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Preface: Drug Testing and Toxicology: Redefining the Plague of Darkness xi

Martin H. Bluth

Narcotic Analgesics and Common Drugs of Abuse: Clinical Correlations and Laboratory Assessment 603

Martin H. Bluth and Matthew R. Pincus

Pain management is an evolving discipline. New formulations mature with promises of improved pain control, better dosing, and fewer side effects. These agents also have an equal risk for abuse. Street chemists are adept at manipulating drugs to more potent versions and creating new compositions of matter. The clinical assessment of the patient is paramount to developing an index of suspicion of overdose, toxicity, or illicit drug use; the clinical laboratory can be a resource to support investigations and guide therapy. The clinical toxicology laboratory needs to keep in step, adapting technology and methodology to facilitate detection of such substances.

Liquid Chromatography–Tandem Mass Spectrometry: An Emerging Technology in the Toxicology Laboratory 635

Yan Victoria Zhang, Bin Wei, Yu Zhu, Yanhua Zhang, and Martin H. Bluth

In the last decade, liquid chromatography–tandem mass spectrometry (LC-MS/MS) has seen enormous growth in routine toxicology laboratories. LC-MS/MS offers significant advantages over other traditional testing, such as immunoassay and gas chromatography–mass spectrometry methodologies. Major strengths of LC-MS/MS include improvement in specificity, flexibility, and sample throughput when compared with other technologies. Here, the basic principles of LC-MS/MS technology are reviewed, followed by advantages and disadvantages of this technology compared with other traditional techniques. In addition, toxicology applications of LC-MS/MS for simultaneous detection of large panels of analytes are presented.

Common Interferences in Drug Testing 663

Michael P. Smith and Martin H. Bluth

Interferences relating to laboratory toxicology testing refer to results which differ from their true value and are often encountered in the setting of a drug screen compared with confirmatory testing. Such interferences fall into two general categories; those that cause false positive results (when a drug screen is positive but confirmatory testing is negative) and those that cause false negative results (when a drug screen is negative when in reality the sample donor has ingested the tested substance). Such interferences can result from differences in laboratory testing methodology, reagent and analyte cross reactivity, limits of analyte detection, instrument resolution, reporting cutoff, sample processing, tissue type and sample

adulteration among others. Awareness of the possible causes of such interferences are integral to proper laboratory result interpretation and patient management.

Toxicology in Pain Management

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Daniel A. Schwarz, M.P. George, and Martin H. Bluth

Toxicology testing in pain management has become the standard of care. The Center for Disease Control and Prevention published guidelines including urine drug testing prior to initiating opioid therapy and for monitoring prescription and illicit drugs. Physicians must know indications for toxicology testing, and the frequency based upon risk stratification. This includes personal and family history of alcohol or substance related disorders, mental illness and smoking. Knowledge of opioid metabolism and various matrices to test are described. Additional knowledge of presumptive vs definitive testing along with algorithms and medical necessity with evidence-based clinical standards are discussed.

Toxicology in Addiction Medicine

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Daniel A. Schwarz, M.P. George, and Martin H. Bluth

Toxicology testing in addiction medicine varies across the spectrum, yet remains a powerful tool in monitoring addictive patients. There are many reference laboratories offering toxicology testing, and physicians should have some understanding of laboratory, methodology, testing portfolio, and customer support structure to aid them in selecting the best toxicology laboratory for their patients. Consultation with a clinical pathologist/toxicologist in conjunction with the consideration of monitoring large numbers of illicit and psychoactive drugs in the addictive patient may provide important clinical information for their treatment.

Precision Medicine in Toxicology

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Daniel A. Schwarz, M.P. George, and Martin H. Bluth

Precision medicine applies primarily to pharmacokinetics in toxicology. Mastering hepatic metabolism through an understanding of the genetics behind Phase I, or oxidation/reduction and some Phase II, or conjugation, enhances the scientific and clinical application of common drug toxicology. This review includes basic hepatic metabolism, the common substrates, inducers and inhibitors of cytochrome P450 along with genetic variants behind the enzymes. Detailed metabolism of commonly measured opioids in clinical practice is provided. Finally, evidence based research and clinical correlations conclude that knowledge of inducers and inhibitors, in conjunction with genetic variations, are integral components for applied precision medicine in toxicology.

Toxicology in Reproductive Endocrinology

709

Roohi Jeelani, Martin H. Bluth, and Husam M. Abu-Soud

Fertility relies on a series of time dependent events, which are largely regulated by hormones. Concentration and function of these hormones can be altered by exposure of consumed and environmental toxins. It is

important to consider the dose and timing of toxin exposures in assessing the impact of them on reproductive health, however the utility of laboratory assessment in this regard is not well established. General laboratory assessment of reproduction and infertility includes hormone evaluation (hCG, prolactin, TSH, free thyroxin, FSH, LH and androgens among others) and treatment is via various assisted reproductive technologies. Reduction and abstinence from exposure to toxins is recommended to improve reproductive health.

Ketamine: A Cause of Urinary Tract Dysfunction 721

Frank Anthony Myers Jr, Martin H. Bluth, and Wellman W. Cheung

Drug addiction as a result of improper use of prescribed and illicit use has been on the increase globally. The effects of such use have implications in the urologic disease space. To this end, Ketamine has been reported to affect urologic function, causing a number of voiding symptoms. It may also confound the differential diagnosis of urologic diseases, such as interstitial cystitis, among others.

Otolaryngology Concerns for Illicit and Prescription Drug Use 745

Nathan J. Gonik and Martin H. Bluth

Concern for illicit and restricted drug use in otolaryngology is similar to other surgical specialties with a few notable exceptions. Many illicit drugs are consumed transnasally. Repeated nasal exposure to stimulants or narcotics can cause local tissue destruction that can present as chronic rhinosinusitis or nasoseptal perforation. Further, the Food and Drug Administration has taken a stance against codeine for pediatric patients undergoing adenotonsillectomy. They have identified an increased risk of death postoperatively with these medications. Because codeine has been the most commonly prescribed narcotic, this has shifted the standard practice.

Forensic Toxicology: An Introduction 753

Michael P. Smith and Martin H. Bluth

This article presents an overview of forensic toxicology. The authors describe the three components that make up forensic toxicology: workplace drug testing, postmortem toxicology, and human performance toxicology. Also discussed are the specimens that are tested, the methods used, and how the results are interpreted in this particular discipline.

Drug Toxicities of Common Analgesic Medications in the Emergency Department 761

Mateusz Ciejka, Khoa Nguyen, Martin H. Bluth, and Elizabeth Dubey

About 75% of patients present to the emergency department with a complaint of pain. There are multiple prescribed and over-the-counter medications that are available for the treatment of pain. Acetaminophen, opioids, and aspirin are commonly used agents that are available as single agents or in combination with other medications. However, all of these agents are susceptible to toxic overdose, which requires prompt recognition through clinical and laboratory assessment modalities and initiation of therapy to reduce the risk of morbidity and mortality.

Use of the Clinical Laboratory in Psychiatric Practice

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Christopher Aloeos, Jonathan M. Wai, Martin H. Bluth, and Howard Forman

In this review, the authors address the general principles of prescribing psychiatric medications and discuss how the clinical laboratory can be used to guide prescribing practices. Treatment considerations in different settings and for different medications are discussed. Because the clinical laboratory is advancing in its technology, so should the clinician's knowledge of how to use the clinical laboratory. The authors propose recommendations and a simple algorithm for how to use medication levels in blood and other fluids to guide care in medications without well-defined therapeutic windows.

Clinical Toxicology and Its Relevance to Asthma and Atopy

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Rauno Joks and Martin H. Bluth

Although both the prevalence of asthma and the prescription drug use, notably the opiate analgesic class, epidemics are increasing, there is a complex interplay between both disorders, with both protective and exacerbating factors involved in the effect of opiates on asthma pathogenesis and clinical severity. This review examines the airway effects, both immunologic and neurologic, of opiates, which may interact and result in protection or exacerbation of asthma.