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# Utilization management in toxicology

Yan Zhang *, Tai C. Kwong

*Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, NY, United States*

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ABSTRACT

Recent upward trends in the prevalence of abuse of prescription drugs and illicit substances have resulted in increased demands for toxicology testing to support the emergency department and drug treatment in pain management programs. This review will discuss the challenges faced by clinical laboratories to manage the utilization of toxicology tests, particularly those ordered in managing poisoned patients in the emergency department and chronic pain patients on opioid therapy.

Optimal utilization of toxicology tests to support the emergency department relies on selecting the appropriate tests for the patient, and the availability of the results in a timely fashion. Two tiers of toxicology testing systems with different requirements for turnaround time will be discussed. In patients with chronic pain urine drug testing, including screening and confirmation testing are used extensively in pain management to monitor patient compliance. A thorough understanding of the performance characteristics of the test methodologies and drug metabolism is a key to making a proper analytical and clinical interpretation of the test results and will contribute to effective utilization of these tests. In addition, the reimbursement system is an important factor in the decision making process for test selection utilization as significant costs can be incurred by both payers and patients.

Collaboration, trust, and effective communication among clinicians, patients, and clinical laboratory professionals are essential for effective utilization of toxicology testing.



## 1. Introduction

Health care expenditures in the United States will total approximately $4.6 trillion by 2020, which is about 19.8% of the projected gross domestic product [1]. Of those expenditures, it is estimated that laboratory testing accounts for 2–3% of the total (though this is less than 2% of Medicare expenditures) [2,3]. There are over 200,000 clinical laboratories, certified by the Centers for Medicare and Medicaid Services under the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88), which conduct about seven billion tests per year and generate an estimated $52 billion in revenue. The average annual growth rate for both test volume and revenue from 1999 to 2006 was 6–7%, and that growth is expected to continue at a similar rate [3]. The value of laboratory medicine goes well beyond the expense of the laboratory testing itself. It has been estimated that approximately 70% of medical decisions related to patient care are based on laboratory testing [4]. Laboratory testing plays a significant role in clinical decisions addressing prevention, diagnosis, prognosis, treatment, and monitoring of disease.

Clinical toxicology, a subspecialty of laboratory medicine, encompasses the analysis of drugs and toxins in biological fluids (e.g., urine, serum, and saliva) for the diagnosis and treatment of those suspected of poisoning as well as the management of patients on drug therapy. This laboratory service has seen increased utilization due to recent increases in drug abuse and drug overdose. Intentional or unintentional poisonings continue to be a significant cause of mortality and morbidity in the United States. The 2011 National Poison Data System Annual Report indicated that there were 2.33 million human exposures recorded in the previous year, with 49.1% involving children under the age of five resulting in 2765 deaths [5]. In addition, the 2011 National Survey on Drug Use and Health estimated that 22.5 million Americans aged 12 or older were illicit drug users representing 8.7% of the population in that age group. Illicit drug abuse continues to be a threat to public health [6].

Drug overdose rates have increased about five-fold since 1990 [7]. In 2007, over 27,000 unintentional drug overdose deaths occurred in the United States with opioid analgesics being the leading cause followed by cocaine and heroin [7]. Drug overdose is thus second only to motor vehicle crash deaths among the leading causes of unintentional injury [7]. In addition, the increasing prevalence of prescription drug overdose, particularly from opioid analgesics (e.g., oxycodone, hydrocodone, and

*Abbreviations:* CLIA, Clinical Laboratory Improvement Amendments; ED, emergency department; EG, ethylene glycol; HPLC, high pressure (performance) liquid chromatography; POCT, point-of-care testing; TAT, turnaround time; UDT, urine drug testing; MDMA, 3,4-methylenedioxymethamphetamine; MDA, 3,4-methylenedioxyamphetamine; EDDP, 2-ethylidene-1,5-dimethyl-3-3-diphenylpyrrolidine; THCCOOH, 11-nor-9-carboxy$^{\Delta 9}$tetrahydrocannabinol; HCPCS, Healthcare Common Procedure Coding System; LC, liquid chromatography; MS, mass spectrometry.

* Corresponding author at: Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, 601 Elmwood Avenue Box 608, Rochester, NY 14642, United States. Tel.: +1 585 276 4192; fax: +1 585 273 3003.
*E-mail address:* yan1_zhang@urmc.rochester.edu (Y. Zhang).

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methadone) that are used for chronic pain management, reflects a trend that has been observed in the past decade [7].

The prevalence of drug abuse and drug overdose has increased the use of clinical toxicology laboratory services, which are under increasing pressure to reduce costs and improve test efficiency while maintaining and indeed improving the standard of patient care. Due to the ever-evolving nature of drug abuse and drug overdose patterns, as well as the different methodologies involved in drug testing (see details in later sections), clinical toxicology tests can be over- or under-utilized. Misinterpretation can also occur even when appropriate tests have been ordered for the correct indications. In addition, the same drug tests can be ordered for different clinical purposes and will therefore require different approaches to utilization management (e.g. testing for suspected drug overdose versus monitoring of compliance in pain management). To date, there are few published reports on strategies for utilization management focusing on toxicology testing. Effective utilization and management of the clinical toxicology service requires a full understanding of the advantages and limitations of the tests and their clinical utility. This review will focus on the utilization of laboratory tests to support poisoned and intoxicated patients in the emergency department (ED) and drug testing to manage patients treated with opioids for chronic non-cancer pain.

## 2. Clinical toxicology service in support of the emergency department

The clinical toxicology service supports the diagnosis and treatment of poisoned patients in the ED by providing *clinically useful* toxicology test results [8]. The clinical usefulness of the toxicology results refers not only to the clinical utility of tests but also to the availability of results in a timely fashion. Appropriate utilization of a well-planned clinical toxicology service can influence the diagnosis and subsequent treatment of the poisoned patient. Thus, validating drug history or identifying drugs and toxins that were not previously reported can be invaluable for initiating further investigations if needed, or prompt execution of a specific treatment protocol. Measurement of serum drug levels for some drugs can be helpful in assessing the severity of intoxication and the need to initiate specific interventions according to criteria in established clinical guidelines. Moreover, continued monitoring of drug levels can be useful in evaluating the effectiveness of the treatment procedure.

In addition to providing appropriate toxicology tests, the clinical laboratory should make other laboratory tests, such as serum osmolality, arterial blood gases, and liver function tests (see full list in Table 1) available on a 24-hour basis to support the evaluation and management of acute poisoning.

### 2.1. Effective utilization of clinical toxicology tests

Most hospital-based clinical laboratories are unable to provide a full spectrum of toxicological analyses in real time, mostly because of cost constraints and limited technical expertise. The laboratory and the ED should jointly decide on a toxicology service that optimizes clinical utility, meets the needs of the treating physicians, and is feasible within the financial and technical capabilities of the laboratory. The key considerations should include the following: 1) which toxicology tests should be available; 2) whether the assays should be qualitative or quantitative; 3) which specimen types (e.g., serum, urine) to use; 4) when the specimen should be obtained; and 5) what turnaround time (TAT) is acceptable. Each of these features must be examined in the context of test utilization that will have real clinical impact on the management of the poisoned patient.

**Table 1**
Utilization of non-toxicologic clinical laboratory tests for evaluation of acute poisoning [9].

| |
|---|
| Sodium, potassium, chloride and bicarbonate, anion gap |
| Urea, creatinine, glucose |
| Arterial blood gases |
| Liver function tests |
| Calcium, magnesium, albumin |
| Serum osmolality (freezing point depression method) and osmolar gap |
| Creatine kinase |
| Complete blood count |
| International normalized ratio (INR) |

There are published guidelines [9,10] that address the issue of clinical utility of toxicological tests in support of the ED. These guidelines also make recommendations regarding provision of serum or plasma and urine tests that have the greatest impact on patient management and that can be realistically delivered. The tests to be made available should be based on the local prevalence of drugs and toxins in the population served by the ED, the clinical usefulness of their early identification and the value of quantification, and the ability of the laboratory to perform the analyses within an acceptable TAT.

The National Academy of Clinical Biochemistry [10] has recommended that the hospital clinical laboratory provides two "tiers" of toxicology testing. The recommended Tier I tests include selected serum or plasma quantitative tests and urine qualitative tests that have a real impact on diagnosis and acute management of a poisoned patient. These tests should be available, stat, at all times, in all clinical laboratories supporting an active ED that admits patients with acute poisoning, regardless of the size or setting (rural or urban) of the institution. Tier II tests are those that detect drugs or toxins not identified by Tier I tests, are more complicated and time consuming to perform, and are infrequently needed. Tier II tests, if not available on site, may be referred to a regional or reference laboratory. The required TAT differs for Tier I and Tier II tests. The TAT for Tier I tests should be one within which the laboratory can receive specimens, complete the analysis, and report results that are still clinically relevant to the acute care of an ED patient. The TAT requirements for Tier II tests are more flexible [8].

### 2.2. Tier I tests

#### 2.2.1. Tier I tests — Quantitative serum assays

For some drugs quickly determining a patient's serum drug concentration is important, because the level of the drug correlates with the severity of intoxication and/or influences treatment strategy. The drugs that qualify as Tier I quantitative serum assays are listed in Table 2. For these drugs, serum drug concentrations play an important role in the decision to initiate: 1) specific antidote therapy (e.g., acetaminophen (N-acetylcysteine), methanol and ethylene glycol (fomepizol), digoxin (digoxin-specific antibody fragments), iron (deferoxamine), carboxyhemoglobin (hyperbaric oxygen) and methemoglobinemia (methylene blue)); 2) hemodialysis (e.g., theophylline, salicylate, methanol, ethylene glycol) or 3) titration of therapy and/or adjusting of dosage (e.g., ethanol, anti-convulsants).

**Table 2**
Tier I toxicology assays for supporting the emergency department [10].

| Quantitative serum (blood) assays | Qualitative urine assays |
|---|---|
| Acetaminophen | Amphetamines |
| Salicylate | Barbiturates |
| Lithium | Benzodiazepines[a] |
| Theophylline | Cocaine |
| Valproic acid | Methadone[a] |
| Carbamazepine | Opiates |
| Phenobarbital | Oxycodone[a] |
| Digoxin | Propoxyphene |
| Ethanol | Phencyclidine |
| Methanol | Tricyclic antidepressants |
| Ethylene glycol | |
| Co-oximetry testing (oxygen saturation, carboxyhemoglobin, methemoglobin) | |

[a] Drug assays not in [10], but included here due to more recent prevalence of abuse.