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Preface: Toxicology Testing xi

Michael G. Bissell

Overview of Progress in Clinical Toxicology Testing 353

Donald L. Frederick and Michael G. Bissell

Clinical toxicology is the branch of the subject focused primarily on the diagnosis, treatment, prevention, and management of human poisoning. Its practice is most typically carried out in hospital and clinic settings where it is supported by a variety of clinical laboratory services, the historical development of which is the subject of this article.

The Prescription Drug Abuse Epidemic 361

Hoi-Ying Elsie Yu

In the United States, the nonmedical use of prescription drugs is the second most common illicit drug use, behind only marijuana. This article discusses the abuse issues with three of the most widely abused prescription drugs: opioids, central nervous system (CNS) depressants (eg, benzodiazepines), and stimulants (eg, amphetamine-dextroamphetamine and methylphenideate) in the United States. Efforts to deal with the problem are described as well.

Urine Drug Testing for Pain Management 379

Barbarajean Magnani and Tai Kwong

An epidemic of prescription drug abuse in the United States has increased the burden on clinical toxicology testing laboratories. Urine drug testing provides objective evidence for compliance and aberrant drug behavior in patients on chronic (non-cancer) pain management. This article describes the testing menu, drug testing assays including tandem mass spectrometry and their limitations, interpretation of opiate results and clinical considerations.

Alcohol Biomarkers 391

Glynnis B. Ingall

Excessive alcohol consumption poses a wide variety of significant immediate and long-term health risks. Ethanol biomarkers have clinical utility for detection, diagnosis, and treatment of alcohol use disorders as well as for screening for fetal alcohol exposure. Indirect biomarkers are those that reflect the toxic effects of ethanol on organs, tissues, or body biochemistry, whereas direct biomarkers are products of ethanol

metabolism. Liver enzymes, carbohydrate deficient transferrin and mean corpuscular volume are discussed as examples of indirect markers of alcohol use. Commentary on the direct ethanol markers includes the following: acetaldehyde adducts, ethyl glucuronide, ethyl sulfate, phosphatidylethanol and fatty acids ethyl esters.

Drug Abuse: Newly-Emerging Drugs and Trends **407**

Gregory G. Davis

Drug abusers have access to new, more potent compounds that evade existing laws by virtue of their novel chemical structures. These drugs are available for purchase at stores and over the internet. The drugs are not illegal because they are so new that laws have not yet been passed to ban them. These drugs are leading to emergency department visits for cardiovascular, neurologic, and psychiatric complications. Standard drug screens are not designed to detect these new substances. The internet provides access to drugs for substance abusers but also provides physicians speed of access to the habits of substance abusers.

Bath Salts **415**

Roy R. Gerona and Alan H.B. Wu

"Bath salts" has attracted young adults primarily due to its stimulatory and hallucinogenic effects akin to amphetamines and cocaine. Although other designer amines have been incorporated to newer generation "bath salts", synthetic cathinones remain to be their major component. This article discusses our current understanding of the chemistry and metabolism of synthetic cathinones. It also presents a comprehensive review of the most recent laboratory analyses done on this class of compounds in drug products and biological samples.

The Utility of Immunoassays for Urine Drug Testing **429**

Stacy E.F. Melanson

Substance abuse is a significant problem in the United States, with cocaine, marijuana, alcohol and heroin as the most commonly abused drugs. This article focuses on urine drug testing to evaluate potential drug abuse or overdose in the emergent care setting using qualitative immunoassays. Discussion is included regarding the principles of how to validate qualitative immunoassays; how to decide on appropriate specimen type, test menu and cutoff; the limitations of immunoassays; how to communicate test results to clinicians; and use of urine drug testing at point of care.

Drug Testing in the Neonate 449

Steven W. Cotten

Drug testing in newborns comes with analytical, therapeutic, and legal issues, and interpretation of results may be left to physicians, nurses, or social services workers. The unique analytical and legal caveats pose a variety of challenges and therapeutic issues. Positive drug screening results can allow for proper medical management of withdrawal symptoms for certain drug classes. Legal implications and involvement of social services for assessment of child safety surround positive urine or meconium drug samples. Because laboratory results can potentially remove newborns from their biological parents, the caveats and limitations of drug testing in this population are of utmost importance.

Toxicology Testing in Alternative Specimen Matrices 467

Donald L. Frederick

Most toxicology testing involves serum, blood, or urine. Sampling from a site of action such as nerve endings or receptors on cells is not usually available, so often blood is used. Plasma and serum are logical sources to monitor without the interference of red cells. Other types of specimens may be tested and may even be required. Most of such testing has become possible as a result of newer instrumentation. Many of these alternative specimens have very low concentrations of the drugs, drug metabolites, or other toxins. Liquid chromatography–tandem mass spectrometry has allowed testing of these alternative specimens.

Principles and Procedures in Forensic Toxicology 493

John F. Wyman

The principles and procedures employed in a modern forensic toxicology lab are detailed in this review. Aspects of Behavioral and Postmortem toxicology, including certification of analysts and accreditation of labs, chain of custody requirements, typical testing services provided, rationale for specimen selection, and principles of quality assurance are discussed. Interpretation of toxicology results in postmortem specimens requires the toxicologist and pathologist to be cognizant of drug-drug interactions, drug polymorphisms and pharmacogenomics, the gross signs of toxic pathology, postmortem redistribution, confirmation of systemic toxicity in suspected overdoses, the possibility of developed tolerance, and the effects of decomposition on drug concentration.

Pharmacogenomics and the Future of Toxicology Testing **509**

Yash Pal Agrawal and Hanna Rennert

Pharmacogenomics is a useful tool in clinical toxicology for characterizing many gene polymorphisms associated with different pharmacokinetics or pharmacodynamics of exogenously administered drugs. These genetic variants may determine ranges of variation in such fundamental aspects as drug-metabolizing enzymes, drug transporters, drug receptors, or targets of drug action. Toxicologically significant drugs for which the FDA has required the manufacturer to identify relevant pharmacogenomics markers on the label include carisoprodol, citalopram, codeine, and risperidone. For personalized medicine, combining pharmacogenomics testing with therapeutic drug monitoring may allow the identification of individuals who need lower or higher doses, or even a different drug.

Regulatory Issues in Accreditation of Toxicology Laboratories **525**

Michael G. Bissell

Clinical toxicology laboratories and forensic toxicology laboratories operate in a highly regulated environment. This article outlines major US legal/regulatory issues and requirements relevant to accreditation of toxicology laboratories (state and local regulations are not covered in any depth). The most fundamental regulatory distinction involves the purposes for which the laboratory operates: clinical versus nonclinical. The applicable regulations and the requirements and options for operations depend most basically on this consideration, with clinical toxicology laboratories being directly subject to federal law including mandated options for accreditation and forensic toxicology laboratories being subject to degrees of voluntary or state government–required accreditation.

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