Salicylate Poisoning
Toxicology

1 Introduction
Acute salicylate poisoning is a potentially life threatening condition which can occur following overdose of aspirin or the ingestion of methyl salicylate (oil of wintergreen).

Chronic salicylate toxicity is much more insidious and difficult to diagnose. It presents more frequently in the elderly population with a delirium, dehydration and unexplained metabolic acidosis.

Toxicokinetics
Aspirin is a weak acid with a pKa of 3.5. As the pH becomes more acidic a larger proportion of salicylate is available in its active un-ionised form worsening toxicity. It is well absorbed in the acidic environment of the stomach, although in overdose pharmacobezoars can aggregate which can lead to greatly delayed absorption. Salicylates are bound to albumin, the fraction of unbound drug increases with higher concentrations and with acidosis such that the volume of distribution increases markedly in overdose as does its ability to penetrate the CNS and lead to adverse effects.¹

Hepatic metabolism is subject to zero order kinetics, which means the half-life is greatly prolonged in overdose from 2 to 4.5 hours to up to 18 to 36 hours. It is renally excreted and this is an important route of elimination in overdose and is greatly enhanced by an alkaline urine.

2 Risk Assessment
The major feature of poisoning is the development of a metabolic acidosis due to the uncoupling of oxidative phosphorylation.¹ Salicylates also directly stimulate the respiratory centre.

Clinical features include¹:
- Initial hyperventilation & respiratory alkalosis
- Nausea and Vomiting
- Tinnitus
- Renal potassium loss with hypokalaemia
- Dehydration
- High AG metabolic acidosis
Princess Alexandra Hospital Emergency Department Clinical Module
Salicylate Poisoning

- Hypoglycaemia (can be hyperglycaemia)
- Hypocalcaemia
- Pyrexia
- CNS toxicity: confusion, hallucinations, seizures, coma, cerebral oedema
- Pulmonary oedema
- Prolonged PT, >2 x normal is common in severe toxicity (corrects with Vitamin K)
- Mild transaminitis (not clinically significant)

A respiratory acidosis is uncommon from salicylate toxicity and should prompt you to look for other causes such as the co-ingestion of a respiratory depressant, pulmonary oedema, aspiration or seizures.

<table>
<thead>
<tr>
<th>Ingested dose mg/kg of aspirin</th>
<th>Estimated Severity</th>
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</thead>
<tbody>
<tr>
<td>&lt; 150</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>150 – 300</td>
<td>Mild to moderate toxicity</td>
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<tr>
<td>300 – 500</td>
<td>Serious toxicity</td>
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<tr>
<td>&gt; 500</td>
<td>Life threatening toxicity</td>
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</tbody>
</table>

Risk Assessment of Acute Salicylate Poisoning based on dose adapted from Temple 1981
5g of methyl salicylate is equivalent to 7.5g acetylsalicylate (aspirin)

Chronic toxicity can manifest from doses of 100mg/kg/d. Patients with cirrhosis, low protein states or renal impairment are more prone to salicylate toxicity and may develop signs of chronic toxicity with smaller ingestions.

Investigations
- VBG (typically see a mixed respiratory alkalosis and metabolic acidosis)
- ELFT, FBC, coags
- Urinary pH
- Plasma salicylate concentration can be performed 6h post ingestion. There is poor correlation between levels and outcome, however levels greater than 300mg/L are indicative of toxicity.³
  - Conversion factor mg/L x 0.0072 = mmol/L
  - Conversion factor mmol/L x 138 = mg/L

3 Management

Decontamination
Charcoal should be offered to all patients ingesting more the 150mg/kg who present within 6 hours.¹ Repeated doses of activated charcoal should be considered for large overdoses given the potential for pharmacobezoar formation and delayed absorption. WBI has been suggested for large ingestions of enteric coated aspirin.
Enhanced Elimination
Urinary alkalinisation and haemodialysis are both used to enhance salicylate elimination.

Urine alkalinisation should be instituted in all symptomatic patients\(^4\) it is important to maintain normokalaemia as it is not possible to produce an alkaline urine in the setting of hypokalaemia;

Give 1-2 mmol/kg sodium bicarbonate bolus followed by an infusion of 25mmol/h. Monitor urinary pH q2h, aiming for a pH > 7.5. Measure VBG q2h and replace potassium as necessary.

Alkalinisation can be discontinued when salicylate levels fall below 350 mg/L.\(^2\)

Haemodialysis
Haemodialysis is indicated in cases of severe toxicity, specifically:
- Pre-existing renal/cardiac failure precluding urinary alkalinisation
- Pulmonary oedema
- Severe acidosis
- Elevated salicylate level > 700mg/L or 5.1 mmol/L

Supportive Measures
Ongoing supportive measures are crucial particularly in maintaining hydration, ensuring electrolyte repletion (particularly correcting hypokalaemia and hypocalcaemia) and maintaining normoglycaemia.

4 Disposition
ICU admission is typically required for severe poisonings, particularly if requiring haemodialysis. Patient with moderate poisoning requiring urinary alkalinisation can be manage in the SSU under the care of the toxicology unit. Patients who are asymptomatic following a low risk ingestion (<150mg/kg) are suitable for discharge from a toxicological perspective.\(^3\)

Long term neuropsychiatric sequelae can persistent following severe poisonings, particularly in elderly patients, those who suffered seizures, coma or severe metabolic acidosis and in those with chronic toxicity.

5 References
1. Wikitox 2.1.1.4 Salicylates; http://curriculum.toxicology.wikispaces.net/2.1.1.4+Salicylates