Patient presents w/ signs & symptoms suggestive of spontaneous intracerebral hemorrhage (ICH)

EMERGENCY MEASURES
- Airway, Breathing, Circulation (ABCs)

DIAGNOSIS
Does imaging show ICH?
- Yes
- No
ALTERNATIVE DIAGNOSIS

MEDICAL THERAPY

BP Management
- Agents to treat elevated BP
  - Enalapril, Esmolol, Hydralazine, Labetalol, Nicardipine or Nitroprusside
- Agents to treat low BP
  - 1st line: Volume replenishment
  - Dopamine, Phenylephrine or Norepinephrine

Elevated intracranial pressure (ICP) management
- Osmotic therapy
  - Mannitol
  - Hypertonic soln
- Analgesia & sedation
- Neuromuscular blockade
- Hyperventilation
- Head-of-bed elevation
- Barbiturate coma
- CSF drainage

SURGICAL THERAPY IN SELECTED PATIENTS

Treatment of other medical conditions
- Elevated glucose
- Seizures
- Body temperature
- Other general measures

Not all products are available or approved for above use in all countries. Specific prescribing information may be found in the latest MIMS.
1 **SIGNS & SYMPTOMS**
- Sudden onset of focal neurological deficit
  - Focal neurologic findings are related to the anatomic location, size & speed of development of ICH
  - Neurological deficit usually progresses over min-hr

**Adjunctive Global Symptoms**
- N/V
- Headache
- Decreased consciousness
- Elevated BP

*Rapid recognition & diagnosis of ICH are essential because of its frequently rapid progression*

2 **EMERGENCY MEASURES**
- Ensure the status of the patient's airway, breathing & circulation
  - Intubate if insufficient ventilation (pO2 <60 mmHg/7.9 kPa or pCO2 >50 mmHg/6.3 kPa), cyanosis, impending respiratory failure, obvious aspiration risk, or depressed level of consciousness
- Detection of focal neurological deficits
- Detection of signs of external trauma
- Observe in an ICU for at least the 1st 24 hr

3 **DIAGNOSIS**

**History & Physical Exam**
- Assess presenting symptoms & associated activities at onset
- Determine time of stroke onset, age & other risk factors
  - Elicit history of trauma, hypertension, prior ischemic stroke, DM, smoking, alcohol use, recreational drug use (eg cocaine), current antithrombotic therapy (eg Warfarin, Aspirin), hematologic or liver disease
- Focus on level of consciousness & degree of neurologic deficit

**Diagnostic/Lab Tests**

**Plain Cranial CT**
- CT scan differentiates ischemic stroke from ICH
  - Scan will also show size & location of hemorrhage
  - May reveal structural abnormalities (eg aneurysms, brain tumors, etc) or structural complications (eg herniation, intraventricular hemorrhage, etc) which may have caused ICH

**Cranial Magnetic Resonance Imaging (MRI)**
- Equivalent to CT in determining the presence, size, location, & progression of acute ICH
- Superior at detecting underlying structural lesions & delineating the amount of perihematomatal edema & herniation

**Angiography**
- Consider for all patients w/o clear cause of hemorrhage who are surgical candidates
  - Eg young, normotensive patients who are clinically stable
  - Useful in diagnosing secondary causes of ICH eg aneurysm, arteriovenous malformation, dural venous thrombosis, vasculitis
- Angiography not required:
  - Older hypertensive patients who have hemorrhage in basal ganglia, cerebellum, thalamus, or brain stem & in whom CT does not show structural lesion
  - Patient's clinical state & neurosurgeon's discretion will determine the urgency & timing of angiography

**Other Diagnostic Tests**
- CBC, INR, PT, aPTT, electrolytes, ECG, chest radiograph
- Toxicology screen to rule out cocaine use
- Pregnancy test

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ELEVATED INTRACRANIAL PRESSURE (ICP) MANAGEMENT

- Elevated ICP: ICP >20 mmHg for >5 min
- Goal ICP <20 mmHg & CPP >70 mmHg
- Treatment should include a balanced & graded approach beginning w/ simple measures to more aggressive therapies

Osmotic Therapy
- Target serum osmolality: 300-320 mOsm/kg
- Should only be used in patients w/ type B ICP waves, progressively increasing ICP waves or clinical deterioration associated w/ mass effect
- Mannitol is the most commonly used IV osmotic agent
  - Produces lowering of ICP w/in 20 min of administering an IV bolus
- Furosemide may be administered simultaneously to maintain osmotic gradient
- Hypertonic saline solutions have been shown to reduce ICP, even in cases refractory to hyperventilation and Mannitol

Analgesia & Sedation
- Titrate to minimize pain & increase in ICP while allowing evaluation of clinical status
  - Can be achieved w/ IV Propofol, Etomidate, or Midazolam for sedation & Morphine or Alfentanil for analgesia

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ELEVATED INTRACRANIAL PRESSURE (ICP) MANAGEMENT (CONT’D)

Neuromuscular blockade
• Used w/ sedation &/or analgesia to prevent elevated ICP due to increased intrathoracic pressure & obstruction in cerebral venous outflow
• Nondepolarizing agents: Eg Vecuronium or Pancuronium

Hyperventilation
• One of the most effective methods to rapidly reduce ICP
  - Reserved for use as a temporizing measure while awaiting more definitive treatments
  - Reduction of pCO2 to 30–35 mmHg lowers ICP by 25-30% in most patients
  - ICP reduction may take up to 30 min to occur after pCO2 is changed
  - Failure of ICP to respond to hyperventilation indicates a poor prognosis

Head-of-Bed Elevation
• Keep head-of-bed elevated at 30° w/ patient’s neck in neutral position to maximize venous outflow, lowering ICP

Barbiturate Coma
• Depresses cerebral metabolic activity, reducing cerebral blood flow & ICP
• Barbiturates effectively reduce brain swelling
  - Eg Pentobarbital, Thiopental
  - Safe limit ≈10 mg/kg/day

CSF drainage
• Effective esp in the setting of hydrocephalus
• Used when an intraventricular catheter is in place to monitor ICP

TREATMENT OF OTHER MEDICAL CONDITIONS

Elevated Glucose
• High blood glucose on admission predicts an increased fatality rate in both non-diabetic & diabetic patients w/ ICH
• Markedly elevated glucose levels should be lowered to <300 mg/dL (16.63 mmol/L)

Seizures
• The majority of seizures occur w/in the 1st 24 hr of ICH onset
• If seizure does occur, patient should be placed on anticonvulsant
• Anticonvulsant can usually be discontinued after 1 mth in patients who do not suffer from further seizures
  - Long-term treatment w/ anticonvulsant may be necessary if patients experience seizures >2 wk after ICH
• Early prophylactic treatment may be considered for selected patients w/ lobar ICH

Body Temperature
• Fever (Temp >38.5°C) is a common occurrence in patients w/ ICH & increased fever duration is associated w/ poor outcomes
• Fever should be aggressively treated even as appropriate testing for systemic infection is being undertaken
  - May use cooling blankets & Paracetamol (IV/PO/rectal)

Other General Measures
• Correct reversible causes of active bleeding (eg coagulopathies, platelet disorders) by administering fresh frozen plasma (FFP), vit K, platelets as needed
• Fluid management, nutrition, & prevention of aspiration pneumonia & bed sores are the same as for patients w/ ischemic stroke
• Low-dose subcutaneous unfractionated Heparin or low-molecular-weight Heparin helps prevent deep venous thromboembolism
• Prophylactic administration of H2 blockers or drugs that can protect the mucosa decrease the incidence of gastric hemorrhage

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**SURGICAL THERAPY IN SELECTED PATIENTS**

- Surgical evacuation may prevent expansion, decrease mass effect, & block the release of neuropathic products from hematomas.
- Minimally invasive procedures including stereotaxy-guided evacuation should be considered as an alternative to craniotomy.
- Early intervention (within 8 hr of symptom onset) is recommended.

**Surgical Candidates**

- Cerebellar hemorrhage >3 cm with the following:
  - Neurological deterioration or
  - Brain stem compression & hydrocephalus from ventricular obstruction
- ICH with mass effect lesion if surgically accessible & patient has chance of good outcome.
- Young patients with moderate-large lobar hemorrhage & who are deteriorating clinically.

**SPECIAL ASPECTS OF MANAGEMENT OF ICH**

**Management of ICH Related to Coagulation & Fibrinolysis**

- Prothrombin complex concentrate, factor IX complex concentrate, FFP & recombinant activated factor VII (rFVIIa) normalize the laboratory elevation of the INR very rapidly.
- Decision to restart antithrombotic therapy after ICH related to antithrombotic therapy depends on the risk of subsequent arterial or venous thromboembolism, the risk of recurrent ICH, & the overall state of the patient.

**Heparin-associated ICH**

- Protamine sulfate may be used to reduce bleeding tendency, with the dose depending on the time from cessation of Heparin.

**Warfarin-associated ICH**

- Should be treated with IV vit K.
- Treatment should also aim to replace clotting factors.
### Dosage Guidelines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACE Inhibitor</strong></td>
<td></td>
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</tr>
<tr>
<td>Enalapril</td>
<td>0.625 mg IV initially followed by 1.25-5 mg IV over 5 min q6h as needed</td>
<td>Adverse Reactions: CV effects (hypotension, angioedema); CNS effects (fatigue, headache); Resp effects (persistent dry cough, upper resp tract symptoms); Dermatologic effects (skin rashes, erythema multiforme, toxic epidermal necrolysis); Hypersensitivity reactions; Renal effects (renal impairment); Electrolyte disturbances (hyperkalemia, hyponatremia); Blood disorders</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Special Instructions: Avoid in patients w/ aortic stenosis or outflow tract obstruction &amp; should generally be avoided in suspected or actual renovascular disease; Use w/ caution in patients w/ history of hereditary or idiopathic angioedema; NSAIDs should be avoided since they can block the beneficial effects &amp; increase adverse effects of ACE inhibitors</td>
</tr>
<tr>
<td><strong>Beta-Blockers</strong></td>
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<tr>
<td>Esmolol</td>
<td>Loading dose: 500 mcg/kg IV over 1 min then Maintenance infusion: 50 mcg/kg/min IV infusion over 4 min If desired response is not achieved repeat loading dose but increase maintenance infusion to 100 mcg/kg/min over 4 min May repeat &amp; increase maintenance infusion by 50 mcg/kg/min to max of 300 mcg/kg/min Once desired response is achieved, continue maintenance infusion Usual maintenance infusion: 50-300 mcg/kg/min</td>
<td>Adverse Reactions: CV effects (hypotension that usually resolves w/in 30 min after decrease in dose or infusion is stopped, peripheral ischemia); CNS effects (dizziness, somnolence, confusion, headache); GI effects (N/V); Local effect (pain on injection); Misc effects (diaphoresis); Less common misc effects: HF, bronchospasm, severe bradycardia/asystole, skin necrosis from extravasation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Special Instructions: Monitor BP during therapy; Avoid in patients w/ sinus bradycardia, heart block &gt;1st degree, cardiogenic shock, bronchial asthma, uncompensated cardiac failure, hypotension; Use w/ caution in compensated HF &amp; monitor for worsening of the condition, also use w/ caution in patients w/ peripheral vascular disease (PVD) or DM; Esmolol can mask signs of thyrotoxicosis</td>
</tr>
</tbody>
</table>

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## Dosage Guidelines

### ANTIHYPERTENSIVES (IV) (CONT’D)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
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</thead>
<tbody>
<tr>
<td><strong>Beta-Blockers (cont’d)</strong></td>
<td></td>
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</tr>
<tr>
<td>Labetalol</td>
<td>2 mg/min IV infusion titrated to response or 50 mg IV over ≥1 min. May be repeated every 5 min until desired response is achieved</td>
<td><strong>Max cumulative dose:</strong> 300 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Adverse Reactions</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- CV effects (orthostatic hypotension, moderate hypotension, may cause or exacerbate CHF, arrhythmias have occurred; rarely heart block); CNS effects (drowsiness, dizziness, mild paresthesia); GI effects (N/V); rarely Hepatic effects (elevated LFT, jaundice, hepatitis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Special Instructions</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Monitor BP during therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Avoid in patients w/ heart block &gt;1st degree, cardiogenic shock, bronchial asthma, severe bradycardia, hypotension, overt cardiac failure</td>
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<tr>
<td></td>
<td></td>
<td>- Use w/ caution in compensated HF &amp; monitor for worsening of the condition, in patients w/ PVD or DM, use w/ caution in patients w/ pheochromocytoma &amp; in patients w/ impaired hepatic function</td>
</tr>
</tbody>
</table>

### Calcium Antagonist

<table>
<thead>
<tr>
<th>Nicardipine</th>
<th>Initial dose: 5 mg/hr IV infusion Increase infusion rate every 15 min as needed until desired response is achieved</th>
<th>Max dose: 15 mg/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Adverse Reactions</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- CV effects (hypotension, depression of cardiac function, worsening heart failure, edema, flushing, tachycardia); GI effects (N/V, constipation); CNS effects (headache, dizziness)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Special Instructions</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Contraindicated in patients w/ overt decompensated heart failure</td>
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<tr>
<td></td>
<td>- Use w/ caution in patients w/ HF, hepatic impairment or reduced hepatic blood flow, patients w/ portal hypertensive, patients w/ impaired renal function</td>
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</tr>
</tbody>
</table>

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### Dosage Guidelines

#### Direct Vasodilators

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<thead>
<tr>
<th>Drug</th>
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<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydralazine</td>
<td>5-10 mg slow IV inj</td>
<td>May repeat if required after 20-30 min or 200-300 mcg/min continuous IV infusion</td>
</tr>
<tr>
<td></td>
<td>Maintenance dose: 50-150 mcg/min IV infusion</td>
<td></td>
</tr>
<tr>
<td>Sodium nitroprusside</td>
<td>Initial dose: 0.3-1.5 mcg/kg/min IV infusion</td>
<td>Max dose: 8 mcg/kg/min</td>
</tr>
<tr>
<td>(Na nitroprusside, Nitroprusside)</td>
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</tr>
</tbody>
</table>

#### Adverse Reactions
- CV effects (tachycardia, palpitations, angina, flushing, postural hypotension, fluid retention, edema); GI effects (anorexia, N/V, diarrhea); Misc effects (dizziness, nasal congestion, tremor, muscle cramps, lacrimation)
- Less common: Pyridoxine depletion w/ resulting peripheral neuropathy; Hematologic effects (blood dyscrasia, hemolytic anemia); Hepatic effect (hepatotoxicity); GU effects (difficulty in urinating, glomerulonephritis); CNS effects (depression, anxiety); GI effects (paralytic ileus, constipation); Hypersensitivity reactions

#### Special Instructions
- Avoid in patients w/ severe tachycardia, heart failure w/ high cardiac output, dissecting aortic aneurysm, cor pulmonale, or myocardial insufficiency due to mechanical obstruction, idiopathic SLE & related disorders
- Use w/ caution in patients w/ ischemic heart disease, patients w/ recent MI, patients w/ heart failure, impaired renal or hepatic function

#### Sodium nitroprusside

- Initial dose: 0.3-1.5 mcg/kg/min IV infusion
- Adjust gradually until desired response is achieved
- Max dose: 8 mcg/kg/min
- Initial dose: 0.3-1.5 mcg/kg/min IV infusion
- Adjust gradually until desired response is achieved
- Max dose: 8 mcg/kg/min

#### Adverse Reactions
- Adverse effects are typically either due to hypotensive effects or from excessive cyanide accumulation
- These effects may be reduced w/ a decrease in infusion rate: GI effects (N/V, abdominal pain); CNS effects (appréhension, headache, dizziness, restlessness); CV effects (retrosternal discomfort, palpitations); Misc effects (perspiration, muscle twitching)
- Excessive cyanide may result in: Tachycardia, sweating, hyperventilation, arrhythmias & metabolic acidosis; methemoglobinemia may also occur
- Thiocyanate may cause: Tinnitus, miosis, hyperreflexia, confusion, hallucinations & convulsions have been reported

#### Special Instructions
- BP & acid-base balance should be monitored closely
- Avoid extravasation
- Avoid in compensatory hypertension
- Use w/ caution not at all in hepatic impairment & in patients w/ low plasma cobalamin conc or Leber’s optic atrophy
- Use w/ caution in patients w/ impaired cerebrovascular circulation, patients w/ hypothyroidism
- If continued for >72 hr, plasma concentrations of cyanide should be monitored
- When discontinuing, reduce dose slowly

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### Dosage Guidelines

#### DIURETIC

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<thead>
<tr>
<th>Drug</th>
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<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Osmotic Diuretic</strong></td>
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<tr>
<td>Mannitol</td>
<td>As a 15-25% soln: 0.25-2 g/kg IV infusion over 30-60 min</td>
<td>Adverse Reactions: Circulatory overload, CHF, headache, convulsions, chills, dizziness, rash, fluid &amp; electrolyte imbalance, water intoxication, dehydration &amp; hypovolemia secondary to rapid diuresis, N/V, pulmonary edema, allergic reactions. Special Instructions: Do not use until renal function adequacy &amp; urine flow is established. Do not use for &gt;5 days because of adverse rebound phenomenon. Serum osmolality goal is: &gt;310 mOsm/L &amp; &lt;340 mOsm/L.</td>
</tr>
</tbody>
</table>

#### MEDICATIONS USED TO INCREASE LOW BP

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac Drug</strong></td>
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</tr>
<tr>
<td>Dopamine</td>
<td>Initial dose: 2-5 mcg/kg/min IV infusion Increase by 5-10 mcg/kg/min until desired response is achieved</td>
<td>Adverse Reactions: CV effects (ectopic beats, tachycardia, palpitations, anginal pain, hypotension, vasoconstriction); Misc effects (N/V, headache, dyspnea). Less common: CV effects (bradycardia, cardiac conduction abnormalities, hypertension may occur if overdosage); Misc effects (piloerection, azotemia). Special Instructions: Hypovolemia should be corrected prior to treatment. Avoid in patients w/ pheochromocytoma or hyperthyroidism &amp; in the presence of uncorrected tachyrrhythmias or ventricular fibrillation. Use w/ caution &amp; in low dose in patients w/ shock secondary to MI, patients w/ history of PVD are at increased risk of ischemia of the extremities. When discontinuing it may be necessary to gradually decrease the dose while expanding blood volume w/ IV fluids to prevent hypotension.</td>
</tr>
</tbody>
</table>

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### Dosage Guidelines

**MEDICATIONS USED TO INCREASE LOW BP (CONT’D)**

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<thead>
<tr>
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<th>Remarks</th>
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</thead>
<tbody>
<tr>
<td><strong>Vasoconstrictors</strong></td>
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</tbody>
</table>
| Norepinephrine (Noradrenaline) | *Initial dose:* 8-12 mcg/min IV infusion titrated to response  
*Usual dose:* 2-4 mcg/min | *Adverse Reactions:*  
- CV effects (hypertension, reflex bradycardia, peripheral ischemia which may be severe); CNS effects (headache, weakness, dizziness, tremor, restlessness, anxiety); Resp effects (resp difficulty, apnea); Misc effects (pallor, intense sweating, vomiting)  
- Severe local adverse effects may occur & extravasation must be avoided  
*Special Instructions:*  
- Correction of hypovolemia prior to administration is recommended  
- Large vein should be used for IV infusion & use very dilute solutions  
- Avoid in the presence of hypertension & monitor BP closely  
- Use w/ caution in patients w/ hypoxia or hypercapnia, cardiac arrhythmias are more likely in these patients  
- Use w/ caution in hyperthyroidism  
- When discontinuing, decrease dose slowly & observe patient for too rapid fall in BP |
| Phenylephrine               | *Initial dose:* 100-180 mcg/min IV infusion  
*Reduce to 40-60 mcg/min according to response* | *Adverse Reactions:*  
- Reflex bradycardia, excitability, hypertension, arrhythmias, peripheral/visceral vasoconstriction, decreased cardiac output, headache, anxiety, decreased renal perfusion, respiratory distress  
*Special Instructions:*  
- Avoid in patients w/ ventricular arrhythmias  
- Use w/ caution in patients w/ hyperthyroidism, partial heart block, bradycardia, myocardial disease or severe coronary artery disease & the elderly |
| **Phenylephrine**           |                                                                        |                                                                         |
| **MUSCLE RELAXANTS**        |                                                                        |                                                                         |
| Pancuronium                 | *Initial dose:* 40-100 mcg/kg IV  
*Incremental doses:* 10-20 mcg/kg IV | *Adverse Reactions:*  
- Tachycardia, elevated BP & cardiac output, edema, skin flushing, rash, excessive salivation, profound muscle weakness, bronchospasm, hypersensitivity reactions  
*Special Instructions:*  
- Use w/ caution in patients w/ renal or hepatic impairment |
| Vecuronium                  | *Initial dose:* 80-100 mcg/kg IV  
*Incremental doses:* 30-50 mcg/kg IV |                                                                         |

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*Please see the end of this section for reference list.*