Salicylate intoxication refers to poisoning from a salt or an ester of salicylic acid—the most common of which is aspirin. Aspirin is used for a wide variety of indications, including as an analgesic, anti-inflammatory, and fever reducer. It’s also used as prophylaxis for stroke, myocardial infarction, and venous thromboembolism in high-risk patients. Aspirin is found in many over-the-counter (OTC) preparations and has a variety of on- and off-label uses, making it one of the most widely used medications today.

In this article, I’ll describe how to identify and treat a patient experiencing salicylate intoxication.

What’s going on?
Salicylate dosing depends on the desired effect and the individual’s age. Because of this, aspirin is available in a wide number of formulations, including regular tablets, chewable tablets, dispersible tablets, enteric-coated tablets, extended-release and delayed-release tablets, suppositories, and gum. Aspirin is also a component of various liniments, keratolytics, and topical rubifacants.

Delayed absorption can be seen with large, sustained-release tablets and enteric-coated preparations. Foods and drugs that acidify urine will increase salicylate levels. Coingestants, such as central nervous system depressants, may also alter the clinical presentation of acute salicylate intoxication.

The half-life of aspirin is 2 to 3 hours following small dosages. However, the half-life may extend to more than 20 hours in patients with salicylate intoxication.

Aspirin dosages of 200 to 300 mg/kg are considered toxic, and dosages of 500 mg/kg or greater are potentially lethal. Salicylate poisoning can be acute or chronic, intentional or accidental, and may occur alone or in combination with other drugs. Acute intoxications are more common and are more likely to be accidental in the pediatric age group (especially preschool children) and intentional in teens and adults. Morbidity and mortality are higher with chronic salicylism. The availability of aspirin alternatives, mass media campaigns about the association of aspirin with Reye syndrome in children, and legislation mandating child-resistant closures and pill limits per bottle have likely all contributed to the decreased incidence of aspirin-related fatalities in young children.

Aspirin is metabolized in the liver and is eliminated through the kidneys. There are four mechanisms of salicylate toxicity:

- stimulation of the central respiratory center, which causes hyperventilation
- intracellular effects, including the uncoupling of oxidative phosphorylation, which causes hyperthermia, and the interruption of glucose and fatty acid metabolism, which causes metabolic acidosis
- possible alteration in capillary integrity
- alteration in platelet function.

The kinetics of salicylates in neonates and elderly patients place them at increased risk for toxicity. In addition, elderly patients who are receiving therapeutic dosages of aspirin are at particular risk because the symptoms of chronic salicylism, such as confusion and dehydration, are nonspecific and severe poisoning can occur at lower salicylate levels.
A classic triad
The classic triad of symptoms indicating acute salicylate poisoning are:
• hyperventilation
• tinnitus
• gastrointestinal (GI) tract irritation.
Symptoms of chronic salicylism may include:
• fatigue
• slight fever
• confusion
• collapse
• rapid heart beat
• uncontrollable rapid breathing.
If you suspect salicylate intoxication, the most important components of the physical exam include:
• vital signs: body temperature, heart rate, respiratory rate and pattern, BP, and oxygen saturation
• neurologic assessment: level of consciousness (LOC), presence or absence of gag reflex, reflexes, pupillary size and response, posture, presence of seizures, and speech
• cardiovascular assessment: heart rate and rhythm, quality of pulses, capillary refill, heart sounds, and liver size
• hydration status: mucous membranes and urine output.
Remember, your examination of the patient must take into account the possibility of unknown and multiple coingestants or exposures. In children there may be clear evidence of an accidental overdose, either from a witness or from the telltale empty aspirin bottle nearby. However, in patients receiving therapeutic dosages of aspirin, you must screen for signs and symptoms of toxicity. Neither chronic ingestion nor enteric-coated aspirin ingestion will provide the classic clinical correlation with increased serum salicylate levels that may be seen with acute intoxication.
The diagnosis of acute salicylate intoxication is suspected based on the patient’s clinical history, the physical exam, and acid-base findings (mixed respiratory alkalemia and metabolic acidosis). Confirmation of the diagnosis requires measurement of serial plasma salicylate concentration, but confirmation isn’t needed before beginning treatment. Suspected or acknowledged salicylate poisoning requires serial levels because a variety of factors may influence absorption.
When evaluating a patient with an altered LOC, acute intoxication is included in the differential diagnosis. Urine/serum toxicology is sent to the lab to screen for multidrug exposures. Baseline and serial urine pH and volume, plasma pH, glucose, potassium, calcium and electrolytes (anion gap calculation), blood urea nitrogen, creatinine, clotting studies, and liver function tests will help guide treatment. Radiographic studies are indicated if your patient has altered mental status (head computed tomography scan) or if pulmonary edema is suspected (chest X-ray).

Monitoring essentials
All symptomatic patients suspected of acute drug intoxication from one or more drugs should be admitted to the ICU for evaluation, monitoring, and treatment. As with all acute emergencies, follow the ABCs (airway, breathing, circulation). In acute salicylate intoxication, intubation is reserved for patients who are unable to protect their airway and those with documented hypoventilation. When mechanical ventilatory support is indicated, remember that hyperventilation is a compensatory response to correct and control metabolic acidosis in patients with acute salicylate intoxication, and manage your patient appropriately. Almost all patients with acute salicylate poisoning require serial levels because a variety of factors may influence absorption.

Salicylate poisoning
Acute salicylate poisoning:
Classic clinical triad
• Hyperventilation
• Tinnitus
• GI tract irritation
Dosages to remember
• Therapeutic: Varies by age and desired effect
• Toxic: 200 to 300 mg/kg
• Potentially lethal: 500 mg/kg or greater

National Poison Control Center
• 1-800-222-1222
• Accessible 24 hours/day, 7 days/week
salicylate poisoning who are intubated and ventilated will simultaneously undergo hemodialysis to help clear the salicylates and organic acids. Oxygen supplementation is provided under usual guidelines.

Because salicylate poisoning has metabolic consequences, including effects on pH, fluid status, glucose, and electrolytes, these levels should be monitored and corrected as necessary, recognizing the inherent risks of coma, seizures, pulmonary edema, and aspiration. Fluid losses may be related to fever, increased respiratory rate, and metabolic activity. Asymptomatic patients who are breathing normally following a potentially toxic ingestion should be monitored for at least 6 hours, depending on coingestants, aspirin formulation and dosage, and clinical history.

There’s no specific antidote for salicylate intoxication. Activated charcoal is used for gastric decontamination in acute salicylate poisonings, while simultaneously paying attention to the correction of any fluid, glucose, and electrolyte abnormalities. Elimination is enhanced with urinary alkalization and hemodialysis. Bicarbonate diuresis should be initiated early on in patients with moderate salicylate poisoning. Hemodialysis is the preferred method to enhance salicylate elimination.

**Patient teaching musts**

Following an accidental ingestion in a child, warn parents to keep medications and household poisons out of reach and in their original bottles. Medications shouldn’t be encouraged as candy and should only be given under direct supervision. Child-resistant caps should be encouraged where young children frequent, recognizing that elderly individuals often opt against them because they’re more difficult to handle. All unused and expired medications should be discarded. Accessible 24 hours a day, 7 days a week, the National Poison Control Center is an important resource for every household. Keep the phone number (1-800-222-1222) handy to both cell phones and landlines.

Following an accidental overdose or chronic intoxication in an elderly patient, encourage the patient to ask members of his healthcare team if he has questions about his medications. Self-medicating and medication sharing should be discouraged. Many elderly patients are on a variety of prescription medications that may interact with OTC and herbal preparations. Expired and unused medications should be discarded. You can help your elderly patients by asking the pharmacy to provide large print labels on their prescriptions and encouraging patients to read the label not only on their prescriptions, but also on all OTC and herbal preparations. They should be aware of the signs and symptoms of chronic salicylism and know to report tinnitus, confusion, persistent GI pain, diarrhea, sweating, and hyperventilation. Alcohol should be avoided.

Patients admitted with intentional ingestions should be evaluated by a mental health professional with firm plans in place for follow-up before discharge.

**Recognizing red flags**

With over 4,800 exposures to aspirin reported to United States poison centers in 2007, resulting in 63 deaths (5% of all fatal poisonings reported), it’s important for you to be able to recognize salicylate intoxication in your patients so prompt treatment can be initiated.

**Learn more about it**


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