

## Toxicology

Acetaminophen Overdose																				
Toxic Dose	200 mg/kg (7.5-10 g in older pts) as a single acute overdose																			
Pathophysiology	Saturation of glucuronidation/sulfate conjugation pathway → ↑ metabolism via P450 pathway and depletion of glutathione → build up of toxic NAPQI → hepatotoxicity +/- renal toxicity																			
Symptoms	See chart below																			
Evaluation	Acetaminophen levels (at ≥ 4 hours post-ingestion, LFTs, coags, electrolytes, BUN/Cr, UA w/ tox screen (serum and urine), urine pregnancy for females)																			
Management	<ul style="list-style-type: none"><li>•Activated charcoal if w/i 1-2 hrs of ingestion and no contraindications (unprotected airway and decreased LOC)</li><li>•Goal: Initiate NAC ≤ 8 hours of ingestion (or ASAP if &gt;8 hours post-ingestion)</li><li>•APAP level → apply NOMOGRAM → estimate risk of hepatotoxicity</li><li>•***KEY POINT: NOMOGRAM can only be used for: single acute ingestion, known time of ingestion, ingestion w/i 24hrs of presentation. Also, caution if co-ingestants that may affect GI motility***<ul style="list-style-type: none"><li>■ Risk of hepatotoxicity → give N-acetyl cysteine</li><li>■ IV: loading dose of 150mg/kg over 1 hour, then 50 mg/kg over 4 hours, then 100 mg/kg over 16 hours; check APAP levels, LFTs, coags 2 hours before 16h infusion is scheduled to end</li><li>■ PO/NG: Loading dose 140mg/kg, then 70mg/kg 14hrs x24 hours</li><li>■ Guidelines for stopping NAC: clinically well, improving LFTs, normalizing coags, APAP level&lt;10 (if patient does not meet guidelines, continue NAC (100mg/kg IV over 16 hours) until they meet criteria.)</li></ul></li></ul>																			
Rule of 150	<ul style="list-style-type: none"><li>•Potentially toxic dose: 150mg/kg</li><li>•Treatment line: 150mcg/mL at 4 hours</li><li>•Loading dose of NAC 150mg/kg over one hour</li></ul> <table><tr><th colspan="3">Acute APAP Toxicity: 4 stages</th></tr><tr><th></th><th>Symptoms</th><th>Labs</th></tr><tr><td>Stage 1: 0-24 hours</td><td>N/V, diaphoresis, malaise <b>May be asymptomatic</b></td><td>Labs, PE generally normal</td></tr><tr><td>Stage 2: 24-72 hours</td><td>Initial symptoms resolve RUQ pain, liver enlargement/tenderness</td><td>↑ AST/ALT, ↑ PT/INR, renal dysfunction, ↑ amylase</td></tr><tr><td>Stage 3: 72-96 hours</td><td>N/V, diaphoresis return<ul style="list-style-type: none"><li>■ Jaundice, hepatic encephalopathy, hyperammonemia, bleeding, hypoglycemia, lactic acidosis</li><li>■ Renal failure, multi organ failure, death</li></ul></td><td>LFTs peak</td></tr><tr><td>Stage 4*: 4-14 days</td><td>Recovery phase Slow normalization of symptoms and lab values (Symptoms typically normalize well before transaminases do)</td><td>Slow normalization</td></tr></table>		Acute APAP Toxicity: 4 stages				Symptoms	Labs	Stage 1: 0-24 hours	N/V, diaphoresis, malaise <b>May be asymptomatic</b>	Labs, PE generally normal	Stage 2: 24-72 hours	Initial symptoms resolve RUQ pain, liver enlargement/tenderness	↑ AST/ALT, ↑ PT/INR, renal dysfunction, ↑ amylase	Stage 3: 72-96 hours	N/V, diaphoresis return <ul style="list-style-type: none"><li>■ Jaundice, hepatic encephalopathy, hyperammonemia, bleeding, hypoglycemia, lactic acidosis</li><li>■ Renal failure, multi organ failure, death</li></ul>	LFTs peak	Stage 4*: 4-14 days	Recovery phase Slow normalization of symptoms and lab values (Symptoms typically normalize well before transaminases do)	Slow normalization
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Aspirin Overdose	
<b>Toxic Dose</b>	150 mg/kg
<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>Stimulates medullary respiratory center → ↑RR, hyperpnea, respiratory alkalosis</li> <li>Inhibits Krebs's cycle enzymes → lactic acidosis, ketoacidosis</li> <li>Inhibits platelet function + vitamin-K dependent clotting factors → coagulopathy</li> </ul>