed the risk of HTN based on DBP.
2. In 1971 the Framingham heart study clearly showed that SBP accurately described the risk of all the complications of HTN.
3. It took 22 years until JNC V in 1993 used SBP to define HTN in USA national guidelines.
4. Since then the paradigm has shifted dramatically and in JNC VI (1997) & JNC VII (2003), it has become the primary focus of risk stratification and treatment goals.
The treatment goal of SBP has become increasingly lower over the past few years, thereby creating numerous hypertensive patients who according to previous criteria would not have fulfilled this definition.
Why ISH has become increasingly important over the past few years?

- We are seeing more and more elderly patients, & ISH is the most common form of high BP in this population.
- Systolic BP is the most powerful predictor of CV morbidity and mortality.
Benefits of Lowering Blood Pressure:

In clinical trials anti-hypertensive therapy has been associated with:

a) 20 - 25% reduction in MI.
b) 35 - 40% reduction in stroke incidents.
c) More than 50% reduction in HF.
Elevated BP should be treated at any age if the person is in a reasonable state of health.
In the systolic HTN trial in Europe, the incidence of dementia was approximately 50% lower among treated patients than among controls.
# Hypertension Prevalence and BP Levels in 6 European Countries, Canada and USA

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>European</th>
<th>Canada &amp; USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-44</td>
<td>27%</td>
<td>14%</td>
</tr>
<tr>
<td>65-74</td>
<td>78%</td>
<td>53%</td>
</tr>
</tbody>
</table>

*JAMA May 14, 2003 – Vol 289 No 18*
Hypertension Prevalence in the USA

Distribution of Hypertension Subtype in the Untreated Hypertensive Population in NHANES III by Age

**ISH** (SBP ≥140 mm Hg and DBP <90 mm Hg)

**SDH** (SBP ≥140 mm Hg and DBP ≥90 mm Hg)

**IDH** (SBP <140 mm Hg and DBP ≥90 mm Hg)

**Numbers at top of bars represent the overall percentage distribution of untreated hypertension by age.**

SHEP & Syst-Eur: Results & Conclusions

**SHEP**

36% total stroke reduction in patients receiving anti-hypertensive treatment for isolated systolic hypertension.¹

**Syst-Eur**

42% total stroke reduction in patients receiving nitrendipine for isolated systolic hypertension.²

⇒ Treatment of hypertension significantly reduces the rate of primary stroke.

¹ SHEP Cooperative Research Group. JAMA 1991;265:3255–3264;
The Following are Key Messages From JNC VII:

1. In persons older than 50, SBP of more than 140 is a much more important CVD risk factor than DBP.

2. For persons aged 40 to 70, the risk of CVD begins at 115/75 and doubles with increment of 20/10 up to 185/115.

3. Individuals who are normotensive at 55 years of age have a 90% lifetime risk for developing HTN.
4. Most patients with hypertension will require 2 or more medications to achieve goal BP less than 140/90.

5. If BP is more than 20/10 above goal BP, consideration should be given to initiating therapy with two agents, one of which be a thiazide-type diuretic.

6. The most effective therapy prescribed by the most careful clinician will control HTN only if patients are motivated.

7. The importance of the physician–patient relationship builds trust and improves motivation and medication adherence.
Patients with office hypertension, normal values at home and no evidence of end-organ damage should undergo AMBPM to find out if they are truly hypertensive.
Comparison of AMBPM & HBPM with Clinic BP

- **It has demonstrated four groups of patients:**
  1. Normotensive by both methods.
  2. Hypertensive by both methods.
  3. Hypertensive by clinic & normotensive by ambulatory or home (W.C. hypertension)
  4. Normotensive by clinic and hypertensive by ambulatory & home (masked hypertension).
# Blood Pressure Thresholds (mmHg) for Definition of Hypertension with Different Types of Measurement

<table>
<thead>
<tr>
<th></th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office or Clinic</td>
<td>140</td>
<td>90</td>
</tr>
<tr>
<td>24-hour</td>
<td>125-130</td>
<td>80</td>
</tr>
<tr>
<td>Day</td>
<td>130-135</td>
<td>85</td>
</tr>
<tr>
<td>Night</td>
<td>120</td>
<td>70</td>
</tr>
<tr>
<td>Home</td>
<td>130-135</td>
<td>85</td>
</tr>
</tbody>
</table>
AMBPM

- It is recommended when facilities are available.
- It is a clinical tool for both diagnosis and assessment of treatment efficacy.
Home BP measurement

- Cheaper and easier to perform than AMBP.
- Improves compliance and BP control.
- Helps reduce white coat HTN and determines the presence of masked HTN.
Masked Hypertension

a. Smokers and the elderly.
b. Family history in both parents.
c. In patients sometimes normal and sometimes elevated BP.
d. Unexplained LVH.
e. Diabetics.
A European trial of elderly treated patients found that the increase of cardiovascular events with elevated home BP, but not in the office (MH) was high and similar to that of patients with uncontrolled HP.

*JAMA* 2004: 291: 1341-1349
Updated large scale epidemiologic studies and meta-analysis of clinical trial data emphasized that the main driver of clinical benefit from blood pressure lowering therapy is the magnitude of BP reduction and perhaps the speed at which it is achieved.

*JACC 2005, 45: 813–27*
Going Beyond Hypertension:

- Statins should and will become routine therapy in people with treated HTN, especially those at highest CVD risk, because they potentially complement the primary objective of anti-hypertensive therapy, notably to reduce the risk of CHD and stroke.

- This is undoubtedly the most effective way “to go beyond blood pressure“.

*JACC 2005, 45 : 813 – 27*
Controversy is the Lifeblood of Science

Sir George Pickering

ISH – Why & How to Treat?
Why Should we Treat?

- The benefits of treatment are well established.
- The decrease in the absolute risk is greater in the elderly compared with the young people.
- The relationship between BP and risk of CV events is continuous, consistent and independent of other risk factors.
How to Treat?

1. Elderly patients have different behaviors.
2. Present a number of co-morbid conditions.
3. Use a broad array of drugs-NSAIDS.
4. The elderly often face socioeconomic constraints that should be taken into account in drug selection.
Non-pharmacological therapy like lifestyle change, weight reduction.

There is some evidence that salt restriction is more effective than in younger patients.
The JNC guidelines recommend thiazide-type diuretics as initial drug therapy for most patients with isolated systolic hypertension unless there are specific contraindications for their use.
The joint guidelines of the ESH and the ESC do not give preference to diuretics and recommend any of the five major classes of antihypertensive drugs for first-line therapy.
Recent guidelines from Great Britain argue against the use of both diuretics and beta-blockers for initial therapy and favor ACE inhibitors, angiotensin-receptor blockers, or calcium-channel blockers.
Beta-blockers are usually not useful in the treatment of ISH?

1. Any decrease in HR is prone to increase SV: a higher SV ejected into a stiff aorta will elevate systolic and lower diastolic BP.

2. Bradycardia often causes systolic hypertension or makes it resistant to therapy.

3. HR progressively slows throughout life and bradycardia is common in the elderly.

4. Elderly have low renin level.

(Low dose is often helpful)
B-Blockers

- The use of B-blockers as first-line therapy for elderly patients with HTN has been questioned recently.

- A meta-analysis of intervention trials for hypertension showed a 16% higher incidence of stroke among patients treated with traditional B-blockers (primarily atenolol) than among those treated with other antihypertensive medications.
The following two-drug combinations have been found to be effective & well tolerated in elderly hypertensive patients:

- Diuretics + BB (SHEP).
- Diuretics + ACEI (PROGRESS).
- Diuretics + ARBS (LIFE, SCOPE).
- Diuretics + CCA (VALUE).
- CCA + ACEI (ASCOT-BPLA)
<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Drug Comparison</th>
<th>Primary Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>STOP-2\textsuperscript{27}</td>
<td>Thiazide-type diuretic plus beta-blocker vs. ACE inhibitor plus calcium-channel blocker</td>
<td>No significant difference</td>
</tr>
<tr>
<td>ALLHAT\textsuperscript{28}</td>
<td>Thiazide-type diuretic vs. ACE inhibitor vs. calcium-channel blocker</td>
<td>No significant difference</td>
</tr>
<tr>
<td>INVEST\textsuperscript{29}</td>
<td>Thiazide-type diuretic plus beta-blocker vs. calcium-channel blocker plus ACE inhibitor</td>
<td>No significant difference</td>
</tr>
<tr>
<td>ASCOT\textsuperscript{30}</td>
<td>Thiazide-type diuretic plus beta-blocker vs. calcium-channel blocker plus ACE inhibitor</td>
<td>No significant difference</td>
</tr>
<tr>
<td>LIFE\textsuperscript{31}</td>
<td>Angiotensin-receptor blocker vs. beta-blocker</td>
<td>Angiotensin-receptor blocker superior</td>
</tr>
<tr>
<td>ANBP2\textsuperscript{32}</td>
<td>Thiazide-type diuretic vs. ACE inhibitor</td>
<td>ACE inhibitor superior in men only</td>
</tr>
<tr>
<td>ACCOMPLISH\textsuperscript{33}</td>
<td>ACE inhibitor plus thiazide-type diuretic vs. ACE inhibitor plus calcium-channel blocker</td>
<td>ACE inhibitor plus calcium-channel blocker superior</td>
</tr>
</tbody>
</table>

\* ACCOMPLISH denotes Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension, ALLHAT Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, ANBP2 Second Australian National Blood Pressure Study, ASCOT Anglo-Scandinavian Cardiac Outcomes Trial, INVEST International Verapamil-Trandolapril Study, LIFE Losartan Intervention for Endpoint Reduction in Hypertension, and STOP-2 Swedish Trial in Old Patients with Hypertension 2.
Nevertheless, despite some important differences between antihypertensive medications, the major benefits of therapy are related to the reduction of blood pressure rather than to other specific drug actions.
Sympathetic nervous system has a role in the pathogenesis of HTN.

Percutaneous renal denervation can achieve an improvement in BP control.
Cardiovascular Disease

- CV diseases are the leading cause of death worldwide.
- Two-thirds of the cerebrovascular disease burden & half of the ischemic disease burden are attributable to non-optimal blood pressure.
Hypertension Represents a Significant Burden on Healthcare

- Worldwide, hypertension is responsible for:
  - 62% of strokes\(^1\)
  - 49% of heart attacks\(^1\)

- Hypertension is the third leading risk factor for disease:
  - Causes 7.1 million premature deaths each year\(^1\)
  - 4.5% of global burden of disease\(^1\)

- Hypertension represents a high burden on healthcare expenditure:
  - In 2004, the direct and indirect cost of high blood pressure in the US was $55.5 billion; drug costs accounted for $21 billion\(^2\)
  - In Germany hypertension represents 23% of total cardiovascular disease costs\(^3\)

- **Thus, hypertension management is a public health priority**

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1. WHO, 2004
2. AHA, 2004
Hypertension represents a systemic disorder characterized by structural, hemodynamic, metabolic, hormonal, humoral, and central nervous system disturbances with elevated BP levels as one of its manifestations.

\[ \text{Hypertension} = \text{Systemic Disorder} + \text{Elevated BP levels} \]
- Educate, communicate the importance of the treatment, control and achieving the goal.
- It is not the drug you use, it is the goal you achieve.

  and how fast you achieve it!
CONCLUSION

- The current trend is to prescribe two or more drugs at low doses and quite often one of them being a diuretic.
- We must establish an alliance with and gain the confidence of the patient.
- We must tailor the treatment considering the particulars of each patient.
In Fact time & eventual aging constitute conspiracy against the human body.

The only way not to live long & become hypertensive is to die young !!
Thank you for your attention