Dear Reader,

Thank you for subscribing to the MEDTOX Journal. We hope that you find this research and first-hand accounts article interesting and educational. This issue ranges from new drugs hitting the American shores to adolescent addiction to research on marijuana and the brain. You may forward a copy on to others by clicking this box.

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Russian Benzodiazepine Hits American Shores

Benzodiazepines are a class of sedative-hypnotic drugs that are prone to misuse and abuse. There are a slew of benzodiazepines produced in laboratories around the world. The drugs are quite effective in treating insomnia, anxiety, seizure disorders, and alcohol withdrawals. Valium (diazepam), Xanax (alprazolam), and Ativan (lorazepam) are benzodiazepines. Most benzodiazepines are controlled substances that are regulated under Schedule IV of the Controlled Substances Act. Brought to market as putative “safe” alternatives to barbiturates, most of these drugs have each been diverted and abused. With the proliferation of prescription drug abuse, the benzodiazepines have become popular “combination” drugs that are frequently taken with opiate prescription drugs, such as hydrocodone and oxycodone to create “loads.” Recent exposes have cited the rapid ascension of methadone and Xanax as a “load” cocktail in places such as New York City and other large east coast cities. When mixed with alcohol, benzodiazepines create a synergy that greatly magnifies the intoxicating effects of both drugs.

It has since been reported that a Russian epilepsy drug named phenazepam has been diverted from Central Europe and has made its way over to American shores. Phenazepam has already

Study Examines Illicit Drugs in Children Being Evaluated for Abuse

In 2004, the University of Iowa’s hospitals and associated medical clinics initiated a drug testing protocol for children suspected of being maltreated...
created some havoc with overdoses in the United Kingdom. As its name suggests, this drug is a benzodiazepine. It is not a controlled substance in the United States; it is not approved or cleared by the FDA as medicine. In Russia and other bordering countries, the drug is used to control the incidence and severity of epileptic seizures. In that sense, phenazepam shares some similar characteristics with Klonopin (clonazepam), a benzodiazepine that is approved for use in the United States. Phenazepam seems to share many of the same effects of clonazepam. The drug is manufactured in small scored white tablets in doses of 0.5 mg and 1.0 mg. The drug can be taken every 6-8 hours as needed.

The fact that phenazepam is not a controlled substance in the U.S. may lead to more sales of the drug to American buyers. The Internet is the primary outlet for phenazepam dealers. The packaging for phenazepam varies. From pill bottles labeled in Cyrillic to English-stamped aluminum foil blister packs, phenazepam can come organized in a variety of different designs. And like all other drugs of the benzodiazepine class, phenazepam abuse can lead to dependency and addiction.

Mystery Drug: How to Obtain the "Businessman's Trip"

This month's mystery drug is a veteran of the psychedelic experiences of the 1960s. With the emergence of the designer drugs "bath salts" and "plant food" in 2010, this month's drug has reappeared in a number of American cities. It is a member of a large chemical class of hallucinogenic substances, many of which can be found naturally in plants and mammals. In fact, this month's drug is a near clone of a substance that can be found as a toxin in Bufo alvarius, a toad that is indigenous to the Colorado River area. In the 1990s, "toad licking" was rumored in drug user circles as an effort by entrepreneurs to collect the hallucinogenic substance from the slimy underbelly of the critter. The toxic secretion of the toad contains bufotenin, a mildly hallucinogenic substance that is central to its defense mechanisms. When under attack, the toad will discharge bufotenin through parotid glands located near the surface of the skin. Bufotenin is fairly toxic to animals, but to humans it is relatively benign. This month's drug is not bufotenin, but again, it is a near clone. To our knowledge, there is no animal that can produce this month's mystery drug.

This month's drug can be smoked, injected, or snorted. The drug is ineffectual when taken orally. Although first identified in plant material in 1931, it was not until 1959 that the drug was finally isolated and extracted in a laboratory. Initially found in the bark of a South American tree, this month's drug has since been identified as an active ingredient in nearly 50 other different plant species. More curious is the fact that this drug has also been identified as a naturally produced endogenous compound in many animals. The structural chemistry of this month's drug and abused. The criteria for inclusion in the testing program were as follows: family history of domestic violence, parental history of substance abuse, patient more than two years of age, and burns or unusual injuries on the patient. The charts of some 572 children were evaluated for the symptoms of abuse between the years 2004 and 2008. Using the criteria described above, some 232 patients were selected for further study and testing. Of those, 15% tested positive for illicit drugs. Half of those presented with positive tests from hair samples, which indicates that these children were all subjected to multiple exposures. Evidence of long-term maltreatment was much more common in children associated with positive drug tests. Statistical regression analysis helped investigators identify factors associated with positive drug tests. The factors included the following: physical abuse or neglect, public or no health insurance, soft tissue injuries, inflicted burns, history of parental substance abuse, and history of domestic violence history in the family.

This study supports the idea that children suspected of being abuse victims should be drug tested, especially when associated factors are present at the time of examination. Skeletal examinations and eye exams should be pursued in the emergency room. Special consideration should be given to situations where parents or guardians are suspected of methamphetamine abuse. Besides the exposure that children endure to the toxic effects of the drug's constituents, methamphetamine-abusing parents are more prone to violent outbursts and crude living arrangements. Children of methamphetamine-abusing parents are at an elevated risk
is quite similar to the central nervous system transmitter serotonin. The drug's principal effects as a hallucinogen can be attributed to its actions at serotonin receptor sites. Hallucinogen effects in humans all stem from disruptions involving serotonin transporters and receptors. This month's drug shares this hallucinogen characteristic. In fact, this month drug is notably more powerful than most other hallucinogens in terms of its affinity for serotonin receptors. Because of the selective action it exerts at serotonin receptors, the high associated with this drug can lead to powerful emotional experiences. Concurrent to the entheogenic effects it exerts, the drug can lead to significant visual distortions and sometimes frank hallucinations. For some, the high generated by this drug can be annoying; for some it may actually be frightening. But for the hardcore hallucinogen fan, this month's drug delivers the goods.

Although this month's drug packs quite a wallop, the span of its effects is relatively short. When smoked, the drug's peak effects are experienced between the 15 and 30 minute mark. Linger ing hallucinogenic experiences may persist through hour two. The drug is found mostly in western and southwestern states. In those locales, the drug consists of a fine white powder that is most commonly smoked. Crack pipes and "meth" pipes suffice for the purpose of smoking. For the DAR and DRE trained evaluator, the symptoms of intoxication move quickly. In that sense, this drug is similar to Salvia Divinorum, the hallucinogen that is highlighted on YouTube and other social media websites with the recorded antics of people under the influence of it. By the time a police officer has a chance to begin a DAR or DRE evaluation, symptoms of intoxication have dissipated or disappeared. For someone who injects this drug, the effects of the high will be somewhat longer lasting. For reasons not well understood, I.V. injectors report more frank hallucinations than others who smoke or snort the drug. Many users report hallucinations where the appearance of phantom characters can be frighteningly real. A good number of these I.V. users describe their experiences as mystical or spiritual. Some have said that their use of the drug led to post-death experiences where they were introduced to family and others who had died and passed on to the next life. For some, this experience beckoned them back to use the drug again. For a good number of the first time users, the first chapter was the last chapter in this drug's use. Because of the nature of this drug's effects, it is believed to be non-addictive. For those who use the drug chronically, there is little chance that they can become dependent on it.

Like many of the designer drugs that have recently emerged in the marketplace, this drug is synthesized and sold through the auspices of various web-based networks. Periodically, labs that produce this drug are raided and seized in the United States, but those incidents are rare. The physical effects of this month's drug include, but are not limited to, the following:

- Very dilated or "rimmed" pupils (7.0 mm or more)
- Normal reaction to light
- No nystagmus
- No lack of convergence
- Very elevated pulse
- Very fast Romberg internal clock
- Piloerection; gooseflesh

for lack of care and malnourishment. Methamphetamine is a powerful anorectic drug that causes parents to eat less. This translates into less food and fewer meals for their children. In cases where methamphetamine is suspected, caregivers should also look for signs of malnourishment with dependent children.


Kratom Testing Now Available at MEDTOX

Prior editions of this newsletter have chronicled the emergence of Kratom as a concerning drug. This substance seems to be widely abused; many opiate abusers turn to Kratom when symptoms of withdrawal ensue. The drug is a partial opiate agonist that is extracted from the Mitragyna tree that is grown in Southeast Asia. The drug is not a controlled substance. It is unclear what action the DEA will take in response to this drug's rise in popularity. Kratom can be easily purchased on the Internet. MEDTOX is currently testing for Kratom in our St Paul - based laboratory. Anyone interested in Kratom testing services should contact a government sales representative at 1-800-832-3244.
Elevated body temperature
Flushed face and extremities
Unremarkable completion of standard field sobriety tests
Difficulty in oral communication
The powerful almost overwhelming effects of this month's drug is challenging to even veteran users. But many of the truly devoted believe that they can mentally prepare for what they think will be an aggressive or intense high because the high does not cause panic or fear. For them, the benefit of the introspection and depth of experience with the use of this month's drug is worth the risk of a frightening high.

This month's drug is a survivor. It emerged as a cult drug in the 60s and 70s. It was sustained through the 80s and 90s, when drugs like cocaine and methamphetamine swept the scene. And today, it persists as a drug of abuse and concern. This month's drug is assigned to Schedule I by the DEA. It has no known or recognized medical utility. A number of South American spiritualists have lobbied the DEA and other agencies in order that they may use the drug for use in their devotions; the government has largely denied those efforts. At present, there are several derivatives of this month drug that can be found on the streets. But providing the names of these drugs would provide direct evidence of this month's drug's identity.

Although some users cite visitations by alien travelers while high, there seems to be relatively little use of this drug beyond North America. A number of Internet sites coordinate and advise the activities of its fans. Several of these sites act as compendiums of experiences and techniques that contemporary users can source for advice and assistance when trying to get high. In fact, several notable drug abuse textbooks are devoted to instruction on the use of the drugs of this class. These books continue to sell.

This month's drug: Dimethyltryptamine (DMT); Street name: DMT

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**Drug Used to Treat Nausea Shows Promise in the Treatment of Opiate Withdrawal**

Withdrawal from opiates stands in the way of a sober lifestyle for many addicts. Withdrawal from drugs such as heroin and methadone can be quite grueling. There have been few pharmacotherapies to choose from in mitigating the pain and discomfort of withdrawal. And with skyrocketing abuse of oxycodone and other prescription opioids, withdrawal management is at the top of the list for addictionists and therapists. According to the 2007 survey by National Survey on Drug Use and Health, nearly 12.5 million Americans ages 12 and older are using prescription pain medications for recreation purposes. Opioid dependency is a national health problem.

The treatment for opiate withdrawal has been traditionally inadequate. From rapid opiate detoxification to “cold turkey,” there have been few options. But researchers from Stanford University's
Department of Anesthesia have discovered that the antiemetic drug Zofran (ondansetron) blocks 5-HT3 receptors, the chemical messaging system that is involved with the triggering of opiate withdrawal. Initially, experiments were carried out with mice. Later, studies were conducted using human subjects. Administration of ondansetron led to a noticeable reduction in withdrawal symptoms. The benefit continued for some time after the drug had disappeared from the blood. That development suggests that ondansetron is influencing activities at the receptor level. Dependency and abuse is not a concern with the use of ondansetron because it is not a controlled substance, it is not an opiate, and it is not addictive.

The weakness in this study relates to the small study population. Future analysis will likely involve larger study cohorts. Ondansetron has a reputation as a go-to drug for patients who are suffering from chemotherapy-related nausea and vomiting. And prior studies reveal that ondansetron may also be helpful in reducing the pain and discomfort of alcohol withdrawal. Experiments with laboratory animals suggest that the drug may exert broad action across an array of substances that are associated with the development of drug dependency. This is good news for frontline addiction medicine and rehabilitation professionals.

**Early Onset of Psychosis: More Bad News for Marijuana Users**

For some time now, this Journal has reported on a stream of research dealing with the relationship between cannabis use and mental illness. The summary of work analyzed so far has established that marijuana use is associated with early onset of mental illness in susceptible people. Unanswered however is the question of whether or not marijuana smoking can actually lead to psychosis. With nearly 16 million regular users of marijuana in the United States, this question about the role of cannabis in triggering psychosis is an important public health question. With the recent emergence and popularity of synthetic cannabinomimetic drugs, such as K2 and Spice, the psychosis concern is even more critical.

In a study reported in the Archives of General Psychiatry, it appears that for adults diagnosed with psychosis, the onset of symptoms was nearly three years earlier in marijuana users than with nonusers[1]. This large meta-analysis of 83 prior studies also revealed that alcohol use was not significantly associated with early onset of psychosis. A number of other variables were analyzed for association with psychosis: gender, schizophrenia, and related conditions did not explain the earlier onset of psychosis. In those studies where cannabis use was heaviest, subjects reported earlier mean age of psychosis onset. The picture of marijuana’s multiple impacts on the health of
smokers is becoming clearer. One area for elucidation in future study is the question as to whether or not people that would otherwise not become psychotic might develop psychiatric condition following a period of chronic marijuana use earlier in life. Is marijuana like methamphetamine in the respect that protracted use of the drug can lead to a distinct type of psychosis that can persist in sobriety? Also unclear is the mechanism involved with this relationship. With cannabis chemistry, a complicated trilogy involving the dopamine, serotonin, and GABA transmitters, the explanation for what has been discovered in this study may remain elusive.


Startling Data for Adolescent Substance Abuse Is Published

According to the National Center on Addiction and Substance Abuse (CASA) at Columbia University, adolescent substance abuse ranks as this country’s greatest health problem. Today, nearly half of all U.S. high school students currently smoke, drink, or use other dangerous drugs; a third of users meet the DSM-IV criteria for addiction according to the report. The 400-page CASA report is being considered the most comprehensive look at teen substance use to date. The study is based on nationally representative online surveys of 1,000 high school students, 1,000 parents of high school students, and 500 school personnel, including teachers, principals, counselors, and coaches. The findings of the report include the following:

- Three-fourths of high school students have smoked cigarettes, drank alcohol, or used another drug.
- Alcohol is the most preferred addictive substance among high school students, followed by cigarettes, marijuana, and controlled prescription drugs, such as narcotic analgesics (hydrocodone and oxycodone).
- Two-thirds of high school students have used more than one addictive substance.
- A quarter of teens that responded to the CASA survey said they consider marijuana to be harmless, and about one in six view it as medicine.

A major concern with these findings is the younger a person is when experimenting with an addictive substance the greater the likelihood the person will become addicted as an adult. People who use addictive substances before age 18 are six times more likely to later develop a substance use disorder than those who did not start using until they were 21 or older. Calibrating prevention programs to deal with the forces that drive junior high and high school drug use could generate exponential benefits in adulthood. Another startling statistic is 90 percent of Americans who meet the medical criteria for addiction started smoking, drinking, or using other drugs before age 18. Previous articles from this Journal have touched upon adolescent drug use and the effects they have on
teens; this new study makes a clear connection between adolescent "start-up" use and lifelong addiction in adulthood. The adolescent brain has an immature development of the prefrontal cortex that can cause poor impulse control and the favoring of low-effort, yet thrilling, drug experiences. They also feel heightened sensitivity to the social benefits of intoxication which may contribute to an initial decision to use drugs and make the experience rewarding enough to repeat.

In a statement in the report, former Representative Jim Ramstad, R-Minn., chair of the CASA national advisory commission on substance use among high school-age Americans, explains, "It is time for America to deal with our Nation's number one public health problem: substance abuse and addiction. While we must provide treatment for those in need, the best cure is prevention." The report emphasizes that "teen substance use is a preventable public health problem and addiction is a treatable disease." There are approximately two million U.S. high school students meeting the criteria for an alcohol or drug use disorder, yet only about 100,000 have received treatment in the past year.


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