Complete Summary

GUIDELINE TITLE

Salicylate poisoning: an evidence-based consensus guideline for out-of-hospital management.

BIBLIOGRAPHIC SOURCE(S)

Chyka PA, Erdman AR, Christianson G, Wax PM, Booze LL, Manoguerra AS, Caravati EM, Nelson LS, Olson KR, Cobaugh DJ, Scharman EJ, Woolf AD, Troutman WG, Americal Association of Poison Control Centers, Healthcare Systems Bureau, Health Resources and Sevices Administration,. Salicylate poisoning: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2007;45(2):95-131. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
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SCOPE

DISEASE/CONDITION(S)

Salicylate poisoning

- This guideline applies to exposure to the specified salicylates alone. Exposure to additional substances could require different referral and management recommendations depending on the combined toxicities of the substances.
- This review focuses on the ingestion of more than a single therapeutic dose and the effects of an overdose. Although therapeutic doses of salicylate can sometimes cause adverse effects in adults and children—some idiosyncratic and some dose-dependent—these cases are not considered.

- The management of Reye's syndrome associated with aspirin use in children is beyond the scope of this guideline.
- This guideline does not address bismuth toxicity resulting from bismuth subsalicylate ingestion.

GUIDELINE CATEGORY

Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Internal Medicine
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Nurses
Pharmacists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To assist U.S. poison center personnel in the appropriate out-of-hospital triage and initial out-of-hospital management of patients with a suspected exposure to salicylates by:

- Describing the process by which a specialist in poison information should evaluate an exposure to salicylates
- Identifying the key decision elements in managing cases of salicylate exposure
- Providing clear and practical recommendations that reflect the current state of knowledge
- Identifying needs for research

TARGET POPULATION

Adults and children with suspected exposures to salicylates

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Assessment of key decision points for triage:

- Patient intent
- Route of exposure and estimated dose
- Time since exposure and symptoms
- Pattern of ingestion (acute or chronic)
- Assessment of symptoms
- Presence of co-ingestants

Treatment/Management

1. Referral to an emergency department
2. Administration of activated charcoal for acute ingestion of toxic dose
3. Washing with mild soap and water for dermal exposures
4. Immediate irrigation for ocular exposures, with referral for ophthalmologic exam, if symptoms of eye injury are present
5. Evaluation by obstetrician or primary care provider of pregnant patients in last trimester who ingest below the dose for emergency department referral and do not have other referral conditions
6. Home observation
7. Follow up monitoring of symptom onset by poison centers

MAJOR OUTCOMES CONSIDERED

- Symptom severity and time of onset
- Mortality
- Dose required for the development of toxicity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Search Strategy

Literature searches for relevant articles were performed by a single investigator. The National Library of Medicine's MEDLINE database was searched (1966 to March 2004) using aspirin or salicylic acid (exploded as Medical Subject Heading [MeSH] terms) with the subheadings poisoning (po) or toxicity (to), limited to humans. The MEDLINE database was further searched using aspirin or bismuth subsalicylate or choline salicylate or ethyl salicylate or glycol salicylate or homomenthyl salicylate or magnesium salicylate or methyl salicylate or methylsalicylate or octyl salicylate or phenyl aminosalicylate or phenyl salicylate or potassium aminosalicylate or potassium salicylate or salicylamide or salicylic acid or salsalate or sodium aminosalicylate or sodium salicylate or sodium thiosalicylate or triethanolamine salicylate or trolamine salicylate as textwords (title, abstract, MeSH term, CAS registry) plus either poison* or overdos* or intox*, limited to humans. This process was repeated in International

Pharmaceutical Abstracts (1970 to March 2004, excluding abstracts of meeting presentations), Science Citation Index (1977 to March 2004), Database of Abstracts of Reviews of Effects (accessed March 2004), Cochrane Database of Systematic Reviews (accessed March 2004), and Cochrane Central Register of Controlled Trials (accessed March 2004). Reactions (1980 to March 2004), the salicylate poisoning management in Poisindex, and the bibliographies of recovered articles were reviewed to identify previously undiscovered articles. Furthermore, North American Congress of Clinical Toxicology abstracts published in the Journal of Toxicology Clinical Toxicology (1995 to 2004) and Clinical Toxicology (2005) were reviewed for original human data.

Four major toxicology textbooks were reviewed for recommendations on the management of salicylate poisonings and for citations of additional articles with original human data in the chapter bibliographies. The Toxic Exposure Surveillance System maintained by the American Association of Poison Control Centers was searched for deaths resulting from unintentional salicylate poisoning. These cases were abstracted for review by panel members. All U.S. poison control centers were surveyed in 2004 to ascertain their out-of-hospital management and triage practices for salicylate poisonings.

Criteria Used to Identify Applicable Studies

The recovered citations were entered into an EndNote library and duplicate entries were eliminated. The abstracts of these articles were reviewed, searching specifically for those that dealt with estimations of doses with or without subsequent signs or symptoms of toxicity and management techniques that might be suitable for out-of-hospital use (e.g., gastrointestinal decontamination). Articles that did not meet either of the preceding criteria, did not add new data (e.g., reviews, editorials), or that exclusively described inpatient-only procedures (e.g., dialysis) were excluded.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level of Evidence	Description of Study Design
1a	Systematic review (with homogeneity) of randomized clinical trials
1b	Individual randomized clinical trials (with narrow confidence interval)
1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it.)

Level of Evidence	Description of Study Design
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality randomized clinical trial)
2c	"Outcomes" research
3a	Systemic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case series, single case reports (and poor quality cohort and case control studies)
5	Expert opinion without explicit critical appraisal or based on physiology or bench research
6	Abstracts

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Extraction Process

All articles that were retrieved from the original search were reviewed by a single trained physician abstractor. The complete paper was reviewed for original human data regarding the toxic effects of salicylates or original human data directly relevant to the out-of-hospital management of patients with salicylate toxicity or overdose. Relevant data (e.g., dose, effects, time of onset of effects, therapeutic interventions or decontamination measures provided efficacy or results of any interventions, and overall patient outcome) were compiled into a table and a brief description of each article was written. This evidence table is available at http://www.aapcc.org/DiscGuidelines/Guidelines%20Tables/Salicylate%20Evidence%20Table.pdf. The table of all abstracted articles was then forwarded to the panel members for review and consideration in developing the guideline. Every attempt was made to locate foreign language articles and have their crucial information extracted, translated, and tabulated. A written summary of the data was created and distributed by the abstractor. Copies of all of the abstracted articles were made available for reading by the panel members on a secure American Association of Poison Control Centers (AAPCC) website.

Criteria Used to Evaluate Studies and Assign Levels of Evidence

The articles were assigned level-of-evidence scores based on the Grades of Recommendation table developed by the Centre for Evidence-Based Medicine at Oxford University (see "Rating Scheme for the Strength of the Evidence" field). Single case reports and case series were classified as level 4.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

An expert consensus panel was established to develop the guideline (see Appendix 1 in the original guideline document). The American Association of Poison Control Centers (AAPCC), the American Academy of Clinical Toxicology (AACT), and the American College of Medical Toxicology (ACMT) appointed members of their organizations to serve as panel members. To serve on the expert consensus panel, an individual had to have an exceptional record in clinical care and scientific research in toxicology, board certification as a clinical or medical toxicologist, significant US poison control center experience, and be an opinion leader with broad esteem. Two specialists in poison information were included as full panel members to provide the viewpoint of the end-users of the guideline.

Guideline Writing and Review

A draft guideline was prepared by the lead author. The draft was submitted to the expert consensus panel for comment. Using a modified Delphi process, comments from the expert consensus panel members were collected, copied into a table of comments, and submitted to the lead author for response. The lead author responded to each comment in the table and, when appropriate, the guideline draft was modified to incorporate changes suggested by the panel. The revised guideline draft was again reviewed by the panel and, if there was no strong objection by any panelist to any of the changes made by the lead author, the draft was prepared for the external review process.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The rating scheme for the strength of the recommendation (A-D, Z) is directly tied to the level of evidence supporting the recommendation.

Grade of Recommendation	Level of Evidence
A	1a
	1b
	1c
B	2a
	2b
	2c
	3a
	3b
C	4
D	5
Z	6

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

External review of the second draft was conducted by distributing it electronically to American Association of Poison Control Centers (AAPCC), American Academy of Clinical Toxicology (AACT), and the American College of Medical Toxicology (ACMT) members and the secondary review panel. The secondary review panel consisted of representatives from the federal government, public health, emergency services, pediatrics, pharmacy practice, and consumer organizations (see Appendix 3 in the original guideline document). Comments were submitted via a discussion thread on the AAPCC web site or privately through email communication to AAPCC staff. All submitted comments were rendered anonymous, copied into a table of comments, and reviewed by the expert consensus panel and the lead author. The lead author responded to each comment in the table and his responses and subsequent changes in the guideline were reviewed and accepted by the panel. Following a meeting of the expert consensus panel, the final revision of the guideline was prepared.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the weight of the evidence (A-D, Z) and classes of recommendations (1a-6) can be found at the end of the "Major Recommendations" field.

1. Patients with stated or suspected self-harm or who are the victims of a potentially malicious administration of a salicylate should be referred to an emergency department immediately. This referral should be guided by local poison center procedures. In general, this should occur regardless of the dose reported **(Grade D)**.
2. The presence of typical symptoms of salicylate toxicity such as hematemesis, tachypnea, hyperpnea, dyspnea, tinnitus, deafness, lethargy, seizures, unexplained lethargy, confusion, or dyspnea warrants referral to an emergency department for evaluation **(Grade C)**.
3. Patients who exhibit typical symptoms of salicylate toxicity or non-specific symptoms such as unexplained lethargy, confusion, or dyspnea, which could indicate the development of chronic salicylate toxicity, should be referred to an emergency department **(Grade C)**.
4. Patients without evidence of self-harm should have further evaluation, including determination of the dose, time of ingestion, presence of symptoms, history of other medical conditions, and the presence of co-ingestants. The acute ingestion of more than 150 mg/kg or 6.5 g of aspirin equivalent, whichever is less, warrants referral to an emergency department. Ingestion of greater than a lick or taste of oil of wintergreen (98% methyl salicylate) by children under 6 years of age and more than 4 mL of oil of wintergreen by

patients 6 years of age and older could cause systemic salicylate toxicity and warrants referral to an emergency department **(Grade C)**.

5. Do not induce emesis for ingestions of salicylates **(Grade D)**.
6. Consider the out-of-hospital administration of activated charcoal for acute ingestions of a toxic dose if it is immediately available, no contraindications are present, the patient is not vomiting, and local guidelines for its out-of-hospital use are observed. However, do not delay transportation in order to administer activated charcoal **(Grade D)**.
7. Women in the last trimester of pregnancy who ingest below the dose for emergency department referral and do not have other referral conditions should be directed to their primary care physician, obstetrician, or a non-emergent health care facility for evaluation of maternal and fetal risk. Routine referral to an emergency department for immediate care is not required **(Grade C)**.
8. For asymptomatic patients with dermal exposures to methyl salicylate or salicylic acid, the skin should be thoroughly washed with soap and water and the patient can be observed at home for development of symptoms **(Grade C)**.
9. For patients with an ocular exposure of methyl salicylate or salicylic acid, the eye(s) should be irrigated with room-temperature tap water for 15 minutes. If after irrigation the patient is having pain, decreased visual acuity, or persistent irritation, referral for an ophthalmologic examination is indicated **(Grade D)**.
10. Poison centers should monitor the onset of symptoms whenever possible by conducting follow-up calls at periodic intervals for approximately 12 hours after ingestion of nonenteric-coated salicylate products and for approximately 24 hours after the ingestion of enteric-coated aspirin **(Grade C)**.

Definitions:

Grades of Recommendation and Levels of Evidence

Grade of Recommendation	Level of Evidence	Description of Study Design
A	1a	Systematic review (with homogeneity) of randomized clinical trials
	1b	Individual randomized clinical trials (with narrow confidence interval)
	1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it.)
B	2a	Systematic review (with homogeneity) of cohort studies
	2b	Individual cohort study (including low quality randomized clinical trial)
	2c	"Outcomes" research
	3a	Systemic review (with homogeneity) of case-control studies
	3b	Individual case-control study
C	4	Case series, single case reports (and poor quality

Grade of Recommendation	Level of Evidence	Description of Study Design
		cohort and case control studies)
D	5	Expert opinion without explicit critical appraisal or based on physiology or bench research
Z	6	Abstracts

CLINICAL ALGORITHM(S)

An algorithm is provided in Appendix 4 of the original guideline document for the triage for salicylate poisoning.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate out-of-hospital triage and initial management of patients with a suspected exposure to salicylates

POTENTIAL HARMS

The benefits of activated charcoal administration should be weighed against the risk of aspiration of gastric contents secondary to vomiting.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline is based on an assessment of current scientific and clinical information. The expert consensus panel recognizes that specific patient care decisions may be at variance with this guideline and are the prerogative of the patient and the health professionals providing care, considering all of the circumstances involved. This guideline does not substitute for clinical judgment.
- This guideline has been developed for the conditions prevalent in the U.S. While the toxicity of salicylates is not expected to vary in a clinically significant manner in other nations, the out-of hospital conditions could be much different. This guideline should not be extrapolated to other settings unless it has been determined that the conditions assumed in this guideline are present.

Limitations of the Literature

Literature based on case reports can be inherently difficult to evaluate because patient histories can be unreliable and are often obtained during a period of extreme emotional stress for patients and caregivers. The exact product, salicylate content, patient weight, patient age, or specific effects were often not known or not documented. There were infrequent mentions whether the accuracy of the history was confirmed by outside sources (e.g., caregivers or witnesses) or objective evidence (e.g., empty product containers or serum concentrations); however, most cases had serum salicylate concentrations reported or salicylate detected in the urine indicating exposure to salicylate. A statement of whether confirmation of the exposure was obtained is included in the data summaries (see Tables 6-11 in the original guideline document).

Wide dosage ranges were observed for all groupings of toxic severity. Besides interpatient variability, the dose ranges could also be attributed to spontaneous emesis in some cases, time of onset for treatment, and inaccuracies in the history of the exposure. Advances in critical care in the past 5 decades have likely had an influence on the assessment, treatment, and outcome of salicylate poisoning. This influence could not be gauged but should be considered in the interpretation of the literature.

Some proprietary products were not sufficiently described and the contents could not be verified in domestic or foreign references. In some reports, only tablet counts were provided without any statement of tablet strength. Some reports did not specify the salicylate and only stated that the dose or product referred to "salicylate." Some reports of case series indicated a percentage of patients with salicylate toxicity and the range or mean of doses, so that specific doses resulting in toxicity could not be determined. When clinical effects were listed as percentages of exposed individuals, it was impossible to determine which effects were associated with a particular dose.

There were inherent difficulties in quantifying exposures to salicylate-containing dermal products. The amount of salicylate in the product, the condition of the skin, surface area of the skin affected, whether occlusive dressings were used, whether the skin was intact, and the frequency and duration of application affected the dose estimation of salicylate.

For the interval to the onset of symptoms, in most cases it was only possible to establish an upper limit of time to onset because often only the time of presentation to a hospital was noted and effects were often present by that time. Few reports documented an exact time of onset after exposure. The times recorded in the summary tables are estimates of the maximum possible delay to onset of symptoms. The data in Tables 6-11 in the original guideline document refer only to the time of first effect and do not give information on the time to achieve maximum effects or the total duration of effects. The practice of documenting essential data, such as dose, patient weight, and time since ingestion, for all salicylate exposures should be reinforced at poison control centers, emergency departments, and in published reports.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Chyka PA, Erdman AR, Christianson G, Wax PM, Booze LL, Manoguerra AS, Caravati EM, Nelson LS, Olson KR, Cobaugh DJ, Scharman EJ, Woolf AD, Troutman WG, Americal Association of Poison Control Centers, Healthcare Systems Bureau, Health Resources and Sevices Administration,. Salicylate poisoning: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2007;45(2):95-131. PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 May 23

GUIDELINE DEVELOPER(S)

American Association of Poison Control Centers - Professional Association

SOURCE(S) OF FUNDING

Health Resources and Services Administration, U.S. Department of Health and Human Services

GUIDELINE COMMITTEE

Not stated

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

There are no potential conflicts of interest reported by the expert consensus panel or project staff regarding this guideline.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Association of Poison Control Centers.

Print copies: Available from the American Association of Poison Control Centers, 3201 New Mexico Avenue NW, Suite 330, Washington, DC 20016

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on November 30, 2006. The information was verified by the guideline developer on December 13, 2006.

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