Hypertension Update: Latest Treatment Recommendations
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Objectives
• Upon completion of this workshop, the participant will be able to:
  – Describe the clinical consequences of hypertension.
  – Identify antihypertensive medications with compelling indications for use in patients with comorbid conditions, hypertensive urgency and hypertensive emergency.

Objectives (continued)
• Upon completion of this workshop, the participant will be able to:
  – Identify preferred drug combinations for the person with hypertension and comorbidities

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7)
JNC-8 to be released Summer 2011 for public review and comment, Summer 2012 for final publication
National Heart, Lung and Blood Institute
National High Blood Pressure Education Program
www.nih.nhlbi.gov

Goal of HTN Tx = Not Just a Good Number but to Avoid Target Organ Damage

<table>
<thead>
<tr>
<th>BP Level</th>
<th>Patient Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;140/&lt;90</td>
<td>Non-DM adults per JNC-7</td>
</tr>
<tr>
<td>&lt;130/&lt;80</td>
<td>All w/HTN per NKF</td>
</tr>
<tr>
<td>&lt;130/&lt;80</td>
<td>Adults w/DM, chronic renal disease per JNC-7</td>
</tr>
</tbody>
</table>

Value of BP Reductions in Hypertensive Patients
• “Even a 2 mm Hg lower usual systolic blood pressure would involve about 10% lower stroke mortality and about 7% lower mortality from ischemic heart disease or other vascular causes in middle age.”

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group

Published at www.nejm.org March 14, 2010 (10.1056/NEJMoa1001286)

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The ACCORD Study Group: Conclusions

• In patients with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, did not reduce the rate of a composite outcome of fatal and nonfatal major cardiovascular events.

Lifestyle Modification per JNC-7

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Average SBP Reduction Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (body mass index 18.5–24.9 kg/m²)</td>
<td>5–20 mm Hg per 10 kg weight loss</td>
</tr>
<tr>
<td>DASH eating plan</td>
<td>Adopt a diet rich in fruits, vegetables, and low fat dairy products with reduced content of saturated and total fat.</td>
<td>8–14 mm Hg</td>
</tr>
</tbody>
</table>

Source: www.nhlbi.nih.gov/guidelines/hypertension

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Algorithm for Treatment of Hypertension

Not at Goal Blood Pressure (<140/90 mmHg)
(<130/80 mmHg for those with diabetes or chronic kidney disease)

1. Without Comorbid Indications
2. With Comorbid Indications

Stage 1 Hypertension
(SBP 160–179 mmHg or DBP 100–109 mmHg)
Thiazide-type diuretic as first-line treatment, add other antihypertensive drugs as needed.

Stage 2 Hypertension
(SBP 180–199 mmHg or DBP 110–119 mmHg)
Thiazide-type diuretic plus an ACEI, ARB, BB, or CCB as needed.

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BP = HR (heart rate) x SV (stroke volume) x PR (peripheral resistance, also known as peripheral vascular resistance {PVR})

Yield = Myocardial Remodeling, Vessel Hypertrophy, Endothelial Dysfunction

How to avoid HTN TOD?
- Avoid target organ damage in part by blunting catecholamine effect
- Attenuate the action of angiotensin II (Ang II)
  - A potent vasoconstrictor that also stimulates adrenal catecholamine release

Medication Comment

<table>
<thead>
<tr>
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<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta adrenergic antagonists (-lol suffix)</td>
<td>Use with caution with COPD, asthma, heart block. In DM, benefit of beta blocker use outweighs the risk of worsening insulin resistance or masking hypoglycemia symptoms. With discontinuation, taper slowly.</td>
</tr>
<tr>
<td>Examples-Atenolol, metoprolol, propranolol</td>
<td></td>
</tr>
<tr>
<td>•MOA-Block adrenergic B-receptor sites, blunt catecholamine response</td>
<td></td>
</tr>
<tr>
<td>BP = HR↓ x SV↓ x PVR↓</td>
<td></td>
</tr>
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</table>

Meta-analysis Results: Beta Blockers in Uncomplicated HTN
- **Stroke**
  - Significantly higher with beta-blockers than with other antiHTN (relative risk, 1.16; 95% CI, 1.04–1.30)
  - Most problematic w/atenolol than w/other non–beta-blocker antiHTN a (RR, 1.26; 95% CI, 1.15–1.38)
Source


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<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha- beta adrenergic antagonists (-lol suffix) Examples: Carvedilol, labetalol</td>
<td>Use with caution with COPD, asthma, heart block. In DM, benefit of beta blocker use outweighs the risk of worsening insulin resistance or masking hypoglycemia symptoms. With discontinuation, taper slowly.</td>
</tr>
<tr>
<td>MOA: Block adrenergic B1-, B2, alpha-1 receptor sites, blunt catecholamine response</td>
<td></td>
</tr>
<tr>
<td>BP = HR↓ x SV↓ x PVR↓</td>
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**American Association of Clinical Endocrinologists**

Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Hypertension
Endocrine Practice Vol 12 No 2 March/April 2006

**Recommendation for HTN with DM per AACE**

• “In addition to lifestyle modifications, the use of an ACEI or ARB, in conjunction with a low-dose diuretic, a calcium channel blocker, a 3d generation beta blocker (such as carvedilol) or some combination of these agents, currently seems to be the preferred initial therapeutic regimen for patients with diabetes.”

**Recommendation for HTN with DM per AACE** (continued)

• “In a study of patients with type 2 diabetes and hypertension, carvedilol and atenolol had similar BP lowering effects...”

**Recommendation for HTN with DM per AACE** (continued)

• “…and action in decreasing left ventricular hypertrophy, but triglycerides, fasting plasma glucose, A1C and insulin levels decreased with carvedilol use but increased with atenolol therapy.”
**Renin-angiotensin Cascade: What works where?**

- **Angiotensinogen**
- **Non-renin (e.g., tPA)**
- **Angiotensin I**
- **Brad y kinin**
- **Renin**
- **Angiotensin II**
- **AT₁**
- **AT₂**
- **ACE**
- **Inactive peptides**

**Medication Comments**

**Angiotensin converting enzyme inhibitors (ACEI)**
- ACEI examples: Lisinopril, enalapril, all with -pril suffix
- Angiotensin receptor blockers (ARB)
  - ARB examples: Losartan, telmisartan, all with -sartan suffix

**Comments**

- Adjust dose in renal insufficiency. Do not use in presence of bilateral renal artery stenosis.
- Hyperkalemia risk, especially with inadequate fluid intake, when used with aldosterone antagonist.

**Medication**

- **Direct renin inhibitor**
  - Example: Aliskiren (Tekturna)

**Comments**

- Use with caution in renal insufficiency.
- Modest hyperkalemia risk, especially with inadequate fluid intake, when used with other potassium sparing drugs.
- Rare angioedema and cough risk with use.
- Do not use during pregnancy (Category D).

**Medication**

- **Calcium channel blockers (CCB)**
  - Dihydropyridine (DHP) examples: Amlodipine, felodipine, others, all with -ipine suffix
  - Non-DHP CCB examples: Diltiazem, verapamil

**Comment**

- Ankle edema, particularly with DHP.
  - Non-DHP-caution w/BB, >1 degree HB.
- Verapamil and diltiazem shown to reduce CV mortality, proteinuria & diabetic nephropathy progression independent of ACE inhibitor use.
- Use with caution in presence of heart failure, renal or hepatic impairment.

**Medication**

- **Aldosterone antagonist**
  - Examples: Spironolactone, eplerenone

**Comment**

- Hyperkalemia risk, particularly w/ACEI, ARB use or volume depletion including excessive diuresis
- Use with caution in renal impairment.
**Medication Comment**

**Alpha adrenergic antagonist**
- Examples: Terazosin, doxazosin, all with -azosin
- **MOA**: Causes vasodilatation
  \[BP = HR \times SV \times PVR \downarrow\]

**Comment**
- Not as solo or 1st agent = Higher rate of stroke, heart failure (ALLHAT)
- Helpful in prostatism

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**Medication**

**Centrally acting agents**
- Examples: Clonidine, methyldopa
- **MOA**: Works at brain BP control center
  \[BP = HR \times SV \times PVR \downarrow\]

**Comment**
- Sedation risk
- Abrupt withdrawal of clonidine can lead to rebound hypertension

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**Medication**

**Direct vasodilators**
- Examples: Hydralazine, minoxidil
- **MOA**: Peripheral vasodilatation through a direct relaxation of vascular smooth muscle
  \[BP = HR \times SV \times PVR \downarrow\]

**Comment**
- Sedation risk
- Autoimmune (hydralazine only)
- Hirsutism (minoxidil only)

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**JNC-7 Compelling Indications for Individual Drug Classes**

<table>
<thead>
<tr>
<th>Compelling Indications</th>
<th>Diuretics</th>
<th>ACE Inhibitors</th>
<th>Calcium Antagonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Post MI</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>High Coronary Disease Risk</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Diabetes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Chronic Renal Disease</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Recurrent Stroke Prevention</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

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**Algorithm for Treatment of Hypertension**

1. **Lifestyle Modifications**
2. **Not at Goal Blood Pressure**
   - (≥140/90 mmHg)
   - Consider weight loss, sodium restriction, increased physical activity.

**Without Compelling Indications**

**With Compelling Indications**

**Stage 1 Hypertension**
- SBP 140–159 or DBP 90–99 mmHg
- Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.

**Stage 2 Hypertension**
- SBP > 160 or DBP > 100 mmHg
- 2-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB)

**Not at Goal Blood Pressure**

**Optimal treatment**

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**You see, Sam, a 68 yo man...**

- ...Who is in for a sick visit with a CC of a skin rash but who states he otherwise feels well.
- He has a hx of HTN but has not taken medications for the past 6 months.
- **BP**: 220/112
- Cardiac: +5/4, no murmur
- Abd: No bruise
You see Tim, a 68 yo man...

- Who is in for a sick visit with a CC of a skin rash.
- He has a hx of HTN but has not taken medications for the past 6 months.
- When question furthered, he admits to a 4-day history of increasing shortness of breath, headache and blurred vision
- BP= 220/112

Tim’s Funduscopic Exam

What is the difference?

- Tim
  - HTN urgency?
  - HTN emergency?
- Sam
  - HTN urgency?
  - HTN emergency?

Hypertensive Crises: Emergencies per JNC-7

- Hypertensive emergency defined
  - Severe elevations in BP (>180/120 mmHg) complicated by evidence of impending or progressive target organ dysfunction (TOD)
Hypertensive Crises: Emergencies per JNC-7 (continued)

• Goal of treating HTN emergency
  – Immediate BP reduction (not necessarily to normal) to prevent or limit target organ

• Goal of treating HTN emergency (cont.)
  – Examples of TOD= Hypertensive encephalopathy, intracerebral hemorrhage, acute MI, acute left ventricular failure with pulmonary edema, unstable angina pectoris, dissecting aortic aneurysm or eclampsia

• Goal of therapy in hypertensive emergencies
  – Reduce mean arterial BP by no more than 25 percent (within minutes to 1 hour), then if stable, to 160/100–110 mm Hg within the next 2–6 hours

• Risk of excessive falls in pressure
  – Can precipitate renal, cerebral or coronary ischemia

“Unfortunately, the term “urgency” has led to overly aggressive management of many patients with severe, uncomplicated hypertension. Aggressive dosing with intravenous drugs or even oral agents, to rapidly lower BP is not without risk.”

“Oral loading doses of antihypertensive agents can lead to cumulative effects causing hypotension, sometimes following discharge from the ER.”
Patients with hypertensive urgencies may benefit from treatment with an oral, short-acting agent such as captopril, labetalol, or clonidine followed by several hours of observation. However, there is no evidence to suggest that failure to aggressively lower BP in the ER is associated with any increased short-term risk to the patient who presents with severe hypertension.

**HTN Urgency per JNC-7 (continued)**

- Captopril 12.5 to 25 mg
  - Onset of action
    - PO route: 15-30 min
    - SL route: 10-20 min
  - Duration of action
    - PO route: 6-8 h
    - SL route: 2-6 h
  - Repeat up to 50 mg or as needed

**Medication Doses for use in HTN Urgency**

- Labetalol 200-400 mg PO
  - Onset of action
    - 1-2 h
  - Duration of action
    - 2-12 h
  - Repeat every 2-3 h

**Medication Doses for use in HTN Urgency (continued)**

- Clonidine 0.1-0.2 mg PO
  - Onset of action
    - 30-60 min
  - Duration of action
    - 8-16 h
  - Repeat with 0.05 to 0.1 mg every 1 to 2 hours to a maximum dose of 0.6 to 0.7 mg

**What about additional or follow-up medications?**

- Furosemide 20-40 mg
  - Brisk BP reduction with rapid onset of action
- CCB
  - Nifedipine SR 30 mg x 1 or felodipine 5 mg x 1
  - Relatively rapid onset of action with 24 h duration of activity

End of Presentation!
Thank you for your time and attention.
Margaret A. Fitzgerald, DNP, FNP-BC, NP-C, FAANP, CSP
www.fhea.com E-mail: cs@fhea.com
Algorithm for Treatment of Hypertension

Lifestyle Modifications

Not at Goal Blood Pressure (<140/90 mmHg) (<130/80 mmHg for those with diabetes or chronic kidney disease)

Initial Drug Choices

Without Compelling Indications

Stage 1 Hypertension (SBP 140–159 or DBP 90–99 mmHg)
Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.

Stage 2 Hypertension (SBP ≥160 or DBP ≥100 mmHg)
2-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB)

With Compelling Indications

Drug(s) for the compelling indications
Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.

Not at Goal Blood Pressure

Optimize dosages or add additional drugs until goal blood pressure is achieved. Consider consultation with hypertension specialist.

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