Abuse of OTC Drugs
By Gerald Gianutsos, PhD, JD

Upon successful completion of this article, the pharmacist should be able to:
1. Describe the characteristics and significance of OTC drug abuse.
2. Identify the signs of dextromethorphan abuse.
3. Explain the effects of dextromethorphan, pseudoephedrine, and antihistamines based upon their pharmacodynamic properties.
4. Recognize the requirements for sales restrictions on pseudoephedrine and prepare for possible regulatory changes for other OTCs.
5. Identify the populations at risk and the effects of laxative abuse.

INTRODUCTION

When pharmacists think about drugs of abuse, illicit street drugs such as heroin, marijuana, and cocaine would most likely be the ones to come to mind. Pharmacists are probably also aware of the growing epidemic of abuse of prescription (Rx) drugs, especially opiate analgesics. In fact, according to recent government estimates, more young people between the ages of 12 and 17 abuse prescription drugs than any illicit drug except marijuana—more than cocaine, heroin, and methamphetamine combined.

However, the abuse of over-the-counter (OTC) drugs, especially by young people, is also a significant problem that is not as well appreciated. As these drugs are more readily obtainable, and are regarded by teens and parents as less risky than the controlled substances, the abuse of OTC drugs has skyrocketed and creates many problems that pharmacists need to address. Most young people abusing Rx and OTC drugs also abuse alcohol or other drugs, and many combine their drug use with alcohol, raising the potential of dangerous drug interactions and other serious medical consequences.

Drugs from several pharmacological classes have been subject to abuse by young people, including cough and cold products, antihistamines, diet pills, anabolic promoters, and even laxatives. A survey of pharmacists in Northern Ireland revealed 112 different OTC products that pharmacists perceived were being abused, with a median of 10 patients raising suspicion in a typical three-month period. (Note however that this survey included OTC opiates which are not generally available in the United States, and may overestimate the scope of the problem in the United States.) In a survey of poison control centers in Utah over a 10-year period, more than one-third of the reported intentional drug abuse among adolescents between 6 and 19 involved an OTC drug; 65 percent of the exposures occurred in the home and an additional 10 percent occurred in school. Some street-drug users also use OTC drugs as a secondary product when their regular drug of choice becomes unavailable or to boost the performance of their preferred drug. This lesson will review the non-medical use of some OTC substances.
with an emphasis on the abuse of cough syrups containing dextromethorphan (DXM) and cold products containing pseudoephedrine (PSE). Recent regulatory efforts to curb the non-medical use of OTC drugs will also be reviewed.

Although beyond the scope of this review, pharmacists also need to be aware of another emerging problem, the abuse of herbal products, some of which are sold as dietary supplements or are available via the Internet. Many of these products are promoted to teens and young adults as “safe, natural highs” and are usually less rigorously regulated than traditional Rx or OTC drugs.

DEXTROMETHORPHAN-CONTAINING ANTI-TUSSIVES

A woman enters the pharmacy with a concern about her teenage son. He had been sent home from school after being found disoriented and slurring his speech. There was no sign of alcohol on his breath. After searching his room, she was relieved to find no needles or bags of marijuana or other apparent illegal substance. The son claimed he had a bad cold and took some cough syrup which he had purchased at the pharmacy and claimed to have had a “bad reaction.” She is questioning the pharmacist as to whether this could have caused his behavior. What should the pharmacist consider?

Scope

The mother in the scenario above has reason to be concerned. Abuse of cough syrups has become a serious problem among young adolescents in the United States.

The cough suppressant dextromethorphan (DXM) is the most popular antitussive in the United States and is found in more than 140 cough and cold medications available without a prescription. DXM was first approved by the Food and Drug Administration for clinical use in the United States in 1958 as an OTC alternative to codeine for cough. Initially marketed as a tablet under the trade name Romilar, the drug was diverted to recreational use and case reports of DXM abuse have surfaced since the 1960s in the United States, Canada, and Europe. Ultimately Romilar was removed from the market in 1973. Shortly after its removal, pharmaceutical companies reintroduced the drug in liquid formulations in an effort to reduce abuse by creating an unpleasant taste if ingested in large amounts. Among users, DXM is known to possess a bad taste and consumption of large quantities of syrup, especially with guaifenesin, is known to induce vomiting.

Nevertheless, intoxication with DXM-containing products has become increasingly popular in the United States, particularly among teens. The drug has profound psychological and physiological effects similar to those of phencyclidine (PCP), and its unrestricted access make it a prime target for abuse.

According to the 2006 National Survey on Drug Use and Health conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA), about 3.1 million young people between the ages of 12–25 had used an OTC cough and cold medication to get high, and nearly one million are estimated to have done so within the year preceding the survey.

The frequency of use among adolescents is particularly high. Teenagers are the greatest risk group for DXM abuse, with some likening the effects to marijuana, but with a perceived lower risk of detection by parents, teachers, or other adults. The demographic group with the largest percentage of misuse is Caucasian males, aged 18–25 (7.7 percent), although abuse has been reported in children as young as nine. Surveys conducted on younger people revealed strikingly high percentages of use; four percent of 8th graders, five percent of 10th graders, and six percent of 12th graders had abused OTC cough and cold remedies. According to data obtained from poison centers, DXM abuse showed a 10-fold increase over the years 1999–2004, with a 15-fold increase among adolescents aged 9–17 years, with the number of children in the 12–14 year old group approaching that of older teens. Most people in the 12–25 year-old group who used OTC cold and cough remedies to get high in the past year also used alcohol and illicit drugs. The lifetime prevalence of DXM abuse in
one sample of 11th- and 12th-grade students in Ohio was higher than the use of anabolic steroids, methamphetamine, heroin, crack, and methylphenidate. Alarmingly, fewer than half of teens believed that abusing cough medicine to get high is risky.

Even if the user is found with a supply of the drug, it would be easy to mislead a parent, teacher or law enforcement agent, as the user would be carrying a seemingly innocuous cold remedy and could readily explain away its presence. Moreover, parents feel that Rx and OTC drugs are safer than street drugs if abused and teens believe that parents don’t care as much if they are caught with an Rx/OTC drug. According to recent surveys, about 70 percent of parents discussed the risks of marijuana “a lot” with their children, but only 36 percent reported doing the same with prescription drugs, and only 33 percent with OTC cough or cold medications.

Others teens cited the ease with which OTC drugs could be obtained, which does not require contact with a dealer or other unsavory environment, but merely necessitates going to a pharmacy or local convenience store. The advent of automated checkout in many stores further reduces the probability of detection. Many youths also admitted to stealing the products off pharmacy shelves; this activity has become so common that many pharmacies have moved DXM products behind the counter to prevent diversion.

Pattern of Use
Adolescent DXM abusers intoxicate themselves at parties and before or after school, as the drug is legal, relatively inexpensive, and easily obtainable. DXM is available in different formulations, including solid and liquid dosage forms. Many users drink large quantities of cough syrup in an effort to get high, but these efforts are minimized by the disagreeable taste and susceptibility to vomiting. Solid dosage forms facilitate abuse.

DXM gelcaps are colloquially referred to as “skittles” or “Red Hots” because of their resemblance to the popular candy. Users call the habit of misusing solid dosage forms as “Skittling.” Some other street terms for DXM include Orange Crush, Vitamin D, and Robo. One particularly popular form of DXM is the product Coricidin, a mixture of 30 mg dextromethorphan hydrobromide and 4 mg chlorpheniramine maleate per tablet. Users refer to this preparation as “Triple C’s” (Coricidin Cough and Cold Tablets). According to at least one survey, as many as 87 percent of dextromethorphan abuse cases reported to poison control centers involved Coricidin HBP (67 percent) or another Coricidin product (21 percent), highlighting the prevalence of this particular product. The manufacturer (Schering-Plough) maintains a Web site which contains information on abuse and tips for parents (www.coricidin.com/InformationOnAbuse/Default.htm). In another survey of persons aged 12–25 who had misused an OTC cough and cold medication in the past year, 30.5 percent misused a NyQuil product, 18.1 percent misused a Coricidin product, and 17.8 percent misused a Robitussin product. These statistics illustrate that pharmacists need to be vigilant when observing young people purchasing or browsing these types of products and should be prepared to take appropriate steps when warranted.

Many Web sites can be found providing recipes for the extraction of DXM from cough and cold products. Essentially, the drug is converted to the free base using a base, typically NaOH or ammonia, which is then extracted using methanol or lighter fluid/naphtha. The organic liquid is evaporated and the DXM is ingested. Alternatively, the DXM is extracted from the organic solution using lemon juice to make a lemon flavored liquid or solid dosage form. These procedures not only provide a more concentrated form of DXM but also lessen the potential for vomiting during intake. Powdered DXM is also available on the street in a concentrated form. The FDA reported in the death of at least five teenagers in 2005 from ingestion of powdered DXM. DXM is also sometimes found in illicitly distributed tablets mixed with other illegal drugs such as ecstasy and/or methamphetamine, and is sometimes mixed with street heroin to increase the pharmacologic effects.

Effects of DXM
Most users of DXM describe profound psychological
effects after consumption consisting of acute euphoria followed by intense craving and dysphoria on withdrawal. Some of the psychological effects noted after acute intoxication include perceptual, cognitive and motor alterations, and are summarized in Table 1 (above).

Intoxicated users often exhibit a distinctive, plodding ataxic gait that has been likened to “zombie-like” walking. Severely intoxicated individuals may become agitated or stuporous. Experienced users describe the effects of DXM as four dose-dependent “plateaus.” (See Table 2, below.) Note that the normal dose for cough suppression is 15–30 mg; the plateaus described by users represent a dose 3–100 fold higher than the normal therapeutic dose.

Anecdotal reports suggest a divergent experience among first time users of DXM with only one-third of those who initially experimented with the drug reporting that they liked it. A toxic psychosis has been reported following chronic use of the drug, characterized by a loss of contact with reality, a confused state, and cognitive deterioration. Some users also exhibit violent behavior, which is also characteristic of PCP abuse. Experienced users describe a rapidly developing and persistent tolerance to DXM. The primary symptoms observed during withdrawal are insomnia, dysphoria, anxiety, depression, restlessness, and intense cravings, although physical dependence has not been reported.

Some non-psychological effects of DXM include: sweating, hot flashes, ataxia, nyctagmus, nausea and dizziness, diarrhea, severe weight loss, tachycardia, hypertension, rashes, itching, and red blotchy skin.

**DXM Toxicity**

The more serious adverse effects of abusing large doses of DXM include hyperexcitability and seizures, increased muscle tone, and ataxia. Hyperthermia may reach dangerous levels and should be managed aggressively. Recent guidelines recommend that patients who have ingested more than 7.5 mg DXM/kg should be referred to an emergency department for evaluation. Death from DXM overdose is rare as the usual method of ingestion induces vomiting. Most deaths result from ingesting the drug in combination with other illegal drugs, alcohol, or other ingredients in the mixtures. DXM-related deaths also occur from impairment of the senses, which can lead to accidents. Anecdotal reports suggest the possibility of brain damage from very high dose and chronic use.

As DXM abuse rises, the incidence of serious adverse consequences also increases. Calls to poison control centers involving abuse or misuse of DXM increased 21 percent overall from 2000 through 2002, but calls involving teenagers increased approximately 100 percent from 2000 (1,623) through 2003 (3,271). Another study of cases involving ingestion of a dextromethorphan-containing product recorded

<table>
<thead>
<tr>
<th>Plateau</th>
<th>Dose (mg)</th>
<th>Behavioral Effects</th>
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<tr>
<td>1st</td>
<td>100–200</td>
<td>Mild stimulation</td>
</tr>
<tr>
<td>2nd</td>
<td>200–400</td>
<td>Euphoria and hallucinations</td>
</tr>
<tr>
<td>3rd</td>
<td>300–600</td>
<td>Distorted visual perceptions Loss of motor coordination</td>
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<tr>
<td>4th</td>
<td>500–1500</td>
<td>Dissociative sedation</td>
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Table 1: Effects of Dextromethorphan

- Increased perceptual awareness
- Altered time perception
- Feelings of floating and dissociation from the body
- Tactile, visual, or auditory hallucinations
- Visual disturbances
- Paranoia
- Disorientation and lack of coordination
- Slurred speech
- Impaired judgment and mental performance
at a poison control center revealed that in the instances where the reason for the adverse re-
action was known, 86 percent were associated with intentional abuse and 89 percent of these were patients 13–17 years old, with one patient being only 11.

Abuse of DXM as the common hydrobro-
mide salt can also lead to signs of bromism in heavy users. Typical signs of bromide toxicity in-clude impaired CNS function including behav-
ioral changes, headache, apathy, irritation, slurred speech, psychosis, tremulousness, ataxia, hallu-
cinations, and the possibility of coma. However, acute bromide toxicity is believed to be relatively rare, as ingestion of large amounts of bromide typically causes vomiting, which limits gastrointestinal bromide absorption.

Another problem associated with abuse of DXM-containing cough syrup is the potential toxicity from other active ingredients found in the mixtures. These may include overdose of antihistamines, sympathomimetic deconges-
tants, guaifenesin, and acetaminophen when large amounts of cough and cold preparations are ingested. Antihistamines can produce anticholinergic signs and symptoms (such as tachycardia, warm, dry, flushed skin, dry mouth, mydriasis, agitated delirium, urinary retention, and decreased gastrointestinal mobility). Se-
vere intoxication has also been associated with seizure activity and hyperthermia. Deconges-
tants may produce cardiovascular complica-
tions, including hypertension and tachycardia, while acetaminophen overdose is associated with liver and kidney damage.

One well characterized drug interaction with DXM is the development of a serotonin syndrome. This condition typically occurs from the interaction between DXM and selective serotonin reuptake inhibitors or monoamine oxidase inhibitors. Some antibiotics (such as linezolid), opiate analgesics (such as meper-
dine and tramadol), or drugs of abuse can also precipitate the condition. Patients with serotonin syndrome may demonstrate the clinical triad of mental status changes, autonomic instability, and increased muscle tone. DXM can also potentiate the dangerous hyperthermia produced by MDMA (Ecstasy).

Treatment of acute DXM intoxication is mainly sup-
portive. Some patients may be severely agitated and require physical restraint. The agitation may be controlled with benzodiazepines. Benzodiazepine sedatives can also help control seizures and may also reduce associated hypertension and tachycardia. Activated charcoal is used in cases of recent intoxication (less than one hour following ingestion), but is of unclear benefit. Respiratory depression and coma have been reported in rare cases and may respond to high IV doses of naloxone. If anti-
cholinergic signs are present, especially if a combination product containing an antihistamine has been ingested, physostigmine may be considered.

Pharmacology

DXM is the dextro isomer of levomethorphan, an opiate analgesic and the methyl ether analog of levorphanol (Levo-Dromoran). However, DXM does not have affinity for the opiate receptors. Instead, DXM and its active metabolite, dextrorphan, act as potent blockers of the N-methyl -D-aspartate (NMDA) receptor, a member of the family of receptors for the excitatory neurotransmit-
ter, glutamate. At high doses, the pharmacology of DXM is similar to the controlled substance phencyclidine (PCP; angel dust) and the veterinary anesthetic ket-
amine, drugs that also antagonize the NMDA receptor. The similarity in their mechanism of action accounts for the PCP-like behavioral effects produced by high doses of DXM. The metabolite, dextrorphan, has a higher affinity for the NMDA receptor than does the parent com-
ound and is comparable to ketamine. DXM may cause a false-positive test result with some urine immunoas-
says for PCP.

DXM also acts on Sigma receptors, which are be-
lieved to account for the anti-tussive activity, and also interacts with serotonergic neuronal systems.

Pharmacokinetics

DXM is well absorbed following oral ingestion. The half-life of the parent compound is approximately two to four hours in individuals with normal metabolism. Effects generally last for six hours, but may vary depending on the amount of DXM ingested, and if it is used in combination.
with other drugs. Dextromethorphan and its metabolites undergo renal elimination.

Dextromethorphan undergoes metabolism via Cytochrome P450 CYP2D6. DXM is 3-demethylated to dextrorphan and, to a lesser extent, N-demethylated to 3-methoxymorphinan; both metabolites are further demethylated to 3-hydroxymorphinan. Dextrorphan is an active metabolite that prolongs the central nervous system effects of DXM. CYP2D6 is involved in the oxidation of a wide variety of drug substrates including opiates, most antidepressants and antipsychotics, and many anti-arrythmics, but there is a wide phenotypical variability among individuals with most of the U.S. population being rapid metabolizers. However, approximately 5 percent to 10 percent of Caucasians are poor DXM metabolizers, which increases their risk for overdose and death. Slow metabolizers show greater psychomotor impairment and sedation. However, slow metabolizers also exhibit less euphoria and greater dysphoria, due to a decrease in formation of dextrorphan, and may be less likely to abuse DXM. Experienced dextromethorphan users describe a tachyphylaxis to the drug, but it is unknown whether this effect is due to alterations in metabolic activity or some other effect.

Regulatory Issues

A teenager walks up to the pharmacy counter with 12 bottles of cough syrup-DM. The pharmacist questions the young man, who tells him that he and his two brothers have a bad cough and his mother sent him to the pharmacy for the medicine. Should the pharmacist take any action?

DXM is not a controlled substance under the Controlled Substances Act (CSA). The CSA specifically excluded DXM from any of the schedules when it was enacted in 1970 because of a lack of significant opiate-like abuse potential despite its structural similarity to opiate drugs. The Drug Enforcement Administration is currently reviewing DXM for possible control, possibly adding it to Schedule IV or V.

Should the DEA decide to further regulate DXM, some other possible regulatory strategies they could use for cough products are restricted access, limits on amounts sold, age restrictions, and the use of a log book similar to Schedule V controlled substances or the recent changes with pseudoephedrine. A bill was introduced in Congress in 2007 (the Dextromethorphan Abuse Reduction Act) which, if passed, would place raw DXM in Schedule V and would restrict the sale of DXM-containing cough and cold products to consumers over 18. Significant for pharmacists, the legislation would make it illegal to knowingly sell DXM-containing products to individuals under 18 years old, and would impose civil penalties of up to $1,000 for a first violation, up to $2,000 for a second violation, and $5,000 for a third violation for retailers who do so. Retailers failing to check a government-issued identification for an individual under 18 years old would be deemed to have knowledge that the person was underage and would be subject to the penalties; however, the bill provides an affirmative defense for retailers who check identification and reasonably believe it to prove that the purchaser is over 18.

Some states are also considering putting age restrictions on DXM sales, while some parent groups believe that DXM, because it’s so accessible, is a bigger problem than other drugs and support taking it off store shelves. Consequently, regulatory changes governing DXM is a very real possibility.

In many states, pharmacies are already voluntarily refusing to sell DXM-containing products to anyone under 18 and/or are limiting the amount that can be purchased at one time. Wal-Mart’s policy is to sell it only to customers 18 or older, and the chain limits the number of boxes people can buy to three.

In the 1980s, an epidemic of adolescent and teenage abuse of DXM in Utah resulted in the voluntary removal of the drug from store shelves to behind pharmacy counters. This measure has resurfaced as a potential solution, but manufacturers are opposed to this idea, claiming that putting it behind the counter would deprive those who need it. Instead, they propose improved warning labels and changing the packaging so that it is harder to shoplift.

In 1986, the Swedish National Board of
Health and Welfare changed DXM to prescription drug status because of teenage abuse of the product. Illinois passed a law in 2006 classifying pure DXM as a Schedule II drug; sale of DXM in this form, including over the Internet, is punishable by three to seven years in prison. Similar legislation has been considered in other states, including Texas, North Dakota, and California.

**OTC DECONGESTANTS**

Other ingredients in OTC cold preparations have also been the subject of abuse. The abuse of OTC sympathomimetic decongestants has long been recognized as a problem due to their amphetamine-like stimulant effects. Over the past few decades, the most commonly available over-the-counter decongestants have been ephedrine, phenylpropanolamine (PPA), pseudoephedrine and phenylephrine. Ephedrine and PPA were also found in OTC weight reduction products and were used to enhance athletic performance. Typically, decongestants act by activation of postjunctional alpha adrenergic receptors in pre-capillary and post-capillary blood vessels of the nasal mucosa, producing vasoconstriction, resulting in a decrease in blood flow through the mucosa and shrinkage of the tissue. Decongestants may act directly on the alpha receptor or indirectly by increasing the pre-junctional release of norepinephrine from sympathetic neurons and this action also contributes to their stimulant properties.

PPA was the subject of an FDA voluntary recall in 2000, due to evidence of an increased risk of hemorrhagic stroke, especially in women and its use in OTC products was banned by the FDA in 2006.

Ephedrine is a naturally occurring alkaloid derived from the Ephedra plant which shares pharmacological properties with other decongestants. Ephedrine was banned by the FDA in 2004 after a lengthy regulatory dispute, because of the risk of producing hypertension and stroke, including at least 10 deaths. As a natural product regulated by the Dietary Supplement and Health Education Act (DSHEA), ephedrine proved to be more difficult for the FDA to remove.

**Pseudoephedrine**

Another substance still commonly found in OTC cold remedies, pseudoephedrine (PSE), has also been associated with a serious public health problem. However, with PSE, the problem is not with the consumption of the parent compound but instead with the illicit manufacturing of methamphetamine, using PSE as a precursor. Formulas for converting PSE to methamphetamine can be found on numerous Web sites and much of the methamphetamine available in the United States is manufactured in small, portable home-based labs, starting with PSE obtained from OTC products, preferably from single ingredient tablets.

Methamphetamine is a widely abused stimulant drug which produces a brief, intense sensation, or rush, in those who smoke or inject it. The rush or “flash” lasts only a few minutes and is described as extremely pleasurable. Oral ingestion or snorting differs by producing a long-lasting euphoric high instead of a rush, which reportedly can continue for a half day. Some identifiable features of methamphetamine abusers include agitation, excited speech, decreased appetite, and increased physical activity levels. In addition to its CNS effects, methamphetamine can cause a variety of cardiovascular problems, including rapid heart rate, irregular heartbeat, increased blood pressure, and irreversible stroke associated damage to small blood vessels in the brain. Other common features include dilated pupils, shortness of breath, nausea, vomiting, diarrhea, and elevated body temperature. Hyperthermia and convulsions can also occur with methamphetamine overdoses, and if not treated immediately, can result in death. In addition, research in laboratory animals suggests that methamphetamine can irreversibly damage brain cells.

Along with the health issues associated with the abuse, small scale methamphetamine manufacturing also results in other important public health and safety problems, including a high risk of child abuse and neglect, criminal activity in the community, risk of fires and environmental contamination due to the prevalence of large volumes of solvents used in the
manufacturing process, and the added toxicity from the IV administration of relatively impure and poorly manufactured products.

In an effort to reduce the clandestine manufacture of methamphetamine, the Combat Methamphetamine Epidemic Act was enacted in 2006. This act modified several previous laws going back almost two decades and placed a number of now familiar restrictions on the sale of PSE. Among the provisions of the act are requirements that each regulated seller (such as a pharmacy) ensure that:

- Customers do not have direct access to the product before the sale is made, meaning that products must be placed in a secure location not ordinarily accessible by the general public. Most pharmacies place them behind the prescription counter, but this is not a requirement.
- A printed or electronic logbook listing sales is kept.
- The amount that can be purchased in a single day and in a month is limited.

Under the revised 2006 law, retail sales may not exceed 3.6g PSE base per day per purchaser, regardless of the number of transactions. The previous law placed limits only on individual transactions. Moreover, individual consumers are prohibited from purchasing more than 9g PSE per 30-day period.

The logbook for retail PSE purchases must contain the following information for each sale:
- Purchaser’s name and address
- Date and time of sale
- Name of product sold
- Quantity sold
- Purchaser’s signature

The retailer is obligated to enter the name of the product and quantity sold and to check information entered by the purchaser against a photo identification. The photo ID must be one issued by a state or the federal government, a passport, or an alien registration receipt card or permanent resident card (“green card”). Each record must be retained for a period of two years after entry. The act exempts the requirements of a logbook for any purchase by an individual of a single sales package if that package contains not more than 60 mg of pseudoephedrine (such as one or two dose units).

The enhanced controls have successfully reduced small scale domestic production of methamphetamine, according to the Bureau of International Narcotics and Law Enforcement Affairs, although the production has shifted to larger labs in Mexico. As mentioned earlier, similar restrictions on retail sales have been recommended by regulatory and consumer groups for DXM and the prudent pharmacist should stay abreast of changes in federal, state and local laws regulating sales of DXM. Pharmacists may also wish to follow the lead of other pharmacies and place DXM-containing products behind the counter, especially if shoplifting has become a problem.

L-desoxyephedrine

L-desoxyephedrine (Vicks Inhaler) is also known by its newer name, levmetamfetamine. This is the optical isomer of methamphetamine and is about one quarter the potency of the more active d-enantiomer. Abuse of levmetamfetamine-containing products, known colloquially as “peanut butter methamphetamine” used to be quite common, but the increased availability of authentic methamphetamine has reduced its desirability. Abuse ordinarily involves opening the inhaler, extracting, and then injecting the drug or, alternatively, swallowing the cotton inside. A similar practice is also followed for propylhexedrine, the active constituent of the Benzedrex inhaler. Internet resources purport to provide methods to synthesize d-methamphetamine from the inhalers.

Substituted Piperazines

While they are not used as decongestants, substituted piperazines (such as N-benzylpiperazine [BZP] and trifluoromethylphenylpiperazine [TFMPP]) produce a stimulant, euphoric effect similar to methylenedioxymethamphetamine (MDMA, “Ecstasy”). Although these products are illegal in the United States (BZP is a Schedule I drug) they can be purchased OTC in Canada, New Zealand, the United Kingdom, and other countries, where they are known as...
“herbal party pills” and can be purchased over the Internet as a “natural” substitute for Ecstasy. (Although synthetic, they are referred to as herbals because of an erroneous association with the pepper plant.) Reported side effects include insomnia, anxiety, nausea, vomiting, hyperthermia, cardiac arrhythmias, tachycardia, abdominal pain, acute renal failure, acute psychosis, and seizures. One form of piperazine that is found in the United States is known colloquially as “rapture.”

ANTIHISTAMINES
Although less prevalent than DXM abuse, antihistamines are known to be abused as a source of a cheap, readily available high among adolescents since at least the early 1970s. The drugs are abused for their hallucinogenic effects and to obtain a sense of euphoria. Usually, very high doses (such as more than 400 mg of dimenhydrinate) are used in an effort to produce the high. The antihistamines can produce a toxic psychosis resembling atropine delirium consisting of visual and auditory hallucinations; this is not unexpected since the most commonly abused anti-histaminic drugs possess anti-muscarinic properties. Initially the effects consist of euphoria, and later disorientation, ataxia, and visual hallucinations. The toxicity from the high doses of antihistamines has been misdiagnosed as a psychiatric disorder. Other antimuscarinic signs accompanying the misuse include tachycardia, mydriasis, hot flushed dry skin, dry mouth, and mild hypertension.

The most commonly reported abused antihistamines are diphenhydramine (Benadryl), dimenhydrinate (Dramamine), and meclizine (Bonine), but any depressant, sedating antihistamine (such as one which penetrates into the CNS) is potentially susceptible to abuse. Antihistamine abuse is especially common in individuals with a history of drug abuse and in individuals with a history of psychiatric disorders. Experienced drug users have used antihistamines with pentazocine (such as “T’s and Blues”) for decades to produce a concoction indistinguishable from heroin, and antihistamines have also substituted for LSD in experienced users. Because of the risk of widespread abuse, some experts have proposed restricting sales of some antihistamines, just as sales of PSE cold medicines have been limited.

LAXATIVES AND EMETICS
Laxatives and emetics are abused under a number of different circumstances. Unlike the previously discussed drugs which are abused for their euphoric CNS effects, laxative and emetic abusers are looking for a different benefit. These drugs are abused by individuals who mistakenly believe that they will prevent the absorption of calories from ingested food and by individuals who believe that daily bowel evacuation will promote good health. However, one of the more serious concerns is the frequent abuse of laxatives and emetics in patients with anorexia and bulimia nervosa. In one survey of patients seeking treatment for eating disorders, more than 25 percent had abused a laxative in the preceding three months. The laxative misusers scored significantly higher than non-misusers on measures of anorexic behaviors and weight and shape concerns and also displayed higher levels of depression and self-directed hostility.

Similarly, laxative abuse in patients with eating disorders has been associated with longer duration of illness, suicide attempts, impulsivity, and greater eating and general psychopathology. Individuals who misused laxatives were older, were perceived to be in poorer physical health, and were less likely to have sought treatment specifically for an eating problem than those who engaged in self-induced vomiting. The abuse of laxatives as well as OTC diuretics is also becoming more common in female athletes, particularly those starting in competitive activities at a young age or those who are engaged in activities such as gymnastics, figure skating, and ballet, where weight and body image are a factor. Data on emetic abuse among patients with eating disorders also suggests that this is a cause for concern. Studies investigating the extent of ipecac abuse in patients with eating disorders report that as many as 7.8 percent of patients had used ipecac, 3.1 percent using the drug chronically. Anecdotal reports suggest that some women with eating disorders may take as
much as four bottles of ipecac per day. Laxative and emetic abuse have also been reported as a factor in Munchausen syndrome by proxy.

The abuse of stimulant laxatives and emetics may lead to a number of metabolic and gastrointestinal complications including diarrhea with associated sodium and water loss and dehydration; potassium loss and hypokalemia, the potential for hypocalcaemia and hypomagnesaemia resulting in tetany, acid-base disturbances; and renal damage. Cardiac and muscle toxicity and cardiac arrest have also been reported. Abuse of emetics was reportedly a major factor in the death of singer Karen Carpenter, who suffered from anorexia. Incidents such as these have prompted the call for a ban on the sale of ipecac and restrictions on laxative sales. In 2003, an FDA advisory panel voted to rescind OTC sales of ipecac.

**SUMMARY AND CONCLUSIONS**

The abuse of OTC drugs is not a new problem but is one that has, along with prescription drug abuse, taken on new importance, especially among the adolescent population. The ease of obtaining the drugs, the low risk of detection, and the relatively poor perception of the risks involved by both teens and parents has contributed to the explosion in the abuse of OTC drugs, which shows no signs of abating. This presentation highlighted the abuse of dextromethorphan, which produces PCP-like effects and the abuse of stimulant OTC decongestants, which substitute for amphetamines. But, interested individuals are able to identify other drugs for possible abuse and the existence of the Internet permits rapid dissemination of information to other potential users.

Pharmacists are familiar with the restrictions placed on pseudoephedrine-containing products in an effort to reduce their diversion, and the possibility exists that similar limitations may be placed on dextromethorphan and potentially other drugs as well. At the very least, pharmacists need to be aware of requests for excessive quantities of OTC drugs, especially by adolescents and by patients with a history of drug abuse or psychiatric illness. Pharmacists should also consider voluntary measures such as keeping certain products out of sight.

The abuse and misuse of a long list of OTC drugs, going beyond those described in this lesson, reinforces the importance that pharmacists need to place on OTC drugs when taking drug histories and during counseling sessions.

Gerald Gianutsos, BS Pharm, MS, PhD, JD is an associate professor of pharmacology at the University of Connecticut School of Pharmacy, Storrs, Connecticut.

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**Editor’s Note:** To obtain the complete list of references used in the article, contact Chris Linville at NCPA (703-838-2680), or at chris.linville@ncpanet.org.
CONTINUING EDUCATION QUIZ

Select the correct answer.

1. The abuse of prescription and OTC drugs:
   a. Is a problem but lags far behind the use of most street drugs
   b. Is rarely associated with alcohol abuse
   c. Is a problem restricted to the United States
   d. Often occurs in the home or school

2. The abuse of dextromethorphan:
   a. Exceeds the abuse of methamphetamine among 12th graders
   b. Remained constant from 1999-2004
   c. Is especially frequent in liquid forms because of the pleasant taste
   d. Is a problem among high school students but is not seen in younger children

3. The demographic with the highest misuse of dextromethorphan is:
   a. African American males, aged 18-25
   b. Caucasian males, aged 18–25
   c. Caucasian females, aged 18–25
   d. Caucasian males, aged 14–17

4. Abuse of OTC cough products is growing because:
   a. Parents are less concerned about non-street drugs.
   b. Teenagers do not appreciate the risks associated with abuse of OTC drugs.
   c. The products are relatively easy to obtain from pharmacies.
   d. All of the above are correct.

5. The subjective effects of dextromethorphan most closely resemble which drug of abuse?
   a. Heroin
   b. Phencyclidine (PCP)
   c. Methamphetamine
   d. Cocaine

6. The term “skittling” refers to:
   a. The use of OTC drugs of abuse at parties where candy is also served
   b. The abuse of dextromethorphan in solid dosage forms that resemble popular candy
   c. Adding candy to cough syrup to mask the taste
   d. The abuse of cough syrup by very young adolescents

7. The usual dose of dextromethorphan for treating coughs is:
   a. 15–30 mg
   b. 50–75 mg
   c. 100–150 mg
   d. 500–1,000 mg

8. Experienced dextromethorphan users refer to drug plateaus. Which statement is correct?
   a. The first plateau (i.e., lowest dose) describes effects at more than 25 times the usual therapeutic dose
   b. Dissociative sedation occurs at plateau four
   c. Effect occurring at first plateau is visual distortions
   d. Euphoria requires a dose of 1,000 mg or more.

9. The active metabolite of dextromethorphan is:
   a. Levomethorphan
   b. Dextrorphan
   c. Ketamine
   d. The metabolites are all pharmacologically inactive
10. The metabolism of dextromethorphan:
   a. Occurs primarily via CYP3A4
   b. Is slow, resulting in a half life of more than 18 hours
   c. Is slower than normal in approximately 5-10 percent of
      Caucasian users
   d. All of the above are correct.

11. Toxicity from an overdose of dextromethorphan includes:
   a. Hyperexcitability and seizures
   b. Fall in body temperature
   c. Hypotension
   d. A contraindication to the use of benzodiazepines

12. Other types of toxicity associated with the abuse of dextromethorphan-containing cough products include:
   a. Liver damage due to acetaminophen
   b. Hypertension and tachycardia from decongestants
   c. Possible signs of bromide toxicity
   d. All of the above are correct.

13. The proposed Dextromethorphan Abuse Reduction Act would change the regulation of dextromethorphan by:
   a. Reclassifying it as a Schedule II drug
   b. Restricting sales of dextromethorphan containing cough syrups to consumers age 18 or older
   c. Placing cough syrups behind the counter
   d. Banning the sale of cough products containing dextromethorphan as the sole ingredient

14. Phenylpropanolamine and ephedrine were removed from the market because of:
   a. Poor efficacy
   b. Excess CNS stimulation
   c. Risk of stroke
   d. Kidney toxicity

15. Sales of pseudoephedrine have been regulated because:
   a. There is a high risk of cardiovascular complications.
   b. It is highly abused for its CNS effects.
   c. It is used in the illicit manufacture of methamphetamine.
   d. It is frequently used as a substitute for heroin.

16. Agitation and excited speech are characteristic signs of the abuse of:
   a. Dextromethorphan
   b. Anti-histamines
   c. Heroin
   d. Methamphetamine

17. Log books for sales of pseudoephedrine require the recording of the following information except:
   a. The purchaser’s names
   b. The purchaser’s address
   c. The purchaser’s driver’s license or alien registration ID number
   d. The amount purchased and the date

18. Abuse of levmetamfetamine inhalers:
   a. Is rarely a problem because the drug is found in a wad of cotton from which extraction is difficult
   b. Is a problem which is becoming more common
   c. Produces effects similar to methamphetamine
   d. Is not a problem because the drug does not produce effects on the CNS
19. Which of the following effects may be associated with the abuse of antihistamines?
   a. Disorientation and ataxia  
   b. Visual hallucinations  
   c. Delirium  
   d. All of the above

20. The signs of antihistamine abuse most closely resemble an overdose of:
   a. Methamphetamine  
   b. An anti-muscarinic  
   c. Heroin  
   d. LSD

Abuse of OTC Drugs

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22. Type of pharmacist:  a. owner  b. manager  c. employee

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24. Did this article achieve its stated objectives? a. yes  b. no

25. How much of this program can you apply in practice?
   a. all  b. some  c. very little  d. none

How long did it take you to complete both the reading and the quiz? ______ minutes

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