**Clinical Pharmacology & Toxicology Pearl of the Week**



**~ Salicylate poisoning ~**

* Salicylate toxicity can be life threatening and results from either acute ingestion or excessive therapeutic use.
* Toxic effects are the result of direct toxicity to the CNS, uncoupling of oxidative phosphorylation, and interference with glucose/fatty acid metabolism and platelet function.
* Toxicity can be delayed and prolonged due to a number of factors: enteric coated (EC) formulation, formation of bezoars (concretions), erratic intestinal absorption, and enzyme saturation.
* Concentrations may continue to rise for 12 hours or more post ingestion, especially with ingestions of EC products.
* Acute toxicity = vomiting, tachypnea, tinnitus, diaphoresis, and lethargy. This may progress to seizures, hypoglycemia, hyperthermia, coma, and pulmonary edema. Blood gas usually reveals a mixed respiratory alkalosis and metabolic acidosis.
* Chronic toxicity = delirium, dehydration, and tachypnea. Cerebral and pulmonary edema occurs more frequently than with acute toxicity. Severe poisoning occurs at lower salicylate concentrations, and the mortality rate is higher than in acute poisoning.
* After the diagnosis has been made, the following management plan is recommended:
* Decontamination:
  + All patients should receive single dose activated charcoal 1.0 g/kg PO/NG unless contraindicated (i.e. unable to protect airway, bowel obstruction, GCS < 15). Note that charcoal may be administered well after 1-2 hours post ingestion to help decrease absorption.
  + Multi-dose activated charcoal (0.5 g/kg PO/NG q4h to decrease salicylate absorption) should follow the initial dose of charcoal if salicylate concentrations are not declining. This may require between 2-6 doses.
  + Whole bowel irrigation should be reserved for large ingestions of EC preparations where activated charcoal has been unsuccessful in reducing salicylate concentrations.
* Urine alkalinization:
  + Urinary alkalinization is indicated in patients with clinical features of salicylate toxicity and a salicylate concentration > 1.8 mmol/L.
  + Urinary alkalinization (“bicarb drip”): add 150ml (“3 amps”) of sodium bicarbonate 8.4% solution to 850ml D5W (remove 150ml D5W from 1L bag first)
  + Potassium supplementation must be included either in a separate minibag or within the bicarb drip (e.g. 40 meq KCl/L of fluid).
  + Run IV at twice the maintenance rate (i.e. 250 ml/hr in adults)
  + Adjust infusion rate appropriately based on pH results
  + Do not exceed serum pH of 7.55
* Ongoing tests:
  + Urine pH q1h (urine dipstick is sufficient)
  + Goal urine pH is 7.5-8.0
  + Salicylate concentrations Q2h
  + Electrolytes (Na, K, Cl, C02) Q2h
  + Blood gases (venous or arterial) as needed
* When to stop urine alkalinization:
  + Two salicylate concentrations declining over at least 4 hours; at least one of these must be below the lower limit of the therapeutic range (0.7-1.8 mmol/L)
  + No increasing anion gap on repeat electrolyte measurements
  + Clinically well (no tinnitus, GI upset, mental status changes)
  + After urinary alkalinization has been stopped, repeat a salicylate concentration, electrolytes, and venous blood gas (if available at your facility) no sooner than 2 hours after stopping alkalinization. This is to ensure that there is no ongoing absorption of salicylate resulting in increased concentrations or increasing anion gap.
* Pearls and pitfalls of salicylate poisoning:
  + Airway – tachypnea is a compensatory mechanism with salicylate toxicity. Intubation of such patients is a high risk event and should be performed by the most skilled person available. Any respiratory acidosis during intubation may suddenly increase salicylate absorption into the CNS and result in acute deterioration. Patients who are intubated require frequent monitoring of ventilator settings and blood gases to ensure their minute ventilation matches their pre-intubation state. Such patients are often best treated with hemodialysis post-intubation.
  + Fluid resuscitation – patients may be volume depleted by several litres on presentation because of vomiting, increased respiratory and metabolic rate. If pulmonary edema is present, intravenous fluids should be restricted; such patients may be best treated with hemodialysis.
  + Potassium – potassium supplementation must be included in the intravenous fluids to ensure successful urine alkalinization. Oral supplementation may also be required if the patient is hypokalemic on presentation. Patients in oliguric or anuric renal failure should not receive supplemental potassium until the renal failure is corrected.
  + Glucose – administer supplemental glucose as needed for hypoglycemia or altered mental status in the setting of normal serum glucose (i.e. possible neuroglycopenia)
  + Imaging – an abdominal X-ray may show radio-opaque material, but a negative x-ray does not rule out salicylate ingestion.
  + Dialysis – patients who may require dialysis include those with renal failure, congestive heart failure/pulmonary edema, altered mental status, seizures, cerebral edema, worsening acid/base status, unable to alkalinize the urine (urine pH < 7.5), a salicylate concentration > 7.2 mmol/L after an acute overdose, and rising salicylate concentration despite treatment.
  + Consider transfer to a higher level of care if investigations (q2h salicylate concentrations and electrolytes) or treatment (hemodialysis) are not readily available in your facility.



**The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click** [**HERE**](https://cumming.ucalgary.ca/ermedicine/files/ermedicine/calgary-clin-pharm-consult-service-poster.pdf) **for clinical issues the CP service can assist with.**

**The Poison and Drug Information Service (**[**PADIS**](https://www.albertahealthservices.ca/topics/Page11975.aspx)**) is available 24/7 for questions related to poisonings.   
Please call 1-800-332-1414, and select option 1.**