Disclosure of Relationships

- No Potential conflicts of interest to announce
- No financial interest in technical or pharmaceutical industry.
- American Society of Hypertension:
  - Nominating Committee,
  - Membership Committee,
  - CME Committee
Hypertensive Crisis: Emergency vs Urgency. Learning Objectives

- Recognize clinical and pathological differences between Hypertensive Emergencies and Urgencies
- Discuss “Hypertensive Crisis” target organ damage: Brain, Heart, Eyes, Kidneys, Arteries
- Explain Cerebral blood flow auto-regulation abnormality in Hypertensive Crisis
- Plan treatment for Hypertensive Emergencies vs Hypertensive Urgencies
- Reduce medical errors
- Improve Health care quality improvement
Grade 4 KWB (Keith-Wagner-Barker) Hypertensive Retinopathy
Which of these men had a Hypertensive Crisis: Emergency vs Urgency? He had Malignant Hypertension? What was his Treatment? Where was this meeting?
'CAME OUT OF CLEAR SKY,'
SAYS PRESIDENT'S PHYSICIAN

Adm. Ross T. McIntire
Asserts There Was No
Indication of Imminent Danger.

DEATH DUE TO CEREBRAL
HEMORRHAGE — BLOOD
VESSEL IN BRAIN BROKE

WASHINGTON, April 13 (AP).
President Roosevelt
Died from what doctors call
a cerebral hemorrhage,
which means a sudden exten-
Systolic and Diastolic Arterial Pressure of Franklin D. Roosevelt from 1935 until His Death on April 12, 1945

- EKG denotes electrocardiogram, and LVH left ventricular hypertrophy
- Data are from the diary of Dr. Howard G. Bruenn

Arterial Blood Pressure (mm Hg)

EKG: LVH
Proteinuria: + ++

350/190 mm Hg

Month and Year from personal diary of Dr. Howard G. Bruenn
Case of Blurred Vision
Hypertensive Emergency

- 55 y/o w/m water meter reader develops blurred vision, headaches, shortness of breath, chest pain, swollen ankles. Previously normal B.P. at age 50. ASA and Tylenol for headache.
- B.P. 230/138 mm Hg in ER
- 4 KWB (Keith-Wagner-Barker) hypertensive retinopathy
- S 3+4 gallop, Rales- both bases, Bruit LUQ
- Pretibial pitting edema bilateral
- UA trace protein, S Creatinine 1.7, eGFR 45 ml/min
- Ultrasound smaller R kidney
- What to do in ER?
What is your first choice Treatment in ER? What route of Admin: IV, IM, SC, PO? Which 1 of 4 meds should not be given?

A. Nitroprusside (Nipride)
B. Nicardipine (Cardene)
C. Labetolol (Normodyne, Trandate)
D. Hydralazine (Apresoline)
What is your first choice Treatment in ER?
What route of Admin: IV, IM, SC, PO?
Which 1 of 4 meds should not be given?

A. Nitroprusside (Nipride)
B. Nicardipine (Cardene)
C. Labetolol (Normodyne, Trandate)
D. Hydralazine (Apresoline)
What is role of diuretic in this case?
What route of Administration?

A. Thiazide
B. Chlorthalidone
C. Loop Blocker
D. Spironolactone
E. Mannitol
What is role of diuretic in this case?
What route of Administration?

A. Thiazide
B. Chlorthalidone
C. Loop Blocker, IV
D. Spironolactone
E. Mannitol
Left Ventricular Hypertrophy without ischemia

Left Ventricular Hypertrophy with ischemia
Hypertensive NonCompliance

- 48 y/o AA/f with 20 history of HBP
- hctz, atenolol, amlodipine, clonidine
- Short of breath, swollen legs, headache, blurred vision for 3 weeks
- Missing medicine doses
- Suddenly diaphoresis, anxiety, palpitations on weekend
- B.P. 228/135 mm Hg, HR 120/minute
- Arterial spasm, Many soft cotton wool exudates, blurred disk
- What to do in ER?
What is Treatment of Choice in this Case?
What route of Administration: IV, IM, SC, PO, SL?

A. Hydralazine
B. Prazosin
C. Clonidine
D. Labetolol
What is Treatment of Choice in this Case?
What route of Administration: IV, IM, SC, PO, SL?

A. Hydralazine
B. Prazosin
C. Clonidine
D. Labetolol
Pregnancy & Hypertension

- 20 y/o AA/f presents with headache, SOB, swollen ankles, missed 4 menstrual periods.
- History: Hypertension Age 17, high school, started on ramipril 5 mg q.d.
- B.P 185/105 mm Hg, S 4, edema pedal, ankle, mid pretibial in E.R.
- Proteinuria 3 +, 450 mg/ 24 h
What is best course of therapy in emergency room?

- A. increase dose of ramipril until BP is controlled
- B. discontinue ramipril and start beta blocker
- C. add amlodipine to ramipril and titrate to control BP
- D. add IV alpha methyl dopa to ramipril and control BP
What is best course of therapy in emergency room?

- A. increase dose of ramipril until BP is controlled
- B. discontinue ramipril and start beta blocker
- C. add amlodipine to ramipril and titrate to control BP
- D. add IV alpha methyl dopa to ramipril and control BP
Systemic Familial Hypertension

- A 38 y/o AA/f, gr 2, p 2, ab 0, hypertensive with 2 pregnancies, LNMP one month ago, presents to E.R. with headaches, blurred vision, SOB, bilateral leg swelling of 2 weeks duration. She was a known hypertensive for 18 years and had been off antihypertensive meds for over one year.

- Family history indicates mother and 2 uncles and a brother are hypertensive. Father died of hypertensive stroke while in ESRD Dialysis program.
Physical Examination

- BP 230/140, P 110, R 20, 65 Kg, dyspneic at rest.
- Fundi show papilledema, flame hemorrhages, soft white exudates, severe arteriolar spasm
- NVD 12 cm, Carotids equal
- Heart, Reg S 3, S4, Lungs bibasilar rales
- Hepatomegaly 14 cm, tender
- 3 + pitting edema to knees
- UA 2+ prot, Sed 10-20 RBC, 5-10 WBC/hpf, granular and hyaline casts
Telescopied urine sediment
Laboratory Values

- S creatinine 5.8 mg/dL, BUN 84 mg/dL
- Na+ 128, K+ 6.5, Cl- 91, tCO2 12, Glu 140
- Hb 7.8, Hct 24, wbc 7,900
- 24 hr proteinuria 1200 mg.

What treatment in ER?

Calculate the estimated GFR; Determine Kidney Ultrasound results; Plan need for kidney biopsy.
Microangiopathic Hemolytic Anemia of Malignant Hypertension
The estimated GFR is:

- A. 5 mL/ minute
- B. 11 mL/ minute
- C. 16 mL/ minute
- D. 22 mL/ minute
The estimated GFR is:

- A. 5 mL/ minute
- B. 11 mL/ minute
- C. 16 mL/ minute
- D. 22 mL/ minute
Kidney Ultrasound Results

- A. Large edematous kidneys bilaterally
- B. Small contracted kidneys bilaterally
- C. One large kidney, one small kidney
- D. Bilateral swollen kidneys, dilated calyces and ureters
Kidney Ultrasound Results

- A. Large edematous kidneys bilaterally
- B. Small contracted kidneys bilaterally
- C. One large kidney, one small kidney
- D. Bilateral swollen kidneys, dilated calyces and ureters
If a kidney biopsy were performed on this patient, the result would most likely be which diagnosis:

- A. Membranous Glomerulonephritis
- B. Proliferative Glomerulonephritis
- C. Nephrosclerosis
- D. Chronic Interstitial Nephritis
If a kidney biopsy were performed on this patient, the result would most likely be which diagnosis:

- A. Membranous Glomerulonephritis
- B. Proliferative Glomerulonephritis
- C. Nephrosclerosis
- D. Chronic Interstitial Nephritis
Funduscopic Examination in Emergency Room on Admission
Six (6) months after admission, Funduscopic Examination in Dialysis Unit
22 y/o w/f slowly develops headaches, diffuse arthralgias, myalgias, shortness of breath, swollen ankles, orthopnea
Hypertensive Emergency and Skin Rash

- 22 y/o w/f slowly develops headaches, diffuse arthralgias, myalgias, shortness of breath, swollen ankles, orthopnea
- B.P. 220/118 mm Hg in E.R., HR 110, facial bimalar erythema, S4, tender hepatomegaly, pitting edema to knees, tender swollen elbows, wrists, knees
- UA proteinuria 4+, rbc casts and wbc

* What medicine should not be given?
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-nuclear Antibody</td>
<td>&gt;1:100 homogen</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-native DNA Antibody*</td>
<td>86.1</td>
<td>&lt; 15%</td>
</tr>
<tr>
<td>Anti-single stranded Antibody*</td>
<td>75.9 % binding</td>
<td>&lt; 15%</td>
</tr>
<tr>
<td>Extractable Nuclear Antigen (ENA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-”Sm” Antibody**</td>
<td>1:64</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-Ribonucleoprotein Antibody**</td>
<td>neg</td>
<td>Negative</td>
</tr>
<tr>
<td>Rheumatoid Factor**</td>
<td>neg</td>
<td>&lt; 1:80</td>
</tr>
<tr>
<td>C3</td>
<td>28</td>
<td>55 - 120mg%</td>
</tr>
<tr>
<td>Complement Components***</td>
<td>&lt;3</td>
<td></td>
</tr>
<tr>
<td>C4</td>
<td></td>
<td>20 - 50mg%</td>
</tr>
<tr>
<td>Immune Complexes*</td>
<td>42.3</td>
<td></td>
</tr>
</tbody>
</table>

* Radioimmunoassay
** Hemagglutination
*** Radial Immunodiffusion
Hypertension Terminology

- Systolic Pressure (mm Hg)/Diastolic Pressure (mm Hg)
- Normal BP = < 120/< 80
- Pre-hypertension = 120-139/80-89
- Hypertension stage 1 = 140-159/90-99
- Hypertension stage 2 = ≥ 160/≥ 100
- Former Hypertension stage 3 = ≥ 180/≥ 120 *
- Hypertensive Crisis = ≥ 180/≥ 120
- Hypertensive Urgency = ≥ 180/≥ 120 ? Without S & S of End Organ Decompensation
- Hypertensive Emergency = ≥ 180/≥ 120 with *
  * Progressive S & S of End Organ Damage
Hypertensive Emergencies and Urgencies

- Therapeutic decisions in accelerated hypertension depend on severity of associated co-morbidities.

- **Hypertensive Urgencies**: BP $\geq 180/\geq 120$ *in absence* of Signs + Symptoms of progressive target organ damage rarely requires emergency therapy and can be managed in the outpatient setting if appropriate follow-up can be provided.

- **Hypertensive Emergencies**: BP $\geq 180/\geq 120$ *plus* acute or rapidly progressive target organ damage; usually requires hospitalization in ICU with BP monitoring and parenteral therapy to reduce BP to a safe, non-critical level, not necessarily to normal BP Level***

- Treatment of hypertensive encephalopathy (caused by abnormal autoregulation of cerebral blood flow) reverses acute neurologic abnormalities.
 Syndromes of **Severe** Stage 2 (formerly Stage 3) Hypertension-to be revised as Stage 3 Hypertension 2014 Recommendations

- Therapeutic decisions in a patient with markedly elevated blood pressure ($BP >180 \text{ mm Hg systolic}$), hypertension, **depend on the severity of the co-morbidities.**
Hypertensive Emergencies: TARGET ORGANS

Severe elevations in BP, complicated by evidence of acute or rapidly progressive life-threatening target organ dysfunction.

- Coronary ischemia
- Cerebrovascular accident
- Pulmonary edema
- Acute arterial bleeding
- Acute renal failure
- Retinopathy: KWB-Gr 3,4 (Necrotizing Arteriolitis)

- require immediate BP reduction (minutes to hours ??)
- to limit or prevent target organ damage and reduce risk.

**Target Blood Pressure ?? 160-170/90-100 mm Hg**
Hypertensive Urgencies

- Severe elevations in BP **without evidence** of acute or rapidly progressive target organ dysfunction.

- Elevated BP alone in the absence of symptoms of progressive target organ damage rarely require emergency therapy.

- BP managed by oral medication in the Emergency Room with appropriate follow-up within 1-3 days.

- If prompt and appropriate follow-up cannot be ensured, some hypertensive urgencies justify admission.
Hypertensive Emergencies

- Hypertensive Encephalopathy
- Malignant Hypertension (?)
- Severe Hypertension plus Acute Complications:
  - Cerebrovascular
    - Intracerebral hemorrhage
    - Subarachnoid hemorrhage
    - Acute atherothrombotic brain infarction (with severe hypertension)
  - Renal
    - Rapidly progressive renal failure
  - Cardiac
    - Acute aortic dissection
    - Acute left ventricular failure with pulmonary edema
    - Acute myocardial infarction
    - Unstable Angina
  -- Retinopathy
Hypertensive Emergencies (Cont.)

- Eclampsia or severe hypertension during pregnancy
- Catecholamine excess states
  - Pheochromocytoma crisis
  - Food or drug interactions (tyramine) with monoamine oxidase inhibitors
  - Rebound hypertension after sudden withdrawal of antihypertensive agents (i.e. clonidine, guanabenz, methyldopa) (Beta Blocker withdrawal)
- Drug induced hypertension (some cases)
  - Overdose with sympathomimetics (ephedrine, pseudafed, neosynephrine) or drugs with similar action (e.g. phencyclidine, lysergic acid diethylamide (LSD), cocaine, phenyl propanolamine, amphetamines, metamphetamine)
- Head trauma
- Post coronary artery bypass hypertension
- Postoperative bleeding at vascular suture site
Hypertensive Urgencies

- Accelerated and severe (?)
- Rebound hypertension, sudden withdrawal of antihypertensive agents
- Drug induced hypertension
  - Sympathomimetic agents
  - Metoclopramide-induced hypertensive crisis
  - Interaction α-adrenergic and nonselective β-adrenergic antagonist
- Extensive body burns
- Acute glomerulonephritis
- Scleroderma crisis
- Acute systemic vasculitis
- Surgically related hypertension
  - Patients requiring immediate surgery
  - Postoperative hypertension
- Severe epistaxis
- Episodic hypertension, chronic spinal cord injury; autonomic hyperflexia syndrome
TRIAGE – Group I
HYPERTENSION > 180/110 mm Hg

Symptoms
- Headache
- Anxiety
- Often asymptomatic

Examination
- No target organ damage
- No clinical cardiovascular disease

Therapy
- Monitor 1-3 h post therapy
- Initiate/resume medication(s)
- Increase Dosage of inadequate agent

Plan
- Arrange follow-up ~ 24 to 72 h
- If no prior evaluation, schedule studies
TRIAGE – Group II
HYPERTENSION > 180/110 mm Hg

Symptoms
- Severe headache
- Shortness of breath
- Edema

Examination
- Target organ damage obvious
- Clinical cardiovascular disease present or stable

Therapy
- Monitor 3-6 h post therapy
- Lower BP with short-acting oral agents
- Adjust current therapy

Plan
- Short hospitalization, 24 h, Monitor therapy, Check Labs
- Arrange follow-up
TRIAGE – Group III
HYPERTENSION - 220/120-140 mm Hg

SYMPTOMS:
- Shortness of breath
- Chest pain
- Oliguria, Nocturia

EXAMINATION:
- Dysarthria
- Weakness
- Altered consciousness
- Encephalopathy
- Pulmonary edema
- Renal insufficiency
- Cerebral vascular accident
- Cardiac ischemia

THERAPY/MANAGEMENT:
- Baseline labs,
- Intravenous line
- Monitor BP
- Initiate parenteral therapy in the emergency room
- Immediate admission to intensive care unit
- Treat to initial goal BP...?? 160-170/90 mm Hg
- Additional diagnostic studies
Neurological Considerations
Acute Hypertension: Pathophysiology & Hemodynamics

SVR = Systemic Vascular Resistance; CO = Cardiac Output; SV = stroke volume; HR = Heart Rate

BP = SVR \times CO \text{ which measured?}

\begin{align*}
&PV_R = \frac{BP}{CO} \\
&SVR = \frac{BP}{CO}
\end{align*}

Cerebral Perfusion Pressure

- **MAP** = DBP + 1/3 PP
  - MAP = Mean Arterial Pressure
  - DBP = Diastolic Blood Pressure
  - PP = Pulse Pressure (SBP – DBP)

- **CPP** = MAP – ICP
  - CPP = Cerebral Perfusion Pressure
  - ICP = Intracranial Pressure

Does your MICU measure ICP?
Calculation of Systemic Vascular Resistance

- Formula for Calculation: The relationship between the variables for calculating SVR is the same as the relationship of variables in electrical circuit defined in **Ohm's law**,

  \[ \text{resistance} = \frac{\text{pressure}}{\text{flow}}. \]

- **SVR**: measured from difference between mean arterial pressure and central venous pressure divided by cardiac output flow. CVP is normally 0 mm Hg ... in this case the calculation becomes:

  \[ \text{SVR} = \frac{\text{MAP}}{\text{CO}} \]

- To convert the resultant value into **dyne.sec.cm}^{-5, (dyne*sec/cm}^5\right)\text{ the result is multiplied with 79.9.} \]

  \[ \text{SVR} = \frac{(\text{MAP} - \text{CVP})}{\text{CO}} \times 79.9 \quad \text{or} \]

  \[ \text{SVR} = \frac{(\text{MAP} - \text{CVP})}{\text{CO}} \times 80 \]

- Normal SVR is 900-1,300 \((\text{dyne*sec})/\text{cm}^5\)

- **Hypertensive Crisis**: \(\text{SVR} = 1,600 \text{ to } 2,000 \text{ dynes} \cdot \text{sec}/\text{cm}^5\)

**MAP** = Mean Arterial Pressure,
**CVP** = Central Venous Pressure,
**CO** = Cardiac Output

**Systemic Vascular Resistance Index** uses **cardiac index instead of cardiac output**. Divide the difference between the mean arterial pressure and central venous pressure by **cardiac index instead of cardiac output**.
RULES: Cerebral Auto-Regulation is Central to Treatment of Hypertensive Crises

Cerebral auto-regulation may be lost

Chronic hypertensive patients are accustomed to higher BP—curve shifted to the right
Patients may have concomitant cardiac disease

- Patients with chronic hypertension
- Auto-Regulate cerebral blood flow around higher BP set points


BP=180/120; MAP=140
Hypertensive Crisis: Autoregulation of Cerebral Blood Flow is Affected by Hypertension Level

Chronic Hypertension pts. — Auto-regulate cerebral blood flow around higher set points. Pts with Cerebral Ischemia lose ability to auto-regulate cerebral blood flow.

Adapted with permission from Varon J, Marik PE. Chest. 2000;118:214-227.
Ischemic Stroke Hypertension

- Cerebral auto-regulation may be lost
- Chronic hypertensive patients are accustomed to higher BP—BP Perfusion curve shifted to the right
- Patients may have concomitant cardiac disease (CAD, CHF)
- Hypertension may resolve spontaneously (?) \(^1\)
  - May be important to maintain adequate perfusion pressures
  - Usually not treated unless:
    - SBP >220, DBP >120 or MAP >130 mmHg \(^2\)
    - Or concomitant medical conditions—
      - acute MI, aortic dissection, hypertensive encephalopathy, severe LV failure
    - Or thrombolytic Rx used: ↓ BP to avoid hemorrhage

References:
Recent Original Article

Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

Craig S. Anderson, M.D., Ph.D., Emma Heeley, Ph.D., Yining Huang, M.D., Jiguang Wang, M.D., Christian Stapf, M.D., Candice Delcourt, M.D., Richard Lindley, M.D., Thompson Robinson, M.D., Pablo Lavados, M.D., M.P.H., Bruce Neal, M.D., Ph.D., Jun Hata, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Mark Parsons, M.D., Ph.D., Yuechun Li, M.D., Jinchao Wang, M.D., Stephane Heritier, Ph.D., Qiang Li, B.Sc., Mark Woodward, Ph.D., R. John Simes, M.D., Ph.D., Stephen M. Davis, M.D., John Chalmers, M.D., Ph.D., for the INTERACT2 Investigators

N Engl J Med
Volume 368(25):2355-2365
June 20, 2013
Study Overview

- In this trial involving hypertension patients with intracerebral hemorrhage, intensive BP lowering (target systolic BP <140 mm Hg) did not significantly reduce the rate of the primary outcome of death or major disability but did significantly improve overall functional outcomes.

- A Negative Study!
Trial: hypertension intracerebral hemorrhage patients- Conclusions

- Intensive BP lowering of target systolic BP <140 mm Hg
- Did not result in a significant reduction in rate of primary outcome of death or severe disability.

Management of Hypertensive Emergencies

- Accelerated Hypertension is often Misunderstood, Mismanaged
- **Delays in therapy** can cause further target end organ damage
- **Overzealous therapy** can result in too rapid reduction in blood pressure and **cerebral ischemia**
- Does rapid decrease of BP improve survival, cognition?

- **Basile, J.** Hypertension in face of acute intracerebral hemorrhage (ICH)”. JCH, January 2014
- **Varon J, Marik PE.** Chest. 2000; 118: 214-227
- **Epstein M,** Clin Cornerstone. 1999; 2: 41-54
How aggressively to treat Hypertension in face of acute intracerebral hemorrhage (ICH) 

- Debate by Stroke Neurologists and Hypertension Specialists. Even in patients without history of hypertension, severe HBP increases ICH.
- Possible adaptive response to increased intracerebral pressure (ICP).
- Is elevated BP after acute ICH just a marker of increased ICP/poor prognosis ??
- Should elevated BP after ICH be potential target for intervention?? Unknown !!
- Increased BP might lead to a greater risk of hematoma expansion and poor outcome,
- Lowering BP with anti-HBP medication in the face of increased ICP might be associated with decreased cerebral perfusion and worsen ischemia.
<table>
<thead>
<tr>
<th>AGENT</th>
<th>DOSE</th>
<th>ONSET/DURATION OF ACTION (AFTER DISCONTINUATION)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PARENTERAL VASODILATORS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium nitroprusside</td>
<td>0.25-10.00 μg/kg/min as i.v. infusion; maximal dose for 10 min only</td>
<td>Immediate/2-3 min after infusion</td>
</tr>
<tr>
<td>Glyceryl trinitrate</td>
<td>5-100 μg as i.v. infusion</td>
<td>2-5 min/5-10 min</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>5-15 mg/h i.v. infusion</td>
<td>1-5 min/15-30 min, but may exceed 12 h after prolonged infusion</td>
</tr>
<tr>
<td>Verapamil</td>
<td>5-10 mg i.v.; can follow with infusion 3-25 mg/h</td>
<td>1-5 min/30-60 min</td>
</tr>
<tr>
<td>AGENT</td>
<td>DOSE</td>
<td>ONSET/DURATION OF ACTION (AFTER DISCONTINUATION)</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Diazoxide</td>
<td>50-150 mg i.v. bolus, repeated or 15-30 mg/min i.v. infusion</td>
<td>1-5 min/3-12 h</td>
</tr>
<tr>
<td>Fenoldopam mesylate</td>
<td>0.1-0.3 mg/kg/min i.v. infusion</td>
<td>&lt;5 min/30 min</td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>0.625-1.250 mg every 6 h i.v.</td>
<td>15-60 min/12-24 h</td>
</tr>
<tr>
<td>Hydralazine ***</td>
<td>10-20 mg as i.v. bolus or 10-40 mg i.m.; repeat q 4-6 h</td>
<td>10 min i.v/&gt;1 h (i.v.), 20-30 min i.m./4-6 hours i.m. ***</td>
</tr>
</tbody>
</table>
## Management of Hypertensive Emergencies

<table>
<thead>
<tr>
<th>AGENT</th>
<th>DOSE</th>
<th>ONSET/DURATION OF ACTION (AFTER DISCONTINUATION)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PARENTERAL ADRENERGIC INHIBIT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labetalol</td>
<td>20-80 mg as i.v. bolus every 10 min; up to 2 mg/min as i.v. infusion</td>
<td>5-10 min/2-6 hours*</td>
</tr>
<tr>
<td>Esmolol (Aortic Aneurysm)</td>
<td>500 μg/kg bolus injection i.v. or 25-100 μg/kg/min by infusion. May repeat bolus after 5 min or increase infusion 300 μg/kg/min</td>
<td>1-5 min/15-30 min</td>
</tr>
<tr>
<td>Phentolamine (Regitine) (Pheochromocytoma)</td>
<td>5 mg as i.v bolus (may repeat)</td>
<td>1-2 min/10-30 min</td>
</tr>
</tbody>
</table>
Specific Emergency Drug Precautions

Sodium Nitroprusside – nausea, vomiting, muscle twitching; with prolonged use, may cause thiocyanate intoxication (especially CKD), methemoglobinemia acidosis, cyanide poisoning (especially Liver disease); bags, bottles, and delivery sets must be light resistant.

Glyceryl Trinitrate – headache, tachycardia, vomiting, flushing, methemoglobinemia; requires special delivery systems due to the drug’s binding to poly-vinyl chloride tubing.

Nicardipine – tachycardia, nausea, vomiting, headache, possible protracted hypotension after prolonged infusions.

Verapamil – heart block (first-, second-, and third-degree) especially with concomitant digitalis or β-blockers; bradycardia.

Diazoxide – hypotension, tachycardia, aggravation of angina pectoris, nausea and vomiting, hyperglycemia with repeated injections.

Fenoldopam – Headache, tachycardia, flushing, local phlebitis

Enalaprilat – renal failure in patients with bilateral artery stenosis, hypotension.
Specific Emergency Drug Precautions (Continued)

Hydralazine – tachycardia, palpitations, headache, vomiting, aggravation of angina pectoris, myocardial ischemia.+++ 

Labetalol – bronchoconstriction, heart block, orthostatic hypotension.

Esmolol – first degree heart block, congestive heart failure, asthma.

Phentolamine – tachycardia, orthostatic hypotension.
What is Ideal Agent for Hypertensive Emergency?

- Rapid Onset of Action
- Cessation of Action Rapid when Dose Stopped
- Predictable Dose Response Curve
- Minimal Side Effects
Hemodynamic Changes
Patients with Hypertensive Emergencies:

- Excessive elevations in SVR.
- Decreased cardiac output.
- Decreased renal blood flow.
- **Volume status?** Evaluate for contraction vs expansion, pulmonary edema)

- Usually diuretic is not recommended unless evidence of fluid overload.
Hemodynamic Effects of What Drug?

- Decrease MAP,
- Decrease Afterload,
- Decrease Preload
- Increase or No Change Cardiac Output
- Increase Renal Blood Flow
- Increase GFR
Hemodynamic Effects of What Drug?

- Decrease MAP,
- Decrease Afterload,
- Decrease Preload

- Increase or No Change Cardiac Output
- Increase Renal Blood Flow
- Increase GFR

Sodium Nitroprusside

- Increased Cerebral Perfusion,
- Usually n/c in ICP due to Powerful Decrease MAP
What Drug is Potent Venodilator?
What Drug is Potent Venodilator?

- Nitroglycerine
  - Moderate Afterload Reduction
  - Decrease Myocardial Oxygen Demand
  - Dilates Epicardial Coronary Arteries
  - Inhibits Vasospasm
  - Favorable Endocardial Blood Flow
  - Increases Cerebral Blood Flow
  - Caution with Increased ICP,
Nitroglycerine drug of choice

- What drug combinations?
- Hypertension Emergency in the setting of:
  - Myocardial Ischemia—
  - Acute Myocardial Infarction—
  - Pulmonary Edema—
  - After CABG—
  - Post Re-Perfusion
Hypertensive Crisis with Myocardial Ischemia, MI

- What drug combinations?
Hypertensive Crisis with Myocardial Ischemia, MI

Rx. Vasodilator plus Beta Blocker

- Combination: Nitrates and Beta Blockers
- Combination: Sodium Nitroprusside and Beta Blockers
What is Combined alpha & beta Blocker?
What is Combined alpha & beta Blocker

Labetalol

- “Combination alpha-and beta-blocker”,
- Orally has a relative beta to alpha-blocking effect of approximately 3:1.
- Dosage begins at 100mg q 12 hours (not BID) and
- Titrate to desired response.
- Onset of action is 30 minutes to 2 hours;
- Duration of action 8 to 12 hours
Caution with Labetalol

- CHF
- Bradycardia
- Heart Block
- Reactive Airways Disease
What Drug is a selective Peripheral Dopamine-1-Receptor agonist?
What Drug is a selective Peripheral Dopamine-1-Receptor agonist?

**Fenoldopam**

- Arterial vasodilator with a
- Rapid onset of action
- Relatively short half-life
- It may be of particular benefit in patients with renal insufficiency
- “Theoretically” shown to improve renal perfusion.
- Contraindicated in Glaucoma, Increased IOP
- May cause tachycardia
What I.V. and I.M. Antihypertensive Drug is Contraindicated in Myocardial Ischemia?
What I.V. and I.M. Antihypertensive Drug is Contraindicated in Myocardial Ischemia?

Hydralazine
Hydralazine

- Bolus Dosage 5-10-20 mg, Long Duration of Action 6 hours I.M.!
- Direct arterial vasodilator
- Decreases Systemic Vascular Resistance
- Induces Compensatory Tachycardia
- Increases Myocardial Oxygen Demand-Ischemia
- Contraindicated in Aortic Dissection
- Increases ICP

- Limited to preeclampsia treatment of pregnant women
- No effect on venous capacitance.
- Crosses the utero-placental barrier
- But has minimal effects on fetus.
What is Diagnosis?
BP 240/130 mm Hg and Chest Pain
Type A aortic dissection, widened mediastinum and enlargement of the shadows of the ascending aorta and descending aorta (arrows).
What I.V. Antihypertensive Drug/Drugs Recommended in Aortic Dissection?
Rational of Medications in Aortic Dissection

- **Beta Blockers and sodium Nitroprusside**, Relieve the shear force of blood on the aortic wall by reducing the heart rate and lowering blood pressure. With reduced blood shear force, the aortic dissection is less likely to worsen.

- **Decrease Aortic dP/dt, shear force.** Medical therapy used to prepare a patient for surgery. Decision concerning location of type B dissection: medication and surgery VS medications alone.

- CT or MRI imaging scans periodically to monitor

- What Anti-Hypertensive drug is contraindicated??
Rational of Medications in Aortic Dissection

- **Beta Blockers and sodium Nitroprusside**: Relieve the shear force of blood on the aortic wall by reducing the heart rate and lowering blood pressure. With reduced blood shear force, the aortic dissection is less likely to worsen.

- **Decrease Aortic dP/dt, shear force.**

- Medical therapy used to prepare a patient for surgery. Decision concerning location of type B dissection: medication and surgery VS medications alone.

- CT or MRI imaging scans periodically to monitor

- What Anti-Hypertensive drug is contraindicated? **Hydralazine**
### Management of Hypertensive Urgencies: Oral Agents

<table>
<thead>
<tr>
<th>AGENT</th>
<th>DOSE</th>
<th>ONSET/DURATION OF ACTION (AFTER DISCONTINUATION)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>25 mg p.o.; repeat as needed; s.l.; 25 mg</td>
<td>15-30 min/6-8 h; s.l. 15-30 min/2-6 h</td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.1-0.2 mg p.o.; repeat hourly as required to total dose of 0.6 mg</td>
<td>15-60 min/8-16 h</td>
</tr>
<tr>
<td>Labetalol</td>
<td>200-400 mg p.o.; repeat every 2-3 h</td>
<td>30 min-2 h/2-12 h</td>
</tr>
<tr>
<td>Prazosin</td>
<td>1-2 mg p.o.; repeat hourly, as needed</td>
<td>1-2 h/8-12 h</td>
</tr>
</tbody>
</table>
Precautions, Oral Urgency Agents

**Captopril** – hypotension, renal failure in bilateral renal artery stenosis.

**Clonidine** – hypotension, drowsiness, dry mouth.

**Labetalol** – bronchoconstriction, heart block, orthostatic hypotension.

**Prazosin** – syncope (first dose effect), palpitations, tachycardia, orthostatic hypotension.
Diuretics
Hypertensive Urgencies/Emergencies

- **Loop Blocker Diuretics**
  - Volume overload exists...must confirm volume excess?
  - Sodium and fluid retention
  - Counteract NaCl & H2O retention by acute BP lowering drugs
  - Furosemide, Butmetanide
  - Ethacrynic acid

- **Fenoldopam** — A Selective Peripheral Dopamine-1-Receptor Agonist for the Treatment of Severe Hypertension.
  Vasodilator in peripheral arteries and Diuretic in the kidneys
What oral drug decreases catechol synthesis in Pheochromocytoma patients waiting for surgery to prevent emergency??

- Phentolamine (Regitine) or
- Phenoxybenzamine (Dibenzyline)
- But not alone, after about 2 days, start
- Beta Adrenergic Blockade but not given alone?
Alpha Adrenergic Blockade in Pheochromocytoma

- Phentolamine (Regitine) or
- Phenoxybenzamine (Dibenzyline)
- But not alone, after about 2 days, start

- Beta Adrenergic Blockade

- Tyrosine Hydroxylase Inhibitor:
  - Metyrosine (Demser)

- reduce catacholamine synthesis preop and chronic combined with Phenoxybenzamine
Hypertensive Emergencies + Urgencies

The End

Become ASH Hypertension Specialist
Niphedipine Sublingual Complications

Case A

Case B
Sublingual Nefedipine for Hypertensive Urgency

Precautions

- Hypotension
- Acute Coronary Insufficiency
- Acute Myocardial Infarction
- Syncope
- Transient Ischemia Attack
- Cerebral Vascular Accidents
Clonidine - by mouth - Benefits vs Precautions

CLONIDINE

ORAL (P.O.)

P.O.  ONSET  ½ to 1 HOUR

PEAK  2 to 4 HOURS

DURATION 7 to 10 HOURS
CLONIDINE

EMERGENCY USE

P.O.  0.1 mg q1HOUR

Until Desired Effect
Grade IV  KWB Hypertensive Retinopathy

Hypertensive Emergency
Allan B. Schwartz, M.D.
Professor of Medicine
Division of Nephrology & Hypertension
Department of Medicine,
Arfonad: trimethaphan camsylate, Ganglionic Blocker

**Graph 7.** Some hemodynamic parameters recorded during treatment of patient. Drug dosage is shown at the bottom in milligrams per minute for Arfonad and milligrams per day for reserpine and guanethidine. Two titrations with Arfonad show the effect first on peripheral resistance and second on contractility.
Nitroprusside (Nipride) peripheral vasodilator

FIGURE 1: Blood pressure response to nitroprusside infusion. Note that excessive hypotension is quickly reversed by discontinuation of the drug.

INTRAVENOUS LABETALOL/HYPERTENSIVE EMERGENCY

BP (mmHg)

SYSTOLIC

DIASTOLIC

HEART RATE (X)

MINUTES

LABETALOL 200mg ORALLY

20 40 80 80 80
Fenoldopam

Reduction in Mean Arterial Blood Pressure in 10 Hypertensive Patients after the Commencement of Infusion


Effects of fenoldopam on renal hemodynamics and renal tubular cells suggest potential to preserve kidney function; however, ultimate clinical importance of these effects remains to be determined.
Minoxidil
For Chronic
Severe
Hypertension (po)
Hypertensive Emergencies + Urgencies

The End

Become ASH Hypertension Specialist
Hypertensive Emergencies + Urgencies

The End

Become ASH Hypertension Specialist