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As the Holiday Season is upon us, we find ourselves reflecting on the past year and on those who have helped to shape our newsletter in a most significant way. We value our relationship with you and look forward to new endeavors in the year to come. We wish you and your families a very Happy Holiday Season and a New Year filled with peace and prosperity.



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The MEDTOX Criminal Justice and Rehabilitation Services Department

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Advisory: Nucynta: A New Narcotic Enters the Pain Management Market

On June 23, 2009 the FDA and DEA approved a new narcotic-analgesic in the U. S. market. Johnson and Johnson developed this medication and released it as the trade name Nucynta (CII). Known generically as tapentadol, this potent opioid is the first new narcotic to enter the market since the mid 70s. Nucynta has classic opioid characteristics as a powerful agonist of the mu opiate receptor. The mu receptor complex is the central player in mediation of narcotic analgesic effects throughout the body. In this sense, Nucynta is no different than older and more widely used opiates, such as morphine and codeine. Nevertheless, the drug possesses some unique properties that distinguish it from the other drugs of the same class.



Nucynta is a DEA Schedule II drug. This means that the drug will be regulated and controlled the same way as other potent opiates, such as Demerol, Morphine, and Dilaudid. The drug was designed to treat acute moderate to severe pain. Nucynta emerges as an alternative to other prescription opioids such as Percocet (oxycodone) and Vicodin (hydrocodone). The potency of the drug is thought to be somewhere between Ultram (tramadol) and Morphine. Although the drug is approved for use in fast-developing episodes of acute pain, the drug has already been used "off-label" for managing chronic pain. Based on the drug's pharmacological properties, Nucynta poses substantive risk for abuse and misuse. Long-term use of the drug will result in classic opioid dependency; tapering off from the drug will be necessary to avoid the discomfort of opiate withdrawal.

In addition to Nucynta's actions as a mu receptor agonist, the drug also demonstrates a unique ability to selectively block the reuptake of norepinephrine (NE). Pain is a complicated physiological process that involves a number of different neurotransmitter and polypeptide systems scattered throughout the body. The intensity of pain and the psychological responses to it are thought to be somewhat mediated through the actions of central nervous system monoamine transmitters. Norepinephrine is one such neurotransmitter. It is rather common for physicians to prescribe a selective serotonin and norepinephrine reuptake inhibitor (SNRI) drugs as adjuncts in the treatment of certain types of chronic pain. The dual action of Nucynta as an opiate and antidepressant makes it an interesting new addition to the drugs currently utilized in pain management. Only time will tell if the drug will be truly effective in that role.

Lessons in the History of Addiction: Dr. William Halsted

All stories of addiction are tragic ones. But in the annals of addict deception, there are some cases that are more tragic than others. One of the most incredible stories of deception involves one of America's most respected pioneering physicians. Dr. William Halsted is noted in history and medical textbooks as one of the most talented physicians to have ever donned surgical gloves. Dr. Halsted was very well educated and he hailed from a prominent family. Nevertheless, his life became a nightmare of cocaine and morphine addiction. Despite repeated "vacations" and trips abroad to shake himself of his addictions, he went to the grave as an incurable addict cloaked in an aura of master surgeon.



Dr. Halsted is recognized as one of the pioneering physicians of the prestigious John Hopkins Hospital. In fact, his appointment to the Hopkins staff came about at the point where most addiction specialists would say that Dr. Halsted had hit "rock bottom." Regardless, Dr. Halsted went on to lead a colorful career as a physician and surgeon. He had a career that earned him accolades and the respect of his peers. Although Dr. Halsted insisted that he had beaten his addiction, it is rather evident that he had not. At best, Dr. Halsted developed a process of addiction management that kept him precariously close to a total physical and mental breakdown. Like most cocaine addicts, Dr. Halsted was a complete prisoner to the drug. No aspect of his humanity went unaffected by cocaine.

Dr. Halsted's emergence as a doctor occurred during the heady scientific discovery days of the late 1800s. In 1884, much of the worldwide medical establishment had come to view cocaine as a safe and effective treatment for a wide array of maladies. Sigmund Freud published a very thorough treatise on the effects of cocaine in the summer of 1884. Freud was the preeminent leader of a group of medical professionals who experimented on themselves. Freud completely missed the most important medical application of cocaine at that time-its topical anesthetic qualities. It was Karl Koller who discovered cocaine's great ability to provide local anesthesia. Koller is now famous for his contributions to eye surgery when cocaine was used as the local anesthetic. Dr. Halsted was well aware of cocaine in 1884. Word was spreading rapidly of cocaine's miraculous qualities. Unable to resist his curiosity, Dr. Halsted began to experiment with the drug. He even started calling cocaine a "wonder drug." Picking up on Koller's work with cocaine as a topical anesthetic, Dr. Halsted published his theory on the application of cocaine for the purpose of anesthesia in localized surgical procedures. His observations were published in the September 12, 1885 issue of the New York Medical Journal.

By all accounts, his report was a mess. His writing was convoluted and unclear. To the knowing observer, Dr. Halsted's writing had been bungled by his use of cocaine. In short order, Dr. Halsted's noble effort to self-experiment with cocaine had transformed him into a compulsive and dependent cocaine user. The good doctor had become a cocaine addict.

Eighteen months following the medical journal fiasco, Dr. Halsted was faltering. A friend of his, William Welch, a respected New York pathologist, intervened and tried to cobble together a coherent treatment plan. Because cocaine's pharmacology wasn't understood yet, treatment programs consisted largely of extended vacations and trips to sanitariums. For Dr. Halsted, it was a long sea voyage. Like most addicts, Dr. Halsted duped his well-intentioned pathologist friend and saw to it that healthy doses of cocaine were carefully hidden in secret spots throughout the sailing vessel. He, of course, planned to cut down his cocaine use through a strict process of titration. His plan didn't work. In fact, Dr. Halsted ran out of

cocaine before he hit landfall. Dr. Halsted was reduced to making late-night trespasses into the ship's medical bay where he broke into the drug cabinet and made off with pharmaceutical cocaine. Dr. Halsted returned to America and resumed his medical practice. He also continued his raging cocaine habit. He made another effort to detoxify by self-admission into a Rhode Island psychiatric hospital. Using an alias, he underwent a very rigorous program designed to rid his body of its dependence on cocaine. In that time, withdrawal syndromes were ordinarily treated with alcohol, chloral hydrate (CNS depressant), and morphine. Tragically, Dr. Halsted's addiction was compounded at this point with a newly emerging dependency on morphine. Leaving the facility, Dr. Halsted was whisked to a safe and sane location by Dr. Welch. His good friend worked hard at keeping Dr. Halsted working and as sober. It was during this period of time that Dr. Halsted conducted research that significantly advanced abdominal surgery techniques. He also developed a nuanced view of sterile operating procedures.

Dr. Halsted's cravings never abated and relapse was a foregone conclusion. In early 1888, he had returned to the psychiatric hospital. Dr. Halsted emerged from the hospital and went back to work at John Hopkins. He went to great lengths to convince his peers that he no longer used drugs. Rumors began to spread about his unpredictable moods, his bitter sense of humor, and his sudden absences from the operating room. No doubt, Dr. Halsted was feeding a poly drug addiction. In addition to cocaine and morphine dependence, Dr. Halsted was a chain smoker of cigarettes. At any given moment of the day, Dr. Halsted was probably experiencing some type of withdrawal. His waking hours must have been a tormenting challenge of feeding each of his individual addictions. The denial and shame of his condition made it difficult for him to come to terms with his affliction. He felt his options to be few. He chose to try and hide the disease. By most accounts, Dr. Halsted was unable to camouflage his addictions.

Cocaine is an insidious drug. In Dr. Halsted's case, the fact that he became addicted to cocaine following an innocent good faith effort at self-experimentation made him no different than a modern day crack addicted cocaine smoker. Although he worked at a prestigious American hospital, Dr. Halsted's disease was unsuccessfully treated. Like many cocaine addicts today, Dr. Halsted was reduced to a painful life of secrecy, denial, and shame.

December Mystery Drug: The Brainchild of a Pharmacy Legend

Dr. Paul Janssen died in 2003. He was 74 years old. Dr. Janssen is a legendary figure in the world of pharmacy and pharmaceutical research. Among other substances that have been produced in his research laboratories is this month's mystery drug. Dr. Janssen's work is prodigious and it carries on today in the form of a pharmaceutical company that bears his name. Currently, Janssen Pharmaceutical specializes in the research and production of drugs that treat menacing mental illnesses, such as schizophrenia and bipolar disorder. For generations, Janssen had been a leader in the development of important disease fighting drugs, products that have probably saved hundreds of thousands of lives. The World Health Organization (WHO) cites Janssen for having discovered and brought to market four of the world's most essential drugs. Some of the medicines created by Janssen and his assistants include Haldol and Resperdal. Both drugs are critical medications that are prescribed in cases of schizophrenia and bipolar disorder. Everyday drugs such as loperamide were also created by Janssen. Loperamide is the main ingredient of Imodium and miconazole, the anti-fungal agent found in Monistat. Janssen also conjured up lesser-known drugs, yet they are critical medicines that have been widely used to treat intestinal parasites and other diseases endemic to many third world countries.



This month's drug is a synthetic narcotic and powerful agonist of the mu opioid receptor. The drug is available in an array of applications and is regulated under DEA Schedule II. This drug is not available in pill, tablet, or capsule forms. Janssen's discovery of this drug dates back to 1960. During the 50s and 60s there was a great deal of pharmaceutical exploration for synthetic substances that could be fashioned to work as opiates. Driving the discovery of this month's drug was the earlier discovery of meperidine, a synthetic narcotic better known by its product name of Demerol. Janssen's synthetic narcotic was quite different than meperidine however. Its equipotency is greater than that of Demerol, but its analgesic effects are shorter in duration. In fact, this month's drug is one the shortest acting narcotics on the market today. Like Demerol, this drug has a high potential for abuse. On the street, the drug is typically found in the form of a sugar-laden lozenge, a lollipop of sorts. In fact, out on the street, dealers took to calling it a Perco-pop. The "perco" being in reference to a different abused narcotic called Percocet. Narcotic addicts who abuse the Perco-pop will frequently experience tooth decay or erosion of the gum line. The concentrated sugar content of the lollipop works as a reverse acting dentifrice causing fast progressing tooth decay.

This application of the drug extends its analgesic properties and creates a sustained, steady delivery of the drug. Patients with chronic or intractable pain often take this drug in order to get much needed around-the-clock pain relief. There have been notable accidental overdoses with the use of the transdermal patch system. The drug must be carefully used and patients need to be monitored closely.

Cephalon is another biopharmaceutical company that produces a special delivery system for this month's drug. Cephalon produces the drug in lollipop or lozenge form. They also manufacture a buccal form of the drug, a small dissolvable lozenge that can be placed inside the mouth between the lining of the cheek and the gum. In that iteration, the drug quickly dissolves through the surface of the gums and absorbed into the bloodstream. The buccal product contains no sugar. Of the various delivery systems, the buccal application seems to be the least abused and least diverted format.

This month's mystery drug can be found on the streets in most large American cities. Although abuse of the lollipop version of the drug has been well covered by various media, the transdermal patch has avoided the same sort of scrutiny. Although harder to abuse, drug addicts can get a powerful high off this product. Abusers acquire used or new patches and then cut them open to expose the gel matrix that is saturated with the narcotic. YouTube and Internet drug use sites can guide abusers with specific instructions for ingestion that helps maximize the drug's narcotic euphoria effects. Abuse of this drug is molecular Russian roulette. The drug is 80 times more potent than an equal dose of morphine. Small amounts of this drug can cause substantial analgesic effects in humans.

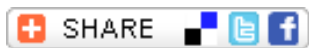
Because of the drug's potency, dosing is rendered in measurements of micrograms (mcg, "mikes") instead of milligrams (mg). Nevertheless, stories are abounding of drug abusers chewing on the fresh gel matrix of a narcotic patch that contains 100 mcg of the drug. Fortunately, the drug is poorly absorbed when taken by mouth. On the street, this drug is referred to as china white, white goat, and tango. Because of the drug's great potency, street users of this drug have come to compare it to the purest known form of heroin called "china white." This drug was the subject of the movie, French Connection. In 2006 and 2007, several large American cities experienced a slew of deadly overdoses tied to this month's drug. In those cases, ordinary street heroin was laced with it. It's likely that the lace came from clandestine laboratories.

This month's drug is one of the most prescribed narcotics in America today. Although approved by the FDA for use in treatment of cancer-caused pain, the drug enjoys extensive off-label utilization in treating other forms of severe, chronic pain. The patch form of the drug competes against other sustained release opiates such as Oxycontin, MS Contin, and Opana. The lollipop lozenge and the buccal dissolvable tablet are prescribed for the purpose of beating back "break thru" pain, discomfort that exceeds the analgesic containment of the extended release drugs. The release of a sugar-free version of the lollipop has been rumored for some time. There is no new information to suggest that it will be delivered to the market anytime soon.

Actiq, Fentora, and Duragesic. Actiq is the product name for the lollipop version. Fentora is the product name for the buccal dissolvable tablet and Duragesic for the transdermal patch. In the hospital setting, the drug is found in a generic I.V. solution. There are several derivatives of this drug where alterations to its chemistry have created even more powerful analgesics. In many of the overdose cases where this month drug was spiked with heroin, the dead were found with the needle still in their arms. The fast and overpowering action of this month's drug led to instant unconsciousness and death.

This month's drug: Fentanyl

Readers who would like more information on fentanyl and the various fentanyl products may do so by contacting the MEDTOX DARS Program at darsprogram@mac.com.



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