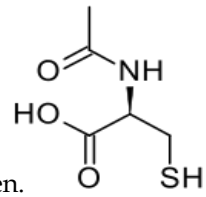
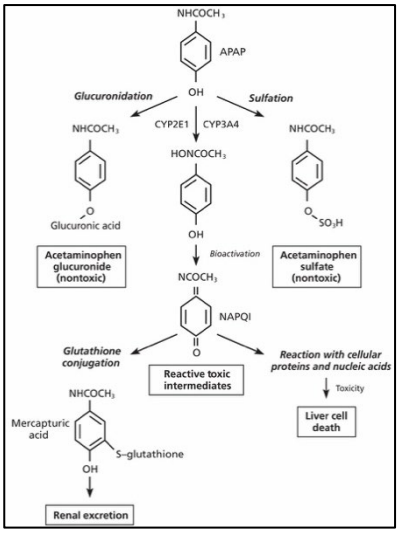
Clinical Pharmacology & Toxicology Pearl of the Week

~ N-acetylcysteine (NAC) & Anaphylactoid Reactions ~



- ✓ N-acetylcysteine (NAC) is the antidote of choice for treatment of acetaminophen (APAP) toxicity.
- ✓ It has several mechanisms of action in APAP toxicity: it acts as a glutathione precursor, glutathione substitute, substrate for sulfation & it enhances reduction of NAPQI (toxic metabolite) to acetaminophen.
- ✓ In patients with hepatotoxicity, it increases free radical scavenging, increases ATP production, and improves hepatic oxygen delivery and blood flow.
- ✓ Anaphylactoid reactions to IV NAC are well-described in the literature. The incidence of such reactions is ~8%.
- ✓ The mechanism is believed to involve either non-IgE mediated histamine release or direct complement activation.
- ✓ Unlike true anaphylaxis, prior exposure to NAC is <u>not</u> required & continued or future treatment is <u>not</u> contraindicated.
- ✓ Symptoms include: cutaneous features (urticaria, flushing, pruritus, angioedema), respiratory features (cough, wheeze, dyspnea), and in severe cases, hypotension and cardiac arrest.
- ✓ Several factors are associated with ↑ risk of anaphylactoid reactions to NAC:
  - history of asthma or atopic disease
  - family history of allergy
  - <u>lower</u> acetaminophen concentrations on admission (APAP decreases histamine release from mononucleocytes and mast cells in a dose-dependent manner)
  - female sex
  - younger age
  - lower alcohol consumption
  - a history of previous reaction to NAC
  - administering the loading dose over any time shorter than 60 minutes
  - longer time interval from ingestion to treatment with NAC



- ✓ Suggestions for managing anaphylactoid reactions to IV NAC include:
  - continue the NAC infusion if the only symptom is flushing.
  - diphenhydramine 1 mg/kg intravenously for urticaria.
  - diphenhydramine and hold the NAC infusion for one hour for angioedema.
  - diphenhydramine, hold the infusion, and consider epinephrine for respiratory symptoms or hypotension.
  - fluid boluses, corticosteroids and beta-2 agonists for patients with hypotension &/or respiratory symptoms.
  - if no symptoms reappear within one hour after stopping the infusion, the NAC infusion be restarted.
  - pretreatment with an antihistamine can be considered in patients who have had previous reactions.
- ✓ If reactions reappear after IV NAC is restarted, switching to oral NAC may be an option. While nausea and vomiting are common with oral NAC, rash and other features of anaphylactoid reactions are extremely uncommon.
- ✓ Newer randomized trials with slower loads of NAC or different dosing schedules have shown fewer adverse effects (especially vomiting or retching, as well as anaphylactoid reactions).

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click HERE for clinical issues the CP service can assist with.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.

References Can be found here →