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News Scan

NIDA ADDICTION RESEARCH NEWS

NEWS UPDATE

Research News

Time to Hepatitis C Infection in Injection Drug Users Lengthening in Developed Countries

Hepatitis C (HCV), a blood-borne infection that can cause liver damage and death, is very common among injection drug users (IDUs) and is transmitted mainly by the sharing of drug preparation or injection equipment. Researchers funded by NIDA have found that the time from onset of injection drug use to HCV infection for IDUs in developed countries has lengthened since 1995. The researchers analyzed 72 studies of HCV infection in IDUs published between 1989 and 2006. In addition, the researchers compared studies from developed countries (such as the United States) with studies from developing countries. They also compared studies completed before 1995 with studies completed after 1995 to measure the impact of increased HIV/HCV awareness in developed countries. They found that in developed countries, HCV prevalence in IDUs who had been injecting drugs for less than 2 years had declined from an estimated 53 percent before 1995 to 38 percent more recently. The prevalence in developing countries remains higher—for example, a 59 percent prevalence of HCV infection at 1 year of drug injection. Whether or not the prevalence in developing countries had decreased at all since 1995 could not be determined because only one study collected data on HCV in developing countries before 1995. Although the results show that many IDUs avoid HCV infection in the first year of drug injection, a substantial proportion of new injectors still acquire HCV rapidly. The authors conclude that a heavy investment in public health resources will likely be needed to make further gains in HCV prevention.

Hagan H, Pouget ER, Des Jarlais DC, Lelutiu-Weinberger C. Meta-regression of hepatitis C virus infection in relation to time since onset of illicit drug injection: The influence of time and place. *Am J Epidemiol.* 2008;168(10):1099–1109.

Male, Female Injection Drug Users in Tijuana, Mexico, Have Different Risk Factors for HIV Infection

Although Mexico has a lower prevalence of HIV infection compared to its bordering countries, the prevalence along the United States–Mexico border is rising and could eventually impact HIV prevalence in the rest of Mexico. In an attempt to better understand risk factors for HIV infection among injection drug users (IDUs) in the border city of Tijuana, Mexico, researchers funded by NIDA surveyed 1,053 IDUs (896 men, 157 women) on demographics, sexual and drug use behaviors, and social networks. Participants were also tested for HIV and syphilis. Overall, female IDUs were almost three times more likely to test positive for HIV compared to male IDUs. Women were also more likely to have an active syphilis infection or a past history of syphilis infection. HIV risk for women increased with age, with a history of being infected with syphilis, and with a longer duration of living in Tijuana—odds of testing positive for HIV increased by 81 percent for female IDUs for every 10 years of living in Tijuana. In contrast, men who lived in Tijuana for shorter durations of time were more likely to test positive for HIV—for every 10 years men lived in Tijuana, their odds of testing positive decreased by 35 percent. When examined more closely, the increased risk with shorter stays in Tijuana is associated with deportation from the United States, with men who had experienced deportation being four times as likely to be HIV-positive as men who had never been deported. The authors propose that frequent deportation may be an indicator of Mexican male migrants already at high risk of contracting HIV; or it may lead to unstable social conditions, which in turn can lead to behaviors that place migrants at high risk for HIV. Other factors associated with HIV infection in men include active syphilis infection and larger numbers of injection partners. This study highlights the need for programs to support the mobile population on both sides of the United States–Mexico border, as well as the need for culturally and gender-appropriate HIV-prevention programs, conclude the authors.

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Strathdee SA, Lozada R, Ojeda VD, Pollini RA, Brouwer KC, Vera A, Cornelius W, Nguyen L, Magis-Rodriguez C, Patterson TL; Proyecto El Cuete. Differential effects of migration and deportation on HIV infection among male and female injection drug users in Tijuana, Mexico. *PLoS ONE.* 2008;3(7):e2690.

HIV Prevalence at the United States–Mexico Border May Change the HIV Epidemic in Mexico

The rapidly changing HIV subepidemic at the border of the United States and Mexico, likely caused by population mobility and the drug and sex trades, may be rapidly affecting the overall HIV epidemic in Mexico. In a recent editorial, NIDA-funded researchers discussed studies of HIV infection at the United States–Mexico border in an effort to better understand factors shaping individual and network-level risks for acquiring HIV. Two different studies in the Mexican border cities of Tijuana and Ciudad Juarez showed a high prevalence of HIV infection among sex workers who were also injection drug users: 6 percent and 12 percent, respectively. Considerable population mobility exists at the Tijuana–San Diego (United States) border in both directions, with one study showing that one-fifth of injection drug users in Tijuana had traveled to the United States in the previous year. This mobility also occurs in other high-risk populations—for example, "nearly half of men having sex with men (MSM) in Tijuana and three-quarters of MSM in San Diego report having male sex partners from across the border," explain the authors. The populations of border cities such as Tijuana largely come from other states in Mexico, and HIV-positive people can carry the infection back to their home states. Mexico now faces several challenges at the national level, including integrating treatment for HIV and other sexually transmitted infections that are risk factors for HIV infection, and increasing the availability of antiretroviral therapy. The authors conclude that due to the high level of migration in all directions, bordering countries must be involved for HIV prevention, diagnosis, and treatment in Mexico to be effective.

Strathdee SA, Magis-Rodriguez C. Mexico's evolving HIV epidemic. *JAMA.* 2008;300(5):571–573.

Varenicline Improves Learning Deficits Caused by Nicotine Withdrawal in Mice

Smokers who attempt to quit experience many negative physical effects, including trouble sleeping and increased hunger. Nicotine withdrawal can also produce mental deficits such as difficulty concentrating and problems with learning and memory. These side effects can lead to relapse to tobacco use. Varenicline is the most recent medication approved by the Food and Drug Administration to aid smoking cessation. While varenicline is known to reduce the severity of physical symptoms associated with nicotine withdrawal, its effects on mental functioning are not well understood. To study the effects of varenicline on mental functioning after nicotine withdrawal, researchers funded in part by NIDA exposed mice to nicotine for 12 days, let them undergo withdrawal, and compared their reactions to unpleasant sensations (loud noise coupled with a small shock to the feet) with and without varenicline administration at various doses. In these experiments, the mice were trained to learn that a specific environment was associated with the unpleasant sensations, and therefore would exhibit a fearful reaction when placed in that environment. Mice undergoing nicotine withdrawal did not make this association. However, the researchers found that a midrange dose of varenicline given during both training and testing sessions improved the ability of the mice to appropriately associate the experimental environment with the aversive stimuli—that is, the nicotine-withdrawn mice that received the effective varenicline dose exhibited the same intensity of fear reactions when placed in the experimental environment as control mice who had never received nicotine. These findings suggest that varenicline may be effective in reducing cognitive deficits associated with nicotine withdrawal in humans, though further experiments are needed to understand how varenicline affects brain functioning on the molecular level, conclude the authors.

Raybuck JD, Portugal GS, Lerman C, Gould TJ. Varenicline ameliorates nicotine withdrawal-induced learning deficits in C57BL/6 mice. *Behav Neurosci.* 2008;122(5):1166–1171.

Denicotinized Cigarettes Affect Nicotine Receptors in Smokers' Brains

Nicotine is thought to exert its effects on the brain by binding to receptors in the brain called nicotinic acetylcholine receptors (nAChRs). However, tobacco smoke contains thousands of chemicals besides nicotine, some of which may also bind to the nAChRs or cause molecules normally found in the body to bind to these receptors. To study the effects of denicotinized cigarettes—cigarettes from which nicotine has been removed—on a specific type of nAChR ($\alpha_4\beta_2$* nAChRs), researchers funded in part by NIDA used a brain imaging technique known as positron emission tomography (PET) to

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visualize these receptors in the brains of smokers during withdrawal and after smoking either low-nicotine or denicotinized cigarettes. Before the PET imaging, all volunteers stopped smoking for approximately 2 days. The volunteers underwent an hour of PET imaging while still undergoing withdrawal and then were assigned to perform one of three activities: smoke a low-nicotine cigarette, smoke a denicotinized cigarette, or not smoke; they then underwent approximately 4 more hours of PET imaging. Withdrawal symptoms were monitored during all imaging sessions. The imaging results showed not only that "inhalation of nicotine during cigarette smoking is solely responsible for occupancy of brain $\alpha_4\beta_2$* nAChRs," but also that the imaging "demonstrated significant $\alpha_4\beta_2$* nAChR occupancy from smoking a denicotinized cigarette," state the authors. This result challenges the assumption that denicotinized cigarettes do not affect the brain's nicotine receptors, the authors further explain. Interestingly, whether or not the receptors were occupied did not correlate with withdrawal symptoms, indicating that factors other than nicotine binding to the receptors play a role in the relief of withdrawal symptoms provided by smoking.

Brody AL, Mandelkern MA, Costello MR, Abrams AL, Scheibal D, Farahi J, London ED, Olmstead RE, Rose JE, Mukhin AG. Brain nicotinic acetylcholine receptor occupancy: Effect of smoking a denicotinized cigarette. *Int J Neuropsychopharmacol.* 2009;12(3): 305–316.

Family-Based Intervention Helps Male Children of Drug Users Avoid Substance Use Disorders

Children of drug users are at high risk for developing substance use disorders themselves later in life. From 1991 to 1993, researchers funded by NIDA recruited families, with a parent in methadone treatment for heroin addiction and at least one young child, into a randomized trial of the Focus on Families (FOF) intervention, which includes relapse prevention services and parent training skills. Results from the original analysis of the trial showed that FOF both reduced parents' drug use and improved children's delinquent behavior compared with participants in the control group, who only received standard services provided by methadone clinics. To assess whether FOF continued to have an effect on children as they grew up, the researchers performed a 12-year followup study—85 percent of the children originally enrolled in the trial participated. Of those, 59 percent had met the criteria for a substance use disorder at some point in their life. Overall, the rates of substance use and dependence were similar between childhood participants in the FOF and control groups. However, when the results are broken down by gender, males who received the FOF intervention had a significantly lower risk of developing a substance use disorder—specifically, alcohol and marijuana disorders—than those in the control group. This may be because the FOF intervention focuses on teaching parents to handle externalizing problem behaviors (such as getting into fights), which are more common in boys than girls, explain the authors. Of concern was the fact that at the time of the followup study, 32 percent of the parents in the FOF group had died, compared to 13 percent of parents in the control group. High mortality is typical in long-term studies of patients on methadone, though the researchers could not find evidence that higher exposure to the FOF intervention was related to mortality in this study. In fact, the highest mortality rate was found among families who were assigned to FOF but never participated in the skills training or case management. FOF participants who attended 75 percent or more of the assigned sessions had about the same mortality rate as participants in the control group.

Haggerty KP, Skinner M, Fleming CB, Gainey RR, Catalano RF. Long-term effects of the Focus on Families project on substance use disorders among children of parents in methadone treatment. *Addiction.* 2008 Oct 8;[Epub ahead of print].

Computerized Cognitive-Behavioral Therapy Has Enduring Effects on Drug Use

Cognitive-behavioral therapy (CBT)—a type of behavioral therapy that teaches people how to unlearn unhealthy behaviors and incorporate more effective behaviors and change strategies—has been shown to be effective in the treatment of substance use disorders. CBT, however, is rarely used in clinical practice due to limited resources in most treatment clinics. In a NIDA-funded clinical trial of a computer-assisted version of CBT for the treatment of drug abuse, known as CBT4CBT, participants who received standard counseling plus the computerized CBT had significantly fewer positive urine drug tests and longer continuous periods of abstinence during treatment than participants who received standard counseling only. To examine whether the CBT4CBT program has enduring effects on drug use, the researchers performed followup interviews and collected urine samples from participants at 1, 3, and 6 months after the end of treatment. Sixty out of the original 73 participants who received treatment attended at least one followup visit. Participants who had achieved longer periods of abstinence during treatment were more likely to report abstinence during followup. Overall, patients assigned to CBT4CBT reported significantly longer continuous abstinence from all drugs during the followup period and were significantly more likely to have a urine test negative for any drug at 1 month after treatment.

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The proportion of negative drug tests remained slightly higher at 3 and 6 months after treatment in the CBT4CBT group. The researchers conclude that the benefit of CBT4CBT remains detectable up to 6 months after the end of treatment.

Carroll KM, Ball SA, Martino S, Nich C, Babuscio TA, Rounsaville BJ. Enduring effects of a computer-assisted training program for cognitive behavioral therapy: A 6-month follow-up of CBT4CBT. *Drug Alcohol Depend.* 2009;100(1–2):178–181.

Vigabatrin Prevents Relapse to Methamphetamine Use in an Animal Model of Addiction

Methamphetamine is a highly addictive stimulant drug, and many people who quit its use experience relapse. Currently, no medications are available for the treatment of methamphetamine addiction. However, an antiseizure medication, vigabatrin, has shown promise in the treatment of addiction. In a new study funded in part by NIDA, researchers tested vigabatrin in an animal model of relapse to methamphetamine use. The researchers trained rats in a conditioned place preference (CPP) scenario, where animals learn to associate a specific environment with the pleasurable effects of drug administration. In the CPP training, rats were exposed to two housing environments that looked and felt different and were connected by a small chamber. Rats were randomly assigned to receive methamphetamine injections in one of the two environments every other day for 10 days. On alternating days, the rats received saline injections in the second environment. All rats came to prefer (i.e., spend more time in) the environment in which they received the methamphetamine injections, and chose that environment over the location of the saline injections when given free access to both places. After developing a CPP, the rats underwent withdrawal from methamphetamine until they no longer preferred the environment they had previously associated with methamphetamine. The researchers then reintroduced the rats to methamphetamine, which immediately retriggered their CPP. When an injection of vigabatrin was given before the next dose of methamphetamine, the rats again lost their preference for the environment associated with methamphetamine injections, even when high doses of methamphetamine were given. The authors explain that though these results show that vigabatrin holds promise in treating people dependent on methamphetamine, humans relapse to drug use for factors other than re-exposure, including environmental cues and stress. Further studies are needed to test whether vigabatrin can help block relapse to methamphetamine use under other conditions, they conclude.

DeMarco A, Dalal RM, Pai J, Aquilina SD, Mullapudi U, Hammel C, Kothari SK, Kahanda M, Liebling CN, Patel V, Schiffer WK, Brodie JD, Dewey SL. Racemic gamma vinyl-GABA (R,S-GVG) blocks methamphetamine-triggered reinstatement of conditioned place preference. *Synapse.* 2009;63(2):87–94.

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- 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 www.drugabuse.gov. To order publications in English or Spanish, call NIDA's new *DrugPubs* Research Dissemination center at 1-877-NIDA-NIH (1-877-643-2644) or 240-645-0228 (TDD), or fax or e-mail requests to 240-645-0227 or drugpubs@nida.nih.gov.

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