Complete Summary

GUIDELINE TITLE

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

BIBLIOGRAPHIC SOURCE(S)

Chyka PA, Erdman AR, Manoguerra AS, Christianson G, Booze LL, Nelson LS, Woolf AD, Cobaugh DJ, Caravati EM, Scharman EJ, Troutman WG. Dextromethorphan poisoning: An evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2007 Sep;45(6):662-77. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Dextromethorphan poisoning

Note:

- This guideline applies to the ingestion of dextromethorphan alone. Co-ingestion of 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 overdoses. Although therapeutic doses of

dextromethorphan can cause adverse effects in adults and children, some idiosyncratic and some dose-dependent, these cases are not considered here.

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
Physicians

GUIDELINE OBJECTIVE(S)

To assist poison center personnel in the appropriate out-of-hospital triage and out-of-hospital management of patients with suspected ingestions of dextromethorphan by:

- Describing the process by which an ingestion of dextromethorphan might be managed
- Identifying the key decision elements in managing cases of dextromethorphan ingestion
- Providing clear and practical recommendations that reflect the current state of knowledge
- Identifying needs for research

TARGET POPULATION

Children and adults with suspected ingestion of dextromethorphan

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Assessment of key decision elements for triage
    - Patient intent
    - Dose and formulation
    - Presence of symptoms

- Time of onset of toxicity
- Presence of co-ingestants and risk for drug interaction

Management

1. Referral to an emergency department
2. Activated charcoal in selected patients
3. Naloxone
4. Intravenous benzodiazepines
5. External cooling measures
6. Close monitoring of vital signs and respiratory, cardiovascular, and neurological status
7. Home observation
8. Follow-up

Note: The following measures were considered but not recommended: routine out-of-hospital use of activated charcoal in patients with unintentional dextromethorphan ingestion, induction of emesis.

MAJOR OUTCOMES CONSIDERED

- Signs and symptoms of toxicity
- Mortality
- The threshold dose 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 PubMed database was searched through March 2006 using dextromethorphan as a Medical Subject Headings (MeSH) term with the subheadings poisoning or toxicity, limited to humans. The PubMed database was further searched using dextromethorphan as a textword (title, abstract, MeSH term, CAS registry) plus either poison* or overdos* or intox* or toxic*, limited to humans. This process was repeated in International Pharmaceutical Abstracts (1970–March 2006, excluding abstracts of meeting presentations), Science Citation Index (1977–March 2006), Database of Abstracts of Reviews of Effects (accessed March 2006), Cochrane Database of Systematic Reviews (accessed March 2006), and Cochrane Central Register of Controlled Trials (accessed March 2006). Reactions (1980–March 2006), the dextromethorphan poisoning management in Poisindex, and the bibliographies of recovered articles were reviewed to identify previously undiscovered articles. Furthermore, abstracts from

the North American Congress of Clinical Toxicology published in the Journal of Toxicology -- Clinical Toxicology (1995–2004) and Clinical Toxicology (2005) were reviewed for original human data.

Six major toxicology textbooks were reviewed for recommendations on the management of dextromethorphan poisonings and for citations of additional articles with original human data in the chapter bibliographies. All United States poison control centers were surveyed in 2006 to ascertain their out-of-hospital management and triage practices for dextromethorphan 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

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.)
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

Level of Evidence	Description of Study Design
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 trained physician abstractor. The articles were reviewed for original human data regarding the toxic effects of dextromethorphan or data directly relevant to the out-of-hospital management of patients with dextromethorphan 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/DM%20evidence%20table%202006-8-8.pdf.

The table of all abstracted articles was then forwarded to the panel members for review and consideration in developing the guideline. Attempts were 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.

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 of 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 guideline draft 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 panel members were collected, anonymously 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 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 of the original guideline document). Comments were submitted via a discussion thread on the AAPCC web site or privately through e-mail 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.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Grades of recommendation (A-D, Z) and levels of evidence (1a-6) are defined at the end of the "Major Recommendations" field.

1. All patients with suicidal intent, intentional abuse, or in cases in which a malicious intent is suspected (e.g., child abuse or neglect) should be referred to an emergency department **(Grade D)**.
2. Patients who exhibit more than mild effects (e.g., infrequent vomiting or somnolence [lightly sedated and arousable with speaking voice or light touch]) after an acute dextromethorphan ingestion should be referred to an emergency department **(Grade C)**.
3. Patients who have ingested 5 to 7.5 mg/kg should receive poison center-initiated follow-up approximately every 2 hours for up to 4 hours after ingestion. Refer to an emergency department if more than mild symptoms develop **(Grade D)**.
4. Patients who have ingested more than 7.5 mg/kg should be referred to an emergency department for evaluation **(Grade C)**.
5. If the patient is taking other medications likely to interact with dextromethorphan and cause serotonin syndrome, such as monoamine oxidase inhibitors or selective serotonin reuptake inhibitors, poison center-initiated follow-up every 2 hours for 8 hours is recommended **(Grade D)**.
6. Patients who are asymptomatic and more than 4 hours have elapsed since the time of ingestion can be observed at home **(Grade C)**.
7. Do not induce emesis **(Grade D)**.
8. Do not use activated charcoal at home. Activated charcoal can be administered to asymptomatic patients who have ingested overdoses of dextromethorphan within the preceding hour. Its administration, if available, should only be carried out by health professionals and only if no contraindications are present. Do not delay transportation in order to administer activated charcoal **(Grade D)**.
9. For patients who have ingested dextromethorphan and are sedated or comatose, naloxone, in the usual doses for treatment of opioid overdose, can be considered for prehospital administration, particularly if the patient has respiratory depression **(Grade C)**.
10. Use intravenous benzodiazepines for seizures and benzodiazepines and external cooling measures for hyperthermia (>104 degrees F, >40 degrees C) from serotonin syndrome. This should be done in consultation with and authorized by emergency medical services (EMS) medical direction, by a written treatment protocol or policy, or with direct medical oversight **(Grade C)**.
11. Carefully ascertain by history whether other drugs, such as acetaminophen, were involved in the incident and assess the risk for toxicity or for a drug interaction.

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 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 triage for acute dextromethorphan hydrobromide (HBr) 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 management of patients with suspected dextromethorphan poisoning

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline has been developed for the conditions prevalent in the United States. While the toxicity of dextromethorphan 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.
- This guideline is based on an assessment of current scientific and clinical information. The expert consensus panel recognizes that specific patient care decisions might 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.

Limitations of the Published Data

The literature on dextromethorphan poisoning generally exhibited a number of limitations: 1) much of the data was determined by retrospective studies and case reports and based on estimates of dose provided by patients or family members, which raise questions about the accuracy of the dose estimate; 2) the dose-effect information was confounded, in most cases, by the presence of co-ingestants, differences in treatment measures provided, the effects of drug withdrawal, chronic substance abuse, and concurrent medical conditions (e.g., cold symptoms, upper respiratory infection) that could have altered the clinical presentation or outcome; 3) product formulations of dextromethorphan alone and in combination might have changed over time and many authors failed to report all ingredients and strengths that were involved in their reported cases; 4) in case series, many of the patients remained asymptomatic and product formulations, ingestion doses, and frequency and severity of effects were typically reported as ranges of values, percentages, or means, so individual doses resulting in specific effects could not be determined; and 5) among the few prospective trials available, dextromethorphan was administered in therapeutic doses, which would be expected to be much smaller than doses likely to be seen in an overdose or poisoning.

The level of clinical detail presented in the case reports and abstracts varied widely. In most, the dextromethorphan ingestion was not independently verified or confirmed by laboratory testing nor could the influence of co-ingestants be adequately evaluated. There were no reports of adults without a co-ingestant or not associated with intentional abuse. The unclear time interval from ingestion to onset of toxicity is confounded by a lack of a definition for consequential toxicity. For example, after a dextromethorphan overdose the development of drowsiness in a child could indicate the onset of toxicity or could represent the approach of nap time.

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, Manoguerra AS, Christianson G, Booze LL, Nelson LS, Woolf AD, Cobaugh DJ, Caravati EM, Scharman EJ, Troutman WG. Dextromethorphan poisoning: An evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2007 Sep;45(6):662-77. PubMed

ADAPTATION

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

DATE RELEASED

2007 May 24

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

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Peter A. Chyka, PharmD; Andrew R. Erdman, MD; Gwenn Christianson, MSN; Lisa L. Booze, PharmD; Lewis S. Nelson, MD; Alan D. Woolf, MD, MPH; Daniel J. Cobaugh, PharmD; E. Martin Caravati, MD, MPH; Elizabeth J. Scharman, PharmD; William G. Troutman, PharmD

Expert Consensus Panel Members: Lisa L. Booze, PharmD, Certified Specialist in Poison Information, Maryland Poison Center, University of Maryland School of Pharmacy, Baltimore, Maryland; E. Martin Caravati, MD, MPH, FACMT, FACEP, Professor of Surgery (Emergency Medicine) University of Utah, Medical Director, Utah Poison Control Center, Salt Lake City, Utah; Gwenn Christianson, RN, MSN, Certified Specialist in Poison Information, Indiana Poison Center, Indianapolis, Indiana; Peter A. Chyka, PharmD, DABAT, FAACT, Professor, Department of Clinical Pharmacy, College of Pharmacy, University of Tennessee Health Science Center, Knoxville, Tennessee; Daniel J. Cobaugh, PharmD, FAACT, DABAT, Director of Research, ASHP Research and Education Foundation, Bethesda, Maryland, Former Associate Director, American Association of Poison Control Centers; Daniel C. Keyes, MD, MPH, Medical Director, Pine Bluff Chemical Demilitarization Facility, Associate Professor, Southwestern Toxicology Training Program, Dallas, Texas; Anthony S. Manoguerra, PharmD, DABAT, FAACT, Professor of Clinical Pharmacy and Associate Dean, School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, Former Director, California Poison Control System, San Diego Division, San Diego, California; Lewis S. Nelson, MD, FACEP, FACMT, FACCT, Associate Professor of Emergency Medicine, New York University School of Medicine, Associate Medical Director, New York City Poison Control Center, New York, New York; Elizabeth J. Scharman, PharmD, DABAT, BCPS, FAACT, Director, West Virginia Poison Center, Professor, West Virginia University School of Pharmacy, Dept. Clinical Pharmacy, Charleston, West Virginia; Paul M. Wax, MD, FACMT, Attending Toxicologist, University of Texas Southwestern Medical Center, Dallas, Texas; Alan D. Woolf, MD, MPH, FACMT, Director, Program in Environmental Medicine, Children's Hospital, Boston, Associate Professor of Pediatrics, Harvard Medical School, Boston, Massachusetts

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

At the time of his work on this guideline, Dr. Erdman was employed by AstraZeneca. Dr. Booze's husband is employed by AstraZeneca.

There are no other 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 Institute on December 17, 2007. The information was verified by the guideline developer on January 14, 2008.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 11/3/2008