

# Overview of Toxicology in Hospital Medicine

Toxicology in hospital medicine involves the recognition, diagnosis, and management of acute poisonings and overdoses, which are common presentations in the inpatient setting, particularly in suicide attempts. Overdoses account for ~2.5 million emergency department visits annually in the U.S. (CDC, 2023), with significant morbidity and mortality if not addressed promptly. Common ingestants include medications like acetaminophen, salicylates, opioids, tricyclic antidepressants (TCAs), baclofen, clonidine, beta-blockers, benzodiazepines, calcium channel blockers (CCBs), as well as anticholinergics, toxic alcohols (e.g., methanol, ethylene glycol), and illicit drugs (e.g., cocaine). Hospitalists play a critical role in early suspicion, stabilization, antidote administration, and coordination with toxicology specialists. This guide provides a comprehensive overview of toxicology, focusing on common ingestants, their physical and laboratory manifestations, when to suspect ingestion, treatment and reversal strategies (including specific antidotes), hospitalist implications, and includes tables and clinical scenarios for practical application.

## Pathophysiology of Common Ingestants

### Acetaminophen:

**Mechanism:** Overdose depletes glutathione, leading to accumulation of NAPQI (toxic metabolite), causing hepatic necrosis.

**Toxicity Threshold:** >150 mg/kg or >7.5 g in adults (single ingestion).

### Salicylates (Aspirin):

**Mechanism:** Uncouples oxidative phosphorylation, causing metabolic acidosis, respiratory alkalosis, and direct CNS toxicity.

**Toxicity Threshold:** >300 mg/kg (acute), chronic toxicity at lower doses.

### Opioids:

**Mechanism:** Mu-receptor agonism causes respiratory depression, sedation, and miosis.

**Common Agents:** Heroin, oxycodone, fentanyl (highly potent).

## Tricyclic Antidepressants (TCAs):

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**Mechanism:** Blocks sodium channels (QRS widening, arrhythmias), inhibits GABA (seizures), anticholinergic effects (delirium), alpha-blockade (hypotension).

**Common Agents:** Amitriptyline, nortriptyline, imipramine.

## Baclofen:

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**Mechanism:** GABA-B agonist, causes CNS depression, respiratory depression, and muscle hypotonia.

**Toxicity:** Overdose leads to coma, seizures, and profound weakness.

## Clonidine:

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**Mechanism:** Alpha-2 agonist, causes CNS depression, bradycardia, and hypotension by reducing sympathetic outflow.

**Toxicity:** Mimics opioid toxidrome (miosis, sedation), often used in suicide attempts.

## Beta-Blockers:

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**Mechanism:** Blocks beta-adrenergic receptors, leading to bradycardia, hypotension, and cardiogenic shock.

**Common Agents:** Metoprolol, atenolol, propranolol (lipophilic, CNS effects).

## Benzodiazepines:

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**Mechanism:** Enhances GABA-A receptor activity, causing CNS depression, sedation, and respiratory depression.

**Common Agents:** Diazepam, lorazepam, alprazolam.

## Calcium Channel Blockers (CCBs):

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**Mechanism:** Blocks L-type calcium channels, causing bradycardia, hypotension, and cardiogenic shock; non-dihydropyridines (e.g., verapamil) also cause conduction delays.

**Common Agents:** Amlodipine, diltiazem, verapamil.

## Anticholinergics:

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**Mechanism:** Block muscarinic receptors, leading to "hot as a hare, dry as a bone, red as a beet, blind as a bat, mad as a hatter" syndrome.

**Common Agents:** Diphenhydramine, atropine, scopolamine (also TCAs).

## Alcohols (Methanol, Ethylene Glycol):

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**Mechanism:** Metabolized to toxic acids (formic acid for methanol, oxalic acid for ethylene glycol), causing metabolic acidosis, organ damage.

**Sources:** Methanol (windshield fluid), ethylene glycol (antifreeze).

## Cocaine:

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**Mechanism:** Sympathomimetic (blocks catecholamine reuptake), causes vasoconstriction, tachycardia, and CNS excitation.

**Toxicity:** Cardiovascular (MI, arrhythmias), neurologic (seizures, stroke).

## When to Suspect Ingestion

### Clinical Clues:

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- Altered mental status (e.g., sedation in opioids/benzodiazepines, agitation in cocaine, delirium in TCAs/anticholinergics).
- Unexplained metabolic derangements (e.g., anion gap acidosis in alcohols, mixed acid-base disorder in salicylates).
- Toxin-specific symptoms (e.g., miosis in opioids/clonidine, anticholinergic syndrome, bradycardia in beta-blockers/CCBs).

### History:

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- Access to medications/illicit drugs (e.g., recent prescription, suicidal ideation, history of substance use).
- Recent ingestion (e.g., antifreeze exposure, alcohol binging).
- Delayed presentation (e.g., acetaminophen toxicity 24-48h post-ingestion, baclofen coma 12-24h post-ingestion).

### Patient Populations:

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- Suicidal patients (e.g., TCAs, clonidine, beta-blockers, benzodiazepines, CCBs).

- Substance use disorders (e.g., opioids, cocaine, benzodiazepines).
- Accidental exposure (e.g., children, alcohols, baclofen in spasticity patients).

## Physical and Laboratory Manifestations

### Acetaminophen:

**Physical:** Early: Asymptomatic or nausea/vomiting; 24-48h: RUQ pain, jaundice (hepatic failure); >72h: Encephalopathy, coagulopathy.

**Labs:** AST/ALT >1,000 U/L (peaks 48-72h), INR >2, Cr rise (renal failure), lactate >3.5 mmol/L (severe toxicity).

### Salicylates:

**Physical:** Tinnitus, vertigo, nausea, hyperpnea (respiratory alkalosis), fever, confusion, seizures (severe).

**Labs:** Mixed acid-base disorder (respiratory alkalosis + metabolic acidosis), anion gap >12 mEq/L, salicylate level >30 mg/dL (acute toxicity), hypoglycemia, hypokalemia.

### Opioids:

**Physical:** Miosis, respiratory depression (RR <12/min), sedation, bradycardia, hypotension.

**Labs:** Hypoxemia (PaO<sub>2</sub> <60 mmHg), hypercapnia (PaCO<sub>2</sub> >50 mmHg), UDS positive for opiates (may miss fentanyl).

### Tricyclic Antidepressants (TCAs):

**Physical:** Anticholinergic syndrome (fever, dry skin, flushed skin, dilated pupils, delirium), seizures, hypotension, arrhythmias.

**Labs:** ECG: QRS >100 ms, QT prolongation, terminal R wave in aVR, UDS positive for TCAs, metabolic acidosis (severe).

### Baclofen:

**Physical:** Coma, respiratory depression, hypotonia, seizures, bradycardia, hypothermia.

**Labs:** Normal acid-base (unless respiratory depression), EEG: Encephalopathy, UDS negative.

### Clonidine:

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**Physical:** Miosis, sedation, bradycardia, hypotension, respiratory depression (mimics opioid toxidrome).

**Labs:** Normal acid-base, UDS negative, glucose normal (unlike hypoglycemia in beta-blockers).

### Beta-Blockers:

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**Physical:** Bradycardia, hypotension, cardiogenic shock, altered mental status (lipophilic agents like propranolol), bronchospasm (non-selective agents).

**Labs:** Hypoglycemia (non-selective agents), ECG: Bradycardia, AV block, UDS negative.

### Benzodiazepines:

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**Physical:** Sedation, respiratory depression, ataxia, slurred speech, coma (severe).

**Labs:** Hypoxemia, hypercapnia, UDS positive for benzodiazepines.

### Calcium Channel Blockers (CCBs):

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**Physical:** Bradycardia, hypotension, cardiogenic shock, altered mental status, hyperglycemia (insulin resistance).

**Labs:** ECG: AV block, bradycardia, hyperglycemia, lactate >2 mmol/L (shock).

### Anticholinergics:

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**Physical:** Fever, dry skin/mouth, flushed skin, dilated pupils, delirium, tachycardia, urinary retention.

**Labs:** Normal acid-base, ECG: QRS widening (TCAs), QT prolongation, UDS may detect TCAs.

### Alcohols (Methanol, Ethylene Glycol):

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**Physical:** Methanol: Visual blurring, blindness, coma; Ethylene Glycol: Flank pain, renal failure, coma.

**Labs:** Anion gap metabolic acidosis (gap >12 mEq/L), osmolar gap >10 mOsm/kg, methanol/ethylene glycol levels, oxalate crystals (ethylene glycol), hypocalcemia (ethylene glycol).

## Cocaine:

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**Physical:** Agitation, seizures, hypertension, tachycardia, hyperthermia, chest pain (MI), mydriasis.

**Labs:** UDS positive for cocaine, troponin rise (MI), ECG: STEMI, arrhythmias, CK rise (rhabdomyolysis).

## Treatment and Reversal Strategies

### General Principles:

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**Stabilization:** Address ABCs (airway, breathing, circulation), fluids (NS 1-2 L bolus), monitor vitals (q1h in severe cases).

**Decontamination:** Activated charcoal (1 g/kg PO) if <1-2h post-ingestion (not for alcohols, caustic agents, or if altered mental status without airway protection).

**Enhanced Elimination:** Hemodialysis for severe cases (e.g., methanol, ethylene glycol, salicylates).

### Specific Treatments:

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- Acetaminophen:
  - **Antidote:** N-acetylcysteine (NAC).
  - **Dosing:** 150 mg/kg IV over 1h, then 50 mg/kg over 4h, then 100 mg/kg over 16h (total 21h).
  - **Indication:** Acetaminophen level above Rumack-Matthew nomogram line (4h post-ingestion), AST/ALT rise, or unknown ingestion time with toxicity.
  - **Supportive:** Fluids, monitor LFTs, INR q6-12h.
- Salicylates:
  - **Antidote:** Sodium bicarbonate (alkalinization).
  - **Dosing:** 1-2 mEq/kg IV bolus, then 100-150 mEq in 1 L D5W at 1.5-2x maintenance rate (target urine pH 7.5-8.0).
  - **Indication:** Salicylate level >30 mg/dL (acute), >20 mg/dL (chronic), severe symptoms.
  - **Enhanced Elimination:** Hemodialysis (level >100 mg/dL, refractory acidosis, renal failure).

- **Supportive:** Glucose (hypoglycemia), K<sup>+</sup> replacement (hypokalemia).
- Opioids:
  - **Antidote:** Naloxone.
  - **Dosing:** 0.4-2 mg IV q2-3min (titrate to RR >12/min), infusion if long-acting (e.g., 2/3 effective dose/h).
  - **Indication:** Respiratory depression (RR <12/min), miosis, sedation.
  - **Supportive:** Ventilation (bag-mask, intubation if needed), monitor for withdrawal.
- Tricyclic Antidepressants (TCAs):
  - **Antidote:** Sodium bicarbonate (for QRS widening).
  - **Dosing:** 1-2 mEq/kg IV bolus, repeat q5-10min until QRS <100 ms (target serum pH 7.45-7.55).
  - **Indication:** QRS >100 ms, hypotension, arrhythmias.
  - **Treatment for Anticholinergic Effects:** Physostigmine (if no QRS widening).
  - **Dosing:** 0.5-2 mg IV over 5min, repeat q10-15min if needed (max 4 mg).
  - **Indication:** Severe delirium, seizures (avoid if QRS >100 ms due to arrhythmia risk).
  - **Supportive:** Benzodiazepines (lorazepam 1-2 mg IV q15min) for seizures, fluids/vasopressors (hypotension).
- Baclofen:
  - **Antidote:** None specific.
  - **Treatment: Supportive:** Intubation for respiratory depression, benzodiazepines (lorazepam 1-2 mg IV) for seizures, fluids for hypotension.
  - **Enhanced Elimination:** Hemodialysis (effective for baclofen due to renal clearance, especially in renal failure).
  - **Supportive:** Monitor EEG (encephalopathy), cooling (hypothermia).
- Clonidine:
  - **Antidote:** Naloxone (partial benefit).
  - **Dosing:** 0.4-2 mg IV q2-3min (may improve sedation, respiratory depression).
  - **Indication:** Sedation, respiratory depression (mimics opioid toxidrome).
  - **Treatment:** Atropine 0.5-1 mg IV (bradycardia), fluids/vasopressors (norepinephrine 5-20 µg/min IV) for hypotension.
  - **Supportive:** Monitor for rebound hypertension (clonidine withdrawal).
- Beta-Blockers:
  - **Antidote:** Glucagon (increases cardiac contractility via cAMP).
  - **Dosing:** 3-5 mg IV bolus over 1-2min, then 2-5 mg/h infusion.
  - **Indication:** Bradycardia, hypotension, cardiogenic shock.

- **Treatment:** atropine 0.5-1 mg IV q3-5min (bradycardia, max 3 mg).
- **High-dose insulin (HDI):** 1 unit/kg IV bolus, then 0.5-1 unit/kg/h infusion (improves cardiac contractility).
- **Vasopressors:** Epinephrine 2-10 µg/min IV (hypotension).
- **Supportive:** Glucose (hypoglycemia), monitor ECG (AV block).
- Benzodiazepines:
  - **Antidote:** Flumazenil.
  - **Dosing:** 0.2 mg IV q1min (max 1 mg), infusion if needed (0.1-0.5 mg/h).
  - **Indication:** Respiratory depression, coma (avoid in chronic users, seizure risk).
  - **Supportive:** Ventilation (intubation if severe), fluids, monitor for withdrawal.
- Calcium Channel Blockers (CCBs):
  - **Antidote:** Calcium (increases cardiac contractility).
  - **Dosing:** Calcium gluconate 1-2 g IV (10% solution, 10-20 mL) q10-20min, or infusion 0.2-0.4 mL/kg/h.
  - **Indication:** Bradycardia, hypotension, shock.
  - **Treatment: High-dose insulin (HDI):** 1 unit/kg IV bolus, then 0.5-1 unit/kg/h.
  - **Vasopressors:** Norepinephrine 5-20 µg/min IV, epinephrine 2-10 µg/min IV.
  - **Supportive:** Atropine (bradycardia), monitor glucose (hyperglycemia).
- Anticholinergics:
  - **Antidote:** Physostigmine (cholinesterase inhibitor).
  - **Dosing:** 0.5-2 mg IV over 5min, repeat q10-15min if needed (max 4 mg).
  - **Indication:** Severe delirium, seizures (avoid in TCAs with QRS widening).
  - **Supportive:** Benzodiazepines (lorazepam 1-2 mg IV q15min) for agitation/seizures, cooling (hyperthermia), sodium bicarbonate (TCA QRS widening >100 ms).
- Alcohols (Methanol, Ethylene Glycol):
  - **Antidote:** Fomepizole (ADH inhibitor).
  - **Dosing:** 15 mg/kg IV loading, then 10 mg/kg q12h x 4 doses, then 15 mg/kg q12h (adjust for dialysis).
  - **Indication:** Suspected ingestion, anion gap acidosis, osmolar gap >10 mOsm/kg.
  - **Alternative Antidote:** Ethanol (if fomepizole unavailable, target level 100-150 mg/dL).
  - **Enhanced Elimination:** Hemodialysis (pH <7.3, renal failure, methanol level >50 mg/dL, ethylene glycol level >50 mg/dL).



- **Supportive:** Folate 50 mg IV q6h (methanol), thiamine 100 mg IV (ethylene glycol), calcium gluconate (ethylene glycol hypocalcemia).
- Cocaine:
  - **Antidote:** None specific.
  - **Treatment:** Benzodiazepines (lorazepam 2-4 mg IV q15min) for agitation/seizures.
  - Nitroglycerin 0.4 mg SL q5min (chest pain/MI), aspirin 325 mg PO (MI).
  - Avoid beta-blockers (unopposed alpha stimulation, worsens hypertension).
  - **Supportive:** Cooling (hyperthermia), fluids, monitor ECG (arrhythmias).

## Hospital Medicine Implications

### Early Suspicion:

Suspect toxicology in unexplained altered mental status, metabolic derangements, or toxidrome (e.g., anticholinergic, opioid, sympathomimetic).

Obtain history from family/EMS (e.g., pill bottles, drug paraphernalia).

### Consultations:

**Toxicology/Poison Control:** For antidote dosing, complex cases (e.g., baclofen, methanol).

**Nephrology:** For dialysis (e.g., methanol, salicylates, ethylene glycol).

**Cardiology:** For beta-blocker/CCB toxicity (bradycardia), cocaine-related MI/arrhythmias.

**Psychiatry:** Post-stabilization for suicidal ideation (common in TCAs, clonidine overdoses).

### Monitoring:

Vitals q1h (HR, BP, RR, temp, SpO2).

Labs q4-6h (lactate, anion gap, LFTs, Cr, salicylate levels, glucose in beta-blockers/CCBs).

ECG q4h (QRS, QT prolongation in TCAs, bradycardia in beta-blockers/CCBs, cocaine).

## Discharge Planning:

**Supportive Care:** Ensure mental health follow-up (if intentional overdose).

**Education:** Avoid re-exposure, safe medication storage.

**Follow-Up:** Primary care, psychiatry within 1 week.

**Table:** Expanded Common Ingestants, Manifestations, and Management

Ingestant	When to Suspect	Physical Manifestations	Laboratory Manifestations	Treatment/ Reversal	Notes
Acetaminophen	Overdose history, delayed RUQ pain	Nausea, jaundice, encephalopathy	AST/ALT >1,000 U/L, INR >2, Cr rise	NAC 150 mg/kg IV over 1h, then 50 mg/kg over 4h, 100 mg/kg over 16h	Use Rumack-Matthew nomogram, monitor LFTs q6h.
Salicylates	Tinnitus, hyperpnea, confusion	Fever, seizures, hyperventilation	Respiratory alkalosis + metabolic acidosis, salicylate >30 mg/dL	Sodium bicarbonate (urine pH 7.5-8.0), hemodialysis (level >100 mg/dL)	Monitor K <sup>+</sup> , glucose, acid-base q4h.
Opioids	Miosis, respiratory depression	Sedation, bradycardia, hypotension	Hypoxemia, hypercapnia, UDS positive	Naloxone 0.4-2 mg IV q2-3min, infusion if needed	Titrate to RR >12/min, avoid over-reversal (withdrawal).
Tricyclic Antidepressants (TCAs)	Delirium, seizures, suicide attempt	Anticholinergic syndrome, hypotension, arrhythmias	ECG: QRS >100 ms, terminal R wave in aVR, acidosis	Sodium bicarbonate (QRS >100 ms), physostigmine (delirium, if no QRS widening)	Benzodiazepines for seizures, avoid physostigmine if QRS >100 ms.
Baclofen	Coma, hypotonia, spasticity patient	Respiratory depression, seizures, bradycardia, hypothermia	Normal acid-base, EEG: Encephalopathy	Supportive (intubation, benzodiazepines), hemodialysis (renal failure)	Monitor EEG, avoid flumazenil (seizure risk).
Clonidine	Sedation, miosis, suicide attempt	Bradycardia, hypotension, respiratory depression	Normal acid-base, UDS negative	Naloxone 0.4-2 mg IV, atropine 0.5-1 mg IV, vasopressors	Monitor for rebound hypertension (withdrawal).
Beta-Blockers	Bradycardia, hypotension, suicide attempt	Cardiogenic shock, altered mental status, bronchospasm	Hypoglycemia, ECG: Bradycardia, AV block	Glucagon 3-5 mg IV, high-dose insulin, vasopressors	Monitor glucose, ECG, avoid unopposed alpha-agonists.

Ingestant	When to Suspect	Physical Manifestations	Laboratory Manifestations	Treatment/ Reversal	Notes
Benzodiazepines	Sedation, respiratory depression	Ataxia, slurred speech, coma (severe)	Hypoxemia, hypercapnia, UDS positive	Flumazenil 0.2 mg IV q1min (max 1 mg), supportive	Avoid flumazenil in chronic users (seizure risk).
Calcium Channel Blockers (CCBs)	Bradycardia, hypotension, suicide attempt	Cardiogenic shock, altered mental status	Hyperglycemia, ECG: AV block, lactate >2 mmol/L	Calcium gluconate 1-2 g IV, high-dose insulin, vasopressors	Monitor glucose, ECG, lactate.
Anticholinergics	Delirium, dry skin, fever	Flushed skin, dilated pupils, tachycardia	Normal acid-base, QRS widening (TCAs)	Physostigmine 0.5-2 mg IV, benzodiazepines for agitation	Avoid physostigmine if QRS >100 ms (TCA).
Alcohols (Methanol)	Visual changes, coma	Blindness, respiratory depression	Anion gap acidosis, osmolar gap, formic acid	Fomepizole 15 mg/kg IV, hemodialysis (pH <7.3)	Folate 50 mg IV q6h, monitor vision.
Alcohols (Ethylene Glycol)	Flank pain, renal failure	Coma, seizures, respiratory failure	Anion gap acidosis, oxalate crystals, hypocalcemia	Fomepizole 15 mg/kg IV, hemodialysis (level >50 mg/dL)	Thiamine 100 mg IV, calcium gluconate for hypocalcemia.
Cocaine	Agitation, chest pain, seizures	Hypertension, tachycardia, hyperthermia	UDS positive, troponin rise, CK rise	Benzodiazepines (lorazepam 2-4 mg IV), nitroglycerin, aspirin	Avoid beta-blockers, monitor ECG, CK.

## Clinical Scenarios

### Scenario 1: Young Female with Acetaminophen Overdose

- **Presentation:** A 20-year-old female presents 6h after ingesting 15 g of acetaminophen in a suicide attempt. She reports nausea and vomiting. Exam shows T 37°C, BP 110/70 mmHg, HR 90 bpm, RR 18/min, RUQ tenderness.
- **Diagnostic Workup:** 4h acetaminophen level: 200 µg/mL (above nomogram line), labs: AST 500 U/L, ALT 600 U/L, INR 1.5, Cr 1.0 mg/dL, lactate 2.0 mmol/L.
- **Diagnosis:** Acetaminophen overdose → High level, early hepatic injury.
- **Management:** Admit to medicine (overdose). Start NAC 150 mg/kg IV over 1h, then 50 mg/kg over 4h, 100 mg/kg over 16h. Fluids (NS 1 L). Consult toxicology: NAC continued. Monitor LFTs, INR q6h. Day 3: AST/ALT peak at 2,000 U/L, INR 2.0, stabilizes by day 5. Discharged with psychiatry follow-up.

## Scenario 2: Middle-Aged Male with Clonidine Overdose

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- **Presentation:** A 45-year-old male presents 2h after ingesting 5 mg of clonidine in a suicide attempt. He is sedated with miosis. Exam shows T 36.5°C, BP 80/50 mmHg, HR 40 bpm, RR 10/min, GCS 12.
- **Diagnostic Workup:** Labs: Normal acid-base, glucose 90 mg/dL, UDS negative, ECG: Sinus bradycardia.
- **Diagnosis:** Clonidine overdose → Sedation, miosis, bradycardia, hypotension.
- **Management:** Admit to ICU (overdose). Start naloxone 0.4 mg IV q2min (total 1.2 mg, partial response). Atropine 0.5 mg IV q5min (total 1.5 mg, HR 60 bpm). Fluids (NS 1 L), norepinephrine 5 µg/min IV (MAP 70 mmHg). Consult toxicology: Monitor for rebound hypertension. Day 2: BP 120/80 mmHg, HR 70 bpm, GCS 15, discharged with psychiatry follow-up.

## Scenario 3: Elderly Female with Beta-Blocker Overdose

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- **Presentation:** A 65-year-old female presents 1h after ingesting 200 mg of propranolol in a suicide attempt. She is hypotensive and bradycardic. Exam shows T 37°C, BP 70/40 mmHg, HR 35 bpm, RR 16/min, GCS 14.
- **Diagnostic Workup:** Labs: Glucose 60 mg/dL, Cr 1.2 mg/dL, lactate 3.0 mmol/L, ECG: Sinus bradycardia, 1st-degree AV block.
- **Diagnosis:** Beta-blocker overdose → Bradycardia, hypotension, hypoglycemia.
- **Management:** Admit to ICU (overdose). Start glucagon 5 mg IV bolus, then 3 mg/h infusion (HR 50 bpm). High-dose insulin: 1 unit/kg IV bolus, then 0.5 unit/kg/h. Fluids (NS 1 L), epinephrine 5 µg/min IV (MAP 70 mmHg). Glucose (D50 50 mL IV for hypoglycemia). Consult toxicology: Monitor ECG, glucose q2h. Day 2: HR 60 bpm, BP 110/70 mmHg, discharged with psychiatry follow-up.