

### Research News

#### **New Research Shows Vaccine May Offer Promising Treatment for Nicotine Addiction**

Each year nearly half of all smokers attempt to quit smoking, but less than 5 percent are successful beyond 3 months to a year. Results from a new study by Dr. Dorothy Hatsukami and colleagues from the University of Minnesota Medical School suggest a new nicotine vaccine may be safe and effective in helping smokers who want to quit.

A total of 68 smokers randomly received a placebo or one of three doses of nicotine vaccine four times over 26 weeks. The researchers then observed the patients for an additional 38 weeks to monitor nicotine antibody levels, smoking behavior, and/or adverse side effects such as nausea, fatigue, or pain.

The scientists observed that nicotine antibodies (molecules that bind to nicotine, reducing its distribution to and its effects in the brain) increased in all nicotine vaccine groups. More patients who received the highest dose of vaccine achieved 30-day abstinence, and in a shorter amount of time, than those who received the other doses or placebo. Moreover, scientists found no evidence of withdrawal symptoms such as craving, irritability, or compensatory smoking (smoking more of a cigarette or puffing more often to increase nicotine intake). More than 90 percent of reported side effects were of mild or moderate severity. The most frequently reported events were upper respiratory tract infection, headache, cough, and inflammation of the nasal passages and throat. There were no observed differences in the frequency of these events among the four treatment groups.

- **WHAT IT MEANS:** Study participants who received the vaccine experienced none of the typical withdrawal symptoms commonly experienced by smokers. The nicotine vaccine may offer a promising new treatment alternative for smokers seeking to quit. Further research is needed to maximize the vaccine's ability to diminish nicotine's effects in humans.

Dr. Hatsukami and her colleagues published this study in the November 2005 issue of *Clinical Pharmacology and Therapeutics*.

#### **Psychiatrists Should Be More Alert to Smoking Practices Among Patients in Routine Care**

Results of a recently published study suggest that psychiatrists tend to significantly underreport patients who smoke and undertreat their smoking problem. This finding, say the scientists who conducted the research, is important because psychiatric patients who smoke are likely to have greater psychosocial needs than those who do not.

Psychiatrists provided information on 1,752 patients, 280 of whom were reported to have a nicotine problem. Of these, only 27 had received treatment from the psychiatrists for nicotine addiction.

The data show that psychiatric patients who smoke are more likely to be males who are single, divorced, or separated; have low levels of educational achievement compared with nonsmokers receiving psychiatric treatment; and have significantly more co-occurring psychiatric disorders, such as schizophrenia and alcohol or other substance abuse.

- **WHAT IT MEANS:** Psychiatrists who routinely treat people who are nicotine-addicted should be more alert to the relationship between smoking and increased medical and psychosocial needs. Educational programs to raise the awareness of psychiatrists to diagnose and treat smoking problems are needed to alleviate this public health problem.

The study, led by Dr. Ivan Montoya of NIDA's Division of Pharmacotherapies and Medical Consequences of Drug Abuse, was published in the October-December 2005 issue of the *American Journal on Addictions*.

## **Numerous Factors Influence Chronic Smoking in Youth, and Many Cross Racial, Ethnic Lines**

Having parents or friends who smoke, dropping out of high school, and trying cigarettes at a young age are among the factors that are linked to adolescents being more likely to become chronic smokers, according to new research supported in part by NIDA.

An analysis of a national sample of more than 14,000 young adults of different racial and ethnic backgrounds found that a number of common factors contribute to daily smoking and nicotine addiction among youth. Depression, however, was uniquely associated with addiction.

Finding cigarettes pleasurable when first trying them and being a "novelty seeker" were other factors associated with youth becoming chronic smokers. However, the researchers found some differences across racial/ethnic groups. Overall, minority youth were less likely than white youth to try cigarettes, become daily smokers once they did try cigarettes, and become addicted to nicotine once becoming daily smokers. Having parents and peers who smoke was associated with chronic smoking among white and Hispanic adolescents, but not African-Americans in the study. African-American youth appeared to be less influenced than whites by the models for smoking in their close interpersonal network.

- **WHAT IT MEANS:** A number of social, psychological, and biological factors predispose youth to become daily smokers or addicted to nicotine. Primary prevention and interventions that address the commonalities could be uniform, irrespective of race and ethnicity.

Dr. Denise Kandel and her colleagues at Columbia University and the New York State Psychiatric Institute published these findings in the February 2006 issue of the *American Journal of Public Health*.

## **Schizophrenics Take In More Nicotine Per Cigarette**

Smokers with schizophrenia and related disorders take in more nicotine per cigarette than people without such mental illnesses, suggesting that such diseases have a neurobiological component that drives people to seek out the drug. This, in turn, indicates that effective treatment for tobacco addiction for people with schizophrenia might include nicotine replacement treatments that mimic smoking behavior.

Dr. Jill Williams and her colleagues at the University of Medicine and Dentistry of New Jersey (UMDNJ)—Robert Wood Johnson Medical School, the UMDNJ—School of Public Health Tobacco Dependence Program, and the University of California—San Francisco compared blood levels of nicotine and its primary byproduct in 81 schizophrenic smokers and 55 smokers without the mental disorder.

They observed that blood levels of nicotine and cotinine (a breakdown product of nicotine from cigarette smoke) were 1.3 times higher in the mentally ill participants despite smoking a similar number of cigarettes per day. They also found that there were no differences between the groups in their ability to metabolize nicotine and cotinine, suggesting that the higher levels in schizophrenia were from differences in their cigarette intake patterns. The research supports anecdotal reports that smokers with schizophrenia seem to take more or deeper puffs than other smokers.

Smokers with schizophrenia have death rates that exceed that of the general population. Such individuals are at greater risk for death from smoking-related illnesses, such as cardiovascular disease and respiratory disease.

- **WHAT IT MEANS:** Smoking in schizophrenics appears to be linked to the unique neurobiological abnormalities of the disorder. Recognizing the differences in nicotine intake by schizophrenic smokers is important not only for developing more effective smoking cessation tools for people with schizophrenia such as a nicotine nasal spray that provides high, intermittent doses, but also for providing additional insight into the nature of the disease.

The scientists published these findings in the November 2005 issue of *Schizophrenia Research*.

## **Low-Dose Naltrexone May Help Reduce Weight Gain in Smokers Trying to Quit**

Many smokers are reluctant to quit because of the perceived risk of gaining weight after smoking cessation. But new research from the first large, prospectively randomized dose-ranging study of naltrexone for smoking cessation suggests that low-dose naltrexone can reduce weight gain in smokers using nicotine patch therapy.

The 6-week study, conducted by researchers at Yale School of Medicine and the NIDA-supported Transdisciplinary Tobacco Use Research Center (TTURC), included 400 patients who smoked at least one pack of cigarettes daily. Patients

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were treated with a nicotine patch and were randomly assigned to receive placebo or one of three doses of naltrexone. The scientists found that continuously abstinent smokers who took the lowest dose of the drug—25 mg—gained significantly less weight (1.5 lbs.) than those who took placebo (4.2 lbs.). In comparison, smokers who took 50 mg of the drug gained 2.4 lbs., and those who took 100 mg of naltrexone gained 3.3 lbs. Of those who completed treatment, 48 percent of the placebo group achieved continuous abstinence, compared with 51 percent of the 25-mg group, 48 percent of the 50-mg group, and 72 percent of the 100-mg group. Given that there wasn't one dose that was effective in both reducing weight gain and improving smoking abstinence over nicotine patch alone, the optimal naltrexone dose for an individual may depend on the greatest motivating factor.

Naltrexone is an opiate antagonist, meaning that it binds to the same receptors in the brain as natural chemicals that are part of the brain's reward system. The Food and Drug Administration originally approved naltrexone for people who are trying to break their addiction to opiate drugs like heroin and morphine.

- **WHAT IT MEANS:** Many people who try to quit smoking are concerned about gaining weight. The study suggests that low-dose naltrexone in combination with the nicotine patch may be useful as a second-line treatment for weight-concerned smokers who are trying to quit. The scientists say the study results support further testing of the 100-mg dose of naltrexone for improving smoking cessation outcomes.

Dr. Stephanie O'Malley and her colleagues published their findings in the March 27, 2006 issue of the *Archives of Internal Medicine*.

### **Lifetime Simulation Model Shows Significant Economic Benefits of Methadone Treatment**

A recently developed mathematical model that simulates the chronic nature of heroin abuse shows that methadone treatment for heroin abusers generates economic benefits that are more than seven times greater than what has been shown by previous models.

The NIDA-funded research is the first to present lifetime estimates of the costs and benefits associated with drug abuse and its treatment. Previous studies examining drug treatment costs and benefits typically have focused on a single treatment episode, treating drug abuse as an acute problem that can be cured in a single episode of therapy, rather than as a chronic disease.

The goal of the scientists was to develop a realistic simulation model that represents the progression of heroin abuse in individuals aged 18 to 60 years with respect to drug treatment, criminal behavior, employment, and healthcare use. Their model demonstrates that increasing a heroin user's access to treatment over that person's lifetime decreases the likelihood of engaging in extended drug abuse, increases employment opportunities, and lessens the probability of committing future crimes and seeking care for addiction-related medical consequences. The study further suggests that the individual and society together reap \$38 in economic benefits for each dollar spent on methadone treatment.

- **WHAT IT MEANS:** Research seeking to conduct cost-benefit analyses of drug treatment regimens need to take the chronic nature of the disease into account. Such models represent a more realistic view of the recurring nature of drug abuse and addiction, and offer a more accurate picture of the social and economic consequences of the disease and its therapies.

Dr. Gary Zarkin, of RTI International, and his colleagues published their research in the November 2005 issue of *Health Economics*.

### **Interim Methadone Treatment Increases Likelihood of Future Comprehensive Treatment**

Men and women who are addicted to heroin and awaiting entry into a comprehensive treatment program can benefit from an interim methadone maintenance program.

Dr. Robert P. Schwartz, of Friends Research Institute, Inc. and the University of Maryland School of Medicine, and his colleagues enrolled 194 heroin-addicted patients in an interim treatment program, which consisted of methadone only, and compared their progress with 120 patients assigned to a waiting list for entry into comprehensive treatment, which can include methadone and other services such as counseling, family therapy, and employment assistance.

The scientists found that only 16 percent of the patients receiving methadone on an interim basis dropped out of the program within 4 months, and that 76 percent of the patients originally assigned to the interim condition entered a comprehensive methadone treatment program. Only 21 percent of those on the waiting list entered comprehensive treatment. In addition, results from a followup interview conducted either at entry into comprehensive treatment or at 120

days from initial data collection showed that 56.6 percent of the interim treatment patients tested positive for heroin, compared with 79.2 percent of the waiting list group. The interim treatment participants also reported spending less money on drugs and receiving less illegal income than the waiting list participants.

- **WHAT IT MEANS:** Participation in interim methadone maintenance treatment can effectively increase the probability that a person will enter a comprehensive methadone treatment program. The results also suggest that interim methadone treatment is associated with a significant reduction in heroin use and a significant self-reported reduction in crime.

The study was published in the January 2006 issue of the *Archives of General Psychiatry*.

### **Cocaine Increases Susceptibility to MPTP, a Toxin Known to Cause Symptoms of Parkinson's Disease in Mice**

After repeatedly injecting mice with an amount of cocaine equivalent to a typical human dose, NIDA-supported researchers found in adult and fetal models that nerve cells in a region of the brain called the substantia nigra were more susceptible to MPTP. MPTP is an environmental agent that functions as a neurotoxin and is known to cause symptoms of Parkinson's disease (PD), such as tremor, stiffness, and slowness of movement.

Chronic cocaine administration interferes with the body's ability to regulate the release and reabsorption of dopamine (a brain chemical that helps control movement and also is involved in feelings of pleasure/reward). It may cause sustained increases in extracellular dopamine, which over time sets off a molecular cascade that can mimic that seen following the administration of parkinsonian toxins. While the researchers found that exposure to cocaine alone or MPTP alone caused comparable neuronal loss in the substantia nigra, exposure to cocaine and MPTP together led to a greater decline in cell numbers than for either agent alone.

The scientists say the study provides additional evidence for a multihit hypothesis for PD development by suggesting that multiple environmental exposures in this region of the brain—including cocaine, and by analogy, other psychostimulants—can work together to increase cell susceptibility to toxins that contribute to PD etiology. However, because the underlying switch in vulnerability is unclear, further research is warranted.

- **WHAT IT MEANS:** Current estimates are that there are 2.7 million chronic, adult abusers of cocaine, and that 1 percent of pregnant women abuse the drug. The findings of this study suggest that exposure to cocaine and other psychostimulants together with other environmental agents may act synergistically to increase susceptibility to PD.

Dr. Richard Smeyne and his colleagues at St. Jude Children's Research Hospital in Memphis published these results in December 2005 in the journal *Neuroscience*.

**For more information about any item in this NewsScan:**

- Reporters, call Sara Rosario Wilson at 301-443-6245.
- Congressional staffers, call Geoffrey Laredo at 301-594-6852.

The National Institute on Drug Abuse (NIDA) is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports most of the world's research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to ensure the rapid dissemination of research information and its implementation in policy and practice. Fact sheets on the health effects of drugs of abuse and other topics are available in English and Spanish. These fact sheets and further information on NIDA research and other activities can be found on the NIDA home page at <http://www.drugabuse.gov>.

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is a component of the National Institutes of Health,  
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES.

