Methamphetamine-Related Effects on Perinatal Morbidity

Methamphetamine (crank, tweak, ice, and glass) is a powerful central nervous system stimulant. Long-term use of the drug can foster a powerful dependency and an addiction that is stubborn to treatment. Chronic use of the drug results in a myriad of serious, oftentimes life-threatening effects. Methamphetamine is a drug that crosses the placental barrier. Babies impacted by maternal methamphetamine use experience many of the effects that adults do when they abuse this drug. Use of methamphetamine in pregnancy or outcomes associated with the use of this substance in pregnancy had not been studied until now. Recently however, investigators conducted a retrospective survey of patient histories of 276 women who self-reported methamphetamine use or who presented with positive methamphetamine screens at or near their time of delivery. This study was conducted at a single institution in Phoenix from 2000 to 2006. Methamphetamine is a primary drug of abuse in Arizona and much of the southwest.¹

From 2000 to 2006, the number of methamphetamine-using women more than tripled. Compared to the larger community of women who presented for obstetrics care during the study period, the methamphetamine-using women were much more likely to be white and of age 20 or older. Many of the methamphetamine users were smokers and reported that they drank alcohol regularly; 61% of these women also tested positive for another drug of abuse. In terms of pregnancy outcomes, 50% of the methamphetamine-using mothers delivered preterm, 17% had high blood pressure outside of a preeclampsia diagnosis, 9% experienced placenta separation, and 4% of the newborn children died. Intimate partner violence in this population was an astounding 23%. Utilization of social services and extra hospital care was high in this group. The group also had increased use of maternal transports, inadequate prenatal care, out-of-hospital deliveries, and mother-child separation.

Methamphetamine abuse in America continues to grow. As the drug reaches into previously unaffected communities, it is likely that more prenatal and perinatal effects will be documented. Social service agencies should prepare and train their caseworkers in identifying and responding to cases in which methamphetamine has impacted the delivery of obstetric and pediatric care to new mothers and their children. Social service agencies can implement programs, such as Drug Abuse Recognition (DAR), as a means of intervention in cases where pregnant women have put their babies in harms way with methamphetamine use. DAR is a special methodology and system designed for social workers and other professionals that allows them to properly recognize and intervene in cases of substance abuse and addiction. Interested organizations can obtain more information about DAR training and certification by calling 661-993-2566.


**FDA Rejects Pharmaceutical Form of GHB for Fibromyalgia**

Gamma Hydroxybutyrate (GHB) is a potent sedative and widely abused drug that is associated with myriad instances of date rape. The drug’s actions in the central nervous system are not clearly understood but they are similar to the effects of alcohol with an addictive potential that may be much worse. GHB addiction and dependency are often difficult to identify. Treatment methods for GHB-dependent patients are unsettled. GHB’s impact as a drug of abuse are amplified by abuse of precursors gamma butyl-lactone (GBL) and 1,4 butanediol (BD).

Jazz Pharmaceuticals manufactures the drug Xyrem, a chemical knockoff of GHB. The drug is currently approved by the FDA for treatment of cataplexy associated with narcolepsy and for excessive daytime sleeping. In recent years, Jazz Pharmaceuticals and a number of physicians have pushed for use of Xyrem to treat fibromyalgia. The disease has proven to be difficult to treat. Physicians have been relying on prescription antidepressants and membrane stabilizing drugs for their patients. The disease afflicts
women disproportionately. Empirically in off-label use of Xyrem, there was some evidence that the drug could be helpful to fibromyalgia patients.

A DFA advisory panel voted 20-2 against approval of the drug. It was clear that the panelists were sensitive to Xyrem and GHB’s abuse potential. Xyrem is sodium oxybate, a salt of GHB. Xyrem has been diverted in much the same way as other prescription drugs. On the street, the drug has widespread potential for abuse. Aside from the drug’s potential for abuse, panelists were taken aback by the drug’s odd dosing mechanism. Like GHB, Xyrem has a very short half-life. For the drug to be clinically effective patients have to take frequent doses of the drug; some patients are instructed to wake up in the middle of the night and mix a dose and then try and get back to sleep. Patient testimonials also point to the very rapid onset of the drug’s effects. In some instances, the drug’s effects are causing some patients to pass out within a minute of administration.

So for the moment, Xyrem has suffered a defeat. But company executives vow to continue meeting with the FDA in an effort to get the drug approved in the future.

**Name that Drug: The Last Standing Member of a Once Potent Drug Family**

The mystery drug for this edition of the DARS Newsletter is a substance that is the final representative of a class of abused substances that was a national scourge from the end of World War II until the end of the Vietnam War. In its current manifestation, the drug can be found as a stand-alone medication or it can be combined with a narcotic, such as codeine to boost its efficacy. This drug can not be found or purchased over the counter; it is regulated under the terms and conditions of federal Schedule III. Interestingly, the drug is more commonly prescribed to women than it is to men. This drug can be addictive and can lead to the development of a painfully strong drug dependency. Withdrawal from the drug can lead to seizures and a host of unpleasant effects.

This drug is a descendant of a large family of substances that were the backdrop to the surge in drug use seen in the 1960s. Hippies and counter-culture warriors hyped the value of this class of drugs in the pursuit of Timothy Leary’s mantra, “Turn on, tune in, drop out.” This month’s drug is not a hallucinogenic. Law enforcement and healthcare officials were acutely aware of the risks associated with its use. During the Nixon Administration, the Drug Enforcement Administration (DEA) came into existence in part as a governmental response to the non-medical use of this class of drugs. The drugs of this class that preceded this month’s mystery drug were nearly all classified in federal Schedule II, the most highly regulated designation that a prescribed medication is assigned. Nearly all of those medications that dominated drug-using scenes of the 60s and 70s have now left the market.

On the street, the drugs of this class were mostly identified by the bright colors of the capsules that contained them. “Reds,” “yellows” and “rainbows” were the street names that attached to these drugs. Police television shows of the era frequently ran episodes of drug investigations where some miscreant
who was trying to lure unsuspecting teenagers was arrested in possession of large plastic bags that were full of red and yellow capsules. Sergeant Joe Friday of the 1960s television series “Dragnet” frequently opined on the insidious nature of these drugs and the dealers who scurried around like cockroaches moving from one dark place to another. Users of these drugs were portrayed as helplessly addicted, and frankly, many of them were. In those days, the drugs were routinely administered through intravenous injection. The injection sites left considerable scarring and bruising. One of the most reliable indicators of use was “tracks” on the hands and in the antecubital space of the forearm. Movie stars and entertainers dabbled in the use of these drugs, some use resulting in death. Marilynn Monroe’s death can be blamed on the dangers of this class of drugs.

A descendant of earlier and more dangerous versions, this month’s drug is a prescription medicine and is of lesser potency than the other drugs and compounds in the larger family. As a controlled substance, physicians must be careful with how the drug is applied to a medical problem. This drug is a central nervous system depressant. For readers who are DAR or DRE trained, signs and symptoms of someone “high” on the drug will be located in the “depressant” category. At low to moderate doses of 50 milligrams, the symptoms will be subtle. At higher doses of 100 milligrams or more, classic presentations of nystagmus and non-convergence will be seen. Droopy eyelids (ptosis) may be present, pupillary reaction to light will be slow. At the higher doses, a user may appear to have been drinking, but without an odor of alcohol. Slurred speech, degraded balance, and loss of coordination are all possible at higher doses. Like other members of its class, this month’s drug is capable of causing an alcohol-like physical dependency. Withdrawal intensity varies based on the daily amount of drug that is consumed. For people using more than 300 milligrams a day, the withdrawals may require supervised detoxification. Ironically, this class of drugs was frequently prescribed in the early and mid-20th century to alcoholics who were experiencing more violent withdrawals. Ultimately, this class of drugs was replaced by benzodiazepines, the family of substances represented by drugs such as Valium, Xanax, and Ativan.

This month’s drug is approved by the FDA for use in the treatment of migraine headaches. The drug is considered a second line treatment for patients who do not respond well to the tryptamine-based drugs (Imitrex, Maxalt, Zomig). The triptans (serotonin receptor agonists) are the first line of defense to abort migraine and cluster headaches. In instances where headaches do not respond well to the utilization of the triptans, this month’s mystery drug is a reliable alternative. In recent years, the drug has also been used in the practice of pain management. In particular, the drug is prescribed for stubborn cases of fibromyalgia. Women are disproportionately felled by fibromyalgia, which is why the drug is more commonly used by women than by men. Physicians know that this drug has potential addiction liabilities; most will avoid prescribing this drug until other pharmaceutical options have failed.

This month’s drug does experience diversion to sources that then deal it on the street. A 50 mg tablet can command $5 to $10 on the streets of Los Angeles. Mixed with alcohol, there is a synergistic potency that occurs with this drug. The drug has been periodically partnered with stimulant drugs, such as cocaine and methamphetamine. In that role, the drug helps create a “speedball” effect where diametrically opposed forces kick the central nervous system into gear going into opposite physiological directions. For some drug users, the “speedball” can be the ultimate thrill. In addition to street use, the drug is often found at adolescent cabinet parties. Kids pour out all the drugs they have taken from the
family medicine cabinet and let friends pick and choose what they want to take to get high. In some east coast reports, users have resorted to smoking this drug by mixing it in with marijuana in a hand-rolled joint.

The drug seems to be more popular with patients when combined with codeine. In its most common iteration, the drug is mixed with acetaminophen and caffeine. The caffeine mix is interesting. Caffeine certainly tends to offset the sleepiness that can attach with the use of the drug, but more importantly is its value as a vasoconstrictor and the role it plays in reversing migraine actions on blood vessels in the brain.

Fiorinal and Fioricet are two of the more common product names for this drug. Its formal chemical name is 5-allyl-5-isobutylbarbituric acid, the latter part of this designation is a giveaway to its identity.

This month’s drug is Butalbital.

**Internet Mania: Kratom is it Real or Not Real?**

In the spring of 2008, the DAR Hotline reported on the emergence of a drug called "Kratom." Billed as a hallucinogen with properties akin to Ecstasy (MDMA), the drug's properties are most like that of an opiate. On the west coast, the Kratom product seems to have gained most traction. Callers to the Hotline from California and are particularly concerned about how Kratom use can be detected and whether or not the drug constitutes a real threat as a drug of abuse? From what the Hotline and our DAR staff can determine, Kratom use and abuse has not changed much since our last report of it in 2008. The drug is widely available on the Internet; it is not a controlled substance in the United States.

Kratom is extracted from the leaf of a tree that grows widely and wildly in Southeast Asia. Concentrated in the Kratom leaf is an alkaloid known as mitragynine. This alkaloid is one of probably many that are concentrated in the plant. The active chemical of mitragynine has some similarities to the tryptamine family of abused drugs here in the United States. That class of drugs has experienced consistent popularity as alternatives to mainstream stimulating hallucinogens. Kratom seems to produce some of the same paradoxical effects as the tryptamines but it does so less powerfully and for shorter lengths of time. The unusual effects of this drug flow from its action as an agonist of the mu opiate receptor. The drug produces sedating effects as a result of this action, but it does so while increasing a users sense of wakefulness, especially at lower doses. In Southeast Asia, it's common to find laborers walking around with a wad of Kratom wedged in their mouth. These people chew the leaf much like coca leaves are chewed and crushed by natives in Bolivia, Peru and Ecuador. The drug is purported to have properties that can cause the release of the neurotransmitter serotonin in the central nervous system too. This sort of effect acts as a biochemical cushion against a crash from its mu opiate receptor activity. Some users have related their tendency to use Kratom to lessen the harsh symptoms caused by withdrawal
from other opiate preparations.

Kratom doesn’t appear to grow here in the United States. Kratom products abound on the Internet, most appear to be extracts of the leaf. There are some sites that cater with actual Kratom leaf. But someone who is taking Kratom in one of its forms is likely to exhibit symptoms of someone under the influence of a low dose opiate. Because it is a mu receptor agonist, evaluators should expect to find constricted pupils (miosis), a sluggish to no reaction of the pupil to light, slowed Romberg clock and a slow deliberate gait and pattern of speech. The span of psychogenic effects for Kratom is 2-3 hours. Kratom use can become chronic for those users who are predisposed to addiction. Kratom can be addicting and it can cause opiate like withdrawals for those users who suddenly stop taking the drug following chronic abuse. It does not appear that Kratom has experienced much diversion and trafficking into adolescent using groups. The drug’s rather limited availability and stiff price tag (for the good stuff) seem to have acted as a barrier to cross over into teenage drug using circles. Some off-key health food stores carry Kratom leaf products on their shelves, but expect most products to come from Internet sites that are headquartered overseas in Thailand. In Thailand, the drug is controlled substance and is popularly abused.

Despite the frequent calls the Hotline receives about this drug, it does not seem to be much of a public safety threat on our streets. The drug seems to be more a curiosity for those users who are attracted to the hallucinogens and opiates. Although most forensic laboratories can screen for the principal alkaloids in Kratom, it can be costly. If you live or work in a community where Kratom has a foothold, contact your laboratory sales representative and discuss the options for testing. DAR users can contact the DAR Hotline for situations where Kratom abuse is suspected. Kratom will likely produce both opiate and hallucinogen groups of symptoms.

**Is Marijuana Smoking Harmful to Schizophrenics?**

An interesting research project recently revealed that schizophrenics who had histories of marijuana use had better neurocognitive scores than nonusers. This study is one of a slew of reports detailing the impact of marijuana smoking on the brain and is touted by cannabis advocates as evidence that the drug is relatively safe to use.

Rates of marijuana use by schizophrenics are thought to be nearly twice that of the general population. Prior reports have spotlighted the fact that heavy marijuana use is a risk to the development of psychotic symptoms. But what has not been investigated is whether or not this risk affects those with

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underlying psychotic symptoms or those with other underlying vulnerabilities. Researchers in this case retrospectively examined lifetime clinical presentations of 455 patients with confirmed schizophrenia or schizoaffective disorder. From this cohort, 175 patients were separately identified and deemed to be heavy cannabis users or were cannabis-dependent. Cannabis dependency can be established when a patient experiences withdrawal following cessation of its use. Cannabis withdrawal is characterized by a variety of notable symptoms that include agitation, nausea, and depression. The effects of cannabis withdrawal may persist for weeks following last use.

In this study, the patients from both groups were administered a battery of neurocognitive tests at admission. All had been drug free for one month. Family psychiatric histories differed little for each group; histories of lifetime severity of positive, negative, and disorganized symptoms were similar in both groups. More men than women had cannabis use histories. Cannabis users exhibited better global functioning than nonusers. More interesting was the fact that cannabis users were found to perform better than nonusers on several tests involving verbal skills and information processing. This component of the research was the most surprising result of the research. Researchers caution that the data does not support a claim that marijuana is helpful in the treatment of schizophrenia. Some of the authors speculate that patients who are cannabis users may represent a higher functioning subgroup. But this data does suggest that schizophrenics who smoked marijuana don’t appear to be clinically worse off than those who didn’t smoke.

This research will no doubt find its way into the growing national debate about legalization of marijuana. In California, a ballot proposition is up for voters to decide if marijuana should be further decriminalized. In a recently passed legislative initiative, Governor Arnold Schwarzenegger signed into law a bill that completely decriminalizes possession of less than an ounce of marijuana. In California, possession of marijuana is penalized less than parking in a handicapped parking space.

**Drug Wins Federal Approval for the Treatment of Opiate Dependency**

In past editions of this newsletter, naltrexone has been spotlighted as a utilitarian drug in the treatment of different types of drug dependencies. Naltrexone is an opioid receptor antagonist that has been successfully used to manage cravings and withdrawal associated with alcohol dependency. In the form of Vivitrol, naltrexone is administered once a month via injection. By blocking opiate receptors in the brain, the drug blocks the effects of narcotics like morphine, codeine, and hydrocodone. In ways that are not entirely understood, the drug’s action at opiate receptors calms the chemical pathways responsible for causing the disquieting effects and cravings experienced by recovering alcoholics.

A recent FDA press release announced Vivitrol’s approval to treat and prevent relapse for opiate dependent patients who have undergone detoxification.
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