Official Newsletter of the **Utah Poison Control Center**

TOXICOLOGY TODAY

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NEW TOBACCO DOSAGE FORMS: A CONCERNING DEVELOPMENT

by Vilayvone Thipsouvan, PharmD

Figure 1: Similarity of Orbs to Tic Tac® mints

Credit: Andrew Seidenberg, Harvard School of Public Health

Introduction

Nicotine is the primary component of tobacco responsible for dependency and acute toxicity. Symptoms of nicotine toxicity range from mild symptoms such as nausea and vomiting, to confusion, convulsions, and death. Delivery vehicles for nicotine containing products have evolved over the years from cigarettes to smokeless tobacco to nasal sprays, and now to dissolvable candy-like tobacco. In 2010, a total of 7,434 exposures to tobacco products were reported to US poison control centers in children less than 6 years of age. Most exposures involved cigarettes and smoking tobacco.[1] The new tobacco products potentially pose an increased risk of exposures in children due to the appealing appearance and palatability.

Sources of Nicotine

Tobacco products have expanded from traditional cigarettes and chews to more compact versions enhanced with flavoring. With the implementation of smoke-free establishments across the US, tobacco companies have introduced smokeless, spit-free tobacco. Snus is finely chopped tobacco contained within small tea-like paper packets and is placed under the user's upper lip. Three additional products of concern are tobacco sticks, strips, and orbs. Sticks are finely milled tobacco formed into a toothpick size stick, strips are a film formulation, and orbs are a pellet-form of tobacco, and all dissolve in the mouth.

Mechanism of Nicotine Toxicity

Nicotine acts as an agonist at nicotinic-type acetylcholine receptors. These receptors are located throughout both the central nervous system and autonomic nervous system.[2,3] Stimulation of these receptors leads to increased action potential propagation and catecholamine release, resulting in tachycardia and hypertension. Direct stimulation of receptors located on the spinal cord result in muscle fasciculations and tremors. Increased parasympathetic activity leads to the development of miosis, salivation, and lacrimation. The stimulatory phase is followed by autonomic and central nervous system depression leading to hypotension, bradycardia, and respiratory depression.[3]

Nicotine Absorption and Toxic Dose

Nicotine absorption occurs through the buccal

Table 1: Nicotine Content: Old Versus New Products*

Traditional Sources of Nicotine[2]		
SOURCE	**CONTENT (mg)**	**DELIVERED (mg)***
1 whole cigarette	13–30	0.5–2.0
1 low-yield cigarette	3–8	0.1–1.0
1 cigarette butt	5–7	–
1 cigar	15–40	0.2–1.0
1 g of snuff (wet)	12–16	2.0–3.5
1 g of chewing tobacco	6–8	2.0–4.0
1 piece of nicotine gum	2 or 4	1.0–2.0
1 nicotine patch	8.3–114	5.0-22/24 h
1 nicotine nasal spray	0.5	0.2–0.4
Snus	3.6–6.3	0.22–1.4
1 Camel Strip	0.6	N/A
1 Camel Stick	3.1	N/A
1 Camel Orb	1 mg	N/A

**Delivered through intended use of standard dose.*

Adapted from references 2,4,5,6

(cont. on pg. 3)

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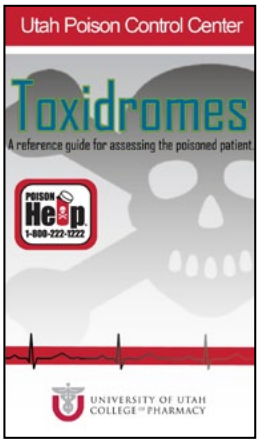
OUTREACH EDUCATION

EMS TOXICOLOGY TRAINING



The Utah Poison Control Center is pleased to announce the completion of our EMS training program on Toxidromes. Our training was developed in conjunction with the Bureau of Emergency Medical Services, Utah Department of Health. An online needs assessment survey was conducted to evaluate toxicology/poisoning education needs and training format preferences for EMS agencies in our state. Based on survey results, we designed an educational program about toxidromes specific to pre-hospital care providers in a train-the-trainer format. The slide presentation and script were made available to EMS trainers on CD. A pocket-sized toxidrome reference booklet was also provided.

We have trained more than 300 EMS trainers and instructors from all 29 counties and provided materials for them to train within their agencies. Based on a sample of 53 EMS trainers who completed a post training survey, each person trained went on to train an average of 15 additional EMS providers. The overall satisfaction score from all trainings was 4.7 on a Likert scale of 1-5. All evaluation respondents would recommend this training to a colleague.

The UPCC is pleased to collaborate with the Utah Department of Health to provide training for our pre-hospital emergency personnel.

AAPCC BLOG

The American Association of Poison Control Centers (AAPCC) is the organization representing America's 57 poison control centers and promoting poison safety and awareness. Their mission is to advance poison centers in their public health mission. As such, they recently extended the reach of poison centers through the use of social media tools.

Blog: The purpose of the blog is to showcase the important work of the nation's 57 poison control centers. The blog discusses current poison issues, such as bath salts and button batteries, as well as ways you can keep your family safe from poisonings. Examples of calls to poison centers are presented. Register here to receive notifications of new posts by email: http://aapcc.wordpress.com

Facebook©: Facebook is used to provide frequent poison prevention tips and highlight important news and research involving poisoning. Check it out here: www.facebook.com/aapcc

Twitter©: Twitter is used to provide poison prevention tips and short entries for the purpose of providing the reader quick access to timely prevention information. See http://twitter.com/#!/aapcc

UPCC TRANSITIONS

Personnel transitions are a natural, but often difficult part of any organization. This year we mark significant transitions in medical direction that provide us with a great opportunity to reflect on the important accomplishments of two individuals who contributed significantly to the Utah Poison Control Center by providing medical direction for the last 30+ years.

E. Martin Caravati, MD, MPH: Dr. Caravati has served as the Utah Poison Control Center's medical director for the last 12 years. Prior to that time he served as associate medical director for 13 years and as a consultant for another 2 years. During his tenure at the UPCC he served on the board of directors of the American Association of Poison Control Centers and the American Academy of Clinical Toxicology. He distinguished himself as an editor serving on the editorial board of several journals, as an Associate Editor of Annals of Emergency Medicine prior to taking on his current role as Editor-in-Chief of Clinical Toxicology; the official journal of the European Association of Poisons Centers and Clinical Toxicologists, and the American Association of Poison Control Centers. Dr. Caravati has made important contributions to the development of consensus guidelines for antidote stocking in hospitals and EDs, as well as national guidelines for poison centers. The UPCC has benefited significantly from his clinical toxicology expertise and his contributions to the published literature Dr. Caravati will continue to take call for the UPCC while he devotes his time to the Medical Toxicology Consult Service at various hospitals in Salt Lake City, the new Toxicology Clinic at Redwood Health Center, as well as to his editorial duties. We are fortunate that he will continue to provide on-call expertise regarding consultation of UPCC cases and work with the UPCC in the coordination of care of the poisoned patient and the education of emergency medicine residents and fellows.

Douglas E. Rollins, MD, PhD: Dr. Rollins served as the UPCC's medical director from 1980-2000. He transitioned to associate medical director in 2000. Dr. Rollins is retiring July 2012 after a successful career as a pharmacologist, toxicologist, researcher and clinician. Dr. Rollins served for 16 years as director for the Center for Human Toxicology, for 3 years as the Medical Director for the Doping Control Program, 2002 Winter Olympic Games and has held numerous grants and contracts during his career. We wish Dr. Rollins all the best as he takes on his next career, retirement.

The Utah Poison Control Center is actively searching for a medical director to be ultimately joined by one or more medical toxicologists to provide full-time coverage to the UPCC. In the meantime, we are pleased to announce that Zane Horowitz, MD will be the interim medical director for the Utah Poison Control Center effective July 1st. Dr. Horowitz is Professor, Emergency Medicine at the Oregon Health & Science University (OHSU) and Medical Director, Oregon Poison Center. He will be onsite at the UPCC 5 days per month. We will use a variety of creative means to interface with Dr. Horowitz and the other medical toxicologists at OHSU the remainder of the month, participating in many educational opportunities and remotely reviewing cases. The OHSU *(cont. on pg. 4)*

Check our website for the 2011 Annual Report
www.utahpoisoncontrol.org

(cont. from pg. 1)

New Tobacco Dosage Forms

and nasal mucosa, GI tract, skin, and respiratory tract.[2,3] Absorption is dependent upon nicotine content, route of exposure, and the pH of the product. An alkaline pH increases the absorption of nicotine.[2] The more alkaline the product the more free nicotine is readily available for absorption. Camel Orbs were found to be more alkaline than cigarettes, most moist snuffs, and most snus products, however, data were not available for the strips and sticks.[4] This would indicate that more nicotine would be absorbed from orb pellets. Toxicity can occur in small children following the ingestion of as little as one cigarette or three cigarette butts (Table 1). Translating this to a potential toxic dose of the newer products is difficult because of the factors affecting absorption.

Clinical Manifestations of Nicotine Intoxication

Clinical effects can develop as early as 15-60 minutes after ingestion of nicotine-containing products and generally last for 1-2 hours.[2,3,5] However, clinical manifestations may last 24 – 72 hours in severe cases.[2,3] Clinical effects related to nicotine ingestion are outlined in Table 2. Gastrointestinal effects occur early and include nausea, vomiting, diarrhea, abdominal pain, and salivation.[2,3] In more severe cases, cardiovascular, respiratory and central nervous system complications can occur (Table 2).

Treatment

Treatment is symptomatic and supportive. Acute ingestions are most likely to present with spontaneous vomiting. The cardiac effects of tachycardia and hypertension are generally short lived and quickly progress to bradycardia and hypotension.[2,3] Hypertensive crisis and seizures should be treated with a short acting intravenous antihypertensive agent and benzodiazepines, respectively. Hypotension should initially be treated with intravenous fluids. If fluids are found to produce an inadequate response, dopamine or norepinephrine may be administered. Atropine may be used to treat bradycardia or other cholinergic symptoms. Avoid the use of H2 antagonists & proton pump inhibitors as these medications will increase the absorption of nicotine by increasing gastric pH. Appropriate monitoring parameters include cardiorespiratory and neuromuscular function, arterial blood gases, blood glucose, and renal function.

Table 2: Symptoms of Nicotine Poisoning[2,3]

Early (15-60 min)	Delayed (0.5-4 hr)
GASTROINTESTINAL	
Abdominal Pain Nausea Salivation Vomiting	Diarrhea
RESPIRATORY	
Bronchorrhea Hyperpnea	Apnea Hypoventilation
CARDIOVASCULAR	
Hypertension Tachycardia Pallor	Bradycardia Dysrhythmias Hypotension Shock
NEUROLOGIC	
Agitation/anxiety Ataxia/dizziness Blurred vision Confusion Auditory disturbance Headache Hyperactivity Muscle fasciculation Seizures Tremors	Coma Hyporeflexia Hypotonia Lethargy Weakness Muscle paralysis

Issues of Concern and Toxic Dose

Although the nicotine content of the new dissolvable products is less than that of traditional tobacco products (Table 1), these new products are packaged in small brightly colored containers, which could easily be mistaken for candy or mints. Camel Orbs bear a resemblance to Tic Tac® mints (Figure 1). The addition of flavoring and the compact size of these products raise concerns that these products will be attractive to small children. Unfortunately, we don't know how many children were exposed to the new dissolvable products. There have been several exposures reported to poison control centers in test markets, with no life-threatening effects noted.[4]

Summary

Poison control centers nationwide receive thousands of calls annually related to pediatric tobacco ingestions. The release of new candy-like tobacco products raises concern for additional ingestions in children due to the attractive nature of these products. Practitioners should be aware of these new products and be prepared for possible increased rates of toxicity.

References

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M-44 Sodium Cyanide

The United States Department of Agriculture, Animal and Plant Health Inspection Service, Bureau of Wildlife Services would like us to remind you that the M-44 sodium cyanide device is used in Utah. The ejector device contains a capsule of sodium cyanide and is baited with meat and placed in the ground. This device is used in specific situations to control coyotes, red fox, gray fox and wild dogs in order to protect livestock and endangered species and to prevent the spread of disease. This device is primarily used on private lands but may also be used on federal land in any county in the state. Areas where the M-44 sodium cyanide device is used are marked with signs. While human exposure to this device is extremely unlikely, be aware this device contains 91% sodium cyanide for which there is an antidote. Please report any exposure to this device to the Utah Poison Control Center at (800) 222-1222. Thank you!

TOXINS IN THE NEWS

Proton pump inhibitors (PPIs) may be associated with an increased risk of ***Clostridium difficile*–associated diarrhea** (CDAD). A diagnosis of CDAD should be considered for patients taking PPIs who develop diarrhea that does not improve.

Dronedarone (Multaq) increases the risk of serious cardiovascular events, including death, when used by patients in permanent atrial fibrillation. It doubles the rate of **cardiovascular death, stroke, and heart failure** in such patients.

(cont. from pg. 2) **UPCC Transitions**

medical toxicologists (http://www.ohsu.edu/emergency/faculty/toxicology.htm) and Dr. Caravati will provide around the clock consultation to UPCC specialists in poison information and will be available for physician to physician consultation by telephone. If you are a provider at the University Hospital, Primary Children's Medical Center, Salt Lake Regional Medical Center, Intermountain Medical Center or LDS Hospital, you can request a bedside consultation from the Medical Toxicology consult service or refer a patient to the Redwood Toxicology Clinic by contacting the Utah Poison Control Center.

POISON PEARLS

RADIATION

Shaneen Doctor, MD
Emergency Medicine Resident

On March 11, 2011 a large earthquake off the coast of Japan created a tsunami that devastated the western coast of Japan. In addition to the tens of thousands of lives that were lost, the tsunami also disrupted the power to the Fukushima Daichi nuclear power plant. The public questioned if they were at risk for radiation exposure and if they should take prophylactic iodine?

There are over 100 nuclear power plants in the United States. These plants generate power via a nuclear fission reaction. Under normal circumstances this reaction is well controlled and the heat byproduct of the reaction is converted to electrical energy. The reaction is kept cool by continuous infusions of cold water. In the event that the plant is no longer able to pump water to cool the reaction (i.e. after a tsunami) there are other control measures in place. In the event that these control measures fail there is the potential risk for nuclear isotopes to be spread outside the facility.

The most radioactive particle that is released in a nuclear reactor accident is iodine 131. This isotope, if inhaled or ingested, has the potential to cause thyroid cancer. The prevention is to take iodine 127 tablets. The theory is that if you occupy your thyroid with iodine 127 (safe) then there is no room for the iodine 131(cancer promoting) to get into your thyroid. This treatment is 96% effective if taken in the correct time frame.

In the event that there is a threat to public health, the Federal, State or local governments will dispense iodine tablets to the public.

UTAH POISON CONTROL CENTER STAFF

Please send comments and suggestions for future articles to the editors of Toxicology Today at:

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Or send e-mail to
poison@hsc.utah.edu

THANK YOU

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.

UNIVERSITY OF UTAH COLLEGE OF PHARMACY

POISON Help 1-800-222-1222