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Emerging Drugs of Abuse

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Patterns of recreational drug use undergo constant change. Health care providers must remain vigilant and informed regarding emerging drugs of abuse to care better for their patients. There is also a role for improved surveillance and characterization of novel drugs. This report reviews the clinical manifestations and toxicity of several new drugs of abuse, including dextromethorphan, hallucinogenic tryptamines (including "Foxy Methoxy"), hallucinogenic amphetamines (including 2C-B and 2C-T-7), as well as the herbal hallucinogen, *Salvia divinorum*.
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The decreased availability of lysergic acid diethylamide (LSD) in recent years has created a niche for novel hallucinogens that are rapidly gaining popularity among adolescents and young adults [1]. Their increased use reflects the intensity of neuropsychiatric effects, ease of procurement, decreased cost, presumed safety, and in some instances, perceived legality. Unfortunately, the emergence of these drugs, which include tryptamines, phenethylamines, and *Salvia divinorum*, has not been well recognized by the medical community [1].

Clinical identification of these new drugs of abuse can be difficult, if not impossible. Routine diagnostic testing may not identify these compounds or differentiate them from more common drugs of abuse. Thus, the medical literature contains few case reports of toxicity from these substances. Essentially, the only method of determining exposure to these hallucinogens may come from information provided by the patient. Increasing awareness of clinicians regarding these emerging drugs of abuse will enable better surveillance and further characterization of both the drugs and their users. All cases of toxicity from recreational drug abuse should be managed in conjunction with a poison control center or toxicologist to facilitate management and improve national surveillance.

Dextromethorphan

Dextromethorphan (also called "DXM" or "Robo") is one of a class of compounds known as dissociative agents that include phencyclidine (PCP, "angel dust") and ketamine ("Special K," "Vitamin K"). Striking increases in dextromethorphan abuse have been observed recently. Toxic Exposure Surveillance System data suggest that abuse or misuse of the drug by adolescents between the ages of 13 and 19 years has increased more than 300% over a 3-year period [2]. Interestingly, dextromethorphan abuse appears to follow a seasonal variation, with the peak exposures occurring between September and May. The abuse of dextromethorphan may be slightly more prevalent in women [3-5].

Younger adolescents may be at greater risk for dextromethorphan abuse [3,4,6,7]. In reports to poison control centers, the most common ages of children abusing the drug were ages 14 (23.1%), 16 (21.8%), 15 (15.4%), and 13 (10.3%) [7]. Dextromethorphan abuse has been reported in children as young as 11 years [5]. Despite the large number of over-the-counter products that contain dextromethorphan, 1 product line appears to be preferred for abuse; up to 87% of dextromethorphan abuse cases reported to poison control centers involved

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Coricidin HBP (67%) or another Coricidin product (21%) [3-5,8].

Dextromethorphan is well absorbed after ingestion, with maximum serum concentrations occurring at 2.5 hours [9]. The major metabolite of dextromethorphan, dextrorphan, is the agent responsible for all biologic activity. Dextrorphan reaches peak plasma concentrations at 1.6 to 1.7 hours after ingestion [10]. Dextromethorphan and its metabolites undergo renal elimination, with less than 0.1% of the drug being eliminated in the feces [11]. The half-life of the parent compound is approximately 2 to 4 hours in individuals with normal metabolism, but clinical effects from overdose may persist for a longer duration.

The clinical presentation of dextromethorphan intoxication depends on the ingested dose. Minimally intoxicated persons may develop tachycardia, hypertension, vomiting, mydriasis, diaphoresis, nystagmus, euphoria, loss of motor coordination, and giggling or laughing [12]. In addition to the above findings, persons with moderate intoxication may demonstrate hallucinations and a distinctive plodding ataxic gait that has been compared with "zombielike" walking [13]. Severely intoxicated individuals in a dissociated state may be agitated or somnolent [3,4,12,14]. Extremely agitated patients may need to be physically restrained by prehospital personnel or police, actions that place patients at risk for hyperthermia, metabolic acidosis, and death.

Experienced dextromethorphan users describe a rapidly developing and persistent tolerance to the drug [12]. Dependence on dextromethorphan is rarely described [15-17]. Although dextromethorphan is not thought to have addictive properties, susceptible individuals may develop cravings for and habitual use of the drug [4,18]. An abstinence syndrome, characterized by dysphoria and intense cravings, may be associated with cessation of dextromethorphan abuse [15,17,19,20]. Toxic psychosis and cognitive deterioration may arise from chronic use of the drug [15,19,20].

Toxicity in the setting of dextromethorphan abuse can arise from coingestants. In addition to dextromethorphan, over-the-counter cough formulations frequently contain other pharmaceutical agents such as chlorpheniramine, acetaminophen, or pseudoephedrine [21]. Chlorpheniramine is an H1-receptor antagonist. Consequently, individuals who have abused chlorpheniramine-containing dextromethorphan formulations may also exhibit anticholinergic signs and symptoms of tachycardia, dry mucosa, mydriasis, agitated delirium, urinary retention, gastrointestinal dysmotility, and warm flushed skin. Severe chlorpheniramine intoxication has also been associated with seizure activity, rhabdomyolysis, and hyperthermia [3]. Pseudoephedrine intoxication may mimic that of chlorpheniramine except that patients may exhibit diaphoresis. It is essential for clinicians to recognize that acetaminophen is a component of more than 100 cough and cold preparations. Accidental overdose may produce delayed hepatic injury and, potentially, death.

Treatment of acute dextromethorphan intoxication is mainly supportive [3,14,22]. Basic life support measures, with rapid assessment of the airway and identification of abnormal vital signs, should be immediately performed. Patients with clinical evidence of dehydration or rhabdomyolysis should receive intravenous saline solution. Physical restraints may be required for severely agitated patients but should be replaced as rapidly as possible by chemical restraint. Agitation is best controlled with benzodiazepines. Hypertension and tachycardia may also respond well to sedating agents such as diazepam. Hyperthermia should be managed aggressively; if benzodiazepines and cooling blankets fail to produce an adequate response, paralysis and orotracheal intubation may be required to reduce muscular thermogenesis. Activated charcoal is indicated in cases of recent ingestion (eg, <1 hour after ingestion) but is of unclear benefit. Respiratory depression is rarely described in severe dextromethorphan intoxication but may respond to high-dose intravenous naloxone [17].

Tryptamines

Tryptamines are a class of natural and synthetic hallucinogenic chemicals [23]. Naturally occurring tryptamines include psilocin and psilocybin, the psychoactive components of *Psilocybe* mushrooms. Bufotenine is an indole alkaloid produced by *Bufo* and *Rana* species toads and has been used in the production of hallucinogenic snuff in South America. N,N-dimethyltryptamine (DMT) is an ingredient of a hallucinogenic mixture known as "ayahuasca" that is used in indigenous Amazonian religious ceremonies [24].

Many of the tryptamines currently used for recreational purposes were first synthesized in the laboratory of chemist Alexander Shulgin, PhD [23]. The synthetic methodology, dose, and clinical effects of many tryptamines were initially described in Dr Shulgin's book, TIHKAL ("Tryptamines I Have Known and Loved"). The most noteworthy of the synthetic tryptamines are 5-Meo-DiPT ("Foxy Methoxy"), alpha-methyltryptamine (AMT, IT-290), and 5-MeO-DMT (5-methoxy-N,N-dimethyltryptamine) [24].

The pharmacology of tryptamines is poorly described. The route of administration, bioavailability, and duration of effect depends upon the chemical modification of the base structure, tryptamine. For example, 5-MeO-DiPT (Foxy Methoxy) may be administered by oral, intranasal, or intrapulmonary routes, but DMT must be smoked (due to extensive first-pass metabolism of the pure chemical). Clinical effects last for as little as 5 minutes with DMT or persist as long as 12 hours with 5-MeO-AMT. Each tryptamine appears to follow a dose-dependent