Over-the-counter Analgesic Toxicity: Exploring the FDA’s Safe Use Initiative
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Frank LoVecchio, DO, MPH, FACEP has no real or apparent conflicts of interest to report.
Learning Objectives

• Evaluate the risks, benefits, and safe use of common analgesics
• Understand the burden and reasons for patient-related medication errors and identify strategies to prevent overdose
• Discuss Advisory Committee recommendations meant to deter overdose and hepatic toxicity
• Recognize the signs and symptoms of overdose from commonly used analgesics and strategies to treat acute toxicity
Scope of the Problem: Acetaminophen

- Acetaminophen is the most widely used antipyretic/analgesic in the United States
  - 8 billion purchased doses of OTC single-ingredient products containing APAP
  - 9.7 billion purchased doses of combination OTC products containing APAP
- Fatal medication errors occurring at home have increased by 564% (1983-2004)

Scope of the Problem: NSAIDs

- >30 million people worldwide consume prescription nonsteroidal anti-inflammatory drugs (NSAIDs) daily
- >100,000 yearly hospitalizations in the US due to NSAID-related complications
- >21,000 salicylate exposures reported to poison centers (2004)

Acetaminophen
Acetaminophen

- ≈80% of people used acetaminophen in last 6 months but only ≈40% knew the liver can be affected
- Far fewer (15%) correctly identified acetaminophen as a component of some Rx opioid analgesics
- Acetaminophen-containing Rx analgesics
  - 11 billion doses
  - 2001—2005: combination Rx use ↑ 38%
  - >182 million prescriptions for combination Rx products
  - Hydrocodone/acetaminophen most frequent

Hepatic Metabolism of Acetaminophen

Conjugation

Glucuronide conjugate (nontoxic) → **Acetaminophen** → N-acetyl-p-benzoquinone imine (NAPQI) (potentially toxic) → Glutathione → Cysteine and mercapturic acid conjugates (nontoxic)

Conjugation

**Acetaminophen** → Sulfate conjugate (nontoxic)
## Routes of Unintentional Adult & Pediatric Overdose

<table>
<thead>
<tr>
<th>ADULT</th>
<th>PEDIATRIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unknowingly ingesting acetaminophen (APAP) from combination products</td>
<td>• Administering wrong pediatric formulation (ie. using infant drops [80 mg/0.8 mL] for children’s suspension [160 mg/5 mL])</td>
</tr>
<tr>
<td>• Unknowingly ingesting APAP from widely used single-ingredient products</td>
<td>• Using multiple products or strengths that cause consumer confusion</td>
</tr>
<tr>
<td></td>
<td>• Incorrect calculation for weight-appropriate dose</td>
</tr>
<tr>
<td></td>
<td>• Incorrect dosing device (i.e., tablespoon instead of teaspoon, dropper versus syringe)</td>
</tr>
</tbody>
</table>

Acetaminophen: Dosing Definitions

- Therapeutic dose defined as $\leq 4\ g$ in adults and $\leq 75\ mg/kg$ in children per 24-hr period
- Acute overdose defined as a toxic amount ($>4\ g$) ingested in $\leq 8\ hrs$
- Repeated supratherapeutic ingestion (RSTI or chronic overdose) refers to multiple ingestions over a period $>8\ hrs$ totaling $>4\ g$ per 24-hr period

Treatment of Acute Overdose

Case Study
Case Study: Acetaminophen Overdose Patient History

- 32-year-old female
- Arrives in emergency department at 9:48 AM
- Complains of bilateral headache, nausea, dizziness, insomnia
- Gets depressed
- Occasional social alcohol use
- No other remarkable past medical history
- Family member reports she ingested 50 x 325 mg acetaminophen early this morning at 12:30 AM
Question

- When NAC is delayed, after what time is increased injury to the liver noted?
  A. 8 to 10 hours
  B. 10 to 18 hours
  C. 18 to 24 hours
  D. 24 to 48 hours
  E. >48 hours
Time Is Liver

- Prompt recognition and treatment of APAP toxicity is essential to prevent morbidity and mortality
- 11/2023 (0.54%) fatalities in those with values above nomogram line and increases in higher-risk patients
- 0 fatalities if NAC started within 16 hrs postingestion

NAC = N-acetylcysteine; AST = aspartate aminotransferase; SEM = standard error of the mean.
Case Study: Physical Examination

- Pulse rate: 74/minute
- Regular heart beats, no murmurs
- Blood pressure: 119/74 mm Hg
- Conscious, but lethargic
- Normoactive bowel
- No tenderness or rebounding pain in abdomen
- Extremities freely movable, no pitting edema
## Presentation: Acute Overdose

<table>
<thead>
<tr>
<th>Stage</th>
<th>Approximate Time Postingestion</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0 to 24 hours</td>
<td>Anorexia, nausea, and vomiting</td>
</tr>
<tr>
<td>II</td>
<td>24 to 72 hours</td>
<td>Right upper quadrant abdominal pain (common); AST, ALT, and, if poisoning is severe, bilirubin and PT (usually reported as the INR) sometimes elevated</td>
</tr>
<tr>
<td>III</td>
<td>72 to 96 hours</td>
<td>Vomiting and symptoms of liver failure; peaking of AST, ALT, bilirubin, and INR; sometimes renal failure and pancreatitis</td>
</tr>
<tr>
<td>IV</td>
<td>&gt;5 days</td>
<td>Resolution of hepatotoxicity or progression to multisystem organ failure (sometimes fatal)</td>
</tr>
</tbody>
</table>

ALT = alanine aminotransferase; PT = prothrombin time; INR = international normalized ratio.

Consider starting acetylcysteine treatment if acetaminophen level will not be available before 8 hr after ingestion. Administer activated charcoal if <4 hr postingestion. Start acetylcysteine and manage in accordance with serum ALT and AST. Determine acetaminophen level at 4 hr postingestion or as soon as possible thereafter. PLOT ON NOMOGRAM. Consider starting acetylcysteine treatment if acetaminophen level will not be available before 8 hr after ingestion. Serum level plots BELOW treatment line. Stop acetylcysteine. Serum level plots ABOVE treatment line. Initiate (or continue) acetylcysteine. Obtain baseline tests (ALT and AST, chemistries) and provide supportive care as indicated. Estimates the time of ingestion. <24 hr since overdose. >24 hr since overdose. Guidelines for the management of acetaminophen overdose. McNeil Consumer & Specialty Pharmaceuticals; 2005.
Management of RSTI

- History of repeated acetaminophen ingestion (>4 g/24 hr over >8 hr)

- Draw serum AST/ALT and serum acetaminophen level

  - AST or ALT >50 IU/L or Serum acetaminophen >10 mg/L (66 µmol/L)
    - Acetylcysteine therapy
      - Repeat AST or ALT in 12 hr
        - Continue acetylcysteine until AST/ALT level static or decreasing, the acetaminophen level is <10 mg/L, and clinical improvement is noted
      - Follow-up call in 48 hr to 72 hr

  - AST or ALT <50 IU/L or Serum acetaminophen <10 mg/L (66 µmol/L)
    - Patient not treated
      - Follow-up call in 48 hr to 72 hr
Case Study: Chemistries

- Hemoglobin = 13.8 g/dL
- White blood cells = 5990/µL
- Platelets = 220 x 1000/µL
- AST/ALT: 52/47 IU/L
- Benzodiazepine (urine): negative
- Acetaminophen (blood): 151.33 µg/mL (10 hr postingestion)
Case Study: Rumack-Matthew Nomogram Check

Patient acetaminophen level at 10 hr: 151.33 µg/mL

Rumack-Matthew Line

Treatment Line: treatment should be administered if level is above solid line

Adapted from Rumack BH, Matthews H. Pediatrics. 1975;55:873.
Case Study: Treatment

• Patient weighs 50 kg

• IV NAC
  – 150 mg/kg (7500 mg) IV + 200 mL diluent over 60 minutes
  – 50 mg/kg (2500 mg) IV + 500 mL diluent IV for 4 hours
  – 100 mg/kg (5000 mg) IV + 1000 mL diluent IV for 16 hours

-OR-

• Oral NAC
  – 140 mg/kg (7000) loading dose
  – 70 mg/kg (3500) every 4 hours for 17 doses starting 4 hours after the loading dose
NAC Administration

- In 2004, the US approved NAC treatment over 20 to 21 hr
- If body weight is >40 kg:
  - Loading dose: 150 mg/kg over 60 min in 200 mL 5% dextrose
  - Second dose: 50 mg/kg infused over 4 hr in 500 mL 5% dextrose
  - Third dose: 100 mg/kg infused over 16 hr in 1 L 5% dextrose
- If body weight is <40 kg:
  - Acetylcysteine solution should be diluted per prescribing information

Treatment Pitfalls and Other Issues

- Not checking acetaminophen and liver enzymes at the end of therapy
- Not checking PT/INR and creatinine if liver enzyme level persists over time
- Other issues
  - Using gastric lavage, activated charcoal; clinical benefit is unclear
  - Acetaminophen levels from extended-relief formulations not as predictable as with immediate-release formulations

Case Study: 2-week Follow-up

• Follow-up at 2 weeks:
  – AST: 25 IU/L
  – ALT: 26 IU/L
  – Creatinine: 0.7 mg/dL
  – INR: 2.0
Summary

- Acetaminophen is the most widely used antipyretic and analgesic, combined with ~125 medications
- Determine when and amount of acetaminophen ingested
- Use the nomogram for single acute exposures
- Early treatment is key, NAC is the antidote
- Hepatotoxicity can occur in acute overdose, but rarely leads to need for transplantation or death
Advisory Committee to the FDA

Acetaminophen
Recommendations
FDA Statement Prior to 2009 Advisory Committee Meeting

- To date, the agency has considered acetaminophen safe when used according to the directions on its OTC and Rx labeling.
- Taking more than the recommended dose of 4 g/d, however, can cause liver damage.
- Many cases of acetaminophen overdose are caused by consumers inadvertently taking more than the recommended dose.
- FDA is not looking to remove acetaminophen from market.
Audience Polling Questions

- Do you think the maximum daily dose should be limited?
  A. Yes
  B. No
  C. I have not decided

- Do you think the single adult dose should be limited?
  A. Yes
  B. No
  C. I have not decided
## Advisory Committee to FDA Recommendations: Pros vs Cons

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes (High/Low priority)</th>
<th>No</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum daily dose &lt;4 g/d</td>
<td>21 (11/10)</td>
<td>16</td>
<td>↑ margin of safety between labeled dose and suggested threshold dose to injury (suggested as low as 7.5 g)</td>
<td>Lower total and single dose will be less effective and potentially prompt ↑ dose, or switching to opioids, or less safe OTC alternatives such as NSAIDs</td>
</tr>
<tr>
<td>Maximum single adult dose of 650 mg</td>
<td>24 (12/12)</td>
<td>13</td>
<td>Single tab/gelcap limited to 325 mg so more tabs/gelcaps would have to be consumed to become toxic</td>
<td>Reduces options for minor pain</td>
</tr>
</tbody>
</table>
Audience Polling Questions

• Do you think the 2 x 500 mg dose should be prescription?
  A. Yes
  B. No
  C. I have not decided

• Do you think Rx combination (opioid/acetaminophen) products should be eliminated?
  A. Yes
  B. No
  C. I have not decided
<table>
<thead>
<tr>
<th>Item</th>
<th>Yes (High/Low priority)</th>
<th>No</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>If single dose lowered, 2 x 500 mg dose to be Rx</td>
<td>26 (8/18)</td>
<td>11</td>
<td>• Potentially decrease unintentional acetaminophen overdoses associated with chronic misuse/abuse of these drugs</td>
<td>• Decoupling makes what was a Schedule III drug now a Schedule II drug</td>
</tr>
<tr>
<td>Recommend pack size limits</td>
<td>17 (2/15)</td>
<td>20</td>
<td>• Control dosing of each drug separately</td>
<td>• Must be written Rx, no call ins. No refills, need follow-up visit. ↑ abuse potential. APAP tox limits use. ↑ diversion</td>
</tr>
<tr>
<td>Eliminate non-Rx combination products</td>
<td>13 (2/11)</td>
<td>24</td>
<td></td>
<td>• Switching to NSAID or opioid combination</td>
</tr>
<tr>
<td>Eliminate Rx combination products</td>
<td>20 (10/10)</td>
<td>17</td>
<td></td>
<td>• Higher costs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Reduces options for pain management</td>
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</table>
FDA Reported Hepatotoxicity for Acetaminophen

• FDA Advisory Committee recognizes APAP hepatotoxicity “rarely occurs from appropriate use”
  – Most hepatotoxicity result of unintended or deliberate overdose

• Postmarketing case reports by FDA Adverse Event Reporting System (AERS)
  – 307 reported* cases of acetaminophen-related hepatotoxicity in adults and children (January 1998 to July 2001)

*Not all cases are reported to AERS.
Acetaminophen Is Safe at Therapeutic Doses in Patients With Comorbidities

• 30,865 adults enrolled in prospective trials treated with multiple-dose acetaminophen (1966-2003)
  – 4,263/30,865 patients received 4 g/d for a mean 5.5 days
• Of 129 (0.4%) of subjects with reported ALT above the ULN, no cases of hepatic failure or clinically significant liver injury reported
• Comorbid conditions included:
  – Acute stroke, CABG
  – Diabetes
  – Multiple sclerosis
  – Advanced cancers
  – Total hip arthroplasty, abdominal surgery

ULN = upper limit of normal; CABG = coronary artery bypass graft.
Hepatotoxicity in Children Is Rare With Therapeutic Dosing of Acetaminophen

- 32,307 children received acetaminophen for a median of 3 days
  - Therapeutic dosing (≤75 mg/kg/d, up to 4 g/d)
- No cases of liver disease or patients requiring liver transplant
- 4 children with ↑ LFTs (highest AST was 375 IU/L and ALT 362 IU/L)
- LFTs normalized quickly and completely without therapy
- All elevations judged to be “possibly” related to acetaminophen exposure (Naranjo score = 3)
- Asymptomatic increases in LFTs happen with therapeutic dosing of acetaminophen

LFT = liver function test.
Special Concerns for Acetaminophen-related Hepatoxicity Following Overdose

- Alcoholic patients
  - Depletion of glutathione stores due to chronic alcohol ingestion
  - Induces P450 2E1
- Unintentional overdose
- Patients with preexisting liver disease
- Dehydration, fasting, or malnutrition

No Change in ALT With Acetaminophen 4 g/d x 3 d in Newly Abstinent Alcoholics

### Summary: No Acute Liver Injury With Acetaminophen 3-4 g/d in Patients With Liver Disease

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Alcoholic cirrhosis</strong></td>
<td>4</td>
<td>2</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td><strong>Alcoholic/Hep C</strong></td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>6</td>
</tr>
<tr>
<td><strong>Hep C cirrhosis</strong></td>
<td>–</td>
<td>3</td>
<td>–</td>
<td>4</td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
<td>–</td>
<td>7</td>
<td>17</td>
<td>–</td>
</tr>
<tr>
<td><strong>Other diseases</strong></td>
<td>–</td>
<td>14</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dosing Regimen</th>
<th>3 g x 5 d</th>
<th>4 g x 5-13 d</th>
<th>3 g x 7 d</th>
<th>4 g x 4 d&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number Exposed</strong></td>
<td>4</td>
<td>26</td>
<td>17</td>
<td>12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Safety</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in ALT</strong></td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
</tr>
<tr>
<td><strong>Change in other</strong>&lt;sup&gt;c&lt;/sup&gt;</td>
<td>NC</td>
<td>NC</td>
<td>NR</td>
<td>NC</td>
</tr>
<tr>
<td><strong>Acute liver failure</strong></td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

<sup>a</sup> = Other includes Laennec’s cirrhosis, unspecified cirrhosis, and primary biliary cirrhosis. <sup>b</sup> = One additional dose given the morning of the fifth day. <sup>c</sup> = Clinical laboratory tests associated with liver function. NC = no change, NR = not reported.
Audience Polling Questions

• Are these data enough to provide clinicians with an evidenced-based argument for the continued use of acetaminophen at currently labeled doses?
• What additional data would you need to support current doses used in practice?
Position Statements and Recommendations
Position Statements Cite Concerns

- **American Pain Foundation**
  - Many will be driven to take medicines with potentially even greater risks
  - Petition site sponsored by the APF to “Educate, Do Not Regulate”
    - [http://www.thepetitionsite.com/1/Acetaminophen-Educate-Do-Not-Regulate](http://www.thepetitionsite.com/1/Acetaminophen-Educate-Do-Not-Regulate)

- **American Academy of Pain Medicine**
  - Recognizes risks of products containing acetaminophen and those combining acetaminophen with other therapies
  - Supports safe and responsible use of acetaminophen

## Recommendations for Acetaminophen Use in Guidelines/Position Statements

<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendation/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009 American Geriatrics Society</td>
<td>325–500 mg every 4 hr or 500–1000 mg every 6 hr. Reduce maximum dose 50%-75% in patients with hepatic insufficiency or history of alcohol abuse.</td>
</tr>
<tr>
<td><em>Recommendation for persistent pain</em></td>
<td></td>
</tr>
<tr>
<td>2009 National Pain Foundation</td>
<td>Do not exceed the recommended single dose and total daily dose of acetaminophen.</td>
</tr>
<tr>
<td><em>Position statement</em></td>
<td></td>
</tr>
<tr>
<td>2009 American Pain Society</td>
<td>Asymptomatic elevations of aminotransferase levels at dosages of 4 g/d.</td>
</tr>
<tr>
<td><em>Recommendation for chronic pain</em></td>
<td></td>
</tr>
<tr>
<td>2000 American College of Rheumatology</td>
<td>Hepatic toxicity with acetaminophen is rare with doses of &lt;4 g/d. Careful monitoring of PT is recommended for patients taking warfarin who subsequently begin high-dose acetaminophen treatment.</td>
</tr>
<tr>
<td><em>Recommendation for osteoarthritis</em></td>
<td></td>
</tr>
<tr>
<td><em>Science Advisory Committee Recommendation</em></td>
<td></td>
</tr>
</tbody>
</table>
Summary

• Advisory Committee recommends limiting the OTC single adult dose to 650 mg and the total daily dose to <4 g/d
• However, therapeutic dosing of acetaminophen ≤75 mg/kg/d or ≤4 g/d is safe in most patients
• At therapeutic doses, transient asymptomatic elevations occur but are unlikely to cause hepatic injury
• Medical societies, physicians, and the public may be hesitant to accept recommendations to limit acetaminophen products
NSAIDs
# NSAID Activity

<table>
<thead>
<tr>
<th>ASA</th>
<th>NSAID</th>
<th>COX-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Inhibits COX-1 and modifies COX-2</td>
<td>• Nonselective for COX enzymes</td>
<td>• Selective inhibition of COX-2</td>
</tr>
<tr>
<td>– COX-1 enables basal cellular homeostasis (platelet function, gastric mucosal integrity, renal blood flow regulation)</td>
<td>• Prevents COX-mediated production of prostaglandin and thromboxanes, but not leukotrienes and other eicosanoids</td>
<td></td>
</tr>
<tr>
<td>– COX-2 increases inflammation and pain states</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Low-dose, long-term use blocks the formation of thromboxane A₂ in platelets</td>
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</table>

ASA = acetylsalicylic acid; COX = cyclooxygenase.

Cyclooxygenase Pathways

Burden of NSAID-related Complications

- ~111.4 million NSAID prescriptions in 2000
- Annual US hospitalizations for serious gastrointestinal (GI) complications is estimated to be ~103,000
- At an estimated cost of $15,000 to $20,000 per hospitalization, the annual direct costs of such complications exceed $2 billion
- Acute overdose fatality is rare
  - 55 NSAID-associated (not including aspirin) fatalities in 2006

Death Rate Following UGIE, MI, or CVA With Recent NSAID Use

- 2008 VA study (N=474,495)
- First report showing absolute risk of death following recent NSAID use
- Significant predictors of mortality:
  - Time spent on a traditional NSAID or COX-2
  - Advancing age
  - Failure to ensure adequate gastroprotection
  - Multiple comorbidities


UGIE = upper gastrointestinal events; MI = myocardial infarction; CVA = cerebrovascular accident; VA = Veterans Affairs; P-Y = person years.
**NSAID-associated Toxicity at Therapeutic Dosing**

- **Dyspepsia:** pain, reflux, bloating, diarrhea
- ~1% of patients treated for 3-6 months and 2%-4% of patients treated for 1 yr will develop ulcers, bleeding, or GI perforation
- The risk is approximately 3.1-4.5 times that of patients not using NSAIDs
- Rates of peptic ulcer and upper GI hemorrhage are similar for diclofenac, naproxen, piroxicam, and sulindac (1989-1991)

FDA Reported GI Toxicity Data for NSAIDs

- Postmarketing case reports by FDA Adverse Event Reporting System
  - 279 cases of GI bleeding associated with the OTC use of NSAIDs between 1998 and 2001
    - 197 cases for ibuprofen, ketoprofen, and naproxen
    - 82 cases for aspirin
    - Data supports nephrotoxic risk with NSAID use
    - Acute renal failure appears to be rare

Management of Acute NSAID Ingestion

- No specific antidote
- Gastric emptying (<1 hr following ingestion)
- Gastric decontamination with activated charcoal 1 g/kg
- Proton pump inhibitor for gastroprotection
- Administer supportive care if needed
  - Airway control with assisted ventilation
  - Arterial blood gases if hypoventilation or acidosis suspected
  - Treat metabolic acidosis with sodium bicarbonate
  - Monitor serum electrolytes and fluids
  - Monitor for renal or hepatic injury
  - Hemodialysis if renal failure develops

Salicylate Toxicity

- >21,000 salicylate (ASA and non-ASA) exposures in poison centers in 2004
  - 2,968 hospitalizations
- ASA alone: 61 deaths in 2006
  - ~50% categorized as intentional overdose
- Incidence of unintentional poisoning is not known, but may be underdiagnosed

Signs and Symptoms of Acute Salicylate Overdose

- Vomiting
- Hyperventilation (~30 minutes)
- Metabolic acidosis (~12-24 hours)
- Dehydration
- Electrolyte imbalance
- Hyperthermia
- Pulmonary and cerebral edema
- Convulsions
- Tinnitus

Salicylate Toxicity Pitfalls

- Failure to recognize salicylate toxicity
- Failure to appreciate continued absorption of salicylate
- Misinterpreting clinical significance of serum salicylate level
- Reliance on 1 or 2 salicylate levels only, unless level is 0
- Misinterpretation of low serum salicylate levels as nontoxic
- Waiting until serum salicylate levels are determined before beginning urinary alkalinization
- Accidentally adding bicarbonate to isotonic saline
- Forgetting to add potassium to the urinary alkalinization infusion
- Failure to recognize emergent need for hemodialysis
- Initiating intubation and mechanical ventilation without hyperventilation and without simultaneous hemodialysis
- Premature discharge without demonstrating metabolic stability

### Diagnostic Studies for Acute Ingestion

- Basic electrolytes to assess levels and acid-base status; baseline renal function

- Arterial blood gas in severe overdose or altered mental status

- Acetaminophen and salicylate levels to rule out concurrent pain medication ingestion

- Fingerstick glucose to rule out hypoglycemia as an etiology of any alteration in mental status

- Screening electrocardiogram to assess for toxin-induced prolongation of the QRS or QTc

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Treatment of Acute Toxicity

• Give GI decontamination with activated charcoal 1 g/kg
  – Weigh risk of aspiration vs possible benefits
• Serum and urine alkalinization with bicarbonate and potassium chloride
• Supportive care
  – Secure airway breathing and circulation (rarely an issue with NSAID poisoning)
  – IV crystalloid to replace volume losses
  – Monitor for need for hemodialysis

Indication for Hemodialysis in Acute Salicylate Poisoning

- Severe acidosis or hypotension refractory to optimal supportive care (regardless of absolute serum aspirin concentration)
- Evidence of end-organ injury (ie. seizures, rhabdomyolysis, pulmonary edema)
- Renal failure
- High serum aspirin concentration (>100 mg/dL) despite relatively stable metabolic picture
- Consider for patients who require endotracheal intubation unless that indication for mechanical ventilation is respiratory depression secondary to a coingestant

Summary

• NSAIDs are common therapies that account for toxicity by unintentional overexposure and gastric or renal injury
• Chronic exposure, even at recommended doses, may result in emergency situations due to GI and CV toxicity
• No antidote available
• Prevention is by education and cautious NSAID use
Conclusions

• OTC analgesic overexposure is common in the US due to ease of availability and lack of physician oversight
• Prompt recognition and treatment may prevent morbidity and mortality associated with analgesic overdose
• Advisory committee to FDA recommends more stringent labeling and lower doses to prevent overexposure and hepatotoxicity
• Subacute toxicity due to chronic NSAID exposure may result in GI or CV AEs
• Patient education and careful use is required for prevention
Thank you!