# Death due to salicylate poisoning in Ontario

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**Acute salicylate poisoning may result in death. A review of seven fatal cases of salicylate poisoning in Ontario in 1984 showed that the average duration of hospitalization before death was 18.1 hours. Factors that contributed to death included failure to administer activated charcoal and sodium bicarbonate, to appreciate the need for hemodialysis and to consult with experts in toxicology.**

**On peut mourir d'intoxication salicylée aiguë. Revue de sept cas mortels survenus en Ontario en 1984. La durée moyenne du séjour en hôpital avant le décès est de 18,1 heures. Les facteurs qui contribuent à l'issue mortelle comprennent le manque à donner du charbon activé et du bicarbonate de sodium, à reconnaître les indications d'une hémodialyse et à recourir à des personnes compétentes en toxicologie.**

Acute salicylate poisoning is common in both internal and pediatric medicine. Although the clinical entity of salicylate poisoning and its treatment have been recognized in the medical literature since the beginning of the century,[1,2] and recent reviews of salicylate poisoning have reiterated and refined the important management concepts,[3-6] salicylate poisoning still claims a surprising number of victims. I reviewed the fatal cases of salicylate poisoning in Ontario in 1984.

## Methods

All deaths identified as drug related in Ontario are reported to the Chief Coroner's Office of the Ministry of the Solicitor General. All Chief Coroner's records concerning deaths due solely to salicylate poisoning in 1984 were reviewed. Deaths due to the use of more than one drug were not included. The cause of death was assigned by the physician who cared for the patient and on the basis of postmortem chemical analysis by the Centre of Forensic Sciences, Toronto. Premortem salicylate levels were determined with colorimetric techniques, postmortem levels with high-pressure liquid chromatography.

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## Results

Twenty-seven adults died from salicylate intoxication in Ontario during 1984; there were no deaths among children. Seven cases were correctly diagnosed in the emergency department, and sufficient information was available to permit an evaluation of the clinical course. All of the involved hospitals were secondary care facilities with subspecialists on staff and ranged in size from approximately 150 to 450 acute care medical/surgical beds.

Six of the seven patients had given a history of acute ingestion and had arrived at the emergency department an average of 5.3 (extremes 0.5 and 9.4) hours after the overdose. The average ingested salicylate dose was 82 (extremes 32 and 123) g. All of the patients had been alert and symptomatic on arrival. Sweating, pallor and vomiting were the most common findings on presentation. The average respiratory rate was 31 (extremes 18 and 40) breaths/min.

The diagnosis was confirmed in all seven patients in the emergency department by documentation of a markedly elevated serum salicylate level. All had increased anion-gap metabolic acidosis and respiratory alkalosis (Table I). The initial therapy consisted of emptying the stomach by vomiting or lavage (in five patients) and administration of activated charcoal (in two) or a saline cathartic (in one). All the patients received fluids, most frequently an electrolyte solution, intravenously; four had sodium bicarbonate added to the

fluids, and two had potassium chloride added.

The seven patients experienced a similar clinical course. The initial clinical picture consisted of a stimulatory phase, which lasted for 5 to 11 (mean 8) hours after arrival, during which the patient was alert, awake, restless, agitated or disoriented, with rambling or incoherent speech. This phase was followed by a depressive phase identified by statements in the records indicating that the patient was sleeping or had become difficult to arouse, lethargic, weak, flaccid or unresponsive to stimuli. Death occurred 2 to 22 (mean 10) hours after the apparent onset of the depressive phase. The average time between arrival in the emergency department and death was 18.1 (extremes 10.7 and 31.8) hours.

The laboratory studies most frequently done were determination of serum salicylate levels and blood gas analysis. The salicylate levels were determined an average of once every 5 (extremes 3 and 12) hours. The salicylate levels in the five patients in whom more than two determinations were done are shown in Fig. 1. Their mean initial salicylate level was 7.1 (extremes 5.6 and 10.0) mmol/L, while their mean final premortem level was 10.6 (extremes 8.2 and 12.0) mmol/L, a mean increase of 49% over 14.7 hours. On average, salicylate levels increased at a rate of 0.3 mmol/L per hour. Only patient 1 had ingested an enteric-coated product and received activated charcoal and a saline cathartic. Blood gas values were measured on average once every 4.5 hours; in one case they were determined more frequently than once every hour, and in another the frequency was once every 12 hours.

In one case peritoneal dialysis was attempted but the patient suffered a cardiac arrest within 1 hour after initiation of treatment. Hemodialysis was not used in any of the patients even though there were hemodialysis facilities in three of the seven hospitals.

In none of the cases was there any indication in the clinical records that a clinical pharmacologist, clinical toxicologist or poison control centre had been consulted.

## Discussion

Since this report is based on a retrospective review of a selected, uncontrolled population, caution must be used in interpreting and extrapolating the results. However, review of the data suggests that many interrelated factors contributed to the deaths of the patients.

### *Diagnosis*

To provide optimal care for a poisoned patient, not only must the correct diagnosis be made but also the severity of the poisoning must be appreciated. The severity of salicylate poisoning can be estimated from the quantity of salicylate ingested (more than 300 mg/kg being potentially

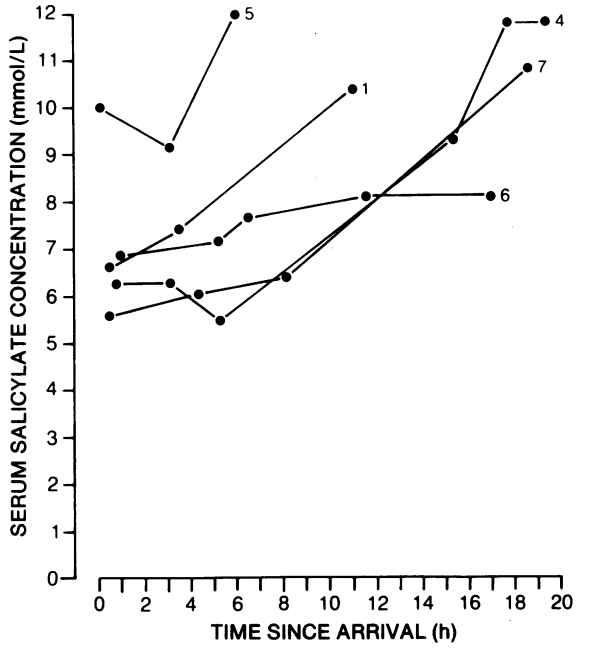


**Fig. 1 — Serum salicylate concentrations in five patients in whom more than two determinations were done.**

Table I — Results of initial laboratory testing in seven patients who died of salicylate poisoning

| Variable | Patient no.; result | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Blood pH | 7.1 | 7.5 | 7.5 | 7.5* | 7.5 | 7.4 | 7.4* |
| Blood levels | | | | | | | |
| $Pco_2$, mm Hg | 27 | 19 | 10 | 28* | 21 | 33 | 25* |
| $Po_2$, mm Hg | 192 | 111 | 108 | – | 99 | 114 | – |
| Bicarbonate, mmol/L | 8 | 14 | 16 | 21* | 15 | 18 | 18* |
| Sodium, mmol/L | 140 | 143 | 146 | 140 | 143 | 144 | 140 |
| Potassium, mmol/L | 4.0 | 4.8 | 5.1 | 3.7 | 3.9 | 4.5 | 3.8 |
| Chloride, mmol/L | 107 | 113 | 109 | 94 | 108 | 107 | 102 |
| Urea, mmol/L | 6.8 | 8.7 | 4.3 | 4.7 | 4.3 | 6.1 | 5.4 |
| Glucose, mmol/L | 8.9 | 12.9 | 7.4 | 8.6 | 8.6 | 8.8 | – |
| Urine pH | – | – | – | 6.0 | 5.0 | – | – |

*Results from capillary blood.

fatal). However, due to the unreliability of the history, Done's nomogram[7] (Fig. 2) is a far more reliable method of determining the prognosis. It was difficult to judge retrospectively whether the severity of the poisoning in the seven patients was appreciated, but in no case was the dose of salicylate calculated in milligrams per kilogram, qualifying terms (such as severe) were never used, and no references were made to Done's nomogram.

*Initial therapy*

The initial or emergency department therapy should consist of decontamination of the gastrointestinal tract and intravenous administration of fluids containing potassium chloride and sodium bicarbonate.[3-6] Techniques for decontamination include administration of ipecac syrup or gastric lavage, and administration of activated charcoal or an osmotic cathartic. The benefit of ipecac-induced emesis and gastric lavage is being questioned, but there is agreement about the usefulness of activated charcoal in preventing gastrointestinal absorption of ingested drugs.[8,9] The fact that activated charcoal was used in only two of the seven patients suggests that its importance was not widely recognized.

Intravenous administration of fluids containing sodium bicarbonate is the basis of treatment of salicylate intoxication. The rationale for using sodium bicarbonate is threefold: to alkalize the urine, to correct metabolic acidosis and to prevent the passage of salicylate into the central nervous system by keeping the plasma relatively alkaline. Potassium chloride is an important adjunct in achieving alkaline urine and thus increasing the excretion of salicylate.

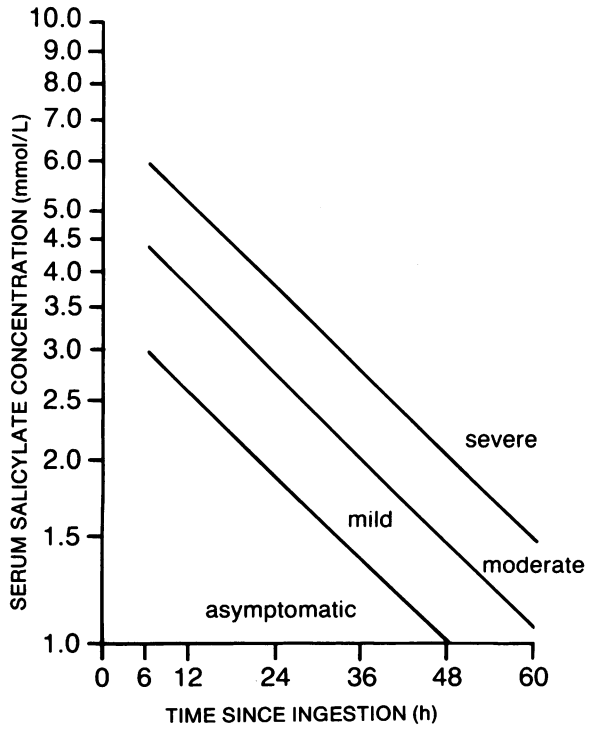


**Fig. 2 — Done's nomogram for determining prognosis in salicylate poisoning (adapted from Done[7]).**

Adding potassium chloride to the fluids did not appear to be a common practice. Sodium bicarbonate was used in only four patients, often at lower dosages than the recommended 225 mEq over the first 3 hours.[5] Presumably the reason for not giving sodium bicarbonate was that the patient did not have acidemia. However, with the degree of ongoing acidosis and hyperventilation that patients with salicylate poisoning demonstrate, administration of 225 mEq of sodium bicarbonate over 3 hours will probably raise the pH of the blood only slightly (from 7.4 to 7.5) and raise the bicarbonate level by less than 6 mmol/L.[10] Moderate alkalemia (arterial blood pH less than 7.5) is not a contraindication to the use of sodium bicarbonate in salicylate poisoning. Patients with increased anion-gap metabolic acidosis, high serum salicylate levels and an arterial pH less than 7.5 should receive sodium bicarbonate intravenously.

*Continuing management*

Continuing management of patients with salicylate poisoning consists primarily of providing appropriate treatment, monitoring progress and correcting or altering the therapeutic course as needed. Ongoing therapy was appropriate in most cases in that salicylate levels, blood gas values and electrolyte levels were monitored. However, undesirable values rarely stimulated a corrective response. The appropriate time interval between measurements of the serum salicylate level is difficult to determine. In patients who have ingested potentially lethal quantities of salicylate, it would be reasonable to measure the levels every 2 hours for the first 8 hours in hospital. Any increase in the level is due to continued gastrointestinal absorption of salicylate and must be treated vigorously with activated charcoal and osmotic cathartics.

The clinical monitoring was similar in the seven cases. The records gave a general impression of a sense of security about the patient who was alert and who had a normal or alkalemic blood pH and a high salicylate level. Patients who were "stable" or were beginning to be quieter were thought to be doing well in spite of increasingly abnormal biochemical values. While clinical impressions are important, they can be misleading in salicylate poisoning. The clinical impression must be integrated with correctly interpreted biochemical values if the patient is to be appropriately assessed. Patients who have ongoing encephalopathy in association with salicylate-induced anion-gap acidosis should have changes made to their therapeutic regimen.

*Aggressive therapy*

Aggressive therapy in salicylate poisoning is hemodialysis.[3,4,6] As none of the seven patients underwent hemodialysis, it must be concluded that the indications for such treatment were not familiar to the physicians who cared for them. A very high salicylate level (greater than 9 mmol/L)[3] or increasing levels indicate the need for prompt hemodialysis. Another indication is failure to alkalize the urine or to control an acid–base disorder.[3,11] Persistence of central nervous system abnormalities is an important sign of therapeutic failure and should indicate the need for hemodialysis.[3,6] Finally, immediate hemodialysis should be considered in any patient in whom complications due to salicylate poisoning develop (e.g., coma, convulsions, pulmonary edema and aspiration).[3,6,11] If there are no hemodialysis facilities nearby, the physician must anticipate the need for hemodialysis by the several hours that are needed to transport the patient to a referral centre.

*Expert advice*

Severe salicylate poisoning is a complex and serious disorder. Physicians, nurses and pharmacists can consult medical personnel with expertise in treating poisoning from salicylates and other agents. In this review the records gave no indication that a poison control centre, clinical toxicologist or clinical pharmacologist was contacted. A physician caring for a seriously poisoned patient should phone the regional poison control centre, if only to make sure his or her knowledge is up to date. The underutilization of expert consultation services may have been an important factor in the deaths of several of these patients.

## Conclusion

**While not all of the critically ill patients described in this review could have been saved, the future death rate can be reduced if emergency physicians, family practitioners and internists recognize the complexity and potential lethality of salicylate poisoning.**

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