Series Editor: Lewis S. Nelson, MD

Smoking Cessation Can Be Toxic to Your Health

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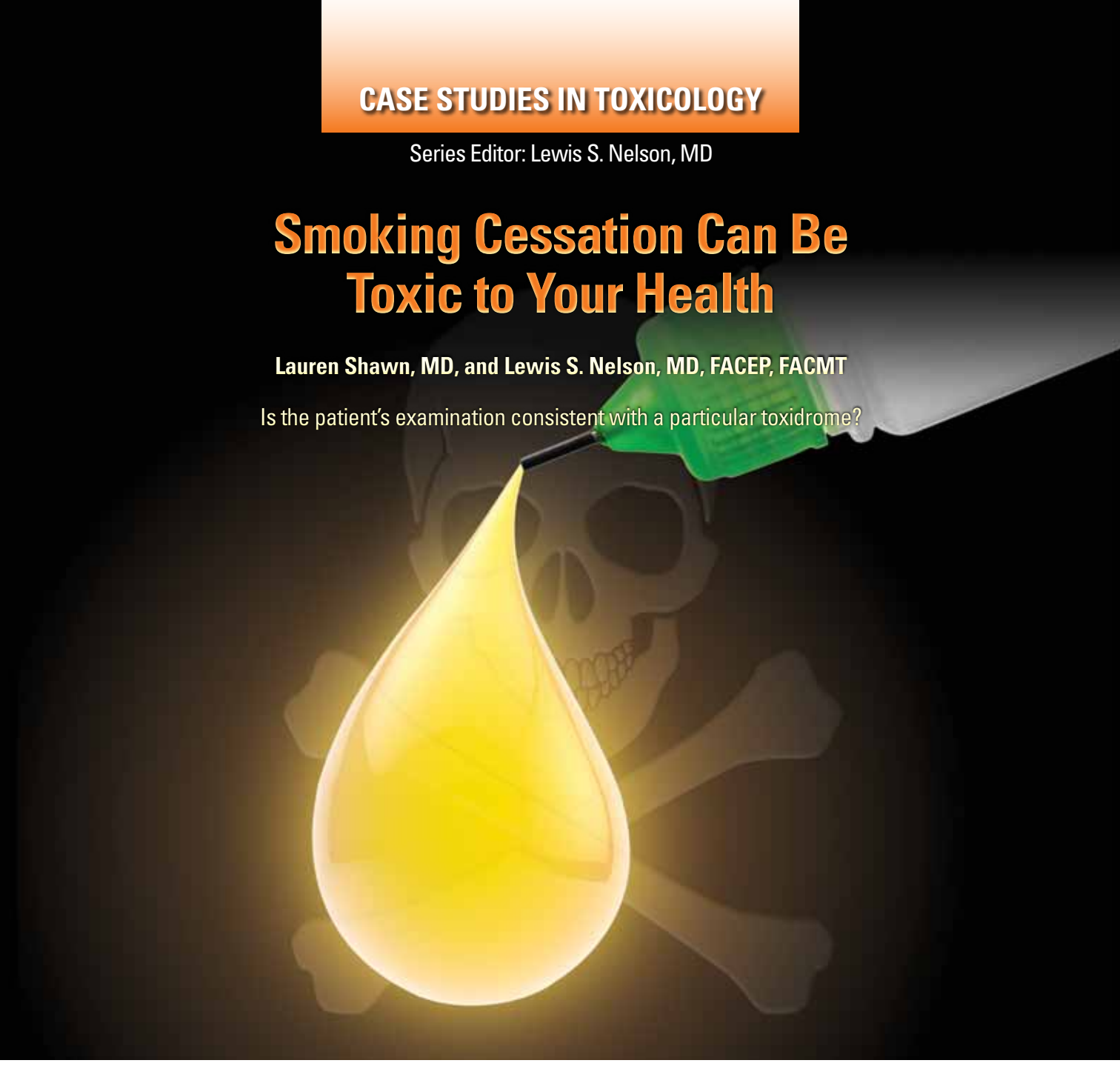
Is the patient's examination consistent with a particular toxidrome?



Case

An 18-month-old girl is found drinking approximately 2 mL of a liquid from a small container she found on her father's nightstand. She begins to vomit and subsequently becomes ataxic and lethargic. She is brought to the emergency department by her parents, and her vital signs on presentation are as follows: blood pressure, 129/89 mm Hg; heart rate, 190 beats/min; respirations, 24 breath/min; afebrile. Her physical exam is significant for pale, diaphoretic skin; pupils approximately 2 mm in size without nystagmus; clear lungs; and increased bowel sounds but no focal tenderness on palpation. Although it is difficult to do a complete neurologic exam on the patient due to her depressed mental status, her

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exam is significant for a slight tremor with movement.

The patient is relatively hypertensive and tachycardic for her age. Sympathomimetics can cause these vital sign changes but should not cause lethargy or small pupils. Although phencyclidine (PCP) is a dissociative anesthetic that can cause hypertension and tachycardia, other physical findings should include nystagmus, normal or increased muscle tone, purposeless movements, and potentially agitation during recovery. Sedative hypnotics like gamma-hydroxybutyrate (GHB) and ethanol can cause ataxia and lethargy, but not the vital sign abnormalities. Antimuscarinics/anticholinergics can produce tachycardia, but the blood pressure is generally normal, the skin dry, and the pupils large. The patient is vomiting and diaphoretic and has small pupils and increased bowels sounds, findings suggestive of the cholinergic toxidrome.

How can her vital signs and examination abnormalities be explained?

The acetylcholine receptor is found in both the central and peripheral nervous system. Acetylcholine is a key neurotransmitter in the autonomic and somatic nervous system that affects nearly every organ system in the human body. There are two broad classes of acetylcholine receptors: nicotinic and muscarinic. The nicotinic receptor is primarily found in the preganglionic synapses of both sympathetic and parasympathetic neurons, the postganglionic neurons of the sympathetic nervous system, and in the neuromuscular junction. The muscarinic receptors are found in the brain and in the postganglionic parasympathetic nerve endings that synapse on various organs.

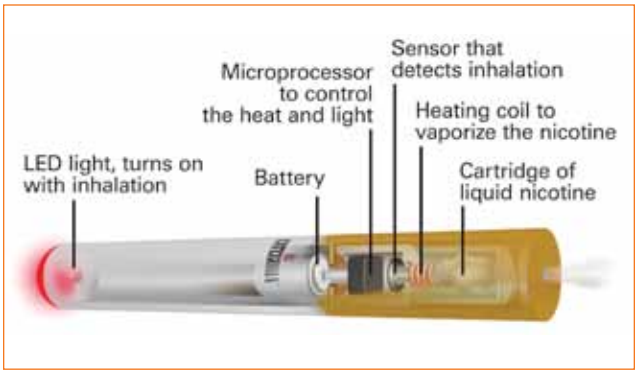

FIGURE. Tip to tip, how an electronic cigarette works to simulate smoking

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Stimulation of the muscarinic receptors causes the classic cholinergic toxidrome of salivation, lacrimation, urination, diaphoresis, gastrointestinal distress (vomiting and diarrhea), miosis, and the "killer B's": bronchorrhea, bronchospasm, and bradycardia. This toxidrome is expected following exposure to a toxin such as an organophosphorus insecticide. Stimulation of preganglionic nicotinic receptors, found in both sympathetic and parasympathetic ganglia, increases outflow of both branches of the autonomic nervous system and produces findings consistent with both parasympathetic and sympathetic excess (sympathetic generally wins!). These findings are typical of nicotine, the receptor's namesake, and account for the physiological effects that cigarette smokers achieve. In addition, central nervous system acetylcholine effects produce euphoria at low doses (which causes nicotine addiction) and altered mental status, vomiting, and seizures as the dose increases. Stimulation of nicotinic receptors in the neuromuscular junction by drugs such as succinylcholine and nicotine can cause fasciculations, tremor, weakness, and subsequent paralysis secondary to excessive, continued stimulation.

Could this be nicotine poisoning?

Nicotine is a familiar drug available in the form of tobacco products such as cigarettes and cigars. It is one of the most addictive substances known and causes a significant health burden from cancers and pulmonary disease in the United States as well as worldwide. There is 10 to 30 mg of nicotine in a standard cigarette, but the average smoker actually inhales only 0.05 to 3 mg per cigarette.[1] There are reports of significant acute nicotine toxicity from cigarettes when small children ingest a cigarette or butt. The median lethal dose in an adult is approximately 1 mg/kg, and a fatal case in a child involved as little as 2 mg of nicotine. Children under the age of 6 generally become symptomatic after ingesting one whole cigarette or three butts.[1]

Nicotine patches are a common form of replacement therapy for those desiring smoking cessation. In a case series of adults who intentionally applied excessive nicotine patches in suicide attempts, the most common findings were dizziness, hypertension, diaphoresis, and altered mental status.[2] Most of the cases were com-

plicated by co-ingestants, and none involved unintentional exposures in children. In one case, an 11-year-old boy placed two of his mother's patches on his arm, resulting in nausea, vomiting, dizziness, and diaphoresis, which resolved within a few hours after the patch was removed.[3]

Nicotine has been used as an insecticide for centuries. Although nicotine is rarely used for this purpose in the United States today, it is still used in many other countries and can be obtained over the Internet. Farmers and gardeners may seek it out because it is a natural pesticide and could therefore satisfy requirements for growing organic produce. Green tobacco sickness is an occupational exposure in which workers who are harvesting tobacco plants develop acute nicotine toxicity as moisture from the plants allows transfer of nicotine onto their skin. A case of fatal poisoning occurred when a 15-year-old boy ingested several milliliters of concentrated nicotine sulfate, which was available decades ago as a household insecticide and has since been discontinued.[4] The patient suffered cardiac arrest and catastrophic brain injury despite return of spontaneous circulation.

Why would liquid nicotine be kept in the home?

The patient's father had recently started using electronic cigarettes in an attempt to prevent second-hand smoke in his home. He had left a 10-mL bottle of liquid nicotine on his nightstand. The entire bottle contained 10 mg of nicotine.

Electronic cigarettes using liquid nicotine have become increasingly popular. First mass-produced in China in 2004, the growing number of manufacturers and Web sites selling the products has expanded the worldwide market.[5] Many view the electronic cigarette as inherently safer because its use does not involve the inhalation of tobacco smoke and therefore poses less risk of cancer and pulmonary disease. Others may view it as a more socially acceptable form of smoking since it is odorless and does not produce second-hand smoke. Recently, it has been marketed as a smoking cessation tool with the idea that the concentration of nicotine can be titrated down while the patient still gets the physical sensation of smoking (as opposed to chewing gum or using a patch).

When a person takes a drag from an electronic cigarette, it triggers a heating coil to vaporize liquid nicotine, and that vapor is then inhaled (see the Figure, page 8).[5] The liquid nicotine is contained in a cartridge that is either fully replaced or can be refilled. The nicotine is usually dissolved in vegetable oil or propylene glycol.[5] Furthermore, many Web sites that sell liquid nicotine allow purchasers to customize the liquid nicotine to be of specific strength and flavor (that ranges from menthol to various fruits to mocha). Although it usually takes as little as 1 mL of liquid nicotine to refill a cartridge, it is possible to buy a 5-L container online. Given the ease of purchase, the exotic flavors, and large quantities that can be obtained, there are significant public health concerns with this product. Teenagers may be able to access electronic cigarettes more easily than traditional tobacco products and could be susceptible to acute and chronic effects of nicotine exposure. Small children are at risk for oral and dermal exposure from large quantities of nicotine that potentially smell or taste appealing to the exploring toddler. Given the relatively large amounts of nicotine contained in a small volume, morbidity and mortality concerns are significant.

➤➤Fast Track

There is no practical antidote for nicotine poisoning. Supportive care is the mainstay of treatment; give benzodiazepines for seizures.

Currently, the Food and Drug Administration's (FDA) Center for Tobacco Products regulates cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco, but not non–tobacco-based nicotine products.[6] Although the FDA's Center for Drug Evaluation and Research regulates electronic cigarettes specifically marketed for therapeutic purposes, manufacturers not making such claims are not subject to FDA regulations. The FDA is attempting to gain regulatory authority over nicotine products like electronic cigarettes, and they caution that the safety of these products, even when used as intended, has not been fully evaluated.[6]

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There is no practical antidote for nicotine poisoning. Supportive care is the mainstay of treatment. The most consequential effect, paralysis, requires respiratory support. Benzodiazepines should be given for seizures. Atropine can limit bradycardia and bronchorrhea, and hypertension can be managed with short-acting antihypertensives. If there is concern for dermal exposure, the patient should be decontaminated with soap and water. Activated charcoal can be administered if the patient presents immediately following exposure, but its use is generally limited by vomiting.

Case concluded

The child vomited several times in the emergency department and was not given activated charcoal. She received intravenous fluids and was monitored closely for 24 hours, during which time her tachycardia and hypertension resolved. The patient became more awake and alert, was able to eat and drink, did not develop any seizures, and was subsequently discharged home. The parents were educated about safe storage of the liquid nicotine refills. **EM**

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"Emergency Imaging"

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- What imaging study should be ordered? How will it aid the diagnosis?