Common Problems and Errors In Treating Hypertensive Urgencies and Emergencies

Colman Ryan, MD FACC
ASH Clinical Specialist in Hypertension
New Recommendations for Hypertension – JNC 8 - 2013
1. Start treatment in patients over age 60 at 150 mm Hg. or above
2. Aim for 140/90 as the upper limits in all patients (except for patients over 80 yrs. old in whom the aim is 150/90)
3. There is no evidence that lower is better in patients controlled to less than 140/90.
4. In those patients in whom the blood pressure is in the lower range of normal and are asymptomatic there is no indication to change medication or allow the pressure to drift up to higher levels.
5. Diastolic pressures in patients over 60 yrs. old may be harmful when consistently less than 60mm Hg.

Home BP monitors (OMRON etc.) consistently need lower diastolic pressures in older individuals than either intra-arterial or audible Korotkoff sounds (C. Ryan)
## Prevalence of Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Blood Pressure</td>
<td>40.6%</td>
</tr>
<tr>
<td>Smoking</td>
<td>13.7%</td>
</tr>
<tr>
<td>Poor Diet</td>
<td>13.2%</td>
</tr>
<tr>
<td>Insufficient Activity</td>
<td>11.9%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8.8%</td>
</tr>
<tr>
<td>Abnormal Cholesterol</td>
<td>13.8% ( &gt; 240 mg / DL )</td>
</tr>
<tr>
<td>Obesity (BMI &gt; 30%)</td>
<td>35%</td>
</tr>
<tr>
<td>Obesity in ages 6-11</td>
<td>18.8%</td>
</tr>
</tbody>
</table>
Death Rates - USA

• 2000 – 2010

- Death rates from CVD declined 31%
- 2150 pts. die each day!
- CAD caused 1/6th of deaths
- Stroke deaths declined 22.8%
- No decline in death from CHF
Cardiovascular Procedures + Costs

• 2000 - 5.9 million procedures done
• 2010 - 7.6 million procedures done

– Cost for CVD Care in 2010
  • $315 Billion.

– Cost for Cancer Care in 2010
  • $201 Billion.
<table>
<thead>
<tr>
<th>1977</th>
<th>2013</th>
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</thead>
<tbody>
<tr>
<td>1. Long hair</td>
<td>Longing for hair</td>
</tr>
<tr>
<td>2. KEG</td>
<td>EKG</td>
</tr>
<tr>
<td>3. Acid rock</td>
<td>Acid reflux</td>
</tr>
<tr>
<td>4. Seeds and stems</td>
<td>Roughage</td>
</tr>
<tr>
<td>Year</td>
<td>1977</td>
</tr>
<tr>
<td>------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>5.</td>
<td>Hoping for a BMW</td>
</tr>
<tr>
<td>6.</td>
<td>Going to a new, hip joint</td>
</tr>
<tr>
<td>7.</td>
<td>Rolling Stones</td>
</tr>
<tr>
<td>8.</td>
<td>Disco</td>
</tr>
</tbody>
</table>
9. Passing the drivers’ test

10. Whatever

Passing the vision test

Depends
Global Health Risks

- High blood pressure
- Tobacco use
- High blood glucose
- Physical inactivity
- Overweight and obesity
- High cholesterol
- Unsafe sex
- Alcohol use
- Childhood underweight
- Indoor smoke from solid fuels

Deaths attributed to 10 leading risk factors, by country income level, 2004

Incidence of Systolic Hypertension Increases With Age

Prevalence of Uncontrolled Hypertension in Treated Individuals by Subtype, %

Age, y

<40 40-49 50-59 60-69 70-79 ≥80

*SBP ≥140 mm Hg and DBP <90 mm Hg.
†SBP ≥140 mm Hg and DBP ≥90 mm Hg.
‡SBP <140 mm Hg and DBP ≥90 mm Hg.

ISH, isolated systolic hypertension; SDH, systolic/diastolic hypertension; IDH, isolated diastolic hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure.


Coronary heart disease death rate (%) per 10,000 person-years

SBP, systolic blood pressure; DBP, diastolic blood pressure.
BP and Cardiovascular Mortality

Risk Doubles With Every 20/10-mm Hg Increment*

*Individuals aged 40-69 years, starting at blood pressure 115/75 mm Hg.
BP = blood pressure; SBP = systolic BP; DBP = diastolic BP.
According to JNC 7, Lowering BP Is Important in Reducing CV Risk

In Clinical Trials, Antihypertensive Therapy Has Been Associated With Reductions in

- Myocardial Infarction (20%-25%)
- Stroke (35%-40%)
- Heart Failure (>50%)

- Each 20–mm Hg increase in SBP or 10–mm Hg increase in DBP doubles the risk of CVD

RAAS: An Important Pathway in Hypertension

RAAS=Renin-angiotensin-aldosterone system; ACE=Angiotensin-converting enzyme.
Intersection of the SNS and RAAS Pathways

SNS activation

Renin-angiotensin system

Norepinephrine

β₁

β₂

α₁

Hypertension

Adrenergic receptors

Selective β₁-blockade

Nonselective β-blockade

Nonselective β-blockade with α₁-blockade

ACE inhibitor

ARB

ACE=Angiotensin-converting enzyme; ARB=Angiotensin-receptor blocker.
Adapted from Packer M. Prog Cardiovasc Dis. 1998;41:39-52.
Use of $\beta_1$-Selective Atenolol and Adverse Outcomes in Patients With Hypertension

All-cause mortality

Cardiovascular mortality

Myocardial infarct

Stroke

Relative risk, 95% CI

0.5
1.0
1.5

Atenolol better
Placebo/Other antihypertensive better

Atenolol vs placebo or no treatment
4 studies included (n=6825)

Atenolol vs other antihypertensive therapy
5 studies included (n=17,671)

Primary outcomes studies in hypertension have not been conducted with COREG CR.

Trials included in meta-analysis vs placebo: Treatment of Hypertension in Elderly Patients in Primary Care (HEP); Dutch Transitory Ischemic Attack Trial; Tenormin After Stroke and TIA (TEST); Medical Research Council Trial of Treatment of Hypertension in Older Adults (MRC Old). Trials included in meta-analysis vs other antihypertensive agent: MRC Old; UKPDS; European Lacidipine Study of Atherosclerosis (ELSA); Heart Attack Primary Prevention in Hypertension Trial (HAPPHY); Losartan Intervention for Endpoint Reduction Study (LIFE).

Renal Sympathetic Activation in Hypertension

- Smooth muscle migration
- Vasoconstriction
- Atherosclerosis

Renal afferent nerves

- Renal ischemia
- Stroke volume↓
- Adenosine↑

Renal efferent nerves

- Renin release
- RAAS
- Systemic sympathetic gain
- Sodium retention
- Hypervolemia
- Wall stiffness
- Decreased renal blood flow
- Proteinuria
- BNP resistance

Hypertrophy
Arrhythmias
Ischemia
Heart failure

BNP = brain natriuretic peptide; RAAS = renin-angiotensin-aldosterone system


theheart.org  Medscape Education
Placement of Renal RF Catheter
### Symplicity HTN-2: Background Medications

<table>
<thead>
<tr>
<th></th>
<th>Renal denervation group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 52)</td>
<td>(n = 54)</td>
</tr>
<tr>
<td>Number of antihypertensive medications, mean (SD)</td>
<td>5.2 (1.5)</td>
<td>5.3 (1.8)</td>
</tr>
<tr>
<td>Patients on medication for hypertension for more than 5 years</td>
<td>37 (71%)</td>
<td>42 (78%)</td>
</tr>
<tr>
<td>Patients on 5 or more medications</td>
<td>35 (67%)</td>
<td>31 (57%)</td>
</tr>
<tr>
<td>Patients receiving (drug class)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker</td>
<td>50 (96%)</td>
<td>51 (94%)</td>
</tr>
<tr>
<td>Direct renin inhibitor</td>
<td>8 (15%)</td>
<td>10 (19%)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>43 (83%)</td>
<td>37 (69%)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>41 (79%)</td>
<td>45 (83%)</td>
</tr>
<tr>
<td>Diuretic</td>
<td>46 (89%)</td>
<td>49 (91%)</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>9 (17%)</td>
<td>9 (17%)</td>
</tr>
<tr>
<td>Vasodilator</td>
<td>8 (15%)</td>
<td>9 (17%)</td>
</tr>
<tr>
<td>Alpha-1 blocker</td>
<td>17 (33%)</td>
<td>10 (19%)</td>
</tr>
<tr>
<td>Centrally acting sympatholytic</td>
<td>27 (52%)</td>
<td>28 (52%)</td>
</tr>
</tbody>
</table>

Symplicity HTN-2: Change in 6-Month Blood Pressure Measured in Office

\[ \Delta \text{From Baseline to 6 Months (mm Hg)} \]

- RDN (n = 49)
  - Systolic: -32
  - Diastolic: -12

- Control (n = 51)
  - Systolic: 1
  - Diastolic: 0

\( P < .0001 \)

RDN = renal denervation

Symplicity HTN-1

Inclusion Criteria
- Office SBP $\geq 160$ mm Hg
- $\geq 3$ antihypertensive medications (1 of them a diuretic)

Exclusion Criteria
- Significant renal artery abnormalities or prior renal artery intervention
- $\text{eGFR} < 45$ mL/min/1.73m$^2$ (MDRD formula)
- Type 1 diabetes mellitus
- Stenotic valvular heart disease, for which reduction of blood pressure would be hazardous
- Secondary cause of hypertension other than sleep apnea or chronic kidney disease
Symplicity HTN-1: 36-Month Follow-up
Sustained Reductions in Blood Pressure

$P < .001$ for systolic and diastolic BP changes from baseline

Krum H, et al.\[^{10}\]
Slide courtesy of Dr Murray Esler
Symplicity HTN-2

Inclusion Criteria
• Office SBP ≥ 160 mm Hg (≥ 150 mm Hg with type 2 diabetes mellitus)
• ≥ 3 antihypertensive medications (1 of them a diuretic)

Exclusion Criteria
• Significant renal artery abnormalities or prior renal artery intervention
• eGFR < 45 mL/min/1.73 m² (MDRD formula)
• Type 1 diabetes mellitus
• Stenotic valvular heart disease, for which reduction of blood pressure would be hazardous
• MI, stroke, or unstable angina in the prior 6 months
Symplicity HTN-2: 12-Month Follow-up
Change in Office Blood Pressure (mm Hg)

*P < .001 for systolic diastolic BP changes from baseline

Esler MD, et al.\textsuperscript{[12]}
Slide courtesy of Dr Murray Esler
Different Approaches That Target the Sympathetic Nervous System in RH

Catheter-based radiofrequency renal nerve ablation (approved for use in Europe, Australia, and other countries; phase 3 trial ongoing in the USA)

Other methodology for renal denervation (under investigation):
- Focused ultrasound
- Heat therapy

Carotid baroreceptor stimulation (under investigation)
Different Approaches That Target the Sympathetic Nervous System in RH

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Carotid baroreceptor stimulation (under investigation)
**SYMPLECTITY-3: Study Design**

- **Initial Screening**
  - Office systolic blood pressure ≥ 160 mm Hg
  - Full doses of ≥ 3 meds
  - No HTN med changes in past 2 weeks
  - No plan to change meds for 6 months

- **Confirmatory Screening**
  - Home blood pressure & med confirmation
  - Office systolic blood pressure ≥ 160 mm Hg
  - 24-hr ABPM systolic blood pressure ≥ 135 mm Hg
  - Documented compliance on meds

- **Renal Angiogram**
  - If eligible anatomy, randomize “on the table”

- **Treatment**
  - 1M
  - 3M

- **Control**
  - 1M
  - 3M
  - 6M

- **Primary End Point**
  - Home blood pressure & med confirmation

- **2 Weeks**
  - 2 weeks
  - Home blood pressure & med confirmation
  - 6M

- **12-36M**

- **Patient and research staff assessing blood pressure and performing follow-ups are blinded to treatment status**

- **No changes in medications for 6 months**

Problems with response to severe hypertension.

- Jumping too fast: responding to single or multiple blood pressures under circumstances of pain, distress, or anxiety – “Emergency room pseudohypertension”

- Reacting too slowly: persistent severe elevations of hypertension being ignored.

- Inappropriate responses... Oral medications, Nitropaste, and failure to move to an intensive care setting.
Choice of Medication

• Oral Nifedipine or Clonidine alone are inappropriate. Sublingual Nitroglycerine and Nifedipine are dangerous.

• Hydralazine (IV or IM) is also dangerous as it may not work at all or work too well. Hydralazine is also associated with tachycardia which is dangerous for most patients.
Choice of Medication (cont…)

• IV Nitroglycerine is **not** the drug of choice at anytime except when hypertension accompanies pulmonary edema or acute coronary syndromes in conjunction with a beta blocker. This is a venodilator with poor arteriolar dilatation.

• Diuretics e.g. IV Furosemide are not useful for hypertensive emergencies or urgencies.

• Relief of pain alone may allow blood pressure to no longer be urgent.
BACKGROUND: Adults who have diabetes mellitus and hypertension are at increased risk for cardiovascular disease. Evidenced-based guidelines from the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) recommends blood pressure goals of less than 130/80 mmHg in people with diabetes. PURPOSE: To assess cardiovascular risk reduction in high risk adults with type 2 diabetes when systolic blood pressure is maintained below 120mmHg. METHODS: 4,733 patients with T2DM, high BP, and either pre-existing CVD or a high risk for developing it from 77 US and Canadian based medical centers were randomly assigned to a target systolic BP of either <120 mmHg or <140 mmHg. Various combinations of blood-pressure-lowering medications were used to achieve goals.

Primary Endpoint: Combined rate for a major CVD event, specifically nonfatal MI, nonfatal stroke, or CV death.
Secondary Endpoints: Total mortality, cardiovascular deaths, nonfatal MI, nonfatal stroke and total stroke.

Results: Systolic BP averaged 119 mm Hg in the intensive-therapy group, 134 mm Hg in the standard-therapy group. Primary Endpoint: No significant difference between the groups in the combined rate of NF heart attack, NF stroke, or CV death (p=.20) after 4.7 y avg. follow up. Stroke risk was significantly lower with intensive therapy (36 vs. 62 strokes; p=.01).
Conclusion: This study does not support the reduction of CV risk by achieving systolic BP goals < 120mmHg in high risk type II diabetic patients.
Management of Hypertensive Emergencies
Vascular Dysfunction: Sequelae of Acute Hypertension
Acute and chronic hypertension: Clinical context

Chronic hypertension

Acute vascular reactivity

Hypertensive emergencies

Courtesy of S Aronson, MD.
Components of blood pressure: New focus on pulse pressure

**PRESSURE**

- HR x SV = CO
- BP*/ CO = SVR
- CO x MAP = work
- MAP = 1/3 PP + DBP

All in the absence of pulsations

**FLOW**

Courtesy of S Aronson, MD.
Acute hypertension: Subgroups and settings

- Hypertensive urgency
  - Emergency department

- Hypertensive emergency
  - Intensive care unit

- Perioperative hypertension
  - Operating room
    - Postanesthesia care
## JNC 7 definitions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive emergency</td>
<td>BP &gt;180/120 mm Hg complicated by evidence of impending or progressive end-organ damage</td>
</tr>
<tr>
<td>Hypertensive urgency</td>
<td>Severe elevation in BP without progressive end-organ damage</td>
</tr>
</tbody>
</table>

Hypertensive urgencies/emergencies: Patients and organ systems at risk

1% of hypertensives (1990 data). Contemporary prevalence may be lower

Cardiopulmonary
- ADHF
- ACS
- Acute pulmonary edema
- Acute aortic syndromes

Ocular
- Papilloedema

Renal
- Acute renal dysfunction

Neurovascular
- Hypertensive encephalopathy
- Stroke

ACS = acute coronary syndrome
ADHF = acute decompensated heart failure

### Hypertensive urgencies/emergencies: Prevalence of organ system complications

N = 449 presenting to Emergency Department with hypertensive urgency/emergency

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Condition</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CNS</strong></td>
<td>Cerebral infarction</td>
<td>24.5</td>
</tr>
<tr>
<td></td>
<td>Hypertensive encephalopathy</td>
<td>16.3</td>
</tr>
<tr>
<td></td>
<td>Intracerebral/subarachnoid hemorrhage</td>
<td>4.5</td>
</tr>
<tr>
<td><strong>CV</strong></td>
<td>Pulmonary edema</td>
<td>22.5</td>
</tr>
<tr>
<td></td>
<td>Acute congestive heart failure</td>
<td>14.3</td>
</tr>
<tr>
<td></td>
<td>ACS</td>
<td>12.0</td>
</tr>
<tr>
<td></td>
<td>Eclampsia</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>Aortic dissection</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Hypertensive urgencies/emergencies: Most common presenting symptoms

**Urgencies**
- Headache (22%)
- Epistaxis (17%)
- Faintness and psychomotor agitation (10%)

**Emergencies**
- Chest pain (27%)
- Dyspnea (22%)
- Neurological deficit (21%)

Effects of Acute BP Elevation on the Vessel Wall
Proposed vascular pathophysiology of hypertensive urgency

Acute ↑ BP triggers ↑ cellular adhesion molecular expression

Courtesy of JJ Ferguson III, MD.
Proposed vascular pathophysiology of hypertensive emergency

- Overwhelmed control of vascular tone leads to coagulation cascade activation
- Loss of endothelial activity coupled with coagulation and platelets promotes DIC


Courtesy of JJ Ferguson III, MD.
Endothelial shear stress

Proportional to the product of blood viscosity ($\mu$) and spatial gradient of blood velocity at the wall ($dv/dy$).

ESS = endothelial shear stress

Implications of low and high shear stress

Effects of **low** shear stress

- Atherosclerosis
- Plaque rupture

Effects of **high** shear stress

- Endothelial dysfunction
- Vascular injury
- Thrombosis
- Neurohumoral activation

Summary: The pathophysiology of acute hypertensive syndromes

Mechanical stress on the vessel wall

- ↑BP
- Release of humoral vasoconstrictors

Further release of humoral vasoconstrictors

- Fibrinoid necrosis of small blood vessels
- Activation of the clotting cascade

Endothelial damage

- Pressure natriuresis
- Volume depletion
- RAAS activation
- Vasopressin
- Endothelin
- Catecholamines

Major physiologic derangements

Courtesy of JJ Ferguson III, MD.
Profile of an ideal parenteral antihypertensive

- Treats underlying pathophysiology
- Rapid onset of action
- Predictable dose response
- Minimal dosage adjustments
- Highly selective
- No increase in intracranial pressure
- Rapidly reversible
- Low risk of overshoot hypotension or adverse reaction
- Easy conversion to oral agents
- Acceptable cost-benefit ratio

## JNC 7: Parenteral antihypertensive treatment

### Currently available

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Onset / Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium nitroprusside</td>
<td>Vasodilator</td>
<td>Faster</td>
</tr>
<tr>
<td>Esmolol</td>
<td>β-blocker</td>
<td></td>
</tr>
<tr>
<td>Phentolamine</td>
<td>α-blocker</td>
<td></td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>Vasodilator</td>
<td></td>
</tr>
<tr>
<td>Fenoldopam</td>
<td>D1 agonist</td>
<td></td>
</tr>
<tr>
<td>Labetalol</td>
<td>α/β-blocker</td>
<td></td>
</tr>
<tr>
<td>Nicardipine</td>
<td>CCB</td>
<td></td>
</tr>
<tr>
<td>Hydralazine</td>
<td>Vasodilator</td>
<td></td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>ACEI</td>
<td>Slower</td>
</tr>
</tbody>
</table>

D1 = dopamine receptor

Sodium nitroprusside: Profile

• Arterial and venodilator
  – ↓Preload and afterload

• Onset: Immediate

• Duration of action: 1-2 min

• Adverse effects
  – Nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication, coronary steal, maldistribution of blood flow

• Light sensitive: requires special delivery system

Esmolol: Profile

- Blocks $\beta_1$ receptors of heart and vasculature
  - ↓Heart rate, cardiac output, and stroke volume

- Onset: 1-2 min

- Duration of action: 10-30 minutes

- Adverse effects:
  - Hypotension, nausea, asthma, 1st degree heart block, HF

Aggarwal M, Khan IA. *Cardiol Clin*. 2006;24:135-146.
Fenoldopam: Profile

- Selective dopamine-1 receptor agonist
  - ↓ Peripheral vascular resistance
  - ↑ Renal blood flow, natriuresis, and diuresis
- Onset: <5 min
- Duration of action: 30 min
- Adverse effects:
  - Tachycardia, headache, nausea, flushing

Labetalol: Profile

• α₁- and β₁-receptor blocker
  – ↓Peripheral vascular resistance (α₁ blockade)
  – No reflex tachycardia (β₁ blockade)
  – Maintains coronary, cerebral, and renal blood flow

• Onset: 5-15 min

• Duration of action: 4-6 hours

• Adverse effects:
  – Vomiting, scalp tingling, bronchoconstriction, dizziness, nausea, heart block, orthostatic hypotension

Nicardipine: Profile

• 2nd generation dihydropyridine calcium channel blocker
  – Coronary and cerebral arterial vasodilation
  – No negative inotrophic or dromotropic effects
  – ↓Systemic vascular resistance

• Onset: 5-15 min

• Duration of action: 15-30 mins

• Adverse effects:
  – Tachycardia, headache, flushing, local phlebitis

BP reduction with IV nicardipine

SBP
Target SBP
MAP
Target MAP Range
DBP

Courtesy of WF Peacock, MD
Nicardipine vs SNP for perioperative hypertension

<table>
<thead>
<tr>
<th></th>
<th>Time to response (min)</th>
<th># Dose changes</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cardiac patients</td>
<td>Noncardiac patients</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>14.1 ± 1*</td>
<td>1.5 ± 0.2†</td>
<td>1.6 ± 0.1‡</td>
</tr>
<tr>
<td></td>
<td>(n = 51)</td>
<td>(n = 18)</td>
<td>(n = 33)</td>
</tr>
<tr>
<td>SNP</td>
<td>30.4 ± 3.5</td>
<td>5.1 ± 1.4</td>
<td>4.6 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>(n = 51)</td>
<td>(n = 15)</td>
<td>(n = 36)</td>
</tr>
</tbody>
</table>

*P = 0.0029 vs SNP, †P ≤ 0.05 vs SNP
‡Significant treatment differences in 2/5 centers (P < 0.05)

Newer Parenteral Antihypertensive Treatment

Pharmacology
## Parenteral antihypertensive treatment

<table>
<thead>
<tr>
<th>Approved</th>
<th>Class</th>
<th>Investigational</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNP</td>
<td>Vasodilator</td>
<td>Nesiritide</td>
<td>B-type natriuretic peptide</td>
</tr>
<tr>
<td>Esmolol</td>
<td>β-blocker</td>
<td>Diazoxide*</td>
<td>K⁺ channel agonist</td>
</tr>
<tr>
<td>Phentolamine</td>
<td>α-blocker</td>
<td>Torsemide*</td>
<td>Loop diuretic</td>
</tr>
<tr>
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<td></td>
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<td>Enalaprilat</td>
<td>ACEI</td>
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</tr>
<tr>
<td>Clevidipine</td>
<td>CCB</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Limited data only

Calcium channel blockers in acute hypertension

1st generation: Nifedipine

2nd generation: Nicardipine

3rd generation: Clevidipine

Clevidipine: Pharmacokinetic overview

• Dihydropyridine calcium channel blocker (CCB)
• $T_{1/2} \approx 1$ min
• Selective arteriolar dilation
  ↓ Systemic vascular resistance
  ↓ Afterload
  ↑ Stroke volume
  ↑ Cardiac output
• No venous dilation
  – No effect on cardiac filling pressure
• No effect on HR

Clevidipine: Principles of use

• Clevidipine is indicated for the reduction of blood pressure when oral therapy is not feasible or not desirable

• Linear relationship between dosage and arterial blood concentrations
  – Relationship maintained for dose rates up to 7 nmol/kg per min

• Rapid clearance following infusion discontinuation
  – BP returns to baseline within 10 min

Nesiritide: Pharmacokinetic overview

- Recombinant B-type natriuretic peptide (BNP)
- Venous and arteriolar dilation
  - ↓Preload
  - ↓Afterload
  - ↑Cardiac output
- No direct inotropic effects
- Approved only for treatment of acute decompensated heart failure

Hypertensive Urgencies/Emergencies: Guidelines
Hypertensive emergencies: JNC 7 consensus recommendations*

- Admit to ICU
- Administer short-acting parenteral antihypertensive with close monitoring
  - ↓BP by ≤25% within 1 hour
  - ↓BP to 160/100-110 mm Hg over next 2-6 hours
  - ↓BP to 130/85 mm Hg over next 24-48 hours

*Expert opinion

Hypertensive urgencies: JNC 7 consensus recommendations*

- Some patients may benefit from short-acting oral antihypertensive treatments
  - However, in one recent study, resting for 60 min was associated with ↓BP of >20% in 1/3 of patients
  - In addition, no evidence that failure to ↓BP in emergency department is associated with ↑short-term risk

- Adjust or reinstitute antihypertensive regimen to gradually ↓BP over next few days

*Expert opinion

# JNC 7: Treatment of acute hypertension in preeclampsia

Consider if childbirth is imminent

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydralazine</td>
<td>5 mg IV bolus, then 10 mg q20-30 min to max 25 mg; Repeat in several hr</td>
<td>Precipitous ↓BP when using with MgSO₄</td>
</tr>
<tr>
<td>Labetalol</td>
<td>20 mg IV bolus, then 40 mg 10 min later, 80 mg q10 min for 2 additional doses to max 220 mg</td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>10 mg po, repeat q20 min to max 30 mg</td>
<td>Cyanide poisoning may occur if used &gt;4 hr</td>
</tr>
<tr>
<td>SNP</td>
<td>0.25 µg/kg per min to max 5 µg/kg per min</td>
<td>Cyanide poisoning may occur if used &gt;4 hr</td>
</tr>
</tbody>
</table>

NEW DATA PRESENTED SEPT. 2013 EUROPEAN STROKE CONFERENCE, LONDON.

• INTERACT 2 TRIAL….LOWERING BLOOD PRESSURE RAPIDLY TO LESS THAN 140 MM HG. IMPROVED THE MODIFIED RANKIN SCALE BUT NOT DEATH OR DISABILITY
Conclusion

• Among patients with acute ischemic stroke, BP reduction with antihypertensive medications compared with the absence of antihypertensive medications did not reduce death and major disability at 14 days or hospital discharge.

• These findings suggest that unless a patient’s BP ≥220/120 mmHg, the decision to lower BP with antihypertensive treatment in patients with acute ischemic stroke should be based on individual clinical judgment.
J He and coauthors for the CATIS Investigators

Effects of Immediate Blood Pressure Reduction on Death and Major Disability in Patients With Acute Ischemic Stroke: The CATIS Randomized Clinical Trial

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Available at jama.com and mobile.jamanetwork.com
1: TREATMENT OF Systolic Hypertension 140-160 mmHg IN ANY GROUP.

2: TREATMENT of PREHYPERTENSION 120/80 TO 140/90.

3: TREATMENT of WHITE COAT HYPERTENSION.