Dear Reader,

Thank you for taking the time to read the MEDTOX Drug Abuse Recognition Journal. We hope you find this newsletter interesting and educational. This issue focuses on the origination of bath salts, a possible new use for ketamine, important news regarding a synthetic cannabinoids study, and the ever-popular name-that-drug article. As always we enjoy hearing your feedback. If you have any questions or topics you would like to see in future Journal issues please email us at medtoxjournal@medtox.com.
News reports recently from all over the country have reported on the spread of K2 and Spice abuse. Synthetic cannabinoids are relatively new substances and society's collective experience with them is scant. However, a growing body of knowledge and information is giving us greater insight as to how these drugs work in the central nervous system. The conventional wisdom here is that synthetic cannabinoids activate the same cannabinoid receptors (CB1 and CB2) that organic cannabis (sativa-L) does. Towards those ends, synthetic cannabinoids will provoke symptoms and signs much like its organic cousin. But that leaves quite a few unknowns to be pondered. To date, law enforcement, poison control, and emergency room personnel point to some decidedly different symptoms aboard people who smoke K2 and Spice, at least when compared to people who smoke organic marijuana. Users often say the same thing. Spice and K2 effects are edgy. They are more powerful than the effects triggered by traditional marijuana smoking. In fact, a good number of users cite visual and auditory distortions while high. The heart rate soars, the mouth gets dry, and sweating begins. A good number of Spice and K2 users put the drug down because it is too potent. The relaxing and loquacious effects of marijuana smoking have been replaced by agitation and anxiousness. It is pretty clear that Spice and K2 use is not universally accepted as a marijuana substitute.

To date, there are no studies about inhaled synthetic cannabinoids in humans; long-term effects are purely speculative at this point. But by using the human experience with marijuana, we can have expectations. Knowing now that marijuana abuse is tied to various forms and types of psychosis, we can gird ourselves for the same experience with Spice and K2 smokers. In fact, reports are coming in of previously healthy Spice and K2 smokers who present to emergency rooms with pretty frank cases of psychosis.

In a recently posted report posted in the American Journal on Addictions, physicians report on a 59-year-old male who was admitted to an inpatient psychiatric unit as a result of effects he experienced while smoking Spice. In fact, the patient had been admitted three separate times over a course of 60 days. A one-time poly drug abuser, the patient had been clean and sober for three years prior to his Spice use. The patient had an additional history of post-traumatic stress disorder (PTSD). He appeared at a hospital emergency room where he
claimed that he was reliving the details of combat trauma he experienced while in the service. The flashbacks were frightening. The patient detailed that he had been smoking Spice on a fairly regular basis before his presentation to the emergency room; he claimed that his use consisted of two Spice "joints" daily. He had also relapsed to Xanax use as well during the same time frame. The patient left the hospital against medical advice. He returned several days later only to report that his symptoms had resumed. He also admitted that he had resumed his Spice smoking. In that instance, the patient reported powerful visual hallucinations; his family reported that he had engaged in bizarre disorganized behavior at home. He was admitted again.

As it turns out, this patient had a significant history of poly-drug abuse that included regular use of organic cannabis, i.e. marijuana. And although he had been clean and sober for the three preceding years, his prior THC use may have in some way provoked his current psychotic episodes. Whatever the etiology of his condition, it is pretty clear in this case that synthetic THC is a potential trigger for serious, psychotic episodes for some users. Although the current menu of Spice products proclaim their legal status and the absence of banned cannabinoids, it is clear that the substances still convey powerful psychoactive effects. Anyone abusing these drugs should be monitored carefully.

For drug court participants and other individuals who are bound by the terms of conditions for probation, synthetic cannabinoid use should be explicitly banned. This also holds true for those participants who may use and abuse other designer drugs such as "bath salts," "plant food," "glass cleaner" and "ant powder."

Signs of someone under the influence of synthetic cannabinoids include, but are not limited to, the following:

- Dilated pupils (rebound with introduction of direct light)
- Lack of convergence (non-convergence)
- Dry mouth
- Odor of burnt plant material on breath
- Organic plant debris in the mouth
- Accelerated speech and mannerisms
- Speech that is out of context or non-responsive to surrounding events
- Problems with coordination; loss of dexterity
- Increased heart rate (90 bpm or more)
- Increased blood pressure (140 mm/Hg or more systolic)

In the future the MEDTOX Journal will maintain a library of recorded webinars that are available for purchase for our readers. Recent presentations include a review of synthetic cannabinoids, "bath salts" etc. and Kratom products, as well as a provocative seminar dealing with prescription opiate abuse. Contact Andrew Gilberts at agilberts@medtox.com for further information about purchase of webinar recordings. Stay tuned to the Journal for announcements of the DAR summer and fall schedule of webinars and podcasts.
Bad News for Marijuana Smokers: The Hits Keep Coming

The MEDTOX Journal has reported on a succession of scientific reports related to short-term and long-term cognitive effects associated with the use of cannabis. It has been established that cannabis use impairs motivation and executive function; it has also been tied to the lowering of thresholds associated with psychotic symptoms. The relationship of cannabis use and the etiology of schizophrenia is currently the subject of scientific examination. Recently published research in the Journal of Biological Psychiatry explores the impacts that cannabis use has on working memory.[1]

The authors of this study treated 17 healthy subjects with tetrahydrocannabinol (THC) or a placebo who then took tests of working memory that involved an exercise of using short-term memory storage and manipulation of memory. The participants then underwent functional MRI imaging. In the patients receiving placebo, there was evidence of increased and progressive activity in the areas of the brain that are associated with working memory, especially the components that make up the prefrontal cortex. For the participants receiving THC, the effects were the reverse. THC significantly retarded the activity in the prefrontal cortex. The THC-treated patients also exhibited lengthened reaction time and degraded accuracy of recall, all indicative of impairment in the prefrontal cortex area. In all, the THC-impaired patients exhibited clear signs of decline in the quality of working memory.

The mounting evidence that marijuana use has serious neuroanatomical consequences must become part of all public service announcements and drug prevention literature. The advent of synthetic cannabinoids makes this situation all the more dangerous as the number of adults and teenagers using THC (organic marijuana and K2/Spice synthetics) appears to be expanding. Based on the societal experience with marijuana to date, it is reasonable to expect that the impacts of synthetic cannabinoids on the brain are decidedly deleterious.

The Netherlands: The Birthplace of "Bath Salts"?

The emergence of "bath salts" as a distinct genre of abused drugs begs a question, where did it all start? Arguably, the concept of phenethylamine and methylated cathinone abuse can be laid at the feet of Alexander Shulgin, the well-known author of the 1991 tome PiHKAL: A Chemical Love Story. The acronym stands for Phenethylamines I have Known and Loved. Shulgin later penned a second generation, a narrative continuation of PiHKAL and expose of tryptamine drugs of abuse. And as you may have guessed, he titled that one TiHKAL for Tryptamines I Have Known and Loved. In any event, Shulgin's first publication was released in 1991; the follow-on effort was released on 1997. In the intervening years, the drugs that are the subject of Shulgin's musings have spurred only marginal interest and activity within the ranks of hallucinogen users. That was, of course, the case until 2010 when many of the drugs showcased by Shulgin wound up in nefarious substances called "bath salts" and "novelty powders." An explosion of designer drug hysteria was unleashed. Almost overnight, the United States market for these drugs exploded. And although federal and state legislation has blunted the further chemical exploitation of these designer drugs, they now are sold and marketed as legal "ant powder," "foot powder," and "glass cleaner." On any given day, it is hard to say what is in these potions exactly, but lab testing results continue to uncover the presence of banned substances such as MDPV and mephedrone.

Looking back on the etiology of the designer drug phenomenon, the Netherlands was one of the first locales that proposed methylenedioxymethcathinone (methylone) as a new and emerging drug of abuse. In fact, in 2005 Dutch researchers published a paper that announced the arrival of methylone on the streets of the Netherland. They announced that methylone, along with a number of abused piperazine compounds, (meta-chlorophenylpiperazine in particular) had been found in various forms in products sold on the streets there[i]. Based on their findings, they opined that these drugs were the avant-garde of a new class of substances meant to compete with methylenedioxymethamphetamine (MDMA, Ecstasy).

Five years after the prescient comments of those Dutch scientists, we find ourselves in a world-wide market that is saturated with on-the-move designer drugs. But often times, evidence of a coming drug abuse tsunami like that which has been ushered in by "bath salts" can be easily seen and anticipated. Let's hope that our current designer drug miasma is on the wane and that there is nothing too bad that will sweep in behind it.

Psychogenic Drug's Success Prompts Calls for Use as an Antidepressant

In a report recently posted in the Journal of Biological Psychiatry, there appears to be mounting evidence that the dissociative anesthetic ketamine has profound abilities in mitigating the effects of depression, especially in patients who struggle with the debilitating diagnosis of bipolar disorder. For these patients, modern pharmacotherapy has been hit-and-miss in the worldwide effort to simmer the wildly fluctuating symptoms of mania and depression. Effective treatments for bipolar disorder are desperately needed.

Ketamine is a drug that is used in specialized medical and veterinary procedures. In humans, the drug is used in pain management for patients who have developed severe tolerance to opioids. The drug is quite effective in that roll. For pediatric patients, ketamine is used as an analgesic and anesthetic; the drug is quite safe for utilization with children and adolescents. The drug is an n-methyl-D-aspartate (NMDA) antagonist, which means that it exerts its effects by blocking the actions of NMDA. It is becoming abundantly clear in modern research that the NMDA receptor complex is intimately involved in modulating antidepressant and anti-suicidal effects in affected patients. The drug's success in this roll opens an entirely new avenue of study for research scientists. The NMDA receptor system is still an unknown factor in the influencing of mood and mood stability. The research reported here begs for new efforts at nailing down the cause and effects of NMDA activity in depression.

As a recreational drug, ketamine is often abused. In America, it has pockets of devoted fans. The drug is chemically related to the insidious dissociative anesthetic PCP. It is also a chemical relative to the over-the-counter drug dextromethorphan. Each of these drugs exerts unique effects on the central nervous system, effects that include a detachment of peripheral nervous system messages from communication with the brain. The resultant experience is one of sedation and detachment from surroundings. The next effect is one of a user sitting passively, quietly, and uncommunicative with surroundings. Ketamine users call this experience as having descended into the "k-hole."

In the study cited in the Journal of Biological Psychiatry, a project headed by the National Institute of Health treated bipolar, depressed patients with a single dose of ketamine. A control group of depressed patients received placebo. In both groups, the patients were carefully monitored and evaluated. Patients kept notes and scores of their experiences. The results were startling. The ketamine-receiving patients reported near immediate improvement in their depression. The improvement in depression symptoms extended for over three days. In addition, ketamine apparently reduced the number and severity of suicidal thoughts in the patients who received the treatment. This particular effect was most startling. Up to this point, no pharmaceutical product has exhibited combined effects as an anti-depressant and as a means of reducing suicidality. Overall, 79% of the patients treated with ketamine improved. No one reported improvement following ingestion of placebo. These effects are staggering.

Ketamine seems to have potential that extends well beyond the emergency room and operating theater. It may be that ketamine and other NMDA receptor antagonists are the opening act in the development of an entirely new class of drugs designed to alleviate the
Varenicline (Chantix®) is an oral medication used by patients to reduce the withdrawals and cravings when quitting smoking. Classified as a partial nicotine-receptor agonist, varenicline has established itself as a first-line drug used to treat the stubborn symptoms experienced by people who try to quit smoking. Despite the drug’s demonstrable effects in easing the experience of nicotine withdrawal, the drug has been linked to a number of physical and psychological side effects. One of the associations involved with Chantix use has been a supposed association between varenicline and higher cardiovascular risk. However, a recently concluded analysis of varenicline clinical trials found that the drug is not associated with a statistical, elevated cardiovascular risk.

The study of varenicline involved 22 separate placebo controlled trials of tobacco smokers of adult age. Participants were provided varenicline or an inactive control. Overall, 5,400 study participants received the drug while 3,800 received the placebo. In analysis of serious cardiovascular events, the risk difference between the two groups was negligible. The University of California, San Francisco (UCSF) scientists who authored the report went on to validate the utilization of varenicline as a first-line drug in the treatment of tobacco dependency.

Tobacco use is frequently encountered in populations of substance abuse patients in recovery. Ironically, it is tobacco dependency that ultimately becomes the most serious health risk for the many patients in recovery. Reducing or eliminating the tobacco dependency can be achieved during early phases of recovery using available pharmacotherapy and cognitive behavioral therapy. The pharmacotherapy involves Chantix being joined with nicotine patch products and the anti-depressant bupropion. This process has proven effective for thousands of recovered smokers.

Name That Drug: A Heavyweight Drug That Toils in the Shadows

This month's mystery drug is a prescription medication; it is a controlled substance. It is unique to its chemical genre in that it is available as an oral, subcutaneous, intramuscular, rectal, and sublingual medication. Although the drug has a moderate potential as a drug of abuse, it has never caught on with the larger substance-abusing world. However, it has been a drug that healthcare workers have become entangled with. Like many drugs of its ilk, it was first "developed" in Germany in 1908. It was not synthesized. (To regular
readers of this column, this is an important clue). In Europe, the drug was instantly popular in the form of an elixir. As an elixir, this month's drug starred as a reliable and long-acting cough suppressant. And as an antitussive, the drug gained the attention of the American pharmaceutical industry. Europe and America were still struggling to control the spread of cough-borne diseases, such as tuberculosis and whooping cough; this month's drug had instantly found its niche. In America, its first utilization was as a cough suppressant. In the modern era, the drug is predominately used as an analgesic, a drug used to treat moderate to moderately severe pain.

This drug is most commonly found in the form of a tablet or capsule. It is ordinarily compounded with adjunct drugs, drugs of lesser potency and little addictive potential. It is manufactured in instant release and time-released formats. The drug is an analgesic. And as an analgesic, it has the potential to create dependency. Considered to be 150% as powerful as codeine, this drug exerts effects for 4-6 hours following ingestion. When utilized for pain management, the drug can be found in some countries as a controlled release drug. In that sense the drug is quite similar to Oxycontin (oxycodone) and Opana (oxymorphone). But unlike those two powerful sustained release drugs, this month's drug has not spawned legions of devoted recreational abusers. In the U.S., this drug is routinely partnered with acetaminophen and aspirin. In other countries it can be found loaded with caffeine, antihistamines, and decongestants. In some places, it can even be found loaded with vitamins. In the U.S., the most commonly encountered commercial product is a drug called Synalgos-DC.

This drug is a chemical descendant from the opium poppy. It bears great structural resemblance to codeine. In fact, one could argue colloquially that this month's drug is a "codeine molecule on steroids." And in that sense, this month's drug will precipitate signs and symptoms that can be said to be classically "narcotic-like." Traditional effects of sedation, muscle relaxation, papillary constriction, and slow and rasp speech will emerge. But of interest to recreational drug users is that this month's drug can cause "ecstasy-like" effects. In fact, many users cite the drug's ability to stimulate feelings of empathy and happiness as being most alluring. Unlike other drugs in its class, this month's drug can provoke mixed feelings of euphoria, relaxation, and stimulation. Some recreational users of the drug have even claimed that the drug has heightened their abilities of interpersonal communication. Recreational users cite improved skills of persuasion and debate. These claims are unusual for drugs of its class.

But for this drug and all others of the class, there are some very insidious side effects. For starters there is constipation. The constipation side effect can be turned to an advantage when applied as a treatment for irritable bowel syndrome. Like Loperamide (Imodium etc.), this month's drug can serve as an effective therapy in treating diarrhea. But unlike Loperamide, the drug will cause central effects that include drowsiness and problems with coordination. People taking this drug will have difficulty in operating machinery and engaging in complex physical tasks. If combined with alcohol, use of this drug will result in significant additive effects that can exacerbate balance and speech. Short-term memory is blunted as well. Tolerance and dependency develop quickly. When that happens, a sudden stoppage in administration will result in rather severe withdrawals.
Because of its euphoria-producing effects, this month drug is believed by some to be a sort of secret. Recreational users of it know that they have a "sleeper." But despite the drug's unique appeal, abuse of it has never risen to a point where public safety authorities have been threatened by it. For those adherents who exclusively abuse this prescription drug, the development of tolerance is a quick and certain. Especially when the drug is ingested in amounts that are much greater than the recommended therapeutic dose. To date, there are no reports of users smoking or snorting this drug. Perhaps the fact that the drug is usually compounded with other non-controlled substances has snuffed out any effort to use the drug in a parenteral form. To snort or inject the drug, a user risks some serious physiological consequences. Especially for those who try to intravenously inject this drug, the result can include life-threatening shock.

This month's drug is obviously an opiate and controlled substance (Schedule II). The intrepid chemist has been known to convert this drug into dihydromorphine. This is a difficult task and one that is not commonly heard of in the recreational drug user world. Additionally, this month's drug was once ventured as a substitute for methadone in cases where opiate substitution therapy was conjured. The arrival of buprenorphine on the scene has put a stop to that idea. The month's drug is a codeine product and in reality can be called a "codeine molecule on steroids."

Answer:
This month’s drug is Dihydrocodeine (also known as Synalgos-DC, Panlor DC, and Dicogesic)

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