



Taming The Wolves Of Addiction

Anti-addiction therapy attempts to hammer a better world out of bent patients and bad drugs. Today's addiction-control medications, supplemented by psychotherapy, help a relative few addicts claw their way back into the sunlight of life. But far more try and falter, plunging again into the neurochemical maelstroms that churn toward self-destruction. This is an old story. The world's addicted stand like actors condemned to endless retellings of the same play, the ordeal of Sisyphus, the Corinthian king condemned to roll a boulder up a hill in Hades, only to see it roll down again once it neared the top.

For more people to permanently free themselves requires better medicines, obviously, but also new formulations of the drugs we already have, formulations aligned with how addicts behave. This is the mission of a handful of small companies committed to what most in the drug industry consider an unattractive medical arena. Although new drug opportunities are possible thanks to better understanding of addiction neurochemistry, what distinguishes these drug makers is their optimism that here are viable, even enormous markets. In freeing legions of wasted souls from chemical bondage, they believe they will both do good and do well.

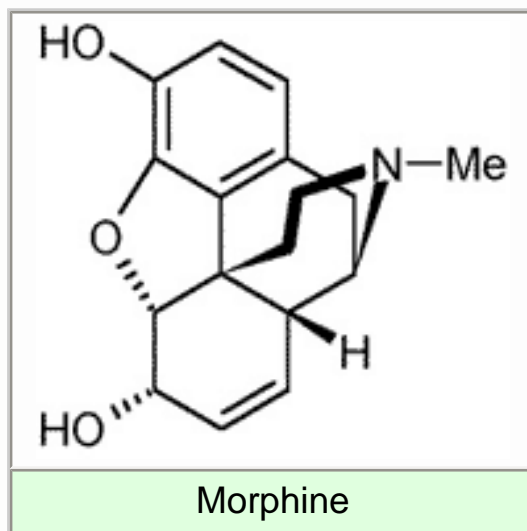
By Tom Hollon
Special To Signals



Let's skip the reams of statistics that drug abuse stories usually begin with to show how awful addiction is. We all know addiction is tragic, a problem maybe as old and permanent as prostitution. Here now is a new aspect of the problem. Osama bin Laden's ABC wish list of weapons he would like to use against us -- atomic, biological and chemical -- is better abbreviated ABCD, including drugs. According to an October 4 story in the *New York Times*, bin Laden tried to develop high-strength heroin to export to the U.S. and Europe. Reportedly the project failed, but -- if he still lives -- he has a good reason to keep trying. As pressure mounts for sovereign states to stop funding terror, financing al Qaeda by selling illicit drugs will grow more attractive. Thus developing anti-addiction medications becomes even nobler: Now it is patriotic, part of the fight against narco-terrorism.

If only it were also good business. Drug companies would naturally like to

help here. But with development costs what they are, the calculus of drug discovery demands the factoring in of potential rewards. Unfortunately, signals about the size of the anti-addiction markets conflict. The patient base is a pearl to catch a pharaoh's eye. A 1997 estimate used by [DrugAbuse Sciences](#) Inc. (DAS), of Hayward, CA is of 22 million alcoholics, 6 million cocaine addicts, and 2 million hooked on heroin in Europe and America -- altogether twice the number who suffer from cancer. Cancer drugs, however, are a multi-billion dollar affair; in comparison, sales of drug abuse medications look nearly Lilliputian. DAS estimates that anti-addiction drugs bring in about \$170 million a year: Top sellers are naltrexone (for heroin addiction and alcoholism), buprenorphine (heroin) and acamprosate (alcoholism). Accordingly, the pharma giants may feel they must stand aside: To sustain themselves, they need far bigger markets.



But a counter argument runs that standing aside is myopic, that flawed medications fog and obscure the true market. This has happened before. The real blossoming of antidepressants, so the story goes, waited until [Prozac](#) coupled efficacy to mild side effects. Many are surprised to hear that an erectile dysfunction market even existed prior to [Viagra](#), but there was one -- for a drug called alprostadil. (Never heard of it? Well, would you want to use a penile injectable?) So the thinking is that if you build a really good anti-addiction drug, addicts who have given up hope will want it. In 1997 -- the most recent statistic -- 2 million addicts sought treatment; with better drugs, that figure could be far higher.

The Pioneer

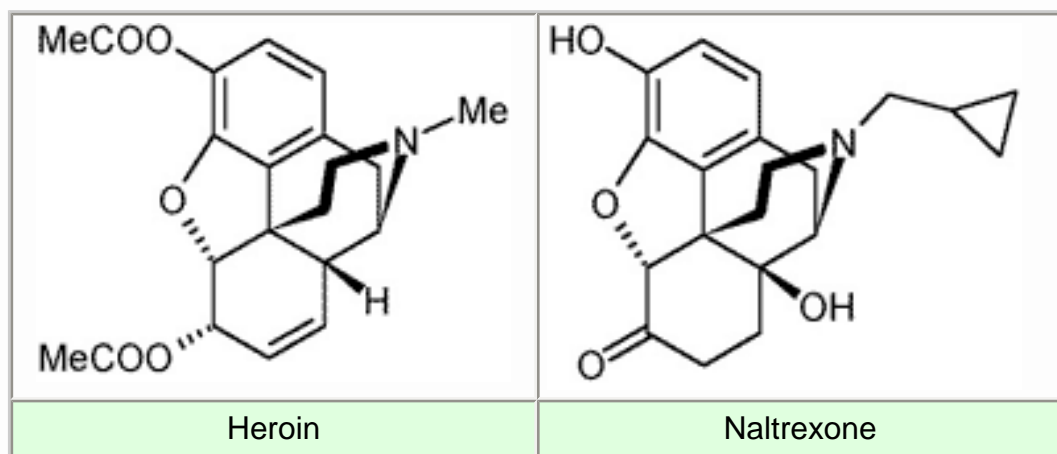


Difficult patients may be another reason the big companies steer clear of addiction therapy, says Elizabeth Greetham, CEO of DrugAbuse Sciences. Addicts have a "very poor compliance rate" in clinical trials. A 30 percent to 50 percent dropout rate is "a fact of life. High compliance just does not happen in this community," she says, whether the patient is in the placebo or treatment arm. Trials for diabetes or heart disease, by comparison, might expect dropout rates of three to four percent.

None of this deterred Greetham from joining DAS after a 30-year career following drug companies on Wall Street. "I liked the business model," she says -- "a therapeutic void with no big company playing in it; where there was a lot of existing knowledge that could be harnessed to make new medicines and improve existing ones." The knowledge comes in large measure from research funded by [NIDA](#), the National Institute on Drug Abuse. Thanks to NIDA research, she says, "the case has been made that addiction is not just a behavioral disease. Clearly there is also a behavioral element, but it's not just a character flaw. It is also a disease of neurotransmitters."

Founded in 1994, DAS is the oldest company entirely dedicated to anti-addiction therapy and has the biggest pipeline. Founder Philippe Pouletty, a French physician, started DAS in California during a period of residence in the States. Today he directs preclinical research in DAS' Paris branch while the U.S. side handles clinical development.

DAS' most advanced product, Naltrexone Depot for treatment of alcoholism, exemplifies the company's use of drug delivery technology to improve anti-addiction medicines already in use. Greetham expects Naltrexone Depot will restore doctors' lost faith in naltrexone, prescribed since 1994 to curb cravings for alcohol and heroin. Naltrexone Depot completed Phase III trials for alcoholism treatment just a few months ago; an NDA submission is planned for 2002.



Naltrexone works by opiate receptor blockade and prevents getting high or overdosing. In the case of heroin, which is extensively metabolized to morphine in the body, it blocks morphine from its receptors. The alcohol connection is that in some patients alcohol upregulates brain endorphins that target the same opiate receptors; naltrexone also blocks endorphins.

Daily naltrexone would cut drinking 40 percent to 60 percent, says Greetham, except that "many alcoholics don't have the discipline to take a daily medication." A recent *New England Journal of Medicine* study (Krystal, J. H. et al. **345**:1734-1739, 2001) documented alcoholics skipping naltrexone 56 percent of the time in 52 weeks. Greetham professes no surprise that the study concluded that oral naltrexone does not work: "If you don't have the drug on board, it can't work, can it?"

Naltrexone Depot reformulates naltrexone to stretch one dose across a month. This involves loading naltrexone into biodegradable microspheres (a proprietary polymer matrix called LACTIZ). After intra-muscular injection, the microspheres dissolve and naltrexone enters the bloodstream by sustained-release. An alcoholic taking naltrexone for a month "has to make 31 daily decisions," says Greetham, whereas, with Naltrexone Depot, "you come for your counseling session, drop your pants, bung in the injection, and you've got your receptor blocked for the next month."

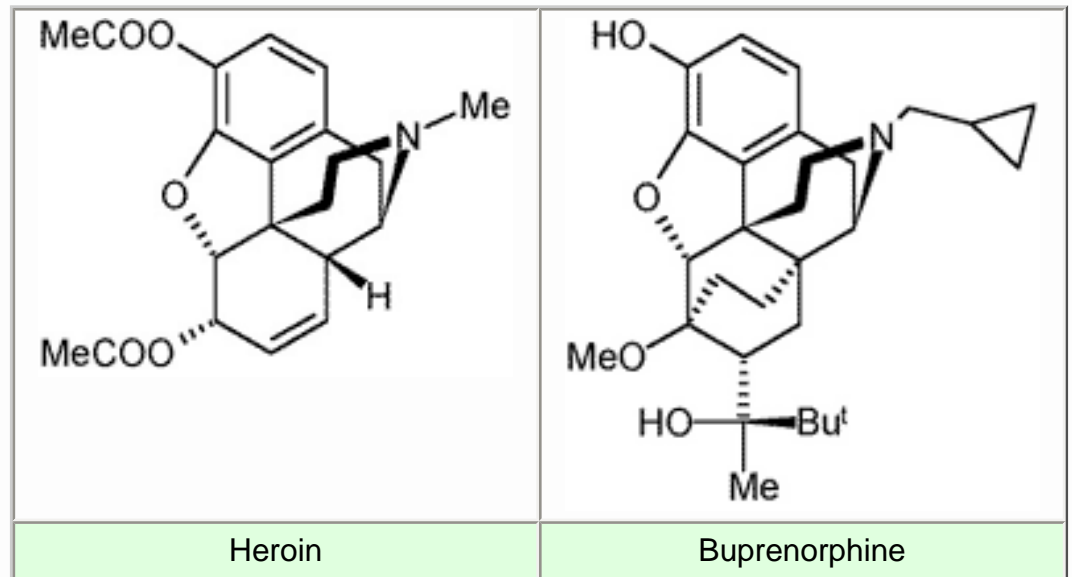
In parallel DAS develops NALTREL -- the same extended-release formulation, but a different brand name -- for heroin addiction. NALTREL begins Phase III trials for opiate dependency in 2002. Anticipating eventual approval of extended-release naltrexone, DAS has its sales force making the rounds in the nearly 3,000 drug clinics in the United States where doctors are on staff. The reps don't go empty handed: In 2000 DAS acquired rights from [EON Laboratories](#) Manufacturing Inc. to market plain old Naltrexone Hydrochloride, in 50 mg tablets (Zeeblok). Zeeblok is a calling card, providing DAS a way to meet and greet the physicians in its target market.



Buprenorphine Depot is DAS' extended-release injectable form of buprenorphine, for detoxification from heroin. In France, where buprenorphine has been used since 1996, the drug has almost completely displaced methadone as a maintenance therapy, and garnered a \$90 to

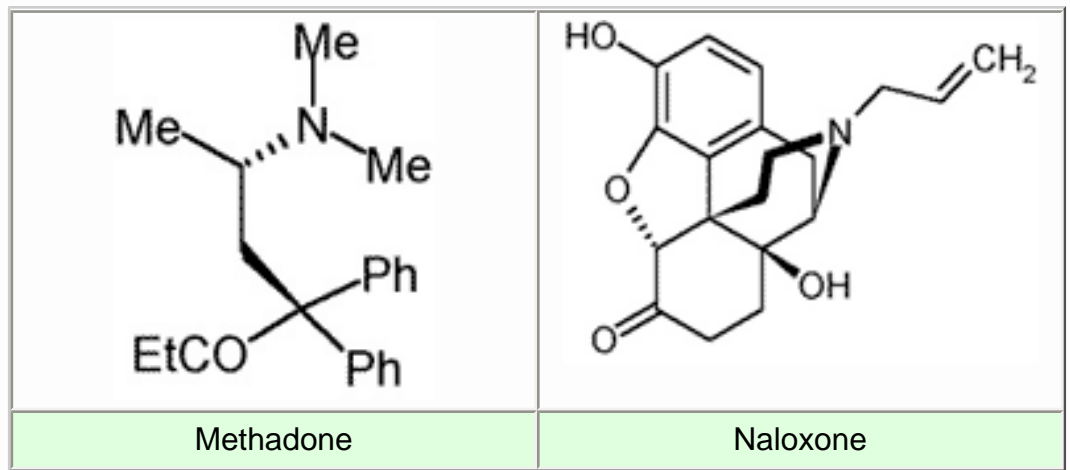
\$100 million dollar annual market, according to Greetham.

Methadone programs have been around since 1970s, with moderate success. Methadone delivers a mild high, enough to leave users able to function. It is a hassle to take, though. Life on methadone is an endless procession of clinic visits, daily lineups for a fix. The grind and inconvenience are reasons methadone users occasionally return to heroin: They didn't make it to the clinic that day.



Methadone's mild-mannered high is not coupled to mild-mannered addiction; it can be just as addictive as heroin. Methadone is "extremely difficult" to get patients off by moving them gradually to lower doses before switching them to antagonists like naltrexone. The pain of methadone withdrawal prevents abrupt switches to naltrexone from being recommended. "You need to get heroin patients detoxified before you give naltrexone," Greetham emphasizes. Here is where buprenorphine comes in. Buprenorphine is a milder narcotic than methadone, harder to overdose with and easier to wean from -- altogether a far better bridge to naltrexone.

Buprenorphine Depot, presently in preclinical testing, will probably deliver a four- to six-week dose of buprenorphine. Patients will benefit from fewer trips to the clinic, heroin holidays may diminish, and extended-release will enhance doctors' control over a drug which, like methadone, can be abused. Physicians can titrate patients to lower Buprenorphine Depot doses and then try switching them to NALTREL.



For treating cocaine addiction DAS has two products. One is the small molecule drug DAS-431, now in Phase II. This is a dopamine D1 receptor agonist intended to reduce cocaine craving and relapse. Cocaine works by blocking the dopamine transporter, the portal through which dopamine re-enters neurons after release at dopamine synapses. Blocking the transporter increases the synaptic concentration of dopamine, which is believed to be the major underlying cause of cocaine euphoria. The premise of DAS-431 is that it will stabilize dopamine levels in cocaine addicts, which in turn may reduce cravings.

The other product, COC-AB, is an antidote for cocaine overdose. Today, no overdose treatment exists for any drug of abuse except the opiates; Narcan (naloxone), a fast-acting opioid receptor antagonist, has a place in medicine as a heroin antidote. "The difficulty of cocaine overdose," Greetham explains, "is that doctors don't know if a case will be mild or severe. Out of the blue," a patient who seems stable dies.

Emergency rooms log about 250,000 cocaine overdoses a year. COC-AB, antibodies against cocaine, should prevent overdoses from becoming lethal by keeping cocaine out of the brain, on the safe side of the blood-brain barrier. The antibodies will act like "a reverse osmotic pump, sucking toxic cocaine out of the heart, muscles, tissues, and brain until you have detoxified the patient." COC-AB, in both polyclonal and monoclonal antibody form, and MAP-AB -- antibodies for methamphetamine overdose -- are both in preclinical development in Paris.

Something For The Hands

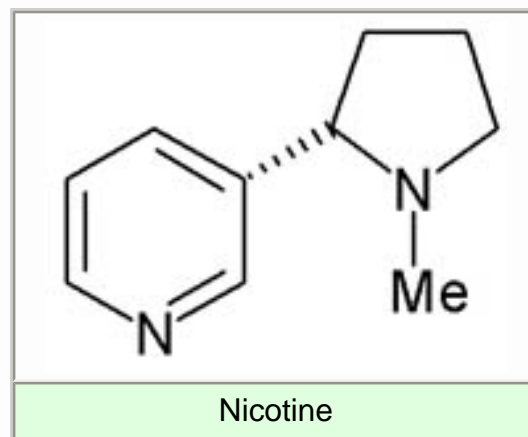


"The idea of naltrexone," says Barbara Fox, president and CSO of [Addiction Therapies](#), Inc. (ATI), "is to block the reinforcing activity of the drug itself. There's nothing wrong with this. It is effective for some people.

But we don't think it's likely to be the most effective approach." Instead, ATI, which she founded in 1998 in Wayland, MA, develops therapies that mesh with the behaviors of addiction.

ATI and DAS use drug delivery technology to address behaviors that cause addicts to stumble, but do it in quite different ways. DAS' extended-release drug delivery deals with the temptation to take a holiday from the daily routine of taking medicine. ATI helps addicts cope with cravings. ATI's lead product, The Straw, helps smokers trying to quit cope with the urge to smoke, the quiet insistence for nicotine that prods the mind with the relentlessness of Chinese Water Torture.

For every addiction, Fox says, pharmacology is only part of dealing with dependency. Smoking behaviors in particular are as critical and as difficult to get around as the pharmacology. "If you're a smoker, you have a dependence on nicotine. But the nicotine signal to the brain has been paired to a set of behaviors -- the tapping of the pack, the feel of the cigarette in your hand, the feel in your mouth." The choreography and ritual of lighting up reinforces the pleasure of nicotine in the same manner conditioning reinforces response in classical animal behavior experiments. And the amount of ritual invested in nicotine is awesome: "A typical smoker trying to quit has had a hundred thousand cigarettes," Fox says.



She adds that much of the disappointment with the nicotine transdermal patch traces to failure to consider how smokers behave. "When the patch came out, everyone thought it was the be all, end all of smoking cessation products. You put it on once a day; that gives you nicotine; that should take care of your craving." In fact, states Fox, it is less efficacious than nicotine gum, and its market share has steadily declined. "Gum has a lot of problems, but at least it gives you something to do when you want a cigarette." That is where the nicotine patch fails. According to Fox, the [American Lung Association](#) sponsored a study a few years ago to find out why smokers couldn't stop. "The lack of something to do with their hands

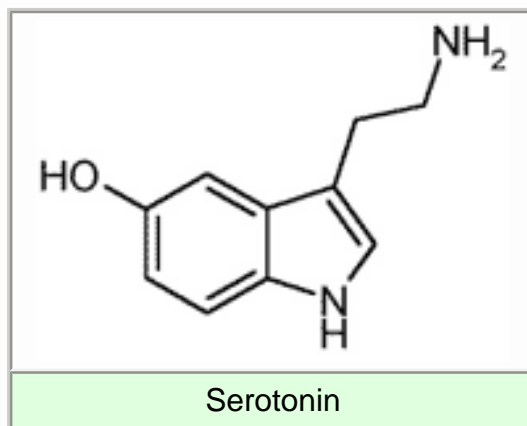
was one of the primary reasons."

A New Ritual

The Straw is a new kind of nicotine replacement therapy, springing from a Fox brainstorm about how to supply the brain with nicotine while delivering empty hands from devil's mischief. The Straw, which recently completed Phase I/II trials, "flips standard pharmaceutical practice on its head," she declares. "We're saying that an effective way to treat addiction is not necessarily to come up with a long-lasting medication like the nicotine patch, but rather to give people a dosing format they can use in response to episodic cravings."

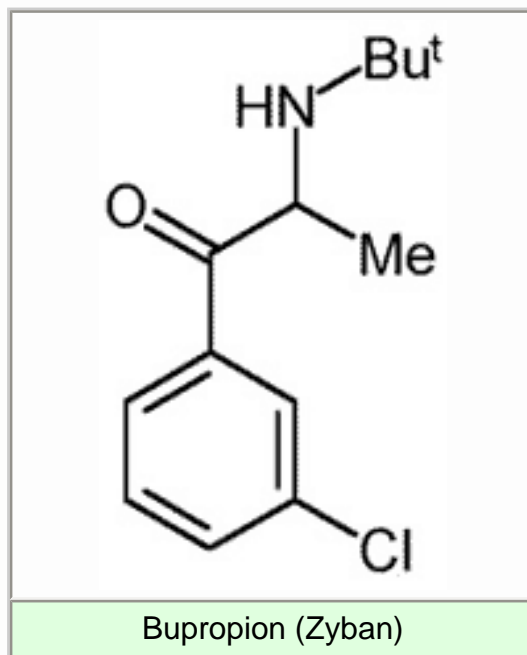
The Straw is based on technology for delivering nicotine in a beverage and looks like just another drinking straw. But appearances deceive. It "contains small beads of nicotine which you sip down with the first sip of the drink," Fox explains. And just as important, a new ritual -- pull out a Straw, put it in a glass, take a sip -- throws idle, jittery, quietly desperate hands a life preserver. The act can be repeated ten or twelve times a day. "Over the course of treatment you taper the number of straws per day and the dose per straw." At first The Straw will be a prescription product; later it will be over-the-counter. As smoking cessation products have "a very well-defined clinical path," Fox anticipates getting her Straw to market by 2004.

The Straw represents her decision to place smoking cessation ahead of treating cocaine addiction and alcoholism, which she also wants to do. Partnership opportunities, lifeblood for ATI, are available in a proven market -- patches, pills, and gums for waging war on tobacco are worth about \$1.5 billion a year -- while, for other addictions, partners must make "a leap of faith to see potential for a much, much larger market."



The company's other smoking cessation product is ATI-823, an anti-craving drug which is expected to enter clinical trials this year. The compound inhibits neurotransmitter re-uptake of dopamine, norepinephrine and serotonin. Fox believes it will be more potent and effective than [Zyban](#), a non-nicotine anti-craving medication that has the distinction of also being an antidepressant (under a different trade name, Wellbutrin). No other antidepressant has an anti-smoking effect. She explains that no other antidepressant inhibits dopamine reuptake -- "To come up with a medication that is going to affect addiction, you have to hit dopamine through one pathway or another." Zyban is not a drug of abuse; Fox thinks ATI-823 will not be, either. Zyban is a money maker; ATI-823 could be too. (Zyban sales estimates are tricky, since, for reimbursement reasons, Wellbutrin is also prescribed to stop smoking. Fox thinks the correct figure is about \$500 million a year.)

Another product in the works is ATI-615 -- a "short-term substitution therapy," Fox says -- for weaning people off cocaine. "It gives people some of the same signals, but in a way that does not make them high." ATI-615 has slower onset than cocaine and stays in the brain longer. "It should relieve the craving." There has never existed a cocaine substitution therapy equivalent to substituting methadone for heroin. One of the reasons why, "is that there are no clinical endpoints to go by to know what is achievable in this indication." So Fox is delighted to receive technical and financial support for Phase I and II clinical trials from NIDA. Phase I, testing ATI-615 in tablet form, should begin in the first quarter of 2003. She hopes the FDA will give ATI-615 fast track approval.



The future to Fox is the neuroscience of remembering the past. "It is

becoming clear," she says, "that addiction is intimately involved with memory. It is a memory disorder. There's no other way to explain the lifelong risk of relapse," to explain how an addict stays clean for 30 years, until one day some stress comes along and all of a sudden, "they fall off the wagon." This is not just theory; it lodges firmly within memories of her own encounter with nicotine. "You miss it forever," she confesses. "I haven't had a cigarette for 25 years, and I still miss it. The future of addiction medication lies at the intersection of memory pharmacology and behavior research."

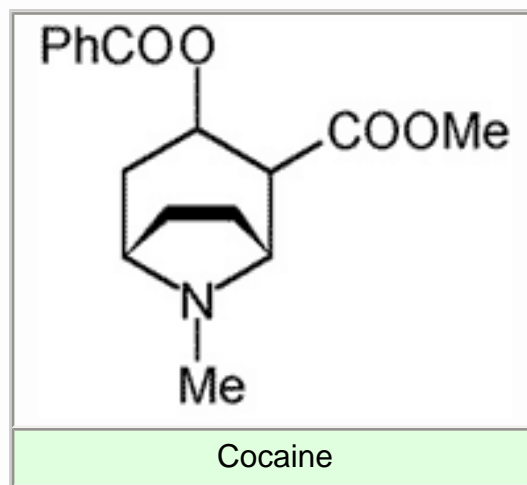
The Core Of Dependence

Perhaps the future is here now. At Addex Pharmaceuticals SA in Geneva, Switzerland, founded only last year, the hunt is on for a drug that treats cocaine addiction by intervening in the neurochemistry of glutamate, the excitatory neurotransmitter associated with learning and memory. Glutamate, it turns out, is more essential to cocaine addiction than dopamine.

Sustaining addiction requires both neurotransmitters, but for cocaine dependence only glutamate is indispensable; at least, this is true for mice. (Because cocaine also binds the serotonin transporter, mice without dopamine transporters can still become addicted to cocaine.) Since researchers can hook mice on the same drugs that hook us, the glutamate connection, discovered by François Conquet, Addex's CEO, likely applies to humans.

The link between glutamate and cocaine came clearly into light last year, when two research groups, one led by Conquet, then head of [GlaxoSmithKline](#)'s experimental pathology unit in Lausanne, Switzerland, engineered knockout mice with deactivated mGluR5 genes. Learning occurs in part from changes in neuronal signals orchestrated through glutamate receptors, including glutamate receptor mGluR5.

A group of Canadian scientists showed that mGluR5 was implicated in fear-related learning, spatial learning and memory. Conquet's team then found that mice without mGluR5 turn up noses and whiskers to cocaine, even though their dopamine neurons respond to cocaine as usual. Cocaine-seeking behavior has been examined in many strains of knockout mice, including some with dopamine neurochemistry defects. None, Conquet declares, were comparable to his, which he calls "the first knockout mice completely unresponsive to this powerfully addictive drug."



What makes this of pharmaceutical interest is that Conquet confirmed his finding with normal mice, using a selective mGluR5 antagonist called MPEP (2-methyl-6-[phenylethynyl]-pyridine). In dose-dependent fashion, normal mice injected with MPEP resist cocaine addiction. MPEP is unsuitable for humans (it dissolves poorly and barely crosses the blood-brain barrier, Conquet explains) but a similar molecule with better pharmacological characteristics might help addicts resist temptation. The market for the son-of-MPEP was judged too small for GlaxoSmithKline, so Conquet started Addex.

Conquet has also found that loss of mGluR5, unlike loss of dopamine receptors and transporters, leaves the so-called natural reward systems undisturbed: Mice lacking mGluR5 eat, drink, mate and nurture normally. This is a first -- proof that a drug addiction can be cleanly dissected from other reward systems controlled by dopamine. This is why Conquet says mGluR5 touches "the core of dependence."

He suggests a distinction in how dopamine and glutamate contribute to cocaine addiction. Dopamine bestows the high people adore; glutamate governs long-term dependence. This appeals to Conquet's view that addiction is a learned behavior. Long-term changes in glutamate transmission are increasingly seen as critical in the brain's adaptation to its environment. Cocaine addiction is one such adaptation.

If Addex finds a good mGluR5 antagonist, therapeutic possibilities may extend well beyond cocaine addiction. Glutamate has been implicated in numerous psychiatric disorders, and mGluR5 inhibitors have been suggested for Alzheimer's disease, Parkinsonian akinesia, muscle rigidity, stroke, anxiety and inflammatory pain. More indications await if mGluR5 antagonists can help people stay away from booze and cigarettes. But Conquet does not know if mGluR5 plays a role in other addictions; the appropriate experiments have not been done. Partly his mice have not had time, since other drugs of abuse, especially alcohol, require longer

training periods. Partly he has not had time, since he is so busy starting Addex.

Bloodstream Barricades

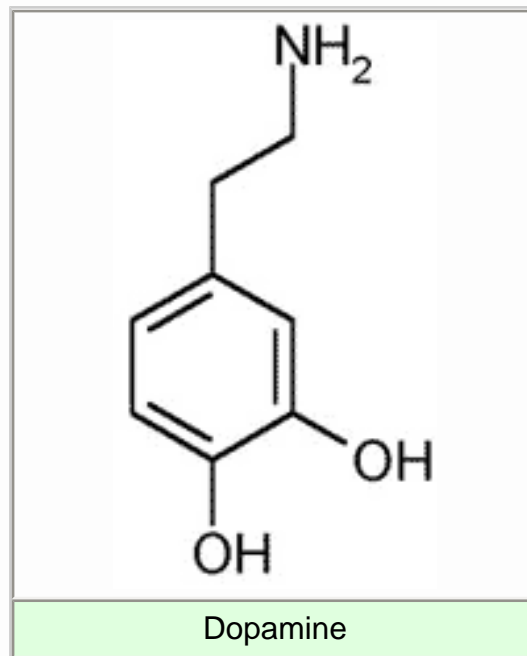


Welcomed or unwanted, nicotine is no concern to the immune system; molecules that small escape immune surveillance. Nicotine cruises the bloodstream without ever being intercepted by antibodies. An old immunologist's trick, however, can force the immune system to produce anti-nicotine antibodies. This is the idea behind NicVAX, the nicotine vaccine being developed by [NABI](#), of Boca Raton, FL.

It has long been known that bonding a small molecule to an immunogenic carrier protein can put an end to joy rides beneath the immune radar. When a protein is of a size the immune system notices, a small molecule saddled to the protein will be noticed too. So when a nicotine-carrier protein complex is injected into a mammal, antibodies against the protein and nicotine result.

The significance of this is that nicotine readily crosses the blood-brain barrier, but nicotine-antibody complexes do not. Without penetration to the brain, nicotine is impotent. So, theoretically, a vaccinated smoker will light up, inflate his lungs with smoke, and then...nothing. The seconds pass, and wonder deepens into astonishment that the cigarette he longed to savor no longer brings that Marlboro Country feeling. All that lingers is a stale, ugly taste in the mouth.

Ali Fattom, NABI's VP of research, and in charge of NicVAX, mentions that it won't be necessary to keep all the nicotine out of the brain. A threshold concentration of nicotine is required before the nicotinic acetylcholine receptor triggers the cascade that ends in the heady glow of extra dopamine in the synapses. All NicVAX has to do is "keep nicotine at a lower level than the threshold that causes release of dopamine." In animals, NicVAX reduces brain nicotine levels 60 percent to 70 percent. Fattom predicts similar reductions would rob nicotine of its pleasure in humans. What's more, smokers won't be able to outsmoke NicVAX -- Fattom believes antibody titers will be so high that simply smoking more cannot surmount the antibody barricades.



NicVAX's protein carrier for nicotine is a recombinant *Pseudomonas* toxin with its active site removed; it is without known toxicity, Fattom says. He expects the vaccine will work gradually. "Take two injections of the vaccine, and you should have antibodies on board within a month." They "will build gradually, which means that you will remove nicotine from your body gradually." Eventually, "you'll actually be smoking a cigarette without getting anything out of it." That would affect perception of the cigarette: It would be like a nicotine-depleted cigarette, which "tastes terrible."

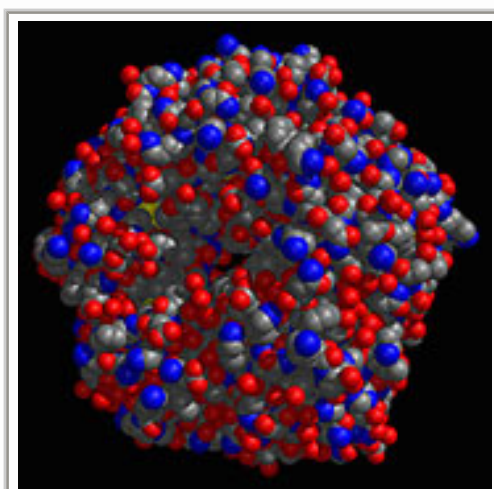
NicVAX will help smokers quit and help smokers who have quit stay quit. Smokers can avail themselves of nicotine patches, gums and medications to cope with craving while antibody titers build. For relapse prevention Fattom believes NicVAX will be a stand-alone therapy. Now that preclinical studies of NicVAX are over, Fattom expects Phase I to begin in 2002. NABI, like some others in this field, has funding from NIDA to help pay for the early phase clinical studies.

The question pops into the mind of any parent -- What about vaccinating kids? Fattom quotes a statistic that 80 percent of Americans who smoke started in middle or high school, so, yes, he's thought about using NicVAX to shield teenagers from the pied piper allure of Joe Camel. But in vaccine development, you cannot go quickly into studies with teenagers, he says. "They are still considered to be children. Unless you are sure that your vaccine is 100 percent safe, you cannot touch them." So this application remains further down the road, after thorough assessments of NicVAX safety in adults.

The Spoiler

Like NABI, [Xenova Group](#) plc, a British company located in Cambridge and the London suburb of Slough, is not an anti-addiction specialist. Xenova conducts small molecule and biologics drug development aimed at the oncology market, while NABI has interests in infectious disease and immune system medications. Both have vaccine projects unrelated to drug abuse. And in nicotine vaccines, they compete. TA-NIC, Xenova's nicotine vaccine, was constructed along the same lines as NABI's and is slightly ahead in development. A TA-NIC Phase I trial started last autumn. Unlike NABI, Xenova also has a cocaine vaccine, TA-CD. Here too, there is competition: DAS has a cocaine vaccine in preclinical stages.

Small like nicotine, cocaine is normally invisible to the immune system. It too must pass through the blood-brain barrier before it produces euphoria, and cannot pass if bound to an antibody. Keeping cocaine out of the brain, or reducing it, says John St. Clair Roberts, Xenova's medical director, should reduce the reinforcing properties of cocaine. Patients could more easily break their addictions. Xenova orchestrates production of anti-cocaine antibodies as with a nicotine vaccine: TA-CD consists of a harmless vaccination protein (inactive cholera toxin B) covalently bonded to cocaine.



Cholera toxin subunit B
(Protein Data Bank,
Brookhaven National Labs)

TA-CD is in two Phase II trials. One is a dose optimization study. Roberts comments that Xenova must figure out the best dose and vaccination timetable -- true for any vaccine -- but a special challenge when pioneering a drug-abuse vaccine, where clinical endpoints may not be

obvious. The problem the cocaine vaccine faces is that, "we don't know how much antibody we need."

In parallel Xenova is conducting what Roberts calls a Phase II cocaine administration study. Addicts receive cocaine under controlled conditions before and after vaccination. Blood samples yield measures of antibody titers and amounts of cocaine bound and unbound. "You can also measure various psychometric parameters to see how they feel about cocaine and whether they're getting the high that they normally get," says Roberts.

Unlike addicts in the dose optimization trial, "these patients really don't wish to quit." (They state that in writing.) How brave of them to risk that Xenova may have created a therapeutic. "We could spoil their party," Roberts admits. But happy days might not vanish forever, because he does not expect the antibodies will be long lasting. "What we're trying to do is protect people for the six to nine months that is the critical time when you're trying to quit. If they then wish to go back to their party, they could just wait until their antibodies diminish."

In truth, the contented are the exception in the sphere in which Roberts moves. "Normally it's difficult to find patients and enrollment is slow," he says. Here he expects the opposite will prove true. Somehow, people from all over the world hear about what Xenova is doing. Then they pick up the phone and call. They beg to test the vaccine. Addicts will cross continents to get away from cocaine. "There are very few countries that haven't called us," Roberts says.

Every Drug A Winner?



You don't just quit drugs, says ATI's Fox. "You need to learn how to do it," she says, noting that the average smoker makes between eight and eleven attempts before successfully quitting smoking.

Recognizing how hard addictions are to break, the trial blazers of anti-addiction medicine modestly say they hope to boost success rates whenever addicts finally decide to quit. They realize their new medicines may not always stand alone, instead finding places beside other drugs; combination therapy may be the surest road out of addiction. This could mean that every new anti-addiction medicine has a chance to be a winner - and if droves of new patients come out of the woodwork, as with Prozac and Viagra, a big winner.

A fly in every drug market's ointment is cost, true here too. Society already spends great sums treating addiction. For heroin, "half of the addicts in the U.S. are covered by Medicaid," says DAS' Greetham. "30 percent comes out of people's back pockets; the rest are charity cases." Eighty percent of alcoholics go to work, so they are covered by their health insurance; cocaine addicts have a similar situation. How much more will we willingly pay? When methadone costs pennies a dose, will we spend much more to replace methadone with Buprenorphine Depot?

Two years ago, Congress changed the rules for treating heroin addiction in a way that eventually may benefit all of these companies. The [Drug Addiction Treatment Act of 2000](#) will allow qualified primary physicians to prescribe buprenorphine to treat heroin addiction. (This is a legal matter because buprenorphine, as an opiate receptor agonist and therefore potentially addictive, is a controlled substance.) The act should encourage people to seek treatment who fear the stigma of going to addiction clinics, or entering the poorer neighborhoods that are often the only places willing to accept the clinics. If the act starts a trend, primary doctors may eventually treat other addictions.

Especially if there are better medicines. None of the anti-addiction companies claims its products will be panaceas. But if the wolves of addiction are to be tamed, so that one day we may look back and wonder how it was that alcohol and cocaine and heroin and nicotine hounded so many to destruction, who are more likely to be the tamers than these?

—Tom Hollon (thollon@starpower.net) is a freelance writer in Rockville, Md.



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