

TOXICOLOGY TODAY



TRICYCLIC ANTIDEPRESSANT (TCA) SCREENING



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PharmD

Introduction

Illicit drug abuse, intentional or accidental overdose, and drug-drug interactions account for a majority of medication related emergency department visits.¹ In 2004, over 12,000 overdoses were exposures to tricyclic antidepressants (TCA), with 11% resulting in serious adverse outcomes or death.² TCA toxicologic screens are included in recommended emergency department toxicology testing and may aid in directing early recognition of a patient with an otherwise unknown ingestion.²⁻⁴ TCA screens have limitations, because of cross-reactive compounds leading to false positives and false nega-

tives for certain TCAs.

Tricyclic Antidepressants

The TCAs are a broad class of structurally similar medications including: amitriptyline, clomipramine, doxepin, imipramine, trimipramine, desipramine, nortriptyline, and protriptyline.⁵ The TCAs have been used since the 1960s for a variety of indications such as depression, anxiety disorders, eating disorders, attention deficit hyperactivity disorders, enuresis in children, and neuropathic pain.²⁻⁵ TCA use has declined over the years due to their relatively serious cardiovascular and central nervous system toxicities in overdoses.

Tricyclic antidepressants have effects on receptors, neurotransmit-

ters, and ion channels. TCAs inhibit muscarinic acetylcholine receptors, alpha-1 adrenergic receptors and presynaptic reuptake of norepinephrine and serotonin. The most worrisome toxicologic effect is that TCAs inhibit fast sodium channels in phase 0 of the cardiac action potential potentially leading to lethal ventricular arrhythmias.

Patients who overdose on TCAs can rapidly decompensate, typically within the first six hours after a TCA ingestion. Anticholinergic symptoms, such as dry mouth, blurred vision, constipation, urinary retention, and decreased sweating can occur early or late in presentation. Central nervous system toxicity presents as agitation and delirium and can progress rapidly to seizures that are usually brief and occur in the first few hours after ingestion. Cardiac conduction delays are typically a widening of the QRS interval (> 100 msec) and a rightward shift of the terminal 40-msec QRS axis. Sinus

TCA Screening

Black Widow Spider Bites

Outreach Education:

- Dosing Devices
- Medication Labels

Meet the UPCC Staff:

- Taylor Rhien

tachycardia is the most common dysrhythmia and ventricular tachycardia is the most common fatal dysrhythmia. The most common cause of death is refractory hypotension.

Early and aggressive management is essential for patients with severe TCA toxicity. Gastric lavage may be considered in life-threatening overdoses and lavage and/or activated charcoal should only be performed if the airway is protected. A 12-lead ECG is recommended as soon as possible for all patients. If the QRS complex is wider than 100 msec or if the height of the upward R wave in lead aVR is taller than 3 mm then alkalinization of the blood is indicated. Sodium bicarbonate is the treatment of choice for conduction disturbances and hypotension, and

benzodiazepines should be used to treat seizures. Class IA and IC antiarrhythmics and physostigmine are contraindicated.

Types of Laboratory Testing

The presence and/or absence of a tricyclic antidepressant can be determined through either screening or confirmatory techniques performed on serum/plasma or urine.⁴ Urine screens are usually qualitative and reported as either positive or negative.¹ The manufacturer of a screening assay sets a cut-off value for the assay – samples screening above this value are interpreted as positive and those screening below this are negative. Confirmatory testing, on the other hand, can provide quantitative results, as long as the quantitation (*cont. on pg. 3*)

DOSING DEVICES – A CUP OF TROUBLE

Pediatric medication errors are frequently attributed to dosing errors. This is particularly a problem with liquid medication¹ and is contributed to by confusing label instructions. Directions use terms such as teaspoon or tablespoon, while the cup or dropper may list doses in milliliters. Some pediatric medications do not come with a measuring device.

A recent article in the Archives of Pediatric and Adolescent Medicine explored the role of health literacy in dosing pediatric medicine accurately.² Caregivers at an urban public health hospital clinic were asked to measure 1 teaspoon or 5 mL of a test medication using 6 different measurement methods [cups, spoon, dropper, syringes]. Caregiver literacy was measured using the Newest Vital Sign (<http://www.pfizerhealthliteracy.com/physicians-providers/NewestVitalSign.aspx>).

Overall, the dosing cups had the highest risk for error; only 30% of caregivers provided



the correct dose with a printed cup. The most accurate dosing was noted with the medicine dropper (94.4% measured the correct dose) followed by syringes and dosing spoon.

For all dosing devices, the rate of error was higher when the caregiver's literacy was lower. Counseling on the accurate use of dosing devices should include strategies to mitigate limited literacy as well.

A recent issue of FDA Consumer Updates was recently published on this topic, available at: <http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM253692.pdf>

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BLACK WIDOW SPIDER BITES

by Jared Koyle, PharmD &
Karen C. Thomas, PharmD, PhD, CSPI



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Roughly 2300 black widow spider (*Latrodectus mactans*) bites were reported to poison control centers in the US in 2011. Approximately 30% of exposures resulted in no or minor symptoms.

Mild envenomations may result in muscle aches and local diaphoresis. Severe envenomations may cause excruciating pain, typically involving the back or abdomen as well as muscle cramping and muscle injury. Symptoms usually present within minutes to hours of a bite and acute symptoms can last for anywhere from 24-72 hours. *Latrodectus* venom contains a protein, α -latrotoxin, which is responsible for clinical symptoms. This toxin acts by depolarizing the presynaptic membrane of sensory and motor neurons, causing them to release large quantities of neurotrans-

mitters like acetylcholine. This causes painful muscle cramping, abdominal pain, back pain and diaphoresis.

Treatment of *Latrodectus* envenomation includes benzodiazepines and opioids to manage pain and muscle cramping. However they do not decrease symptom duration. Black widow spider antivenom contains antibodies against components of *Latrodectus* venom. Antivenom generally relieves symptoms within one to three hours of administration and shortens the duration and intensity of symptoms in envenomated patients. Black widow spider (*Latrodectus mactans*) antivenom is currently on the national drug shortage list. Contact the Utah Poison Control Center for assistance in locating antivenom or with any questions regarding management of black widow spider bites.

References

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WHAT'S ON THE LABEL?

To assist with educating families about using over-the-

counter (OTC) medications, Scholastic, Inc. in conjunction with McNeil Consumer Healthcare and American Association of Poison Control Centers has developed an OTC literacy education program (<http://www.scholastic.com/otcliteracy>). A companion poster and OTC label guide are available to download (http://www.scholastic.com/otcliteracy/pdf/McNeil_56_Poster.pdf) and (http://www.scholastic.com/otcliteracy/pdf/McNeil_56_NWP_WhatsOnTheLabel.pdf)

NORTH AMERICAN CONGRESS OF CLINICAL TOXICOLOGY POSTERS

Poison Center Plant Identification

Dahl B, Crouch BI, Thomas KC, Bennett HK
Utah Poison Control Center, College of Pharmacy, University of Utah, Salt Lake City, Utah

Utilization of a Regional Poison Center

Malheiro MC, Crouch BI, Thomas KC
Utah Poison Control Center, College of Pharmacy, University of Utah, Salt Lake City, Utah

Health District Mini-Grant Program

Pace ST, Malheiro MC, Crouch BI
Utah Poison Control Center, College of Pharmacy, University of Utah, Salt Lake City, Utah

Maternal-Fetal Lead Poisoning From Pottery Pica Treated with DMSA and Exchange Transfusion

Caravati EM, Donnelly ML, Birdsall S
University of Utah, Health Sciences Center, Salt Lake City, Utah

Check our website for more poison prevention information at www.utahpoisoncontrol.org

(cont. from pg. 1)

TCA Screening

of the sample falls between the lower and upper limit of quantitation of the given assay.

Immunoassays are common screening techniques. Immunoassays use monoclonal or polyclonal antibodies directed at the structure of one compound but may have broad cross-reactivity with a class of compounds, like the tricyclic antidepressants. TCA screens are commonly directed at imipramine and desipramine.⁶ Most screening and point-of-care tests are in the form of an immunoassay. Immunoassays are generally inexpensive, and turn-around-times (TAT) are usually rapid. Immunoassays, however, are prone to both false positive and false negative results. In the case of marketed tricyclic antidepressant assays, compounds that are similar in structure to tricyclic antidepressants can produce positive test results.⁷ These cross-reactive compounds can be structurally related compounds or other endogenous compounds. Cross-reactive compounds are usually reported in the package insert for an assay (available from your toxicology laboratory) or in the medical literature and can differ between marketed immunoassays for a given class of substances.

Confirmatory testing can provide definitive identification of a specific TCA and its metabolites.¹ Confirmatory testing is usually performed using gas chromatography mass spectrometry (GC/MS) or liquid chromatography tandem mass spectrometry (LC/MS/MS) only available in large, regional laboratories. These methods are able to detect and quantify small amounts of a substance with accuracy and sensitivity.⁴ A confirmatory test can either be ordered specifically for a compound, or can be performed to confirm a positive screen value. Confirmatory testing, however, is expensive, time consuming, and technically demanding.¹ Average TAT for tricyclic antidepressant confirmation is one to three days, making this type of testing of little clinical utility in the acute management of a patient with suspected TCA toxicity.⁸

Common Medications that Cross-React with TCA Screens

Reported medications that cross-react with TCA screens, resulting in false positives, include the following:^{1, 2, 4, 7, 9}

- Carbamazepine
- Cyclobenzaprine
- Quetiapine
- Phenothiazines, such as prochlorperazine
- Diphenhydramine
- Cyproheptadine
- Hydroxyzine

Summary

Tricyclic antidepressant screens have their limitations. TCA screens should not be used alone to diagnose a TCA toxicity, but rather be used in conjunction with continuous cardiac monitoring and serial ECG monitoring for a minimum of 6 hours in a suspected TCA overdose. Interpretations of TCA values are dependent upon the instrumentation used to obtain the screen, and clinicians need to be aware of the specifics of the TCA screen they are ordering. Obtaining a thorough medication history (prescription, non-prescription, supplements) may aid in determining any cross-reactive compounds that may lead to TCA false positive results. The Utah Poison Control Center is available to provide recommendations in the management of a TCA overdose and/or assist in the interpretation of laboratory results.



Photo Credit: Glowsource.com

GLOW JEWELRY

Glow sticks are self-contained light sources that contain a chemical that luminesces and can be used to enhance visibility in the dark, including emergency situations. Glow products, including glow jewelry are particularly popular around Halloween. The Utah Poison Control Center experiences an increase in calls in October related to these products. The chemical in the glow product can be irritating.

Most exposures to glow products occur when someone bites into them, gets the chemical on their skin or splashes it in their eyes. Most exposures result in minor irritation that can be treated with a drink to take the taste away or irrigation of the skin or eyes. However, since each situation may be unique, the UPCC encourages people to call with any questions or concerns following an exposure to a glow product.

Research has shown that calls to poison centers keep the vast majority of callers out of the hospital and decreased length of stays for patients who are admitted. Poison centers save lives, protect the public's health, and save millions of taxpayer dollars.



AAPCC Press Release – Oct 2012

In 2012, an average of 21 Utah adults died as a result of prescription pain medications each month. The prescription pain medication death rate has leveled off since 2012, when funding for the prescription Pain Medication Program was eliminated.

Utah Department of Health, Violence & Injury Prevention Program Prescription Pain Medication Deaths in Utah, 2012
<http://health.utah.gov/vipp/pdf/FactSheets/2012RxOpioidDeaths.pdf>

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WELCOME DR. MARTIN



The Utah Poison Control Center is pleased to welcome Dr. Thomas Martin as our new medical director. Dr. Martin is trained in emergency medicine and medical toxicology and holds a masters of public health with an environmental and occupational health emphasis. He is a fellow of the American College of Emergency Physicians and the American College of Medical Toxicology. Prior to coming to the Utah Poison Control Center, Dr. Martin was associate professor of medicine and attending physician in the emergency department at the University of Washington and the associate medical director at the Washington Poison Center. Dr. Martin received his medical degree from Pennsylvania State University and completed his emergency medicine training at the Truman Medical Center, University of Missouri Kansas City and his medical toxicology training at the Georgetown University Hospital.

MEET THE UPCC STAFF



TAYLOR RHIEM, BS joined the Utah Poison Control Center in May 2013. He grew up in Farmington, New Mexico and attended Brigham Young University, earning a BS in exercise science. He is currently pursuing a PharmD at the University of Utah and will graduate in the spring of 2016. In his opinion, working at poison control is the best student pharmacist job around. He enjoys the patient interaction, the uniqueness of the job, and learning from experienced poison specialists. Outside of school and the UPCC, Taylor loves bicycles, banjos, and woodworking. He enjoys the great outdoors, especially the parts of New Mexico and Colorado where he grew up. His favorite poison cases involve spiders, scorpions, and other critters.



FDA's MedWatch Safety Alerts: September 2013

To decrease risk of accidental exposure the FDA is requiring the manufacturer of **Duragesic (fentanyl) pain patches** to print the name and strength of the drug on the patch in long-lasting ink, in a clearly visible color. This will enable patients and caregivers to more easily find patches on patients' bodies, and see patches that have fallen off.

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The Utah Poison Control Center expresses its sincere thanks to the health care professionals, public health officials and toxicology colleagues that work together to treat and prevent poisonings.



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