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Aspirin Overdose

Aspirin overdose may be thought by some to be an "old" problem. While there are many other pain relief products on the market, and aspirin is generally avoided in children, aspirin overdose remains a serious problem. At times the diagnosis is not apparent, especially when aspirin is taken as part of a multi-drug ingestion. The presence of an unexplained acid-base abnormality may be the only clue. Treatment can be tricky and falls to the emergency physician to initiate. This article will serve as a comprehensive review of this "old" ingestion.

— Sandra M. Schneider, MD, FACEP, Editor

Background/Epidemiology

Salicylate poisoning remains a major clinical problem involving accidental ingestion in children and intentional overdose in adults. Aspirin may be found in combination with other agents such as narcotics, barbiturates, and caffeine. Although historically aspirin has been the most common cause of poisoning and death in children younger than 5 years of age, the incidence of salicylate overdose during the past two decades has significantly decreased.[1,2] Poison control surveillance data now rank salicylate poisoning as the 13th most common fatal ingestion. This decrease may be due to the fact that pediatricians currently prefer acetaminophen/ibuprofen preparations, and the FDA limits baby ASA bottles to 36 tablets per bottle and mandates child-resistant caps. It is estimated that the use of child-resistant packaging for salicylate-containing medications has resulted in a 34% reduction in the salicylate-related child mortality rate.[3]

Salicylism is the result of acute ingestion in about 60% of cases and chronic ingestion in the remaining 40%. There are several factors that work in concert to make chronic salicylate intoxication so common. The primary factor is aspirin's elimination pattern. As serum salicylate concentrations increase, the ability of the liver to metabolize the drug diminishes until predictable, first-order elimination kinetics (excretion is proportional to the salicylate concentration) are replaced by unpredictable, dose-dependent, zero-order (metabolic rate is constant) elimination. Also, much of the aspirin elimination is through urinary excretion of unchanged drug.[4-6] Therefore, in the face of dehydration and decreased glomerular filtration, drug clearance is impaired. The purpose of this paper is to review the pathophysiology and management of salicylate poisoning that is of concern to the practicing emergency physician.

Although aspirin is the most common cause of salicylate poisoning, several compounds can cause similar toxic manifestations.[7-9] Methyl salicylate (oil of wintergreen), generally meant for topical application, causes a disproportionately high number of salicylate poisoning deaths when ingested or used topically in excess. The severe toxicity of this agent is related to its high salicylate content. A potentially lethal dose for a 2-year-old child is one teaspoon (5 cc) containing the equivalent of 6.9 grams of aspirin or almost 22 adult aspirin tablets. Bismuth subsalicylate (Pepto Bismol), an over-the-counter preparation containing up to 236 mg/15 mL of salicylate, is used in the treatment of diarrhea and prophylaxis for traveler's diarrhea. There is a case report describing a 4-year-old who died after ingesting 3 ounces of Pepto Bismol.[10] Dermal

Executive Summary

- Methyl salicylate contains very high levels of salicylate and can be fatal if ingested or used in large amounts.
- The presence of primary respiratory alkalosis and metabolic acidosis should suggest possible salicylate toxicity.
- The Done nomogram has several limitations. It is not useful in chronic ingestions or in patients who ingest enteric-coated preparations. It cannot be used in the first 6 hours after ingestion.
- Urine alkalinization helps to "trap" the salicylate in the urine and increases excretion. However patients with elevated levels or who have CNS findings may need hemodialysis.

salicylate formulations typically do not result in tissue penetration much deeper than 4 mm in human volunteer experiments. Significant amounts of salicylates typically are not absorbed through the skin except in select patients, such as children and patients with compromised skin such as burn patients and those who apply salicylate medications to large surface areas.[11-13] There is a case report of a newborn with ichthyosis who was treated with twice-daily topical 20% salicylate ointment from day 1 through the 9th day of life who developed salicylate toxicity (salicylate level on day 7 was 119 mg/dL).[14] The toxic effects of ASA, methyl salicylate, and sodium salicylate are qualitatively identical, so the following discussion applies to poisoning with any of these agents. Absorption of large, potentially lethal doses may be much slower than absorption of therapeutic doses, particularly due to salicylate-induced gastroparesis. Rectal absorption is slower and less complete in that only 60% of a therapeutic dose is absorbed. Enteric-coated formulations designed to dissolve in the alkaline medium of the small intestine may cause bezoars[15] and prolong drug absorption.

Aspirin, primarily prescribed for its analgesic, antipyretic, anti-inflammatory, and antiplatelet properties, is probably one of the most frequently used drugs in the world. More than 14,000 tons of aspirin is produced annually in the United States, and more than 200 drugs on the commercial market contain this ingredient. Although salicylate in the form of willow bark (Salix Alba) was used by Hippocrates 2500 years ago for treating pain and fever, salicylates in the form of acetylsalicylic acid were introduced in 1899 by Dresser. Three years later, the first adverse reaction to aspirin, in the form of angioedema, was reported in the literature. Salicylate may be combined with antihistamines and decongestants, or caffeine in cold and allergy preparations (e.g., Alka-Seltzer, Bayer PM). Several products contain combinations of opiates and salicylates (e.g., fiorinal with codeine and Percodan®).[7-9]

Aspirin poisoning remains a common concern in the practice of emergency medicine and is often under-reported and therefore not completely reflected in poison center surveillance data.[1,16,17] There were more than 20,000 aspirin/non-aspirin salicylate medication exposures reported to U.S. poison centers in 2008, with 24 deaths and 5,882 patients requiring hospital treatment.[2] (Refer to 2008 Annual Report of the American Association of Poison Control Centers in the appendix.) Almost 80% of the reported exposures (4,793) were categorized as intentional overdoses. The mortality rate for unrecognized/undiagnosed patients admitted to the hospital who are subsequently found to have salicylate poisoning is estimated to be three times higher than if the diagnosis is made in the emergency department.[18] Thus, it is very important for the emergency provider to be familiar with the clinical spectrum of presentations of aspirin poisoning.

Among preschool children, 90% of the salicylate ingestion cases were managed at home, whereas only 31% of adolescents/adults were cared for at home. This difference is apparently based on the fact that children accidentally ingest smaller amounts than do adolescents/adults who ingest the drug intentionally.[19-21] Similarly, hospitalization rates for children younger than 5 years of age were low, whereas those for adults were considerably higher (7% vs. 26%, respectively).[3]

Salicylate readily crosses the placenta and is found in high concentrations in fetal plasma. In fact, the fetus may act as a "sink" for salicylate due to the fetal circulation being more acidic. Chronic maternal ingestion may be associated with an increased incidence of stillbirths, antepartum and postpartum bleeding, prolonged pregnancy and labor, and lower birth-weight infants. There is no conclusive evidence that salicylate is teratogenic, but a case series described an increased incidence of intracranial hemorrhage in infants whose mothers ingested aspirin during the last week of pregnancy.[22] Nursing infants of mothers who take large doses of aspirin daily may receive considerable exposure not only due to increased intake of the drug but also because of slower elimination by the infant.[19] However, therapeutic doses of aspirin taken by the mother are considered safe for the infant.

The diagnosis of salicylate

Table 1: Imitators of Salicylate Toxicity

- Encephalitis
- Diabetic ketoacidosis
- Alcoholic ketoacidosis
- Psychosis
- Seizures
- Pulmonary edema
- Sepsis
- Altered mental status
- Iron intoxication
- Ethylene glycol, methanol, isopropyl alcohol ingestion
- Acute renal failure

intoxication is often delayed because there is an accompanying illness[23], the symptoms of which often are similar to those of salicylate intoxication. Illnesses that can be confused with salicylate poisoning include respiratory tract illnesses and gastroenteritis since these illnesses are often manifested by fever, nausea, vomiting, and tachypnea, which are similar to those of aspirin poisoning. (*See Table 1.*)

Pathophysiologic Basis for Poisoning

Salts of salicylic acid taken at therapeutic doses are rapidly absorbed from the gastrointestinal tract, with appreciable serum concentrations achieved in 30 minutes and peak levels in 2-4 hours. Absorption of enteric-coated tablets is unpredictable, and peak salicylate concentrations may occur as late as 6-9 hours after ingestion. Large oral doses of aspirin can delay gastric emptying (gastroparesis) by several hours. In the circulation, salicylates are rapidly hydrolyzed to free salicylic acid, which is reversibly bound to serum albumin. Once albumin binding sites are saturated, a marginal increase in the dosage can result in a large increase in unbound salicylate. Salicylate half-life may approach 15-30 hours with toxic doses.

The metabolic derangements induced by salicylate poisoning are multifactorial, but the principle pathophysiologic mechanisms in salicylate poisoning include direct stimulation of the central nervous system respiratory center and interference with aerobic metabolism by uncoupling mitochondrial oxidative-phosphorylation.[24-26] This leads to the interruption of a series of enzyme-mediated mitochondrial functions and anaerobic metabolism with cellular conversion of pyruvate to lactate and the subsequent development of a lactic (metabolic) acidosis. The inefficiency of anaerobic metabolism results in less energy (ATP) being produced per gram of glucose and the release of energy in the form of heat, so a salicylate-toxic patient may be hyperpyretic. Note, however, that the absence of a fever does NOT rule out the possibility of salicylate toxicity. An increased production of carbon dioxide occurs as well as increased oxygen use.

Interference with oxidative-phosphoylation by salicylate will also impact glucose homeostasis negatively by causing glycogen depletion via increased glycolysis and increased catabolism of free fatty acids and proteins (alternate energy sources). The end result is low serum glucose levels and central nervous system hypoglycemia relative to serum glucose levels (confirmed in animal studies).[25] The metabolism of lipids leads to increased formation of ketone bodies.

The above-noted mechanisms result in a primary respiratory alkalosis and a secondary metabolic acidosis with occasional hyperpyrexia and hypoglycemia. The combination of respiratory alkalosis with metabolic acidosis, particularly in adults who ingest salicylate, produces an arterial blood gas that is almost pathognomonic for salicylism. Because these effects are so important in the management of salicylate intoxication, it is essential to review the mechanisms associated with each. Stimulation of the CNS respiratory center seems to be a direct toxic effect of salicylates, independent of increased oxygen consumption or of carbon dioxide production associated with anaerobic metabolism. This respiratory stimulation is characterized by increases in both the depth and rate of respiration (Kussmaul respiratory pattern) resulting in hypocapnia and respiratory alkalosis.

Depending on the balance between these two pathophysiologic mechanisms, either or both respiratory alkalosis or the metabolic acidosis can be present. Early in the course of most adult salicylate poisonings, respiratory alkalosis is initially limited by compensatory mechanisms, including buffering by the hemoglobin-oxyhemoglobin system, the exchange of intracellular hydrogen ions for extracellular cations, and the urinary excretion of bicarbonate. But in cases of severe poisoning in the pediatric population, especially those younger than 2 years of age, a mixed metabolic acidosis and respiratory alkalosis is often present, with the acidosis predominating presumably secondary to the early fatiguing of respiratory muscles. The dominant metabolic acidosis commonly seen in young children (which increases CNS salicylate levels) predisposes them to serious toxicity and is often associated with altered level of consciousness. A common error at this stage of the poisoning is to misinterpret a serum pH of 7.4 as reflective of a stable patient. Patients with a pH of less than 7.4 with decreased pCO_2 and low bicarbonate are dangerously unstable and are likely to rapidly decompensate and develop end-organ injury.[26]

Initially, patients may have either transient or prolonged hyperglycemia in response to failure of the tissues to utilize glucose adequately.[27,28] Eventually, however, as supplies of glucose are depleted, hypoglycemia may develop. While hypoglycemia

Table 2: Signs and Symptoms of Salicylate Intoxication

- Nausea/vomiting
- Tinnitus (ototoxcity)
- Hyperpnea
- Hyperpyrexia
- Altered level of consciousness
- Convulsions
- Hypo- or hyperglycemia
- Electrolyte imbalances (esp. hypokalemia)
- Acidemia
- Hypothrombinemia
- Altered hepatic (Reye's syndrome)/renal function tests

is a less common manifestation than hyperglycemia, it is found mainly in chronic salicylate intoxication or late in the course of acute intoxication.[29-34]

One well-recognized problem associated with salicylate intoxication is water and electrolyte imbalance, particularly hypokalemia. The reasons for these imbalances include:

- increased metabolic rate and resultant heat production with diaphoresis;
- increased respiratory rate causing increased insensible water losses;
- organic aciduria with obligatory losses of sodium and potassium;
- emesis caused by the gastroparesis induced by a metabolic acidosis and stimulation of the medullary chemoreceptor trigger zone;
- increased renal excretion of sodium and potassium as a compensatory response to the respiratory alkalosis.

In addition to inhibiting platelet function (via salicylate inhibition of cyclo-oxygenase and reduction of prostaglandin formation), aspirin intoxication is associated with disturbances in clotting factor VII synthesis, resulting in prolonged protime/INR, although frank hemorrhage is notably uncommon. Mild elevations in hepatic enzymes are also common. Salicylate is a potential renal toxin, and non-oliguric renal failure may be caused by salicylate-induced decreased renal perfusion or direct nephrotoxicity. Oliguria may occur as a result of salicylate-induced SIADH. Tetany, caused by a decrease in ionized calcium, may occur as a result of respiratory alkalosis.[26]

Tinnitus[15,35] and hearing loss are common complaints in patients with salicylate intoxication and are associated with blood salicylate concentrations exceeding 30 mg/dL. Tinnitus or hearing loss often is the first symptom reported, although its absence cannot be reliably used to exclude the possibility of salicylate intoxication. Salicylate toxicity is characterized by a completely reversible sensorineural hearing loss. This is a bilateral symmetrical loss of 30 to 40 decibels for pure tones. One of the most remarkable features of deafness produced by salicylate intoxication is the speed with which hearing returns to normal, in contrast to other ototoxic drugs such as aminoglycosides, which cause morphologic damage to the cochlea resulting in permanent hearing loss. The exact mechanism of salicylate-induced hearing loss is not known.

Lastly, salicylates cause an increase in pulmonary capillary permeability resulting in noncardiogenic pulmonary edema. Cerebral edema may also occur. In adults, risk factors include age older than 50 years, cigarette smoking, chronic salicylate ingestion, metabolic acidosis, neurologic symptoms, and salicylate level greater than 40 mg/dL. In children, risk factors include large anion gap, hypokalemia and low pCO_2. Failure to recognize pulmonary edema as part of the salicylate toxidrome increases morbidity and mortality. From a study of the cause of death in salicylate intoxication, Hill[36] pointed out that the salicylate level in the central nervous system tissue correlated with death better than any other variable measured in a canine model, leading to speculation that CNS salicylate intoxication might cause centrally mediated pulmonary edema. The exact cause of pulmonary edema is obscure, but whatever the pathogenesis, health care providers should be aware that it is an often fatal yet potentially reversible complication of aspirin toxicity.

It is not surprising that salicylates are suspected of causing Reye's syndrome.[37] Salicylates were often used in children with Reye's syndrome during the prodromal phase of their viral illness. The exact mechanism by which aspirin may cause Reye's syndrome is not clear and is based largely on epidemiology. Because salicylate intoxication, particularly that which occurs during therapeutic dosing, and Reye's syndrome occur in similar settings and have similar symptoms (emesis, hyperventilation, delirium, coma, respiratory alkalosis, and hypoglycemia) following a viral illness, clinical differentiation may be difficult.

The progression to death results when mitochondrial dysfunction and basement membrane leakage overwhelm the compensatory capacity of the patient. This leads to marked metabolic acidosis with the development of pulmonary and cerebral edema.[37-39] Myocardial depression and hypotension secondary to acidosis and volume deficit occur, and CNS depression with seizures secondary to hypoxia, hypoglycemia, and direct CNS toxicity preceded cardiopulmonary arrest. In two studies, 40% of the patients who died from salicylate poisoning arrived in the ED alert and decompensated subsequently.[18]

Clinical Presentation

Physiologic changes of aging predispose elderly patients to salicylate

Table 3: Pitfalls in the Emergency Department Management of Salicylate-poisoned Patients[18]

- Failure to recognize the presence of salicylate toxicity
- Failure to appreciate the presence of continued absorption of salicylate
- Single determinations of salicylate levels are not sufficient because absorption may be delayed/erratic
- Misinterpretation of low serum salicylate levels as nontoxic
- Waiting until serum salicylate levels are determined before beginning urinary alkalinization
- Accidentally adding bicarbonate to isotonic saline (creating a hypertonic solution) rather than 5% dextrose solution to alkalinize the urine
- Forgetting to add potassium to the alkalinizing solution
- Failure to recognize the emergent need for hemodialysis on the basis of impending end-organ injury
- Prematurely intubating a patient without recognizing the need for hyperventilation
- Prematurely discharging patients without demonstrating declining salicylate levels and the absence of an aspirin bezoar

Reprinted with permission from: O'Malley GF. Emergency department management of the salicylate poisoned patient. *Emerg Med Clin North Am* 2007;25:333-346.

toxicity. Decreased hepatic perfusion and decreased renal function reduce salicylate biotransformation and clearance.

The initial clinical signs and symptoms, the estimated dose ingested, and the measurement of salicylate levels all serve to gauge the severity of a given acute aspirin poisoning.[18,27,28,36,40-42] However, in chronic salicylism (ingestion of more than 100 mg/kg/day over two days), the clinical picture is the most useful guideline.[29-34,42] Because of the nonspecific nature of symptoms with salicylism, the initial differential diagnosis is broad and may include considerations noted in Table 1. MUDPILES may serve as a useful mnemonic that lists the causes of high anion gap metabolic acidosis: methanol, uremia, DKA, phenformin, iron, isoniazid (INH), lactic acidosis, ethylene glycol, and salicylate.

Signs and symptoms of salicylism depend on the severity of intoxication. Acute ingestion of 150–300 mg/kg is associated with mild symptoms, 300–500 mg/kg is associated with moderate toxicity, and more than 500 mg/kg is potentially lethal.[43,44]

Patients who present with mild toxicity (serum concentration 30–50 mg/dL and a blood gas analysis demonstrating isolated respiratory alkalosis) may only present with modest hyperventilation and may be mistaken for emotional excitation/anxiety. GI irritation (anorexia/nausea/vomiting and dehydration/epigastric discomfort) may be present, and tinnitus may be overlooked. Vital signs are consistent with emotional agitation with tachycardia and tachypnea. Fever is uncommon. Clinical symptoms will be variable when more than one drug was ingested, such as aspirin formulations that contain CNS depressants, and may blunt the hyperventilation typically noted.[18,27,28,36,40,41] With moderate salicylate poisoning (serum level 50-100 mg/dL) more visible signs of toxicity, including fever, diaphoresis, and agitation appear. ASA-induced nephrotoxicity may occur in patients with prior history of nephropathy. With severe salicylate poisoning (serum level > 100 mg/dL), signs and symptoms are primarily neurologic and consist of altered consciousness and seizures. Non-cardiogenic pulmonary edema and cerebral edema may appear in severe cases. In chronic salicylism, these same signs and symptoms appear at significantly lower levels.[29-34]

Emergency Department Evaluation of the Salicylate-poisoned Patient

Assessment of the victim of salicylate intoxication begins with an accurate history and addressing the adequacy of ventilation and perfusion. Laboratory assessment is extensive and includes serum salicylate concentration (every 3 hours until levels have peaked and are declining), electrolytes (every 3 hours until clinical improvement), blood gas repeated as needed, liver function tests, complete blood counts, prothrombin time, partial thromboplastin time, urinalysis, and an electrocardiogram. In the case of intentional ingestions, a comprehensive toxicology panel may be obtained with particular attention to acetaminophen, a common coingestant that cannot be recognized by any other clinical means but testing. Consider obtaining a cranial CT scan for patient with altered mental status.

The characteristics of ASA make gastric decontamination particularly problematic. Gastric irritation and induction of nausea combine to put the salicylate-poisoned patient at substantial risk for vomiting and aspiration from any attempt at GI decontamination.[45] Emergency practitioners must weigh the risk of aspiration versus the possible benefits from any method of gastric decontamination. Activated charcoal should be considered in any patient who presents within 2 hours of a significant ingestion, can adequately protect his or her airway, and has no alteration in mental status. Consider administering activated charcoal to patients with large ingestions who present after 2 hours, as salicylate absorption can be delayed and erratic. It may enhance postabsorptive elimination of salicylates through gastrointestinal dialysis[46-48], although

Table 4: Assessment of Severity of Salicylate Intoxication Based on the Estimated Dose Ingested

Ingested Dose (mg/kg)	Estimated Severity
< 150	No toxic reaction expected
150-300	Mild toxic reaction
300-500	Serious toxic reaction
> 500	Potentially lethal

*Some institutions report salicylate level as mg/dL, and some report it as mg/L. This represents a 100-fold difference and must be recognized.

this has not translated into improved morbidity and mortality. Given that multiple doses of activated charcoal are safe and well tolerated in awake patients and may result in lower total body burden of aspirin, it is reasonable to recommend 25 grams in adults (0.5 gram/kg in children) of activated charcoal without sorbitol every four hours while the patient is being monitored with serum aspirin and blood gas measurements. A study in adult volunteers given 1.9 grams of aspirin showed that 50 grams of activated charcoal given every 4 hours for three doses resulted in a significant decrease in salicylate absorption when compared with one or two doses of charcoal. Charcoal is contra-indicated if bowel sounds are absent, or if obstruction, bowel perforation, hematemesis, and/or shock are present. Whole bowel irrigation is not recommended in aspirin-poisoned patients because there is very little data to support its use and the available data does not demonstrate an improved outcome.[49-51] Gastric lavage has largely been abandoned in the management of aspirin poisoning with the possible exception of patients with life-threatening overdoses who present early in the course of the poisoning.[52] Enteric-coated aspirin has the potential to form concretions in the stomach, and it is therefore reasonable to consider gastric lavage with a large-bore endogastric tube if substantial ASA poisoning is suspected, and there is no likelihood of airway compromise.[18]

The aspirin nomogram, commonly referred to as the Done nomogram[53] after its creator Done, was first published in 1960. Data from pediatric patients who ingested a one-time dose of aspirin were plotted over time to create an instrument to predict toxicity. To confirm the diagnosis of salicylate intoxication, a blood level should be obtained six hours or more after an acute ingestion or at any time chronic ingestion is suspected. Blood levels determined before six hours are still in the absorption-distribution phase of salicylate pharmacokinetics, and although they may be useful in confirming a salicylate overdose, such early levels cannot be used as predictors of severity of poisoning. Several important limitations exist[54] with regard to the development of the Done nomogram that limits its generalizability, including:

- Patients who had polydrug ingestion were included in the analysis, making the clinical correlation difficult to interpret.
- The nomogram assumed an elimination half-life of 20 hours in all patients and did not allow for the change from first-order to zero-order elimination kinetics that occurs when serum levels exceed the elimination enzyme system.
- Its utility is confined to the evaluation of patients with acute salicylate intoxication and it is not helpful in predicting the severity of chronic salicylate intoxication.
- It begins at 6 hours postingestion, by which time the patient may have a significant serum salicylate concentration.
- Severity is best assessed by physical examination, and electrolyte and arterial blood glass analysis rather than by the nomogram.
- Levels may continue to rise for 12 hours or more, especially with ingestion of enteric-coated products.

Although often accurate for the pediatric population[19-21], the Done nomogram has been demonstrated to have very limited applicability for most aspirin-poisoned patients, and its routine use is discouraged. Symptomatic patients suspected of salicylate poisoning should have serial aspirin levels and blood gas analyses performed until a clear trend toward decreasing levels and metabolic stability as described by the blood gas is present.

A few drops of 10% ferric chloride added to 1 mL of urine will turn purple in the presence of even small quantities of ASA (not necessarily toxic levels), although a positive qualitative result should be confirmed with a serum salicylate level. The FeCl test has a sensitivity of 94%, a specificity of 75%, and a negative predictive value of 98% in detecting salicylate in urine in patients with salicylate levels of > 30 mg/dL. There are many false positives. The phenistix turns brown when either salicylate or phenothiazines are present in the urine, although the FeCl test is preferred as the color change is easier to detect (Micromedex Health Services).

Large bezoars[55] of ingested enteric-coated aspirin tablets may or may not be visible on a radiograph, and the absence of opacity on an abdominal film is not adequate to rule out the presence of a large amount of salicylate in the gut.

Treatment of the Salicylate-poisoned Patient

Therapeutic endeavors embrace three objectives: prevention of further salicylate absorption, correction of fluid and electrolyte abnormalities, and reduction of tissue salicylate

Table 5: Effectiveness of Hemo/Peritoneal Dialysis in Clearing Salicylate

Procedure	Approximate Half-life During Procedure	Approximate Clearance During Procedure
Hemodialysis	3.5 hours	86 mL/kg/hr (Jacobsen 1998)
Peritoneal dialysis w/o alkalinization	16 hours	10 mL/kg/hr (Summitt 1964)
Peritoneal dialysis with alkalinization	5 hours	28 mL/kg/hr (Summitt 1964)
Adapted from Micromedex		

levels by increasing renal excretion. Initially hyperthermia should be treated with external cooling. Most patients who have consequential aspirin overdose will be volume deficient, and volume resuscitation with alkalinized intravenous fluids should be initiated early in the course of management. Alkalinization of the urine appears to act as a "trap" increasing salicylate excretion. If dehydration is significant, then fluid boluses of 20 mL/kg should be administered with care to prevent the precipitation of pulmonary/cerebral edema, particularly in patients with severe intoxication. Patients who develop worsening respiratory function consistent with pulmonary edema should have their hydration and urinary alkalinization interrupted and should be evaluated immediately for hemodialysis. Recommended alkalinizing fluid consists of placing three 50 cc ampoules (150 cc total volume) of $NaHCO_3$ (43 mEq Na/ampoule) into a liter of 5% dextrose (the resulting solution should have 132 mEq of sodium, which is essentially the same sodium as normal saline) and infuse at 2-3 mL/kg/hour for the first two hours with subsequent adjustments of the dose and monitoring to maintain the urine pH at greater than 8. This will substantially enhance the elimination of salicylates and promote brisk urine output.[4-6] Urinary alkalinization shortened the half-life by 48% compared to a control group and 43% compared to activated charcoal alone.[6] A total of 20-40 mEq of KCl per liter should be added to prevent hypokalemia unless the patient is anuric. The following illustrates the rationale for alkalinization of the urine:

$HSal <=> H^+ + Sal^-$

$NaHCO_3 <=> Na^+ + HCO_3^-$

Salicylate in its undissociated form readily moves from the tissue/intravascular compartments. Alkalinization of the urine favors the movement of salicylate from the tissue/intravascular sites to the urine and decreases tubular reabsorption of ionized salicylate back into the intravascular compartment (this is termed "ion trapping"). Of importance is the recognition that urine alkalinization cannot be accomplished until potassium depletion has been corrected because hypokalemia increases reabsorption of potassium and excretion of hydrogen ion in the proximal renal tubules. Forced diuresis does not necessarily enhance salicylate excretion more than the clearance accomplished by alkalinization alone. Therefore, fluids are given as needed to restore normovolemia and to produce 1-2 mL/kg/hour of urine. Both urine alkalinization and repetitive oral charcoal should be continued until salicylate concentration falls below 30 mg/dL. Alkalinization is a potentially dangerous treatment, and meticulous monitoring of urine output, serum pH (many authors recommend limiting serum pH to no higher than 7.55), serum potassium and calcium, and mental and pulmonary status should be performed.

Patients with a salicylate level greater than 30 mg/dL and symptoms should be treated with urinary alkalization. The presence of a large anion gap metabolic acidosis or altered mental status indicates a more severe poisoning.

Salicylate-intoxicated patients who have depressed mental status possibly from cerebral hypoglycemia, or coingestants who require endotracheal intubation[56] and mechanical ventilation present a conundrum for emergency practitioners because positive pressure ventilation simply cannot maintain the respiratory rate and metabolic demands of a seriously salicylate-poisoned patient. Salicylates in solution have a pKa of approximately 3.5. Consequently, an acidic environment favors the nonionized state and thus facilitates the ability of salicylate to cross the blood-brain barrier. Hemodynamic instability and worsening acid-base status will be the consequence. Although there is little in the medical literature that directly addresses this critical clinical phenomenon, it is imperative that health care providers who treat salicylate-intoxicated patients be aware that endotracheal intubation may have deleterious effects in the setting of aspirin poisoning. Because suppression of the patient's respiratory drive can be rapidly life-threatening in this setting, it is recommended that endotracheal intubation be withheld unless absolutely necessary. Once the patient is near cardiorespiratory arrest, acidosis is usually predominating and the shock-seizures-death sequence may not be avoided. Intubation is a decision that is hard to make in this setting, even for experienced clinicians. Even is such cases, it is essential that the patient be manually ventilated as rapidly as possible to try to prevent a precipitous decline in serum pH and consequent rush of salicylate into the brain. Avoid administering respiratory depressants and treat seizures aggressively to prevent precipitating the development of "acidemia." It is imperative that respiratory alkalosis be maintained.

A final area of controversy is when patients with salicylism

Table 6: 2008 Annual Report of the American Association of Poison Control Centers' National Poison Data System

Drug	# Cases	Age < 6 yrs	Age 6-19 yrs	Age > 19 yrs	Adverse rx	Tx in Hospital	No health problems	Minor/ moderate health problems	Major health problems	Death
ASA – adult formula	7208	1733	1021	1272	81	2077	1027	1020	61	8
ASA– Ped formula	867	431	94	34	16	98	176	21	10	0
ASA – unknown formula	10290	1711	1442	2065	126	3245	1170	1831	108	16
ASA with other drugs – adult formula	1676	341	138	429	59	356	207	231	14	0
ASA with other drugs – adult formula	12	7	3	0	0	3	8	1	0	0
ASA with narcotics/ narcotic analog	239	23	74	49	13	64	30	42	0	0

Adapted from: Bronstein A, Spyker D, et al. 2008 Annual Report of the American Association of Poison Control Centers National Poison Data System. *Clin Toxicol* 2009;47:911-1084.

should undergo hemodialysis.[57] Hemodialysis should be reserved for seriously ill patients. Hemodialysis rapidly increases salicylate clearance and corrects acid-base, fluid, and electrolyte disturbances. It remains the procedure of choice to treat severe salicylate intoxication. In an animal model, exchange transfusion removed approximately 18%, peritoneal dialysis removed about 15%, and hemodialysis removed about 50% of a standard intravenous dose of 125 mg/kg of sodium salicylate.

Indications include:

- serum salicylate level > 100 mg/dL after an acute ingestion;
- serum salicylate level > 50 mg/dL after a chronic ingestion;
- severe acidosis or other electrolyte disturbance refractory to optimal supportive care (regardless of serum ASA concentration);
- evidence of end-organ injury (seizures, pulmonary edema, renal failure, persistent neurologic dysfunction);
- consider for patients who require intubation unless the indication for mechanical ventilation is respiratory depression secondary to a coingestant;
- progressive deterioration despite standard treatment;
- inability to tolerate $NaHCO_3$ secondary to renal insufficiency, pulmonary edema, or congestive heart failure.

Patients may have metabolized their ASA and have a low measured serum concentration of salicylate, but they still may benefit from hemodialysis to remove the by-products of mitochondrial poisoning. The clinical condition of the patient is more important than the serum salicylate concentration in determining the need for hemodialysis, especially in patients with chronic toxicity or delayed presentation after an acute overdose.

A four-month-old was treated successfully with double volume exchange transfusion after persistent salicylate toxicity.[58] The procedure reduced the salicylate concentration from 70 mg/dL to 34 mg/dL in 8.5 hours, and all laboratory parameters normalized within 48 hours. The elimination rate in a toddler attributable to the exchange transfusion was 152 mL/hr.

Treatment of Acute Salicylate Poisoning[52]

1. GI decontamination/activated charcoal

2. Repeated doses of activated charcoal

50–100 grams loading dose

25–50 grams q 2 hours

3. Treat dehydration — maintain urine output at 1–2 mL/kg/hr (consider Foley placement to monitor fluid status)

4. Correct potassium depletion

5. Alkalinize urine

150 cc $NaHCO_3$ into a liter D5W and infuse at 2-3 mL/kg/hour

Monitor pH (do not cause systemic alkalosis)

6. Consider hemodialysis.

Patient Disposition

In cases of chronic intoxication, low serum salicylate levels can accompany severe degrees of salicylism. Symptom severity determines admission. The mortality rate for chronic salicylate intoxication is 25% compared with a mortality rate of 1% in acute salicylate intoxication.[29]

Emergency Department Management: Patients with minor symptoms (nausea/tinnitus) following an acute overdose may be managed in the ED with decontamination and alkaline diuresis if the salicylate level is shown to be declining.

Home Criteria: Inadvertent ingestions of a single dose of less than 150 mg/kg in children who are asymptomatic.[59]

Admission Criteria: Patients with a rising or non-declining salicylate level, metabolic acidosis, or altered mental status should be considered for intensive care management. Admission should be strongly considered regardless of the salicylate level or symptoms in children younger than 2 years of age, the elderly, or when the ingestion includes enteric-coated tablets.[59]

Observation Criteria: Patients with intentional ingestions and those with unintentional ingestion greater than 150 mg/kg should be observed until salicylate levels are shown to decline and mild to moderate symptoms resolve. For children younger than 6 years of age, ingestions greater than a lick of oil of wintergreen should be observed.[59]

In any case of intentional overdose, psychiatric evaluation is essential, and social work consultation should be seriously considered in pediatric and geriatric cases of salicylate poisoning. Lastly, the poison center (1-800-222-1222)/clinical toxicologist in your community is an important resource that can assist in the management of these difficult patients.

Summary

Aspirin carries both significant adverse effects in therapeutic doses and a substantial risk in overdose for which there is no antidote. Acute overdose in preschool children is generally a relatively benign condition, although intentional ingestions of ASA, as in attempted suicide, are more serious. Its risk-benefit profile is probably the poorest of all analgesics currently available over the counter. Emergency physicians must have a healthy respect for the erratic and unpredictable absorption and elimination kinetics of ASA and the devastating physiologic effects of ASA overdose. Consultation with the regional poison control center is advised to assist with the management and follow-up of all poisoned patients.

References

1. Watson WA, Litovitz TL, Rodgers GC Jr, et al. 2004 Annual Report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 2005;23:589-666.
2. Bronstein A, Spyker D, et al. 2008 Annual Report of the American Association of Poison Control Centers National Poison Data System. *Clin Toxicol* 2009;47:911-1084.
3. Rodgers GB. The effectiveness of child resistant packaging for aspirin. *Arch Pediatr Adolesc Med* 2002;156:929-933.
4. Schwartz R, Landy G. Organic acid excretion in salicylate intoxication. *J Pediatrics* 1965;66:658-666.
5. Miller MR: Suppression of urine in aspirin poisoning. *Lancet* 1955;1:596-597.
6. Proudfoot AT, Krenzelok EP, Vale JA. Position paper on urine alkalinization. *J Clin Toxicol* 2004;42:1-26.
7. Leist ER, Banwell JG: Products containing aspirin. *N Engl J Med* 1974;291:710-712.
8. Settipane G. Adverse reactions to aspirin and related drugs. *Arch Intern Med* 1981;141:328-332.
9. Jones A. Over-the-counter analgesics: A toxicological perspective. *Am J Therapeutics* 2002;9:245-257.
10. Fisher CJ, et.al. Salicylate induced pulmonary edema: Clinical characteristics in children. *Am J Emerg Med* 1985;3:33-37.
11. Singh P, Roberts MS. Skin permeability and local tissue concentration of non-steroidal anti-inflammatory drugs after topical application. *J Pharmacokinetic Biopharmacology* 1993;21:368-370.
12. Cross SE, Anderson C, Roberts MS. Topical penetration of commercial salicylate esters and salts using human isolated skin and clinical microdialysis studies. *Br J Clin Pharmacol* 1998;46:29-35.
13. Taylor JR, Halprin KM. Percutaneous absorption of salicylic acid. *Arch Dermatology* 1975;11:740-743.
14. Yamamura S, et.al. Neonatal salicylate poisoning during the treatment of a collodion baby. *Clin Pediatrics* 2002;41:451-452.
15. Morgan E, Kelly P, Nies K, et al. Tinnitus as an indication therapeutic serum salicylate levels. *JAMA* 1973;226:142-145.
16. Temple AR, Veltri JC. One year's experience in a regional poison control center. The Intermountain Regional Poison Control Center. *Clin Toxicol* 1978;12:277-289.
17. McGuigan MA. A two-year review of salicylate deaths in Ontario. *Arch Intern Med* 1987;147:510-512.
18. O'Malley GF. Emergency department management of the salicylate poisoned patient. *Emerg Med Clin North Am* 2007;25:333-346.
19. Chrichton JU, Elliott GB. Salicylate — a dangerous drug in infancy and childhood. *CMAJ* 1960;83:1144.
20. Jepsen F, Ryan M. Poisoning in children. *Curr Pediatr* 2005;15:563-568.
21. Segar WE. The critically ill child: Salicylate intoxication. *Pediatrics* 1969;44:440-444.
22. Rumack B, et al. Neonatal intracranial hemorrhage and maternal use of aspirin. Obstetrics and Gynecology 1981;58(5 supp):52S-6S.
23. Anderson RJ, Potts DE, Gabow PA, et al. Unrecognized adult salicylate intoxication. *Ann Intern Med* 1976;85:745-748.
24. Tenney SM, Miller RM. The respiratory and circulatory actions of salicylate. *Am J Medicine* 1965;19:498-508.
25. Brem J, Pereli EM, Gopalan SK. et al. Salicylism, hyperventilation, and the central nervous system. *J Pediatrics* 1973;83:264-266.
26. Gabow PA, Anderson RJ, Potts E, et al. Acid base disturbances in the salicylate-intoxicated adult. *Arch Intern Med* 1978;138:1482-1483.
27. Worthley LI. Clinical toxicology: Part I. Diagnosis and management of common drug overdosage. *Critical Care Resuscitation* 2002;4:192-215.

28. Done AK. Aspirin overdosage: Incidence, diagnosis, and management. *Pediatrics* 1978;62(supp):890-897.
29. Bailey RB, Jones SR. Chronic salicylate intoxication: A common cause of morbidity in the elderly. *J Am Geriatrics Society* 1989;37:556.
30. Gaudreault P, Temple AR, Lovejoy FH. The relative severity of acute verses chronic salicylate poisoning in children: a clinical comparison. *Pediatrics* 1982;70:567-568.
31. Temple A. Acute and chronic effects of aspirin toxicity and their treatment. *Arch Intern Med* 1981;141:364-369.
32. Gittelman DK. Chronic salicylate intoxication. *South Med J* 1993;86:683-685.
33. Vivian AS, Goldberg IB. Recognizing chronic salicylate intoxication in the elderly. *Geriatrics* 1982;37):91-97.
34. Fink CW. Acute verses chronic salicylate poisoning. *Pediatrics* 1983;71:862-863.
35. Myers E, Bernstein J, Fostiropolous G. Salicylate ototoxicity — A clinical study. *N Engl J Med* 1965;273:587-590.
36. Hill JB. Salicylate intoxication. *N Engl J Med* 1973;288:1110-1113.
37. Starko, KM, Mullick FG. Hepatic and cerebral pathology findings in children with fatal salicylate intoxication: Further evidence for a causal relation between salicylate and Reye's syndrome. *Lancet* 1983;1:326-329.
38. Fisher CJ, Albertson TE, Foulke GE. Salicylate-induced pulmonary edema — clinical characteristics in children. *Am J Emerg Med* 1985;3:33-37.
39. Hrnicek G, Skelton J, Miller WC. Pulmonary edema and salicylate intoxication. *JAMA* 1974;230:866-867.
40. Done AK. Treatment of salicylate poisoning: Review of personal and published experiences. *Clin Toxicol* 1968;1:451.
41. Yip L, Dart RC, Gabrow PA. Concepts and controversies in salicylate toxicity. *Emerg Med Clin North Am* 1994;12:351-364.
42. Daly FF, Little M, Murray L. A risk assessment based approach to the management of acute poisoning. *Emerg Med J* 2006;23:396-399.
43. Graham CA, Irons AJ, Munro PT. Paracetamol and salicylate testing: Routinely required for all overdose patients? *Eur J Emerg Med* 2006;13:26-28.
44. Wood DM, Dargan PI, Jones AL. Measuring plasma salicylate concentration in all patients with drug overdose or altered consciousness: Is it necessary? *Emerg Med J* 2005;22:401-403.
45. Osterhoudt KC, Durbin D, Alpern ER, et al. Risk factors for emesis after the therapeutic use of activated charcoal in acutely poisoned children. *Pediatrics* 2004;113:806-810.
46. Kirshenbaum LA, Mathews SC, Sitar DS, et al. Does multiple dose charcoal therapy enhance salicylate excretion? *Arch Intern Med* 1990;150:1281-1283.
47. Park GD, Spector R, Goldberg MJ, et al. Expanded role of charcoal therapy in the poisoned and overdosed patient. *Arch Intern Med* 1986;146:969-973.
48. Vale JA, Krenzolak E, Barceloux GD. Position statement and practice guidelines on the use of multidose activated charcoal in the treatment of acute poisoning. American Academy of Clinical Toxicology, European Association of Poison Centres and Clinical Toxicologists. *J Clin Toxicol* 1999;37:731-751.
49. Lheureux P, Tenenbein M. Position paper: Whole bowel irrigation. *J Clin Toxicol* 2004;42:843-854.
50. Tenenbein M. Position statement: whole bowel irrigation. American Academy of Clinical Toxicology, European Association of Poison Centres and Clinical Toxicologists. *J Clin Toxicol* 1997;35:753-762.
51. Heard K. Gastrointestinal decontamination. *Med Clin North Am* 2005;89:1067-1078.
52. Dargan PI, Wallace CI, Jones AL. An evidence-based flowchart to guide the management of acute salicylate overdose. *Emerg Med J* 2002;19:206-209.
53. Done AK. Salicylate intoxication: Significance of measurements of salicylate in blood in cases of acute ingestion. *Pediatrics* 1960;26:800-807.
54. Dugandzic RM, Tierney MG, Dickinson GE, et al. Evaluation of the validity of the Done nomogram in the management of acute salicylate intoxication. *Ann Emerg Med* 1989;18:1186-1190.
55. Taylor JR, Streetman DS, Castle SS. Medication bezoars: A literature review and report of a case. *Ann Pharmacotherapeutics* 1998;32:940-946.
56. Greenberg MI, Hendrickson RG, Hofman M. Deleterious effects of endotracheal intubation in salicylate poisoning. *Ann Emerg Med* 2003;41:583-584.
57. Higgins RM, Connolly JO, Hendry BM. Alkalinization and hemodialysis in severe salicylate poisoning: Comparison of elimination techniques in the same patient. *Clin Nephrology* 1998;50:178-183.
58. Manikian A, et.al. Exchange transfusion in severe infant salicylism. *Veterinary & Human Toxicology* 2002;44:224-227.
59. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as cause of admission to hospital: Perspective analysis of 18,820 patients. *BMJ* 2004;329:15-19.

Physician CME Questions

21. The most toxic preparation based upon available concentration of the salicylate component is:
    A. acetylsalicylic acid
    B. methyl salicylate
    C. bismuth subsalicylate
    D. salicylate-containing liniments

22. Most preschool children with accidental aspirin ingestions will require hospitalization.

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to evaluate their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. *After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a credit letter.* When your evaluation is received, a credit letter will be mailed to you.

Emergency Medicine Reports

CME Objectives

Upon completion of this educational activity, participants should be able to:

- recognize specific conditions in patients presenting to the emergency department;
- apply state-of-the-art diagnostic and therapeutic techniques to patients with the particular medical problems discussed in the publication;
- discuss the differential diagnosis of the particular medical problems discussed in the publication;
- explain both the likely and rare complications that may be associated with the particular medical problems discussed in the publication.

A. true
B. false

23. The most significant metabolic derangement caused by ASA is:
    A. It interferes with cyclo-oxygenase.
    B. It interferes with oxidative phosphorylation in the electron transport system.
    C. It interferes with the urea acid cycle.
    D. It interferes with glycolysis.

24. An adult patient with a respiratory rate of 28 and a diminished level of alertness, on supplemental oxygen has the following ABG: pH 7.4; pO_2 507; pCO_2 24. He:
    A. may be discharged because the pH is normal
    B. should be admitted
    C. should emergently be considered a candidate for the administration of emetics and activated charcoal
    D. is not a candidate for urine alkalinization

25. The classic acid-base derangement in an aspirin poisoned patient is:
    A. respiratory acidosis/metabolic acidosis
    B. respiratory alkalosis/metabolic alkalosis
    C. respiratory acidosis/metabolic alkalosis
    D. respiratory alkalosis/metabolic acidosis

26. Since aspirin is an antipyretic, toxic doses cause hypothermia.
    A. true
    B. false

27. A patient with aspirin toxicity develops tachypnea, hypoxia, and dyspnea. Which of the following statements is true?
    A. Mechanical ventilation with low levels of PEEP is beneficial.
    B. Mechanical ventilation may lead to decreased tissue (brain) levels of the drug.
    C. Mechanical ventilation may lead to worsening respiratory alkalosis.
    D. Mechanical ventilation helps increase urinary excretion of the drug.

28. The following aberrations in laboratory results are seen with aspirin toxicity *except*:
    A. elevated protime time
    B. elevated AST/ALT
    C. hypoglycemia
    D. hypokalemia
    E. white blood cell count of 25,000

29. The following toxins can cause a high anion gap metabolic acidosis:
    A. aspirin
    B. iron
    C. isoniazid
    D. all the above

CME Answer Key

21. B; 22. B; 23. B; 24. B; 25. D; 26. B; 27. C; 28. E; 29. D; 30. B

30. The ability to alkalinize urine may be difficult in the patient with:
    A. hypercalcemia
    B. hypokalemia
    C. coingestion of acetaminophen
    D. hypoglycemia

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Aspirin Overdose

Imitators of Salicylate Toxicity

- Encephalitis
- Diabetic ketoacidosis
- Alcoholic ketoacidosis
- Psychosis
- Seizures
- Pulmonary edema
- Sepsis
- Altered mental status
- Iron intoxication
- Ethylene glycol, methanol, isopropyl alcohol ingestion
- Acute renal failure

Signs and Symptoms of Salicylate Intoxication

- Nausea/vomiting
- Tinnitus (ototoxcity)
- Hyperpnea
- Hyperpyrexia
- Altered level of consciousness
- Convulsions
- Hypo- or hyperglycemia
- Electrolyte imbalances (esp. hypokalemia)
- Acidemia
- Hypothrombinemia
- Altered hepatic (Reye's syndrome)/renal function tests

Reprinted with permission from Temple A. Acute and chronic effects of aspirin toxicity and their treatment. *Arch Intern Med* 1981;141:364-369.

Pitfalls in the Emergency Department Management of Salicylate-poisoned Patients

- Failure to recognize the presence of salicylate toxicity
- Failure to appreciate the presence of continued absorption of salicylate
- Single determinations of salicylate levels are not sufficient because absorption may be delayed/erratic
- Misinterpretation of low serum salicylate levels as nontoxic
- Waiting until serum salicylate levels are determined before beginning urinary alkalinization
- Accidentally adding bicarbonate to isotonic saline (creating a hypertonic solution) rather than 5% dextrose solution to alkalinize the urine
- Forgetting to add potassium to the alkalinizing solution
- Failure to recognize the emergent need for hemodialysis on the basis of impending end-organ injury
- Prematurely intubating a patient without recognizing the need for hyperventilation
- Prematurely discharging patients without demonstrating declining salicylate levels and the absence of an aspirin bezoar

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Assessment of Severity of Salicylate Intoxication Based on the Estimated Dose Ingested

Ingested Dose (mg/kg)	Estimated Severity
< 150	No toxic reaction expected
150-300	Mild toxic reaction
300-500	Serious toxic reaction
> 500	Potentially lethal

*Some institutions report salicylate level as mg/dL, and some report it as mg/L. This represents a 100-fold difference and must be recognized.

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2008 Annual Report of the American Association of Poison Control Centers' National Poison Data System

Drug	# Cases	Age < 6 yrs	Age 6-19 yrs	Age > 19 yrs	Adverse rx	Tx in Hospital	No health problems	Minor/ moderate health problems	Major health problems	Death
ASA – adult formula	7208	1733	1021	1272	81	2077	1027	1020	61	8
ASA– Ped formula	867	431	94	34	16	98	176	21	10	0
ASA – unknown formula	10290	1711	1442	2065	126	3245	1170	1831	108	16
ASA with other drugs – adult formula	1676	341	138	429	59	356	207	231	14	0
ASA with other drugs – adult formula	12	7	3	0	0	3	8	1	0	0
ASA with narcotics/ narcotic analog	239	23	74	49	13	64	30	42	0	0

Adapted from: Bronstein A, Spyker D, et al. 2008 Annual Report of the American Association of Poison Control Centers National Poison Data System. *Clin Toxicol* 2009;47:911-1084.

Effectiveness of Hemo/Peritoneal Dialysis in Clearing Salicylate

Procedure	Approximate Half-life During Procedure	Approximate Clearance During Procedure
Hemodialysis	3.5 hours	86 mL/kg/hr (Jacobsen 1998)
Peritoneal dialysis w/o alkalinization	16 hours	10 mL/kg/hr (Summitt 1964)
Peritoneal dialysis with alkalinization	5 hours	28 mL/kg/hr (Summitt 1964)
Adapted from Micromedex		

Supplement to *Emergency Medicine Reports*, January 17, 2011: "Aspirin Overdose." *Author:* **Marc S. Lampell, MD**, Associate Professor, Pediatric Emergency Medicine, University of Rochester, NY.