



Clinical Pharmacology & Toxicology Pearl of the Week

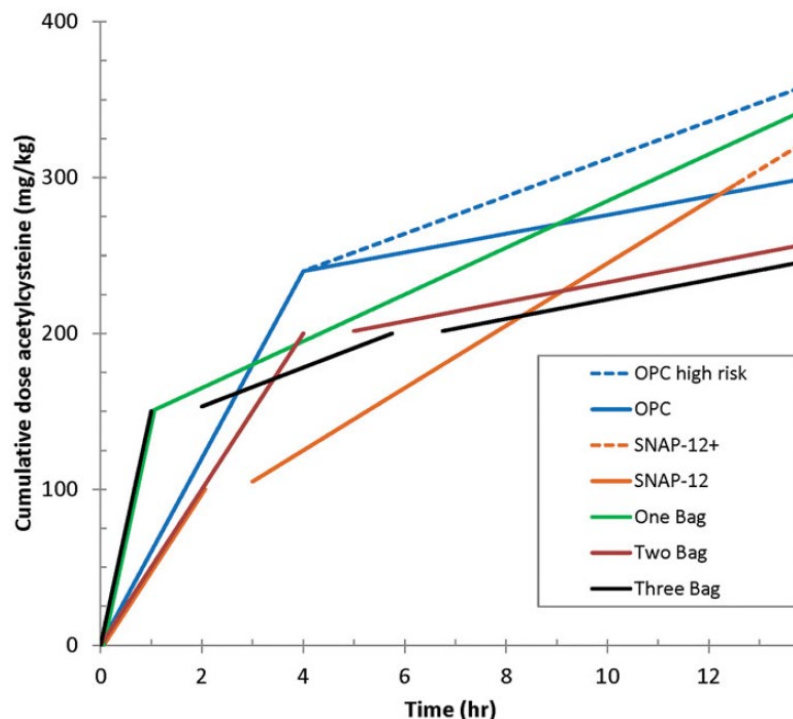
~ Newer IV Acetylcysteine regimens, Part 2 ~

Case:

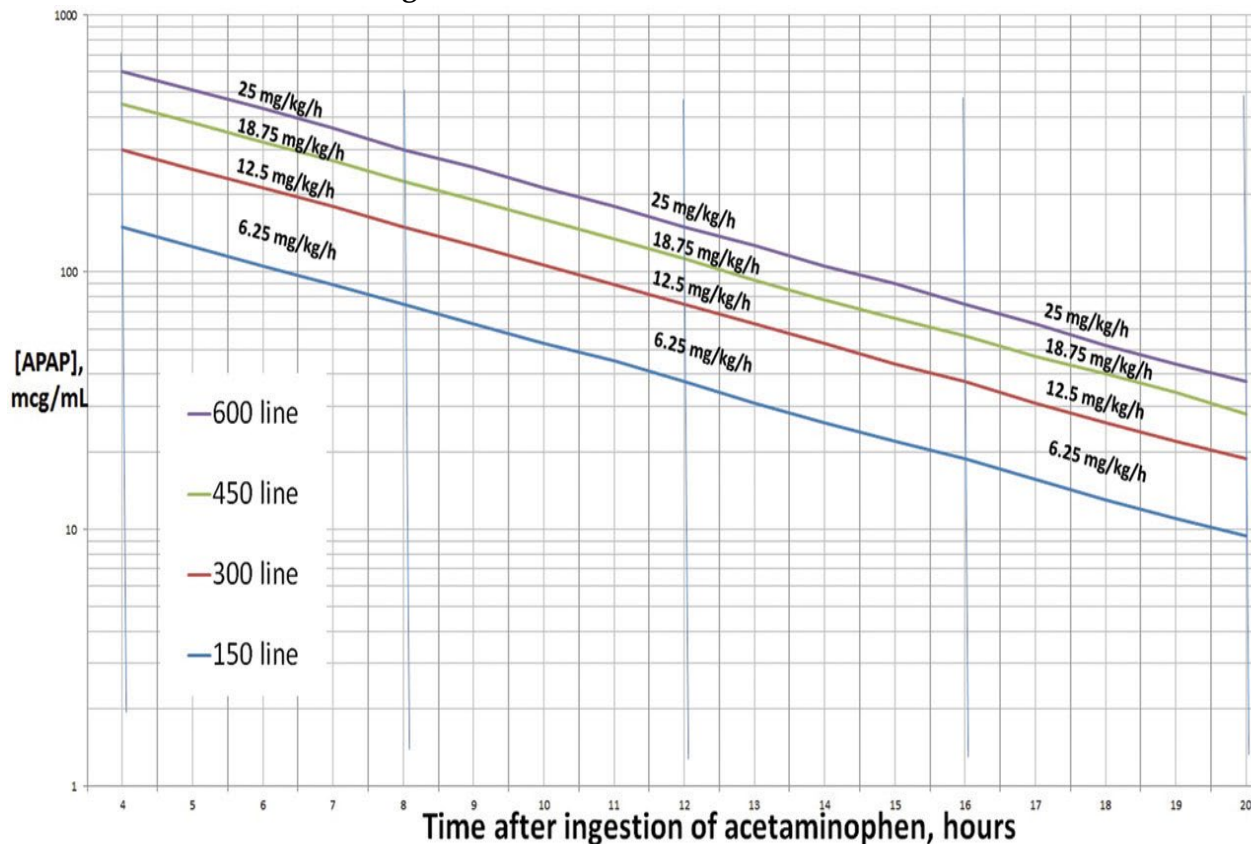
- ✓ A 25-year-old female ingested a supratherapeutic amount of acetaminophen (APAP) at 10am.
- ✓ The 4-hour APAP concentration was 1200 $\mu\text{mol/L}$, indicating that hepatotoxicity (serum AST or ALT > 1000 IU/L) was likely.
- ✓ The patient was started on IV N-acetylcysteine (NAC) and made a full recovery. No evidence of hepatotoxicity occurred during her hospital stay.

IV NAC regimens:

- ✓ The graph below shows the differences in IV NAC infusion rates when comparing rate and duration of loading and maintenance dose (Mullins et al, 2019)
- ✓ Breaks in the black (3-bag), red (Australia/New Zealand 2 bag), and orange (SNAP) regimens are to account for the delays in stopping one bag and switching to the next bag. Ontario Poison Centre (OPC) and 2-step regimens do not have any delay between loading dose and maintenance infusion
- ✓ While the optimal dose and duration of IV NAC varies depending on patient risk, most infusions provide at least 300 mg/kg of NAC over a 12-21 hour period for patients with an average risk of hepatotoxicity



What about massive APAP ingestions?



- ✓ Varying definitions of massive ingestion include: an ingestion > 30 grams, an ingestion > 500-600 mg/kg, or a 4-hour [APAP] > 300 ug/ml (1986 umol/L).
- ✓ The above graph shows the suggested rate of IV NAC maintenance infusion based upon the patient's equivalent 4-hour [APAP] (Hendrickson, 2019).
- ✓ With the traditional 3-bag regimen, this is accomplished by doubling or tripling the rate of the 3rd bag from 6.25 mg/kg/hr to 12.5 or 18.75 mg/kg/hr.
- ✓ With newer regimens, the maintenance infusion can also be increased as needed. Given the higher maintenance dose of the two-step IV NAC regimen, adjustment for higher risk patients is less likely to be necessary.
- ✓ With massive ingestions, other therapies such as fomepizole and dialysis are often recommended in addition to IV NAC. This is especially if the 4-hour [APAP] is close to 6000 umol/L, the patient is comatose, and if metabolic acidosis and elevated lactate are present.

- ✓ It is also important to ensure that GI decontamination is performed if there are no contraindications. 1 g/kg of activated charcoal can be given up to 4 hours post-ingestion.

Side by side comparison of the different IV NAC regimens:

Variable	Traditional '3 bag'	SNAP	Australia '2 bag'	Two-step
Loading dose	150 mg/kg over 1 hour	100 mg/kg over 2 hours	200 mg/kg over 4 hours	150 mg/kg over 1 hour
Maintenance	50 mg/kg X 4h then 100 mg/kg X 16h	200 mg/kg over 10 hours	100 mg/kg over 16 hours	15 mg/kg/hr for 20 hours
Duration	≥ 21 hours	≥ 12 hours	≥ 12 hours	≥ 12 hours
Dose at 12 hours	244 mg/kg	300 mg/kg	250 mg/kg	315 mg/kg
Dose at 21 hours	300 mg/kg	300 mg/kg	300 mg/kg	450 mg/kg
Stopping rules at 12 hours?	No	Yes	Yes	Yes
Dose adjustment in HT or dialysis?	Yes	Yes	Yes	No

References:

1. Mullins et al. Comment on "transition to two-bag intravenous acetylcysteine for acetaminophen overdose," Clinical Toxicology 2019, DOI: 10.1080/15563650.2019.1649418
2. Hendrickson R. What is the most appropriate dose of N-acetylcysteine after massive acetaminophen overdose? Clin Tox 2019.
3. Dart et al. Management of Acetaminophen Poisoning in the US and Canada. A Consensus Statement. JAMA Network Open. 2023;6(8):e2327739. doi:10.1001/jamanetworkopen.2023.27739.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching "Pharmacology" from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching "Toxicology" from the ARD home page.

More CPT Pearls of the Week can be found [HERE](#).

Created: September 26, 2022

Reviewed: March 7, 2025