



## **Inoculate Yourself Against . . . *Cocaine*?**

**by Charles Sigler, D.Phil.**

Can you believe it? A vaccine is being developed that tricks antibodies into identifying and neutralizing cocaine molecules, so that the cocaine cannot pass through the blood–brain barrier and cause an individual to get high. A researcher at the Baylor College of Medicine, Tom Kosten, M.D., has developed a cocaine vaccine; and he plans similar vaccines for methamphetamine and nicotine. Preliminary results from the first clinical trials in humans suggest that the cocaine vaccine holds tremendous promise.

Cocaine and many other drugs consist of particles so small, that the human body cannot fight them because they aren't recognized by the immune system as foreign particles—therefore they're able to make it past the blood-brain barrier to the brain. Kosten attached the cocaine molecules to a larger protein molecule, an inactive cholera protein, and this combination is what the body learns to attack. Inactivating the cholera proteins prevents them from causing disease. However, the immune system can see them when they are injected and will make antibodies for cholera and cocaine. So the person is vaccinated against both cholera and cocaine at the same time! Once the cocaine/cholera combination is recognized, antibodies attach to all parts of it. Some of the antibodies attach only to the cholera part, some attach only to the cocaine part, and some attach to both. The body's immune system is then able to recognize the cocaine by itself since some antibodies now recognize cocaine alone and therefore will clean it out of the blood, preventing it from reaching the brain to create the high.

It's like having a big sponge for cocaine in the bloodstream, said Kosten. The idea is to "soak up" enough cocaine with the antibodies so that addicts cannot get "high." Hopefully, if the inability to get high continues long enough, the addict will be able to quit the drug. During early clinical trials in humans, researchers vaccinated subjects

repeatedly over a period of three months; and the subjects made large amounts of cocaine-specific antibodies. Although the antibody levels drop within a year, they remained significantly high during the first few months. In that early time period, if a vaccinated subject used cocaine, the antibodies prevented the cocaine from entering the brain and giving the person the cocaine “rush.”

However, the vaccine, isn't 100% effective. While 35% of the test subject produced a good antibody response that blocked the cocaine fully, 25% of the subjects didn't produce enough antibodies for the vaccine to work. The remainder of the subjects produced a reasonable amount of antibodies so that some of these subjects stopped their cocaine use while others reduced their use. “It doesn't work on everybody. Not all of us have equally robust immune systems,” said Dr. Jim Patton, a professor in the department of psychology and neuroscience at Baylor. “As with any medical breakthrough, there's the possibility of people seeing it as a silver-bullet type thing,” said Dr. Doug Matthews, an associate professor of neuroscience.

There are ethical questions being raised as well—who would get the vaccine? Would it just be individuals seeking to address their own cocaine problem? Could parents “inoculate” their children as they do for chicken pox? What about convicted cocaine abusers? Could they be required to get the vaccination? As to whether or not parents should be able to give their children the cocaine vaccine, Matthews said, “Parents should use the platform that God's given them with their children. In my opinion it's not the best route.”

### **Cocaine-induced Brain Damage**

Cocaine and other drugs of abuse are addictive because they affect the normal pathways used by brain neurotransmitters such as dopamine and serotonin. Cocaine, for example, uses the dopamine reward pathway in the brain.

Laboratory experiments upon humans and animals indicated that elevations in dopamine continued throughout the 12 to 24 hours during which the subjects were able to use cocaine. During the period of withdrawal that followed, a marked suppression of dopamine, below the levels released before the cocaine high, occurred.

The degree of dopamine suppression was positively correlated with the number of hours of continuous cocaine use before withdrawal. Deficits in brain stimulation reward also increased as a function of the duration of continuous cocaine use. These

findings suggest that long term cocaine abuse alters the brain mechanisms that mediate positive reinforcement. “Drugs of abuse [like cocaine] activate pathways to a 20–fold extent greater than the usual pleasures of life; good food, sex, music, etc. When you are doing that repeatedly, the whole system down–regulates, meaning that it simply doesn't respond to the usual rewards in life anymore, because they are below the threshold.”

In other words, you suffer anhedonia—the inability to experience pleasure from normally pleasurable life events. This marked disinterest or pleasure in normal life events is recognized as one of the key symptoms of depression. A similar process with serotonin suppression occurs after cocaine withdrawal, further reinforcing the experience of depression and several other psychiatric disorders shown to be related to serotonin deficiencies (panic disorder, insomnia, impulsiveness, and aggression-symptoms).

Usually dopamine is broken down into a harmless inactive state very quickly. But when large amounts of dopamine are released by stimulants like cocaine, dopamine accumulates in the brain. Once it builds up to a point that the usual enzymes cannot dismantle it fast enough, other enzymes start working on the dopamine; but they convert it into a substance that is toxic to the brain.



The graphic is from the cited article: “Methamphetamine Nicotine Cocaine Vaccine.”

So many abusers of cocaine and other stimulants develop Parkinson's disease-like symptoms. Parkinson's is defined as having damage to 80 percent of the neurons in the

part of the brain that controls motor function and aspects of cognition, emotions and learning. “In brain imaging studies of 20- to 25-year-old cocaine or stimulant abusers, their brains have deteriorated enough to look like that of a 60-year-old Parkinson's patient,” said Thomas Kosten. “It does not take much of an imagination to realize that their prognosis is not good.” The hope is that the vaccine will encourage cocaine addicts to stop using the drug and thus prevent substantial brain damage. See the graphic above.

As of August 2009 there were two additional cocaine vaccine studies registered on [clinicaltrials.gov](http://clinicaltrials.gov), “Therapeutic Cocaine Vaccine: Human Laboratory Study” measured the relationship between antibodies and the effects of cocaine on subject ratings of intoxication, craving as well as its cardiovascular effects. This study was completed in August of 2009. “Multi-site Controlled Trial of Cocaine Vaccine TA-CD09,” which begins in January of 2010, will test the efficacy of TA-CD, a newly developed active vaccine against cocaine. It is estimated to be completed by July of 2014.

Kosten and his research team have published the results of their most recent research in the October 2009 issue of the *Archives of General Psychiatry*. It is the first placebo-controlled study of a vaccine against an illicit drug of abuse. Thirty-eight percent of the participants achieved blood levels of cocaine-antibodies thought to be sufficient to block cocaine's euphoric effects. This “high-antibody” group had significantly more cocaine-free urines than those in the placebo or low-antibody groups. Fifty-three percent of the high-antibody group were abstinent from cocaine more than half the time during weeks 8 to 20 of the study, compared with only 23 percent of the low-antibody group. Dr. Kosten noted that while the study did not complete abstinence from cocaine, “Previous research has shown, however, that a reduction in use is associated with a significant improvement in cocaine abusers' social functioning and thus is therapeutically meaningful.” NIDA Director, Nora Volkow, felt the study was a promising step towards an effective medical treatment for cocaine addiction: “Provided that larger follow-up studies confirm its safety and efficacy, this vaccine would offer a valuable new approach to treating cocaine addiction, for which no FDA-approved medication is currently available.”

Icro Maremmani, professor of addiction medicine at the University of Pisa and University of Siena, believed the vaccine would only be useful for highly motivated individuals: “Hard users of cocaine probably will not accept this kind of treatment.” He noted that there is a risk that some people will increase their intake of cocaine to

overcome the antibody effect. The result could be similar to the use of naltrexone for heroin addicts: “a perfect drug but poor clinical results.” Kosten said it usually takes about two years for addicts to become drug-free, requiring vaccination every three months to maintain antibody levels. While the vaccine can stop relapses, it doesn't solve the issues that lead to drug use. Kosten noted that “The vaccine doesn't get you new friends, change your depression, get you out of jail, or all the other things that people have trouble with. People could conceivably be on it for the rest of their life if they can't get it together.”

### **The Implications of the Research**

The above findings on the cocaine vaccine although preliminary, still hold tremendous promise for the future of addiction treatment; but I wonder. The vaccine only prevents the cocaine-attached antibodies from penetrating the blood-brain barrier, so mere cocaine molecules can still get through. If you use an inordinate amount of cocaine and overwhelm the existing cocaine-attached antibodies in your system, could you still get enough cocaine through the blood-brain barrier to get high? Also, the vaccine imposes an unusually high tolerance for cocaine upon the vaccinated individual, meaning they would have to ingest a large quantity of cocaine while attempting to get high, but what would that do to other parts of the body, like say the heart?

The vaccine may create a biochemical roadblock that impedes cocaine from reaching the dopamine neurotransmitters in the brain, but it cannot and would not impede the desire or craving for the high. In the hands of the truly desperate cocaine addict, you may just be giving him a loaded biochemical gun.

**For more information on the above topics, see the following:**

[“Anhedonia.”](#)

[“BU medical school discovers vaccine for cocaine addiction.”](#)

[“ClinicalTrials.gov.”](#) Search for “cocaine vaccine.”

[“Cocaine Dependence and Withdrawal.”](#)

[“Cocaine Vaccine Could Help Addicts.”](#)

[“Cocaine Vaccine Shows Promise for Treating Addiction.”](#)

[“Methamphetamine Nicotine Cocaine Vaccine.”](#)

[“US Scientists Working On Cocaine Vaccine.”](#)