Complete Summary

GUIDELINE TITLE

Recommendations for the use of laboratory tests to support poisoned patients who present to the emergency department.

BIBLIOGRAPHIC SOURCE(S)

Wu AH, McKay C, Broussard LA, Hoffman RS, Kwong TC, Moyer TP, Otten EM, Welch SL, Wax P. National Academy of Clinical Biochemistry laboratory medicine practice guidelines: recommendations for the use of laboratory tests to support poisoned patients who present to the emergency department. Clin Chem 2003 Mar;49(3):357-79. [118 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Poisoning

GUIDELINE CATEGORY

Diagnosis
Evaluation
Screening

CLINICAL SPECIALTY

Emergency Medicine
Internal Medicine

INTENDED USERS

Clinical Laboratory Personnel
Emergency Medical Technicians/Paramedics
Physicians

GUIDELINE OBJECTIVE(S)

To present recommendations on the use of clinical laboratory tests to support the diagnosis and management of the poisoned patient who presents to the emergency department

TARGET POPULATION

Patients with suspected poisoning presenting to the emergency department

INTERVENTIONS AND PRACTICES CONSIDERED

1. Drug testing to support emergency department (ED) toxicology including
    - Stat quantitative serum or plasma toxicology assays
    - Stat qualitative urine toxicology
    - Comprehensive or broad-spectrum urine drug screen including thin-layer chromatography, liquid chromatography, gas chromatography (GC) with mass spectrometry (MS), and liquid chromatography-tandem MS
2. Analytical and reporting issues for drugs-of-abuse testing by immunoassays
    - Establishing close relationship between the clinical laboratory and ED and understanding the limitations of existing immunoassays
    - Listing the major cross-reaction substances for each drug class
    - Targeting antibodies in immunoassays for testing benzodiazepines toward the parent compound and conjugated metabolites or utilizing online hydrolysis
    - Detecting most opioids (e.g., oxycodone, hydromorphone, meperidine, tramadol, buprenorphine, etc) and not just codeine and morphine
    - Directing immunoassays for amphetamines toward a broad spectrum of amines as a class
    - Confirmation of positive immunoassays if needed
3. Specific analysis of ethyl alcohol and other toxic alcohols
    - Establishing quality assurance (QA) and quality-control (QC) program for clinical breath alcohol testing
    - Utilizing essential operator procedures for breath alcohol analysis
    - Selection and validation of breath alcohol devices
    - Direct measurements for methanol and ethylene glycol in serum or plasma
    - GC or "Acetest" for detection of isopropyl alcohol and propylene glycol
4. Laboratory assays for other toxicants
    - Quantitative serum or plasma acetaminophen assay
    - Screening for salicylate by assessing patient's signs and symptoms

- History and physical examination for determining the exposure to cyanide or hydrogen sulfide
- Monitoring for coagulation status by the prothrombin time (PT) test for determining exposure to anticoagulants
- Heparinized blood samples for lead testing
- History and clinical examination, serum or plasma transferrin measurement or direct unsaturated iron-binding capacity (UIBC) assay to identify iron poisoning
- A 12- or 24-hour timed urine collection in a metal-free container for arsenic and mercury analysis
- Stat pseudocholinesterase testing to screen for exposure to pesticides
- Recognizing signs of inhalant abuse
- Measurement of the fraction of oxyhemoglobin with a co-oximeter
- Establishing regional toxicology centers to serve the toxicologic needs of a larger community of medical centers

Tests Considered but Not Recommended

- Regular testing of urine for benzodiazepines
- Stat testing for the following drugs for ED patients with acute symptoms: tetrahydrocannabinol (THC; marijuana), lysergic acid diethylamide (LSD), methaqualone, ibuprofen, and cotinine (nicotine metabolite).
- Specific drug test panels based on toxidromes
- Testing of gastric contents in clinical management
- Maintenance of chain-of-custody documentation for samples collected for clinical toxicology purposes
- Broad-spectrum screening for trace elements or other analytes in the absence of probable cause

MAJOR OUTCOMES CONSIDERED

- Prevalence of drug and alcohol use in association with emergency department visits
- Sensitivity and specificity of laboratory tests

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Recommendations for the use of clinical laboratory tests were prepared by an expert panel of analytical toxicologists and emergency department (ED) physicians specializing in clinical toxicology. These recommendations were posted on the worldwide-web and presented in open forum at several clinical chemistry and clinical toxicology meetings during the year 2001: a local clinical chemistry section meeting at the Royal Brisbane Hospital (Brisbane, Australia) in January; the Midwest Association for Toxicology and Therapeutic Drug Monitoring, William Beaumont Hospital (Royal Oak, MI), in May; Edutrak Sessions at the American Association of Clinical Chemistry (AACC) Annual Meeting (Chicago, IL) in August; and in October, The North American Congress of Clinical Toxicology (Montreal, Canada), The Society of Forensic Toxicology (New Orleans, LA), and the Scientific Assembly Toxicology Section meeting of the American College of Emergency Physicians (Chicago, IL). Participants at each meeting discussed the merits of the recommendations. A summary of these discussions are presented in the original guideline document.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

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

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the degree of consensus (A or B) are provided at the end of the "Major Recommendations" field.

General Principles for Drug Testing to Support Emergency Department (ED) Toxicology

Tier I Toxicology Testing

Guideline 1.

The clinical laboratory should provide two tiers of drug testing. The first tier includes stat testing of selected target quantitative tests in serum or plasma (see Table 1 below) and qualitative tests in urine (see Table 2 below). If the patient is in no acute distress, additional or even most initial toxicology testing may be unnecessary.

***Degree of consensus*: A** for the analytes listed in Table 1, **B** for the analytes listed in Table 2.

Table 1. Stat quantitative serum toxicology assays required to support an ED*

- Acetaminophen (paracetamol)
- Lithium
- Salicylate
- Co-oximetry for oxygen saturation, carboxyhemoglobin, and methemoglobin
- Theophylline
- Valproic acid
- Carbamazepine
- Digoxin
- Phenobarbital (if urine barbiturates are positive)
- Iron
- Transferrin (or unsaturated iron-binding capacity [UIBC] assay if transferrin is not available)
- Ethyl alcohol
- Methyl alcohol**
- Ethylene glycol**

*Turnaround time (TAT) of 1 hour or less.

**More realistic TATs for these assays are 2-4 hours. These tests are largely unnecessary in countries where these agents are not widely available.

Table 2. Stat qualitative urine toxicology assays required to support an ED*

- Cocaine
- Opiates
- Barbiturates
- Amphetamines**
- Propoxyphene**
- Phencyclidine (PCP**)
- Tricyclic antidepressants (TCAs***)

*In general, urine toxicology screens such as these have a lower urgency and utility than do serum assays. They do not correlate well with clinical effects and suffer from problems with sensitivity and specificity, as discussed in the text. Although widely available, these assays (with the exception of that for the cocaine metabolite) require clinical interpretation.

**Need for these assays may be based on prevalence of drug use, which may vary from region to region. Regular review of drug usage is important.

***Recommended only if the clinical staff fully understands the specificity limitations of this assay (i.e., results are used in conjunction with the electrocardiograph to support a clinical suspicion of TCA toxicity, but not in cases where a positive urine drug test is the sole evidence for this suspicion.)

Assay Turnaround Times for Tier I Tests

Guideline 2.

The ideal TAT for Tier 1 toxicology tests is 1 hour or less except where noted on Table 2.

***Degree of consensus*: B**

Tier II Testing: Comprehensive or Board-spectrum Testing

Guideline 3.

The second tier of drug tests is for patients admitted to the hospital who remain intoxicated, obtunded, or comatose, where a broad-spectrum ("comprehensive") screening panel and would not be identified based on the findings of the first tier of laboratory tests. Results of these tests might be used for more long-term management and/or counseling of patients. Laboratorians should work closely with intensive care providers to determine the appropriate menu of tests and TATs that are necessary.

***Degree of consensus*: B** is necessary to cover drugs and substances that may have clinical significance

Guideline 4.

Testing for toxins beyond those outlined in Tables 1 and 2 should be performed only after the patient is stabilized and the attending physician has received

toxicology input from a poison control center or, preferably, bedside evaluation by personnel trained in medical toxicology.

***Degree of consensus*: A**

Selectivity of Testing

Guideline 5.

Stat testing for the following drugs is not recommended for ED patients presenting with acute symptoms: tetrahydrocannabinol (THC; marijuana), lysergic acid diethylamide (LSD), methaqualone, ibuprofen, and cotinine (nicotine metabolite). Testing for some other drugs, such as amphetamines, PCP, and propoxyphene, should be conducted in areas where these drugs exhibit notable prevalence.

***Degree of consensus*: B**

Drug Panel by "Toxidromes"

Guideline 6.

Clinical laboratories should not set up specific drug testing panels based on toxidromes. The failure to recognize a particular toxidrome may lead to the failure to order an important drug test.

***Degree of consensus*: A**

Gastric Samples

Guideline 7.

There is no role for the testing of gastric contents in clinical management, although premortem collection and specimen retention may be important for cases with medico-legal considerations.

***Degree of consensus*: A**

"Chain-of-Custody" for Clinical Specimens

Guideline 8.

Maintenance of chain-of-custody documentation is unnecessary for samples collected for clinical toxicology purposes, and such practice should be discouraged. As with any laboratory specimen, proper procedures for collection, transport, results reporting, and storage are necessary.

***Degree of consensus*: A**

Recommendations of Analytical and Reporting Issues for Drug-of-Abuse Testing by Immunoassays

Immunoassays

Guideline 9.

Optimum use of urine drug testing assays for ED patients requires an understanding of the limitations of existing commercial immunoassays for drugs of abuse. A close relationship between the clinical laboratory and ED staffs is necessary. The laboratory should clearly communicate to the ED staff the extent of the toxicology services available to them, such as the menu, target TATs, cross-reactivity data, and contact information for consultations.

***Degree of consensus*: A**

Listing of Cross-Reacting Substances on Immunoassays

Guideline 10.

When immunoassays are used, the laboratory should list the major cross-reacting substances for each drug class when a positive result is reported. It may also be appropriate to indicate in a final report (e.g., in the "notes" section) that a negative urine drug result does not indicate absence of all drugs of abuse.

***Degree of consensus*: A**

Immunoassay Cutoffs

Guideline 11.

Cutoff concentrations optimized for workplace drug testing are not necessarily appropriate for clinical toxicology. Although a true-positive result indicates use, it does not presume impairment or intoxication of the patient at the time of specimen collection.

***Degree of consensus*: A**

Inadequate Spectrum of Benzodiazepine Detection by Immunoassays

Guideline 12.

Some immunoassays for testing benzodiazepines are inadequate. Antibodies in optimum assays should be targeted toward the parent compound and principal conjugated metabolites or should utilize an online hydrolysis procedure to convert the conjugated metabolites to the unconjugated forms.

***Degree of consensus*: A**

Guideline 13.

Antibodies for benzodiazepines should be updated to identify the newer drugs in this class as they become approved and available for clinical use.

***Degree of consensus*: A**

Opiate versus Opioid Detection by Immunoassay

Guideline 14.

Immunoassays should detect most opioids (e.g., oxycodone, hydromorphone, meperidine, tramadol, buprenorphine, propoxyphene, and pentacozine) and not just codeine and morphine.

***Degree of consensus*: B**

Immunoassays for Amphetamines versus Sympathomimetic Drug Class

Guideline 15.

The optimum immunoassays to test for amphetamines in ED patients are those directed toward a broad spectrum of amines as a class, rather than assays that are directed specifically toward the illicit amines. An assay directed toward phenylethyl amines would largely cover this class. The name of the test should be changed from "amphetamines" to "sympathomimetic amines" or "stimulant amines."

***Degree of consensus*: A**

Confirmation of Positive Immunoassays

Guideline 16.

When reporting results of immunoassay screening, there must be proper notation given that the assay used is considered as a "screening test'' and that any positive results are to be considered as "presumptive''.

***Degree of consensus*: A**

Guideline 17.

The laboratory should not routinely perform confirmative analyses on positive screening results.

***Degree of consensus*: A**

Guideline 18.

When confirmation is needed, the laboratory should store these specimens for an indefinite period or until the case is resolved. The laboratory should consult with the hospital's risk management department for further guidance.

***Degree of consensus*: B**

Recommendations for Specific Analysis of Ethyl Alcohol and Other Toxic Alcohols

Need for a Breath Alcohol Quality-Assurance/Quality-Control Program

Guideline 19.

Clinical breath alcohol testing is point-of-care (POC) testing and must meet the same quality-assurance (QA)/quality-control (QC) requirements as any POC test. As a part of the laboratory's ongoing QA effort, a program must be in place to monitor and evaluate policy, protocols, and the total testing process so that breath alcohol results are accurate and reliable. The clinical laboratory should be involved in the design, implementation, and monitoring of the quality assurance program.

***Degree of consensus*: A**

Selection and Validation of Breath Alcohol Analysis

Guideline 20.

The laboratory should be involved in the selection, validation, and deployment of the breath alcohol devices used.

***Degree of consensus*: A**

Reporting Units for Ethyl Alcohol

Guideline 21.

Alcohol concentrations should be reported in units clearly defined by the laboratory, with a notation as to the sample matrix that was tested (serum or plasma, urine, whole blood, breath) and methodology.

***Degree of consensus*: A**

Assays for Methanol and Ethylene Glycol

Guideline 22.

Clinical laboratories should provide direct measurements for methanol and ethylene glycol in serum or plasma. If gas chromatography (GC), the assay should target glycolic acid, the toxic metabolite, in addition to the parent intoxicant, ethylene glycol.

***Degree of consensus*: B**

Osmolality Measurement for Toxic Alcohol Surveillance

Guideline 23.

Inherent problems with the measured osmolality and calculation of the osmolal gap reduce the reliability of these measurements in the differential diagnosis of volatile and ethylene glycol alcohol intoxication in patients. A very high osmolal gap (e.g., > 50 mOsm/kg) requires investigation of a toxic alcohol or other agents that can increase the osmolality.

***Degree of consensus*: B**

Isopropyl Alcohol, Propylene Glycol Intoxication and Acetoacetic Acid

Guideline 24.

Quantification of isopropyl alcohol and propylene glycol by GC is the preferred approach to their identification. Measurement of lactate is appropriate for monitoring patients exposed to propylene glycol because this is the major metabolite.

***Degree of consensus*: A**

Guideline 25.

Because propylene glycol is used as a vehicle in some drug preparations and there can be inadvertent exposure, this alcohol should not be used as an internal standard for the GC analysis of volatile alcohols.

***Degree of consensus*: A**

Guideline 26.

In the absence of GC testing for isopropanol, the "Acetest" may be used as an insensitive surrogate because there is some reactivity of this reagent toward acetone. However, the name of the test should be listed as "acetoacetic acid" and not "ketones," "ketone bodies," or "acetone," as this test has the highest sensitivity toward acetoacetic acid.

***Degree of consensus*: A**

Recommendations on Laboratory Assays for Other Toxicants as Causes of Poisonings

"Universal" Acetaminophen and Salicylate Screening

Guideline 27.

All ED patients who present with intentional drug ingestion and chronic overuse secondary to chronic pain should be screened with a quantitative serum or plasma acetaminophen assay.

***Degree of consensus*: A** for quantitative serum or plasma screen.

Guideline 28.

Screening for the presence of salicylate can be guided by clinical findings or acid-base abnormalities.

***Degree of consensus*: A**

Cyanide and Hydrogen Sulfide

Guideline 29.

The ED must rely on history and physical examination to determine whether treatment with cyanide antidote is appropriate. Collection of a blood sample for later cyanide and sulfide testing may be useful to document exposure.

***Degree of consensus*: A**

Anticoagulants

Guideline 30.

Patients who intentionally ingest anticoagulants, particularly the long-acting formulations, should be monitored for coagulation status by the prothrombin time (PT) test. Samples should be collected at 24-36 hours after exposure to monitor anticoagulation effects without prophylactic vitamin K administration. There is no stat clinical need for determining the identity or concentration of the specific anticoagulant taken.

***Degree of consensus*: A**

Lead Poisoning

Guideline 31.

Emergency testing for lead is not required to support ED practice. The ED should be prepared to collect heparinized blood samples for lead testing when lead exposure is suspected; however, specific treatment is usually not initiated in the ED. Because lead is ubiquitous in the environment, needles and collection and transfer tubes need to be free of lead contamination (<5 micrograms/L). Next-day availability of the blood lead result is adequate to ensure appropriate follow-up. Collection of serum or plasma for lead evaluation is not appropriate. The erythrocyte protoporphyrin (EPP) test is not useful for detecting low-level exposure.

***Degree of consensus*: A**

Testing for Iron Toxicity

Guideline 32.

The clinical laboratory should be prepared to provide serum or plasma iron results on a stat basis to aid in the diagnosis of iron overdose. Because of analytical limitations, heterogeneous assays for the total iron-binding capacity (TIBC) cannot be used to determine the absence of free iron and toxicity. Serum or plasma transferring is a more reliable marker for estimating free and potentially toxic iron. If this assay is not available on a stat basis, the homogeneous unsaturated iron-binding capacity (UIBC) assay is more useful than TIBC assays that require a pretreatment step.

***Degree of consensus*: A**

Arsenic and Mercury

Guideline 33.

A 12- or 24-hour timed urine collection in a metal-free container (use opaque plastics with no metal caps) is the best sample for arsenic and mercury analysis and falls outside the realm of ED practices. Results of urine testing should be available within 48 hours of specimen collection.

***Degree of consensus*: A**

Broad-Spectrum Screening for Trace Elements and Environmental Pollutants

Guideline 34.

In the absence of probable cause, such as occupational and/or accidental environmental exposure, broad-spectrum screening for trace elements or other analytes is inappropriate and would rarely be indicated in the ED or any general office practice. These tests have not been sufficiently validated in a general patient population, nor have the implications of clinical decisions based on one-time measurements been discussed sufficiently to warrant any use other than research and biomonitoring for occupational exposure.

***Degree of consensus*: B**

Pesticides

Guideline 35.

Clinical laboratories should provide access to stat pseudocholinesterase testing to screen for exposure to cholinergic agents and not for monitoring of therapy.

***Degree of consensus*: B**

Inhalants

Guideline 36.

Because of a lack of stat availability, there are no clinical laboratory tests that are currently appropriate for monitoring acute inhalant abuse or solvent exposure.

***Degree of consensus*: A**

Methemoglobinemia

Guideline 37.

For patients suspected of having methemoglobinemia, measurement of the fraction of oxyhemoglobin (oxygen saturation) should be performed with a co-oximeter and not a pulse oximeter, as the latter overestimates the actual O_2 saturation. If a request for oxygen saturation is received, all results of a four-part co-oximetry panel should be reported even if the specific requests for carboxyhemoglobin and methemoglobin are not received. Laboratories should not charge separately for the inclusion of these additional results.

***Degree of consensus*: A**

Regional Toxicology Centers

Guideline 38.

A cooperative effort should be made to establish regional toxicology centers where specialized methods can be made available to service the toxicologic needs of a larger community of medical centers.

***Degree of consensus*: A**

Definitions:

Degree of consensus:

A - indicates general consensus by most participants

B - indicates either no consensus or that the recommendation was not applicable to all situations

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation. The guideline recommendations are based upon expert consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of laboratory tests to support poisoned patients presenting to the emergency department
- Development of new and improved toxicology tests

POTENTIAL HARMS

False-positive and/or false-negative laboratory test results

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The material in this monograph represents the opinions of the editors and does not represent the official position of the National Academy of Clinical Biochemistry or any of the co-sponsoring organizations. The National Academy of Clinical Biochemistry is the official academy of the American Association for Clinical Chemistry.
- These recommendations identify laboratory support measures that can improve patient care. They will need to be adapted to specific situations, such as the evaluation of possible child abuse or so-called emergency psychiatric clearance. They do not address every question or identify every substance that might cause an individual to seek emergency care. For example, certain substances are explicitly identified as not requiring stat analytic identification, whereas many are not mentioned at all. The former are often agents that manufacturers have historically included on instrument menus or that certain third-party regulators or agencies have required. When there is no current rationale for these practices, the guideline developers hope this document can be used cooperatively by laboratory and emergency department (ED) directors and their respective organizations in concert with manufacturers to make changes locally and nationally. On the other hand, these recommendations are designed to be useful to the ~30,000 physicians making decisions in EDs across the US. As such, they do not represent the minimum laboratory evaluation that may be used by a specialist in medical toxicology, nor do they reflect all of the current analytic limitations present in various areas of the country. However, they can serve as a forum for discussion of the toxicology laboratory support that can and should be provided within a given patient population, institution, or geographic region of the country.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

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)

Wu AH, McKay C, Broussard LA, Hoffman RS, Kwong TC, Moyer TP, Otten EM, Welch SL, Wax P. National Academy of Clinical Biochemistry laboratory medicine practice guidelines: recommendations for the use of laboratory tests to support poisoned patients who present to the emergency department. Clin Chem 2003 Mar;49(3):357-79. [118 references] PubMed

ADAPTATION

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

DATE RELEASED

2003 Mar

GUIDELINE DEVELOPER(S)

National Academy of Clinical Biochemistry - Professional Association

SOURCE(S) OF FUNDING

National Academy of Clinical Biochemistry

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site:

- Portable Document Format (PDF)
- Word Format

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 9, 2006. The information was verified by the guideline developer on June 6, 2006.

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