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Know Someone Who Can't Stop Spitting? Maybe It's Pilocarpine
The DAR Program at MEDTOX receives a never-ending set of tales about bizarre and sometimes unbelievable instances of drug use. Our staff of senior DAR instructors, veteran drug enforcement officers, and healthcare professionals has an easy time with most of the calls that come into our Hotline call center. But once in awhile, the Hotline is presented with a bizarre set of facts and circumstances and we are asked to explain to a caller what is going on. These unusual cases are pharmaceutical jigsaw puzzles that require our staff to do research, sometimes necessitating a call to other experts. Recently, our Hotline was asked for assistance with a very strange situation involving a suspicious group of drug-using teenagers from upstate New York. The kids were all members of a local high school group who were attending a party where local police had been called to deal with excessive noise and a large crowd. As is typical for large weekend parties of teenagers, bodies of partygoers were pushed together that spanned across several rooms and the front yard of a home. Despite all the sameness found in the undulating mass of high school kids, sheriff's deputies quickly focused their attention on a group of 30-35 kids who had drifted off into their own small gathering away from the larger core of the party. Deputies noticed something was different with these kids. Something was quite odd with both the boys and girls in this group. All of them were spitting. Not spitting a "tough guy" spit, or professional baseball player sort of spit, these kids were "hawkling" large "loogies" of saliva, one right after another. In the estimation of one of the deputies, the spitting seemed to be unwilled; it appeared to be automatic or an autonomic response. The kids could not stop spitting. Each of the kids in this group exhibited the behavior. Some of the kids said that they couldn't stop spitting because their mouths were producing too much saliva. Some laughed and joked about the predicament as they continued their non-stop spitting.

Besides the growing puddle of loogies, the deputies noticed some physical signs and symptoms of possible drug use. It was obvious that these kids had used alcohol, the telltale odor of alcohol was present and the speech of some of the kids was slurred. However, most of the kids were engaged in alternating periods of laughter and loud talk that was followed by quiet restlessness and continued spitting. Then there were periods of agitation and sweating accompanied by spitting. Some of the kids exhibited piloerection (gooseflesh) and patterns of incoherent speech. Almost all of the kids there presented with pupil constriction at about 3.0 to 3.5 mm. As was expected, the kids denied taking any type of drug other than a sip or two of an alcoholic beverage that had been given to them by someone else. But as the examinations and questions proceeded, the spitting continued.

The question to the Hotline staff was obvious. What drug or combination of drugs could produce the physical signs and symptoms observed with this group of teenagers?

In our modern era of "cabinet" and "flier" parties organized by kids through wide and skillful use of social networking systems, teenagers are experimenting with an array of drugs that heretofore have never made it to the party scene. The contemporary cabinet party is a big fishing net that brings dozens of different classes of drugs and narcotics center stage for kids to experiment with. Whatever happens to be in mom and dad's medicine cabinet is likely to make it to a party and into the hands of a young person who is interested in experimenting with drugs. This means that drugs across the panorama of prescribed and non-prescribed medications will make it into the young bodies and brains. And although youngsters recognize big name drugs like Vicodin, Percocet, and Valium, they are not nearly as astute when it comes to identifying drugs used to treat high blood pressure, diabetes, depression, and infections. Often times, dangerous drugs manufactured for relatively rare conditions get mixed in for use with the popular drugs that teenagers usually seek.

In this case, there are two types of drugs that could cause the hyper salivation that the deputies witnessed in their evaluations of the inebriated youngsters. The first case might involve ingestion of a potent opiate, a narcotic analgesic of some kind. Some of the drugs in this class of drugs can cause excessive salivation and relaxation of the muscles in the face and oral cavity. When this happens, drooling can occur. But the facts in this case tend to indicate that the teenagers are not so much drooling as they are spitting. If the culprit were opiates (narcotic analgesics), the kids would also be rather laid back and exhibit more somnolent like features. They would not be
agitated or otherwise "jacked up." But constricted pupils again are suggestive of opiate use here. Opiates are one of the few categories of drugs that cause pupils to constrict and become non-reactive to light. Larger doses of the opiates can also slow speech. In higher concentrations, opiates can cause slurred speech. Laughter and excitation are not hallmark effects of the opiates though.

In light of the influence of cabinet parties on adolescent and young adult drug use trends, we have to look a little below the radar to better identify the main drug culprit in this incident. In recent years, a relatively obscure prescription medication has found its way out onto the streets and into the hands of adolescent drug users. The drug is Pilocarpine. It is better known by its product names of Dioptic and Alcon. The drug is approved by the FDA to treat glaucoma. To that end, it is a parasympathetic alkaloid and a powerful muscarinic receptor agonist. The drug is sold in both eye drop and tablet form. Like all drugs in its class, it can create noticeable and unwanted side effects. The first and most profound effect is the drug's ability to stimulate the production of saliva. Significant volume increases in saliva may force the user to have to spit or frequently expectorate. The drug directly causes miosis in the pupil of the eye. This means that the drug will cause rapid constriction of the pupil (like the opiates) down low to levels of 1.5 mm to 3.5 mm. While under the influence of this drug, the eyes will not respond to changing light environments. The drug in sufficient concentration can cause sweating and agitation.

In this case, the most likely cause of the symptoms exhibited by the party-going students was the use of pilocarpine. Further, it is likely that the drug was skinned from a medicine cabinet and brought to a central party location where others could experiment with the drug and then watch over one another while high. Alcohol was added to the mix at some point in the evening. The drug's most notable side effects took hold and caused each of the kids to hyper-salivate, the accumulation of saliva then prompted the kids to frequently spit. The constricted pupils documented by the deputies were also the direct effects from the use of this alkaloid. The slurring of speech and the odor of alcohol were related to concurrent consumption of alcoholic beverages and were not caused by pilocarpine ingestion.

The cause of the spitting students from upstate New York: pilocarpine ingestion.

Questions readers may have about this report may obtain more information by contacting the MEDTOX DAR Program at darsprogram@mac.com.

**Tainted Cocaine Increases the Number of Woes for Chronic Drug Users?**

A recent Drug Enforcement Agency advisory released in April announced a significant increase from 2008 in the use of levamisole as a cutting agent in powdered cocaine. Levamisole is a deworming agent used in the livestock business. Dealers and traffickers are using the widely available compound as an additive. Experts differ on why levamisole is being utilized as a cutting agent for cocaine. Some believe that levamisole enhances the release and neuro-chemical effects of dopamine in the central nervous system. Cocaine powerfully stimulates dopaminergic networks that cause feelings of confidence, control, and motivation. It appears that levamisole adds to these effects.

In addition to its role as a veterinary deworming agent, levamisole has been widely utilized as a therapy in the treatment of colon cancer in humans. In Colombia, where a great deal of domestic cocaine undergoes final processing and packaging, levamisole is a common ingredient in farm feed and other animal nutritional products. Chronic ingestion of levamisole in humans can trigger an immune disorder called agranulocytosis. This condition results in the suppression of a type of white blood cell necessary to fight infection. This condition can be fatal for many of those who contract it. In Spokane, Washington, a woman in her mid-40s who tested positive for cocaine was admitted to a local hospital. She
suffered from a variety of illnesses and a rash that covered most of her body. Despite her admission to the intensive care unit, this patient died. Her doctor suspected that the patient had used levamisole that had been laced with cocaine. As it turns out, there have been other fatalities from the ingestion of cocaine contaminated with the deworming agent. In states like Colorado, officials have come to suspect that up to half of the drug circulating there contains levamisole.

From the start of its modern run in the 1970s as a drug of abuse, cocaine has been cut with or altered with a diverse array of powders and concoctions. Some of the additives have bolstered the stimulant effect of the drug, others have had no effect other than to color and add weight to the final product. Levamisole seems to impact the final product more than other additives in the past. The problem is that levamisole is not on the radar of those who use and abuse cocaine. If the drug comes to a buyer from a trusted or regular source of cocaine, it is unlikely that much thought will go towards consideration of what has been mixed with the drug. Not until a buildup of toxic side effects occurs will the users slow down to consider that something is wrong.

A levamisole-tainted cocaine preparation will not appear out of the ordinary to a user. The deworming agent is a white powder and easily blends in with white to off-white colored cocaine HCL. It is unclear what levamisole's fate is when cocaine is put through a process of freebasing, but it is reasonable to suspect that a fair portion of the additive probably does make it in to a final piece of crack cocaine. When smoked, the levamisole effect on dopamine and dopamine transporter systems will likely enhance the core euphoric effects of cocaine.

What Is The Latest Treatment In Marijuana Abuse?

Marijuana is the most frequently used illicit drug worldwide. A 2005 National Survey on Drug Use and Health (NS-DUH) reported that over 70% of 19.7 million illicit drug users abuse marijuana. The incidence of new marijuana use in 2005 was 2.1 million, a number that is constant year to year. This means that there are over 6,000 marijuana initiates every day. Marijuana (cannabis, THC etc.) has been a seminal focus of the MEDTOX Newsletter this year. In this article, the Newsletter staff has placed special emphasis on the explanation of the core elements of marijuana abuse and dependency.

Marijuana abuse typically starts in adolescence. Well-regarded studies put the peak initiation of marijuana use at age 18. Within 10 years of that mark, 8% of that group will become marijuana dependent. About 1 in 10 new cannabis users will become marijuana dependent.[1] A substantial number of teens and adults use marijuana regularly. Marijuana is the most commonly cited drug by those who admit to illicit drug use in the past month. And although marijuana use by teens and adults has steadied in recent years, the numbers of those who admit to chronic cannabis use warns of the need for extensive drug treatment services in the future.

Despite the claims of the marijuana decriminalization crowds, marijuana abuse does have immediate, sometimes significant, medical consequences. Past Drug Abuse Warning Network (DAWN) reports have chronicled marijuana use in more than 20% of emergency room drug abuse visits; the numbers are greater still for drug users under the age of 20. Admissions to treatment programs for marijuana dependency now rival the rates for cocaine and heroin.

Marijuana is a drug that is most commonly smoked. Medical marijuana shops now push a variety of food products that contain cannabis. Nevertheless, smoking marijuana "joints" or bowls of water pipe fed (bong) marijuana is most popular. Once it enters the bloodstream, THC is quickly dispersed and its accumulation into the body fat begins. The major metabolite of THC is THC-9-COOH; it is this product that most urine tests are dialed into. Because of variations in individual pharmacokinetics, assessments of THC-9-COOH concentrations can be difficult. As a result, THC-9-COOH is frequently normalized and reported with creatinine levels in drug test results and reports.
THC interacts with a battery of cannabinoid receptors, mostly located in the central nervous system. Identified as "CB-1" and "CB-2," THC can influence these receptors and a number of functional states in humans. Cannabis use can impact a number of important biological processes that can then lead to continued self-administration. Systems of reward, cognition, memory (short and long term), appetite and analgesia are all influenced by THC in the bloodstream. Recent evidence suggests that THC also exerts effects on dopaminergic processes in the central nervous system. This set of putative effects makes THC a much more complicated substance than scientists and treatment professionals had previously understood.

Of concern to most persons working in the field of marijuana abuse and addiction treatment are the long-term effects of marijuana smoking on its users. And although there is contradictory evidence on the long-term psychological and health effects of chronic marijuana abuse, there are some effects that are downright frightening. A long-term investigation of marijuana users undertaken by Gruber et. al compared a cohort of chronic marijuana users against a similarly matched group of non-users.\[2\] For both groups, each had relatively equal status for college graduation by parents. But for the subjects themselves, the differences in graduation rates could not be more dramatic. In the non-cannabis using control group, 80% achieved a college degree of some type. Less than half of the cannabis users reported achievement of a college degree. And although parents of subjects of both groups reported similar levels of income, the marijuana using subjects reported low-income levels that were twice as low as that of the control group. Motivation, achievement, and educational attainment appear to be significantly reduced in association with marijuana use. Marijuana users also provided commentary of the effects of chronic cannabis abuse on the status of their health and well-being. They gave overwhelmingly negative ratings to the effects of marijuana on their social lives, physical health, mental health, cognition, memory, and careers.

The impacts of marijuana abuse extend beyond those effects on the individual abuser. The Gruber study indicated that ninety seven percent of heavy abusers reported that they regularly drove while intoxicated. Fifty five percent of the heavy users have children. It's not a stretch to assume that some of these heavy users drove while intoxicated with children in the car. It is also likely the negative cognitive effects factored into the overall levels of supervision and parenting rendered by heavy marijuana users. With statistics as sobering as these, it becomes all the more important that effective treatment methods be fashioned, especially for those abusers who are actively seeking treatment. Relapse rates are significant and can be demoralizing for those seeking sobriety. Defining and establishing the most effective therapies and making them widely available in treatment is vital.

Behaviorally based outpatient treatments have demonstrated efficacy for both adolescent and adult marijuana abusers. Cognitive behavioral therapy (CBT) and motivational enhancement (MET) interventions are both effective for reducing marijuana consumption and creating a regimen of abstinence and sobriety. Many of these techniques are adapted from alcohol treatment protocols. Voucher programs and escalating compensation systems that pay for clean drug tests have also proven themselves to be effective in treating cannabis abuse.

Pharmacotherapies have been less encouraging in the treatment of cannabis dependency. It is clear that marijuana dependency has connected to it a clear-cut withdrawal syndrome, as well as to an extensive abstinence syndrome driven by intense craving and anxiety. A number of antidepressant medications have been evaluated in treating marijuana withdrawal. Nefazodone seemingly possesses the most potential in mitigating withdrawal effects. Bupropion, on the other hand, seems much less effective in that role. Oral THC (dronabinol) displayed some potential in reducing THC withdrawal and craving. Taking a page out of the opiate treatment manual, THC substitution appears to lessen some of the more odious impacts of withdrawal-like chills, anxiety, muscle pain, and overall misery. Buspar (buspirone), Prozac (fluoxetine), and lithium are examples of other drugs that have demonstrated some level of efficacy in boosting the success of withdrawal from cannabis dependency. In addition, the opiate antagonist naltrexone has been evaluated as well for its ability in mitigating the more unpleasant symptoms of cannabis withdrawal. It appears that more research is needed to elucidate the role of opiate antagonists in the treatment of marijuana dependency and addiction. Certainly, physicians and patients
would benefit from the addition of new pharmaceuticals to help treat the painful symptoms of abstinence that often trigger the mechanism for relapse to THC use.

Marijuana dependence is not easy to overcome. The rate to relapse for marijuana is similar to that of other drugs such as cocaine, opiates, and alcohol. The good news is that behavioral-based interventions work. There have been steady gains in our understanding of THC dependency. With widespread recognition of marijuana as a drug of abuse and a drug capable of causing a distinct dependency and withdrawal, the groundwork has been laid for real progress. Marijuana dependence is a condition that is largely established early in adulthood. Programs designed to attack marijuana abuse at that critical junction in life should be strongly supported.

Now, is anyone up for a discussion of medical marijuana? Stay tuned for the June edition of this Newsletter where this issue will be stripped down to its most essential elements.


How Widespread Is Adolescent Inhalant Abuse and What Does It Mean for Adulthood?

Although the abuse of gaseous, intoxicating agents by adolescents is believed to be a significant problem, there is a lack of data about the impacts and consequences of the behavior later in life. Does experimentation with these drugs lead to patterns of substance abuse and bad behavior later in adulthood? Does adolescent recreational or social inhalant abuse lead to the development of psychiatric or emotional problems later in adolescence or further into adulthood? The use of these types of drugs is widespread. A 2006 Monitoring the Future Survey pointed out that 16% of 8th graders had used or experimented with inhalants. Preceding the Monitoring the Future Survey, Sakai et. al studied a cohort of 847 adolescents who had been drawn from a substance abuse treatment program and discovered a high rate of lifetime inhalant abuse in the cohort. The teenagers who identified themselves as inhalant abusers also displayed a variety of social and psychiatric impairments. Some of these youngsters were diagnosed with legitimate inhalant use disorders (IUD) per the criteria set forth in DSM-IV, but many of the adolescent users did not reach that point of addiction and dependency. It was unclear what sets a more recreational inhalant abuser apart from another user who goes on to develop an addiction and dependency. This is the age old conundrum that scientists face in assessing the factors that allow some social users of drugs to remain in control of their substance use while others go on to develop dependencies and addictions that are impossible to control or otherwise manage. In that sense, abuse of an inhalant is no different than alcohol, opiates, marijuana, and stimulants in terms of patterns of use and abuse.

As a class of abused drugs, inhalants are comprised of a large group of substances that include liquids, gels, and solids. The gases emanating from these substances are often inhaled into the lungs and held there for extended periods of time in order to bring about maximum absorption. Volatile solvents (paints, glues, gasoline) are some of the most insidious forms of inhalants. The fumes from these substances act as deliriants. These powerful, euphoria-causing fumes cause a mixed bag of depressant and stimulant effects. Chronic users of these inhalants can develop addictions and dependencies that are indistinguishable from those of an alcoholic. But in some cases, ironically, alcohol is less onerous and destructive than inhalants. Solvent inhalant abusers develop medical complications from their drug use that is often more difficult to treat than those occurring from the use of opiates, marijuana, and depressants. In the last decade, inhalant abuse trends shifted from solvent-based to a more diverse lineup of drugs that included aerosol can propellants and electronic parts cleaners. The effects of these drugs were noticeably different, and in some cases more deadly than earlier generations of glues and paints. The utilization of pressurized aerosol products led to frequent cases of asphyxiation and unconsciousness. Inhalation of some of these products has directly led to overdose and death. At present, adolescent inhalant abuse continues to revolve
around utilization of aerosol-based products, whereas adult inhalant abusers still trend toward the use of solvents, paints, and glues.

In a study published in 2009 from a survey of wards in the Missouri Division of Youth Services conducted in 2003, researchers were able to peel away the issues that are raveled together in the histories of adolescent inhalant abusers[2]. The results of the survey help make clear the relationship between early adolescent abuse of inhalants and the impact that this behavior has on drug use later in life. Adolescents who met criteria for having a lifetime inhalant use disorder were mainly Caucasian males who lived in rural areas and small towns. Inhalant users were also more likely to have engaged in delinquent behavior in the past year compared to those young males who did not. Those who indicated that they had inhalant use problems displayed higher scores for impulsiveness, non-conformity, and fearlessness than those boys who did not use inhalants. Inhalant abusing boys also displayed higher scores on scales for depression and anxiety. Those who were inhalant dependent were noticeably higher in their delinquency scores than those subjects who abused inhalants but who were not yet dependent. Boys and girls scored similarly in most measurements of dysfunction. Scores for suicidality and suicidal ideation were also much higher for those subjects who were identified as being inhalant dependent. The contrast was greatest between the inhalant dependent and non-users. Inhalant use disorders among young offenders (male and female) are a strong prognostication for an array of delinquency and substance abuse problems later in life. It appears that the more severe the inhalant abuse disorder is for a young drug abuser, the greater the substance abuse problems will be later in adulthood. It is clear that abuse of inhalants early in life is a fast track to serious psychiatric problems and anti-sociality later on in adulthood.

Inhalant abuse is commonly featured in social media networks frequented by teenagers and young adults. And although the antics of young people high on inhalants borders on the comic, the truth of the matter is that inhalant use is a serious facilitator towards development of graphic social dysfunction. Early abusers of inhalants are logarithmically more likely to become dependent on nicotine, develop alcohol abuse disorders, or become addicted to methamphetamine. Inhalant abuse must become a centerpiece of adolescent and young adult drug prevention efforts. The abuse of inhaled intoxicants is a proven gateway to a plethora of bad outcomes, some deadly. Flippant disregard of inhalants by parents, schools, police, and probation serves to exacerbate the problem. Drug prevention programs, drug detection systems, and drug testing protocols must all orient themselves towards more aggressive approaches to the problem. Drug testing protocols for juvenile probation programs should include assays designed to screen for the most abused inhalant drugs in the region where a given program is located. Drug use trends can be easily obtained by contacting local police, sheriff's office, or state trooper office.

Readers who have questions about inhalant abuse disorders can obtain more information by contacting the MEDTOX Drug Abuse Recognition (DAR) program at darsprogram@mac.com.

Six Flags Theme Park (SFTP) is among the largest theme park and entertainment companies in the world. Their parks are popular destinations for Americans of all ages. In 2009, Six Flags welcomed nearly 25 million visitors to its parks. To safeguard park visitors, Six Flags management vigorously maintains a drug-free workplace. One of SFTP's most important drug-free efforts involves widespread use of urinalysis-based drug testing. In 2008, MEDTOX was awarded the Six Flags drug-testing contract. In addition to urinalysis and oral fluid testing, MEDTOX provides Six Flags with Drug Abuse Recognition (DAR) services. DAR training is used by Six Flags to heighten management's awareness and expertise in an effort to prevent substance abuse from impacting park safety and security.

In March of this year, Six Flags management personnel contacted the DAR Hotline because they had suspected drug use by an employee. Suspicions on the part of a supervisor led to a drug test of the employee. Six Flags, among other methods, employs the use of MEDTOX drug-testing systems. In this instance, a MEDTOX test uncovered evidence of opiate abuse in a specimen provided by the employee. A positive result for opiates suggests the presence of one of an array of opiate drugs. Substances such as codeine, hydrocodone, morphine, and opium are some of the potential drugs involved. Because of chemistry quirks, oxycodone is nearly impossible to screen for in a standard opiate assay. Because of this characteristic, oxycodone must be screened and tested by using a stand alone customized assay. Clients who live and work in regions of the country where oxycodone is widely abused should strongly consider the use of a screening panel that includes a separate oxycodone test. In this case, management knew the employee was suffering from lingering back pain. As a result, a positive opiate drug screen made sense. The supervisors confronted the employee with the result. The employee quickly responded that the positive opiate screening result was due to his prescription use of Lexapro, a popular drug used to treat depression. Many message boards on the Internet contain testimonials from people who claim that Lexapro is an effective alibi to cover up opiate abuse on a drug test, although there is scant scientific evidence to make the case. In this case, supervisors were not swayed by the employee's Lexapro claims.

As the investigation moved forward, the employee allowed supervisors to examine his uniform pockets. A cursory scan of the items revealed a small pink tablet. This discovery prompted the employee to explain to the supervisors that a friend had given him the pill, but that he was unsure of what it was. A check of DAR reference materials identified the tablet as methadone. Despite its reputation as a drug used in opiate detoxification, methadone is more widely used as a pain reliever and analgesic. Because of its long half-life, the drug works well in the management of intractable and/or chronic pain. And although methadone is an opiate, in this employee's case, the positive opiate drug test could not be explained by the presence of a methadone tablet. Like oxycodone, methadone is a unique chemical that requires a specially designed assay in order for it to be screened from a urine specimen. Unlike oxycodone though, methadone is a synthetic narcotic that has a decidedly unique chemical organization. So in the case of this employee, the positive opiate screen that he produced had still yet to be properly explained. The supervisor knew that some other explanation existed for the positive drug test. The supervisor pressed on. Flustered and out of alibis, the employee asked to use the restroom. The employee headed off down the hall towards the bathroom. He was never seen again. He never returned to work and ended up forfeiting his job.

It's unknown as to what exactly was going on with the employee involved in this case. It could be that he was struggling with issues of chronic pain and somehow had come into possession of methadone from an illicit source. Currently, methadone is a popularly abused narcotic in the chic club and rave scenes. The drug is frequently diverted to the street from pain clinics as well. It could be that this employee was opiate dependent and may have been using methadone as a pharmaceutical replacement for some other opiate drug. If that were the case and the employee was in fact dependent or addicted, he would have been eligible for treatment under terms of the company's employee assistance program. But the employee left the building before assistance or intervention could be rendered.
This case illustrates the challenge that employers and public safety agencies face in their efforts to prevent and detect substance abuse. Especially in cases of opiate use, there are many prescription opiates on the market that are not currently tested for in commercial drug test systems. Many substance abusers understand these testing blind spots and choose to use drugs that they know will not be detected in forensic examinations. It's vital that managers, supervisors, and others who have responsibilities for drug testing keep abreast of trends and developments in substance abuse. Training in Drug Abuse Recognition (DAR) goes a long way in developing the needed skills and abilities for supervisors and managers in the maintenance of drug-free workplaces.