

Behavior Game Played in Primary Grades Reduces Later Drug-Related Problems

Positive effects are most pronounced in disruptive boys.

BY NIDA NOTES STAFF

Awarding smiley-face stickers to teams of first-graders in Baltimore for the good behavior of the individual team members greatly increased the likelihood that the students would experience an adolescence free of substance abuse and dependence. Teachers gave out the stickers and other token rewards and penalties

in the Good Behavior Game (GBG), a classroom activity designed to inculcate appropriate behavior during children’s first 2 years in school.

“The GBG gives teachers an effective method of managing behavior in the classroom and of teaching children how to be students,” says Dr. Sheppard Kellam of the American Institutes for Research in Washington, D.C.

Dr. Kellam and colleagues began the longitudinal study of the GBG while at Johns Hopkins

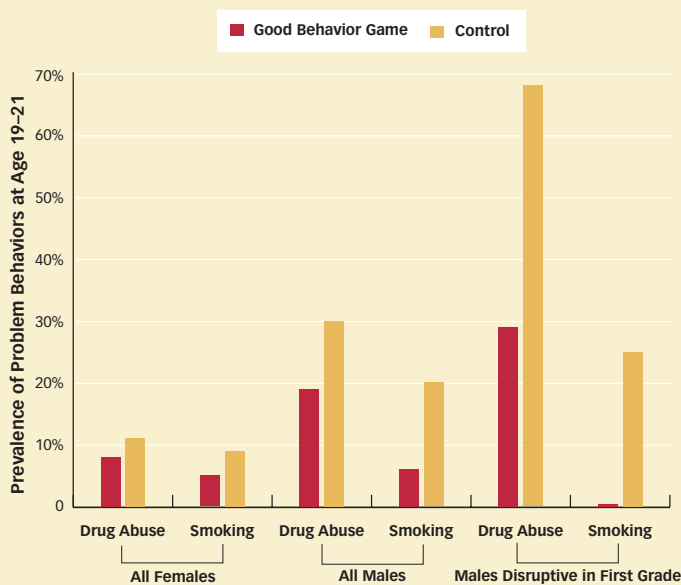
University in close partnership with the Baltimore City Public School System. Dr. Kellam suggests that the activity produces a broad spectrum of long-term benefits by steering 5- and 6-year-olds away from aggressive and disruptive behaviors, which have long been recognized as precursors of many negative adolescent and adult outcomes. The study found that the GBG was protective not only against substance abuse and dependence but also against teenage delinquency, antisocial personality disorder, and suicide attempts.

HOW TO PLAY THE GAME

Teachers first set the rules of the game, presenting a list

[Continued on page 6]

AS THE TWIG IS BENT Young adults who had played the Good Behavior Game in first and second grade were less likely to smoke cigarettes or abuse drugs than those who hadn’t played the game. Males whose first-grade teachers identified them as aggressive and disruptive benefited the most.



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Helping Doctors Become First Responders to Substance Abuse

Every day, the Nation's primary care and family physicians see patients whose use of addictive substances causes them problems. Too often, physicians cannot appropriately diagnose and treat those problems because the patients do not disclose their substance abuse. Patients' fear of revealing sensitive and potentially stigmatizing information and the omission of the topic of addiction in many physician training programs lead to suboptimal medical care.

To remedy this situation, NIDA has developed **NIDAMED**, the Institute's first comprehensive Physicians' Outreach Initiative. **NIDAMED** aims to integrate screening and treatment for the disease of addiction with mainstream medical care. A toolkit developed by **NIDAMED** guides doctors in assessing a patient's risk of developing an addiction problem, advising patients on the health effects of substance abuse and, if needed, arranging a referral to specialty care. The toolkit contains:

- **NIDA-Modified Alcohol, Smoking and Substance Involvement Screening Test (NM-ASSIST)**—This evidence-based instrument, available on an interactive Web site or in print, guides clinicians through a brief screening interview about use of addictive substances, including illicit drugs, prescription drugs taken for nonmedical purposes, tobacco, and alcohol.
- **Clinician's Resource Guide**—This accompanying online guide presents clinicians with more detailed instructions, directions on how to access further information on substance abuse, and comprehensive referral resources.
- **Screening Tool Quick Reference Guide**—This pocket-size resource summarizes the screening tool, risk levels, and followup actions.
- **Patient Information Card**—This postcard-size handout for physicians' waiting rooms encourages patients to "Tell Your Doctors About All the Drugs You Use" to get the best care and also offers Web links to more information.

Another critical component of **NIDAMED** is outreach to medical students, residents, and those who train them. Through a partnership with eight medical schools around the country, NIDA's Centers of Excellence for Physician Information provide innovative, science-based curriculum resources on substance abuse, addiction, and their health consequences.

Doctors can access the new tools at www.drugabuse.gov by clicking on the **NIDAMED** icon. The Institute also recently updated *Principles of Drug Addiction Treatment: A Research-Based Guide*, which summarizes more than three decades of research. In addition, a poster that encourages patients to disclose their drug use is available by calling 1-877-NIDA-NIH. NIDA is collaborating with the U.S. Health Resources and Services Administration, Food and Drug Administration, and New York City Health Department to place the poster in health clinics throughout the Nation. ■

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Some Teens Reporting Nonmedical Use of Prescriptions Develop Disorders

Dr. Li-Tzy Wu and colleagues at Duke University and the Pacific Institute for Research and Evaluation found that 1 percent of the 36,992 respondents age 12 to 17 to the 2006–2007 National Survey on Drug Use and Health (NSDUH) met the criteria for a diagnosis of abuse or dependence on opioid analgesics, which are prescription pain relievers. The teens reported one or more abuse symptoms—such as interference with school and home life, exposure to physical danger, and problems with family and friends—resulting from the nonprescribed use of these pain relievers; or they reported symptoms of dependence disorder—such as experiencing pain-reliever tolerance or withdrawal and giving up activities.

Seven percent of the NSDUH teen respondents reported that they had used prescription painkillers on a nonmedical basis during the past 12 months. Of this group, 7 percent met diagnostic criteria for abuse and 9 percent for dependence; another 20 percent had symptoms that did not reach the threshold for a diagnosis. The teens who misused painkillers had done so for

56 days, on average, in the year under review, and those who were dependent on the drugs had used them for 87 days. Girls were significantly more likely to become dependent on nonprescribed pain relievers than boys, a finding that the researchers suggest may reflect, in part, girls' greater tendency to share prescribed pain relievers with friends.

> *Journal of the American Academy of Child and Adolescent Psychiatry* 47(9):1020-1029, 2008.

Peer Interaction Enhances Adolescent Rats' Drug Reward

For adolescent rats, drugs are better with company, and vice versa. Given the opportunity to spend time in two cage compartments, young rats preferred the one in which they'd twice visited with a peer and also received a low dose of either nicotine or cocaine over the compartment that had furnished neither companionship nor a drug. In contrast, they showed no such partiality for a compartment in which they had previously received only companionship or only the low dose of drug.

Dosage mattered: Rats did gravitate to compartments where they had experienced either a higher dose of drug or more than two previous social opportunities. Dr. Janet Neisewander, graduate student Kenneth Thiel, and colleagues at Arizona State University say that their findings emphasize the importance of examining drug reward in a social context. Animal protocols that

include peer contact may more closely mimic early stages of drug abuse, which typically occurs in a group setting

> *Psychopharmacology* 204(3):391-402, 2009.

> *Drug and Alcohol Dependence* 96(3):202-212, 2008.



Stroop Test Identifies Patients at Risk for Treatment Dropout

The Stroop test, a widely available, easily administered assessment of a person's ability to screen out distractions and inhibit inappropriate responses, may predict which cocaine abusers are likely to drop out of therapy. In a study of 74 cocaine abusers, Dr. Chris Streeeter and colleagues at Boston University School of Medicine and Harvard Medical School found that Stroop scores predicted treatment retention better than addiction severity, symptoms of depression, or other clinical and demographic characteristics. The researchers suggest that programs might use the test to assign patients to appropriate treatment interventions and intensities.

The Stroop test measures the difference in response times between instances where the automatic response is appropriate and instances where that response must be

inhibited. In the Boston trial, this difference—of about 30 seconds, on average—was 24 percent greater among patients who dropped out than among those who completed therapy.

> *Neuropsychopharmacology* 33(4):827-836, 2008.

Genetic Overlap Between Substance Abuse and Bipolar Disorder

According to a recent literature analysis by Dr. Ranga Krishnan of Duke University Medical Center, more than half of people with bipolar disorder also have a substance use disorder. New findings suggest that genes contribute to this comorbidity. One-third of the genes that have been linked with bipolar disorder in four recent studies have also been associated with substance dependence, according to Dr. George R. Uhl and colleagues at the NIDA Intramural Research Program. The team analyzed data from comparisons of genetic profiles of European-Americans with and without bipolar disorder. Bipolar disorder was linked with 69 genes, and Dr. Uhl's team had previously tied 23 of those genes to risk for substance abuse (see "New Technique Links 89 Genes to Drug Dependence," *NIDA Notes*, Volume 22, Number 1). Variants of these genes may affect the two disorders directly and may also interact to increase vulnerability to one or both conditions.

> *American Journal of Medical Genetics: Part B Neuropsychiatric Genetics* 150B(2):182-190, 2009.

NIDA's Genetics Workgroup

Workgroup Directs Search for Genes That Influence Addiction

BY DEBRA P. DAVIS

NIDA Notes Associate Editor

About half of a person's risk for drug dependence resides in his or her genes, with the rest attributable to circumstantial and environmental factors. Genes influence vulnerability to drug abuse by affecting personality traits, physiological responses to drugs, frequency of drug use, and the neurobiological mechanisms of learning, memory, and behavior.

NIDA funds a robust research portfolio to identify the genes and genetic processes responsible for these effects. The ultimate objective is to uncover information and mechanisms that can be exploited to improve and personalize prevention and treatment of drug abuse and addiction.

NIDA's Genetics Workgroup is charged with overseeing and monitoring these efforts. Led by Dr. Jonathan Pollock, chief of NIDA's Genetics and Molecular Neurobiology Research Branch, the Workgroup comprises approximately 20 scientists representing all NIDA divisions. They meet monthly to review developments in the field and identify needs and opportunities for further research, then issue calls for grant proposals on promising approaches.

A Workgroup subcommittee, the NIDA Genetics Coordinating Com-

mittee (NGCC), oversees all genetic research involving human subjects, ensuring that it is designed to answer important questions and takes full advantage of collaborative opportunities within NIDA and with other parts of the National Institutes of Health (NIH). The NGCC, chaired by Dr. Joni Rutter, associate director of human population and applied genetics for the Division of Basic Neuroscience and Behavioral Research, also coordinates the work of the NIDA Genetics Consortium. This is a group of approximately two dozen investigators who conduct human subject studies.

Under an agreement with NIDA and NIH, Consortium scientists contribute blood and DNA samples collected during research, as well as clinical data, to an NIH repository; in exchange, they receive access to the repository's extensive collection. Scientists outside the Consortium can also gain access to the collection if they agree to share their own samples and data. The repository, which is located at Rutgers University's Center for Genetic Studies, has a collection of over 40,000 human DNA

Individuals with high-risk genes might have traits that make them likely to experiment with drugs or susceptible to drug effects that promote addiction.

samples. Information on ongoing studies and data from completed studies can be found at the Center's Web site (zork.wustl.edu/nida).

STAGES OF GENE IDENTIFICATION

The initial clue that some of the risk for drug abuse and addiction is inherited was the observation that the problems tend to run in families. NIDA-funded twin studies added support for the idea, by showing that siblings who share more genes are more alike in terms of developing or not developing a drug disorder. High-risk genes may make individuals more likely to experiment with drugs or susceptible to drug effects that promote addiction. Some high-risk genes may only manifest under certain conditions, such as familial abuse or neglect.

Early projects initiated and overseen by the Workgroup included studies of genes related to biological pathways known to play roles in drug addiction, such as the nicotine receptor and the dopaminergic neurotransmitter system. Comparisons of addicted versus nonaddicted individuals implicated specific DNA variations within such genes.

Researchers also studied genetically engineered animals to examine how their behavior changed when particular genes were turned off. For example, a NIDA-funded study found that disrupting a mouse's *Clock* gene increased its propensity to self-administer cocaine and seek out new experiences ("Manic Mice Show Heightened Sensitivity to Rewards," *NIDA Notes*, Volume 22, Number 4).

Although research on single genes has yielded important information, complex brain disorders such as substance abuse and addiction likely reflect convergent effects of many genes. New technologies are being exploited to

identify these genes and the ways their combinations and interactions may alter risk. The Workgroup is fostering research and analytic methodologies that capitalize on ongoing NIH-wide efforts such as the International Hap-Map Project (see hapmap.ncbi.nlm.nih.gov) and the 1000 Genomes Project (see www.genome.gov/27528684 and www.1000genomes.org).

Many projects apply the powerful technique of genome-wide association (GWA) scanning. Researchers simultaneously test thousands of individuals' DNA for hundreds of thousands of genetic variants that may correlate to drug abuse. "Through GWA studies, we are finding associations with specific genetic variants. Now, we need to understand their functions," says Dr. Rutter. This work is facilitated by databases that compile findings from many investigations of specific genes, their functions, and their links to disease. (see www.ncbi.nlm.nih.gov/gene).

For example, researchers are using GWA and other methods to compare the genetic profiles of smokers who have become dependent on nicotine with the profiles of those who have not. Of particular interest is a family of genes that determine the structure and functions of nicotinic acetylcholine receptors, to which nicotine attaches to produce many of its effects ("Studies Link Family of Genes to Nicotine Addiction," *NIDA Notes*, Volume 22, Number 6).

The Workgroup also funds studies on the related topic of epigenetics. Virtually every cell in the body contains the same genes, but the epigenome determines which genes are active in each cell at each moment in time. Chemical changes, such as methylation, determine the epigenome. Dr. Rutter uses a computer as an analogy: "The DNA is equivalent to the hardware and

MULTIFACETED VIEW NIDA's Genetics Workgroup calls for projects applying a wide range of methods.

Research Question	Examples of Approach
Does a particular trait have a genetic component?	Twin studies
Where in the genome are the genes that influence the trait?	Genetic marker study Genome-wide association study
What specific genes are involved?	Candidate gene study Fine mapping
How does the gene influence the organism?	Knock-out gene study
Does variation in the gene influence human health?	Clinical study
How does epigenetics influence gene expression?	DNA methylation Chromatin modification

the epigenome is akin to the software because it acts on top of the DNA to dictate changes in gene expression." She says, "If we can better understand how epigenetic changes take place, we can create better treatment approaches."

SHARING FOR OUTREACH AND ECONOMY

The Genetics Workgroup's mission includes keeping scientists up-to-date on advances in genetics as they apply to drug abuse. For example, last year the group sponsored a week-long course that drew 80 researchers from approximately 40 universities to learn about recent findings in the genetics of addiction. "The course introduced addiction researchers who lacked genetic expertise to experts in the field of genetics

of addiction," says Dr. Pollock, who organized the program. "It provided a networking opportunity for both the

"The DNA is equivalent to the hardware and the epigenome is akin to the software..."

—Dr. Joni Rutter

instructors and the participants." Slides and videos of the course may be viewed at drugabuse.gov/about/organization/Genetics/geneticsepigenetics/index.html.

In July 2009, the Workgroup sponsored the travel of nine junior investigators to the 50th Annual Short Course on Medical and Experimental Mammalian Genetics at the Jackson Laboratory in Bar Harbor, Maine. ■

■ GOOD BEHAVIOR GAME

[Continued from page 1]

of behaviors, such as sitting quietly, that will be rewarded. They then divide their classes into teams for the GBG. Later, when students are working independently, the teacher announces that the game is in play. Teams whose members maintain the stated behaviors during the game period receive prizes, such as stickers. Students who act out or commit other infractions incur a checkmark, lessening their teams' chances for prizes.

The game is played for brief intervals at first; the time and frequency are gradually lengthened as the children gain practice in controlling their behaviors. Eventually, to instill constant attentiveness to appropriate behavior, the teacher stops announcing when the game is in play and awards the prizes to successful teams only at the finish of a GBG period.

The GBG was devised in the 1960s by Harriet H. Barrish, Muriel Saunders, and Montrose M. Wolf at the University of Kansas. Its underlying concept is that team members, wanting to win, will pressure—and help—each other to meet the behavioral objectives.

“When kids come to school, they often don’t know how to behave like students. They have to be taught. It’s not intuitive, parents don’t always get it, and teachers aren’t being trained to deal with it,” says Dr. Kellam. “This is the issue the GBG attempts to address.”

And the stakes are high: Children who do not adapt to the student role early in their school careers risk rejection by peers, failure to achieve academically, and conflict with their teachers and other authority figures. The consequences of these problems in the teen years include increased risk for self-destructive and antisocial behaviors, Dr. Kellam explains.

Small-scale, more limited studies have provided evidence that the GBG might

alleviate behavioral problems in the early grades. The Baltimore project is the first randomized field trial of the GBG’s effectiveness, and the first to examine its impact on adolescent outcomes outside of school. Dr. Kellam notes that the participation of entire classrooms, representative of large areas of Baltimore, makes the results applicable across that city and perhaps similar ones.

LONG-RANGE BENEFITS

In 1985, Dr. Kellam and colleagues identified three to four schools in each of five demographically distinct neighborhoods, ranging in ethnicity from mostly African-American to mostly White and in economic status from very low to moderate income. Altogether, more than 1,000 children from 41 first-grade classes in 19 schools either used the GBG or served as controls in the study.

During the first weeks of school, teachers in both the GBG and the control classes assessed each student’s behavior; about 12 percent of the males and 3 percent of the females were classified as aggressive and disruptive. Teachers in the game-playing classrooms divided these high-risk students roughly equally among the teams.

The teachers using the GBG began by implementing the game for 10 minutes three times a week; they then increased its frequency and duration as the school year progressed. The same children continued to play the GBG or serve as controls through second grade. The game did not cut into instructional time because it took place when students were at their desks reading, completing work assignments, or engaging in other quiet activities.

About 15 years later, the researchers located and interviewed approximately 75 percent of children, now aged 19 to 21. The proportion of GBG alumni who reported a drug use disorder was 12 percent, compared with 19 percent among former con-

trols. The youths who played the GBG were also less likely to smoke, to report alcohol use disorder or antisocial personality disorder, or to have considered or attempted suicide.

The GBG was more advantageous to boys than to girls, except with respect to alcohol abuse, where the game’s impact was similar in both genders. The greatest benefits were realized by boys whose first-grade teachers classified them as aggressive and disruptive. Among these boys, 29 percent who played the GBG reported

MALES BENEFIT ACROSS THE BOARD

As they grew, boys who had participated in the Good Behavior Game in first and second grade in 1985–1986 used fewer social services than a control group.

	Game Players	Controls
School Services*	9%	14%
Mental Health or Medical Services	13%	18%
Drug Abuse Treatment	4%	9%
Social Services	1%	6%
Criminal Justice System	12%	20%

*For problems with behavior, emotions, drugs, or alcohol.

drug use disorder, compared with 68 percent of controls (see graph, page 1).

“We did not anticipate that a single intervention would have such a major impact,” says Dr. Kellam, who led the study. “The key to the GBG’s efficacy seems to be its effect on aggressive and disruptive boys. These are the kids who get sent to the principal’s office and eventually expelled, so these are the kids who most need help.”

Saving Money on Treatment and Social Services

By lowering teens' rates of smoking, substance abuse and addiction disorders, antisocial personality disorder, and suicidal tendencies, the Good Behavior Game (GBG) yielded economic dividends to public agencies that address those problems. Study recipients' self-reports and researchers' reviews of school and court records indicated that from first grade to age 19–21, GBG alumni, compared with controls, were assigned to fewer school-based services such as individual therapy or placement in special classrooms; they also has less involvement with juvenile and adult criminal justice systems.

The GBG's effect on males accounted for the entire reduction in service use. Roughly 25 percent of males who played the game received one or more services, compared with 38 percent in the control group. In contrast, among females about 19 percent of both players and controls received at least one service.

The greatest reduction was in the use of school services by males who were classified by their first-grade teachers as aggressive and disruptive. Among this group—who made up about 12 percent of all study participants—17 percent of those who played the game used school services, compared with 33 percent of those who did not play. “That’s twice the number of aggressive children that receive these expensive school services,” notes Dr. Jeanne Poduska, who oversaw the young-adult followup while employed by Johns Hopkins and has analyzed the service data while employed at the American Institutes for Research in Washington, D.C.

Dr. Poduska and colleagues propose an overall strategy of using the universal intervention in early grades, followed by more



targeted interventions for children who have persistent behavioral problems, and finally mental health treatment for an even more selective group.

Dr. Elizabeth Robertson, chief of prevention research in NIDA's Division of Epidemiology, Services and Prevention Research, says the report shows that behavioral training in the elementary grades can place students on a more productive course and reduce costs for a wide range of social programs. “It is an example of why early intervention makes sense from an economic standpoint,” she says.

SOURCE

Poduska, J.M., et al. Impact of the Good Behavior Game, a universal classroom-based behavior intervention, on young adult service use for problems with emotions, behavior, or drugs or alcohol. *Drug and Alcohol Dependence* 95 (Suppl.1):S29–S44, 2008.

TRAINING REQUIREMENTS

In 1986, the teachers who had implemented the GBG in their classrooms the previous year did so again with another cohort of over 1,000 first-graders. The teachers had received 40 hours of preliminary training plus mentoring during the first year, but none during the second year. Followup interviews when these children

were 19–21 years old revealed that the magnitude of reductions in smoking and drug abuse were not as great as they had been for the original 1985 cohort. According to the researchers, this falloff in efficacy of the GBG indicates a need for continued teacher mentoring and support.

The researchers have refined their training methods since 1985, but Dr.

Jeanne Poduska of the American Institutes for Research in Washington, D.C., continues to search for better ways to train and motivate teachers. “The question we’re trying to address is: What support does a teacher need to learn a new practice and sustain it over time?” Dr. Poduska says.

[Continued on page 9]

Young Opioid Abusers Benefit From Extended Buprenorphine-Naloxone Treatment

Despite shorter addiction histories, youths' risk of relapse following detoxification resembles that of adults.

BY LORI WHITTEN,
NIDA Notes Staff Writer

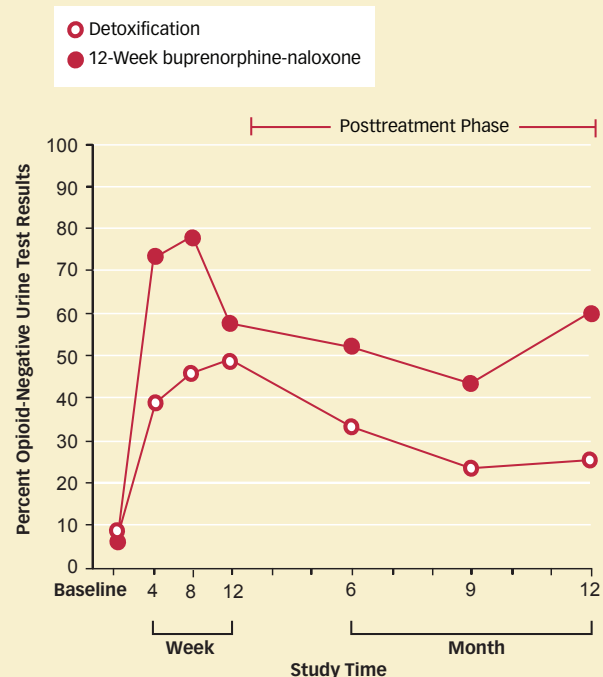
Opioid-addicted youths benefit from extended opioid maintenance therapy, reports NIDA's Clinical Trials Network (CTN). In a study by Dr. George Woody of the Delaware Valley Node of the CTN, the Penn/VA Addiction Treatment Research Center, and the Penn Center for AIDS Research in Philadelphia, participating 15- to 21-year-olds who received drug counseling and 12 weeks of therapy with buprenorphine and naloxone abused a wide range of drugs less often than others who received only counseling and a 2-week detoxification regimen.

Although buprenorphine-naloxone is an approved medication for people age 16 and over, until now clinicians have had little research to guide them on its use in teens and young adults. A common approach, offering only short-term medication and counseling to young people, is based partly on the expectation that youths, with their shorter duration of addiction, do not require extended medication-assisted treatment, as many adults do. However, the CTN findings suggest that risk of relapse following detoxification and the potential benefit of extended buprenorphine-naloxone therapy are similar in youths and adults. The findings are timely: Rates of opioid abuse among young people have risen during the past 10 years, increasing the need for effective treatments for this population.

The study included 152 outpatients from rural and urban community-based, CTN-affiliated treatment programs in Delaware, Maine, Maryland, New Mexico, and North Carolina. On average, the participants were 19 years old and had abused opioids for 1.5 years at the start of the study. Fifty-five percent primarily abused heroin, the majority by injection; about 35 percent primarily abused painkillers; and 10 percent abused multiple opioids. The researchers used randomization procedures to assign approximately equal numbers of

participants to receive either a detoxification treatment of 2 weeks of outpatient buprenorphine-naloxone (up to 14 mg/day for 3 days, followed by a tapering of the dose) or extended treatment of 12 weeks of buprenorphine-naloxone (up to 24 mg/day for 9 weeks, followed by dose tapering that ended in week 12). All patients were scheduled to receive their clinics' standard counseling interventions in one individual session and one group session

EXTENDED BUPRENORPHINE-NALOXONE TREATMENT HELPS YOUNG OPIOID ABUSERS Opioid-addicted 15- to 21-year-olds who received counseling and continued buprenorphine-naloxone for 12 weeks with a dose taper in weeks 9-12 abused fewer opioids than others who received counseling and a 2-week detoxification. They continued to submit more opioid-negative urine specimens throughout a year of follow-up.



per week for 12 weeks, with more sessions available if necessary.

The impacts of the two interventions diverged quickly. At the first assessment, 2 weeks after the end of the detoxification regimen, 74 percent of the participants in the extended-maintenance group and 39 percent of those who had received only detoxification submitted opiate-free urine samples (see graph above). A similar gap continued through week 8 but

narrowed to 57 percent versus 49 percent at the 12-week assessment and widened again to 60 percent versus 25 percent at the final assessment, which took place 1 year after the start of therapy. Extended therapy still yielded superior results at every assessment when the researchers tallied any missed visit as a positive urine sample. Patients in the extended therapy group also stayed in drug counseling longer, required less additional addiction treatment, reported less injection drug abuse, used less cocaine, and smoked less marijuana.

“The results of our study suggest that there is no hurry to stop providing buprenorphine-naloxone, an effective medication, regardless of a patient’s short duration of opioid abuse,” says Dr. Woody. “In my experience as a clinician, most opioid abusers—adolescent or adult—prefer to get off medication eventually. When to stop medication is an individual decision that depends on a patient’s

response to treatment, his or her commitment to achieving full remission without medication, and whether he or she has attained a sustained period of abstinence and a stable over-all living situation.”

Clinicians need additional long-term evaluation of opioid addiction treatments for young people—including intensive behavioral therapy, buprenorphine-naloxone, and the opioid-blocking medication naltrexone—to identify the regimens that are most effective over the long haul, Dr. Woody says.

Dr. Betty Tai, director of NIDA’s Center for Clinical Trials Network, says that Dr. Woody’s findings suggest that “extended treatment with buprenorphine-naloxone is safe and effective and expands the treatment options for

LONGER MEDICATION REGIMEN LEADS TO BETTER RESULTS Extended treatment with buprenorphine-naloxone improved retention in therapy and reduced abuse of several drugs by the 12-week assessment.

	Percentage of Detoxification Patients	Percentage of Extended-Therapy Patients
Dropped Out of Therapy	79	30
Abused an Opioid During the Past Week	55	38
Abused Marijuana During the Past Week	26	16
Abused Cocaine During the Past Week	12	2
Injected a Drug During the Past Month	33	16

adolescents and young adults who are addicted to opioids, including prescription painkillers.” ■

SOURCE

Woody, G.E., et al. Extended vs. short-term buprenorphine-naloxone for treatment of opioid-addicted youth: A randomized trial. *JAMA* 300(17):2003–2011, 2008.

■ **GOOD BEHAVIOR GAME**

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In addition to improving student outcomes, Dr. Kellam notes, the GBG gives teachers a method of managing classroom behavior. He says that many teachers find that their preparation for behavioral management is insufficient, and struggles with class behavior are a primary cause of teacher burnout.

Overall, the researchers conclude, their recent work supports “real optimism” that a single early, inexpensive intervention can improve a wide variety

of outcomes, especially for the children at highest risk. Dr. Kellam says that the study is the first to link a universal childhood intervention with reduced frequency of a psychiatric disorder.

Dr. Elizabeth Robertson, chief of prevention research in NIDA’s Division of Epidemiology, Services and Prevention Research, calls the study results “stunning.” She says, “What we are seeing is a change in the life-course trajectories of these kids as a result of putting them on the right path early on.” If the GBG were to be widely adopted in schools, she adds, the public health impact could be huge. ■

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Vouchers Boost Smoking Abstinence During Pregnancy

Benefits of therapy include improved fetal growth.

BY SHARON REYNOLDS,
NIDA Notes Contributing Writer

When obstetricians' advice was reinforced with voucher payments for not smoking, pregnant women attained much higher abstinence rates, a recent NIDA-funded clinical study found. In addition, the women who earned vouchers scored higher than a control group on two out of three measures of third-trimester fetal growth, a predictor of newborns' health. The pay-for-proof approach has helped patients addicted to smoking and other drugs in previous trials; it was adapted to motivate pregnant women and new mothers.

A LITTLE ADDED INCENTIVE

Dr. Stephen Higgins, Dr. Sarah Heil, and colleagues at the University of Vermont recruited 82 pregnant low-income smokers for a trial of voucher-based reinforcement therapy (VBRT). Originally developed to treat cocaine abuse, VBRT dispenses cash-value vouchers to patients when they meet objective criteria for treatment progress. The value of the voucher awarded mounts with each consecutive favorable test result but resets to the base amount if the patient fails to meet the assigned monitoring criterion. Patients exchange vouchers for retail goods of their choice.

"VBRT uses the same basic principle to treat dependence that's operative in producing dependence," explains Dr. Higgins, the developer of VBRT. "Whereas the rewarding effects of drugs reinforce

drug use, the rewards in the intervention reinforce abstinence from drug use."

In the Vermont study, the women chose a day, shortly after their recruitment, to stop smoking. To enhance motivation during the difficult early days of quit attempts, the researchers scheduled monitoring appointments daily for the first week after each woman's quit date. At these appointments, the women exhaled into a machine that measured levels of carbon monoxide, a component of cigarette smoke, in their breath. The 42 women randomized to VBRT received a voucher worth \$6.25 for their first carbon monoxide reading below 6 parts per million. Each successive time they met this criterion, the value of their voucher increased by \$1.25. A control group of 40 received vouchers worth \$15 for showing up for monitoring, regardless of the results. All women in both groups also received advice and encouragement to

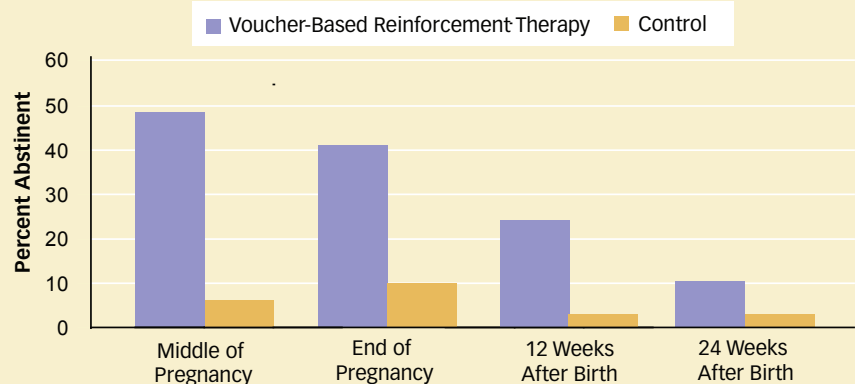
quit smoking from their obstetricians.

After the first week, the researchers changed the reward criterion. To earn vouchers, the VBRT women now needed to submit a urine sample containing less than 80 ng/ml of cotinine, a nicotine metabolite. This more exacting criterion required a longer duration of abstinence. The researchers also monitored the women only twice weekly and eventually reduced the visits to every other week. Each lengthening of the interval between monitoring sessions reduced opportunities for the women to earn vouchers and increased the relative importance of a session in terms of reward. After delivery, when women who quit smoking for their infants' sake might have been vulnerable to starting again, the monitoring interval was shortened to once a week for 4 weeks. From weeks 5 to 12 postpartum, the every-other-week monitoring schedule was resumed.

The women in the VBRT group main-

[Continued on page 13]

ABSTINENCE AT END OF PREGNANCY QUADRUPLES WITH VOUCHERS More women receiving voucher-based reinforcement therapy, compared with women in the control group, were not smoking at the end of their pregnancy and were abstinent 12 weeks after giving birth, when the intervention ended. However, the difference between the groups was smaller later.



Attention to Bipolar Disorder Strengthens Substance Abuse Treatment

Integrated group counseling improves outcomes in a difficult-to-treat dual-disorder population.

BY NIDA NOTES STAFF

Substance abuse compounds the problems of people with bipolar disorder. Individuals with this comorbidity get less benefit from their mood disorder treatment, recover more slowly from mood swings, spend more time in hospitals, and commit suicide more often. They also are less responsive to drug abuse treatment than noncomorbid individuals, but a new psychosocial intervention may partially alleviate this disadvantage. The intervention, called integrated group therapy (IGT), simultaneously focuses on substance abuse and bipolar disorder. In a recent NIDA-funded clinical trial, IGT reduced patients' substance use more than standard substance abuse group counseling did.

"People with these disorders often feel hopeless about ever getting better," says Dr. Roger D. Weiss, professor of psychiatry at Harvard Medical School and chief of the Division of Alcohol and Drug Abuse at McLean Hospital in Belmont, Massachusetts. "They often feel that no matter what they do, it doesn't help; so they may stop trying." Dr. Weiss and colleagues developed and tested IGT with support from NIDA's Behavioral and Integrative Treatment Development Program.

TESTING THE APPROACH

All of the study's 62 participants had both bipolar disorder and substance dependence, and all were taking mood-stabilizing prescription medications. The

majority had both alcohol and drug disorders; the most common primary drugs of abuse, in order of prevalence, were marijuana, cocaine, sedatives, and opioids. The researchers randomly assigned them to receive either IGT or standard, manual-based substance abuse counseling once per week in groups of six to eight. The two treatment groups did not differ in terms of patients' diagnostic categories, mood-stabilizer regimens, baseline substance use problems, or concurrent participation in individual counseling and 12-step programs.

The IGT intervention is based on a cognitive-behavioral therapy model for relapse prevention. In each session, patients reported on their previous week's substance use, mood swings, medication adherence, and high-risk situations. Clinicians addressed the connections between bipolar disorder and substance abuse, covering topics such as methods to deal with depression without using alcohol or illicit drugs.

In the standard group drug counseling format, sessions began with patients' reports on substance use and craving. These groups focused primarily on sub-

stance use without providing explicit references to bipolar disorder signs or symptoms. When patients raised mood-related issues, counselors responded briefly and referred them to the physicians who had prescribed their mood-stabilizing medications. Counselors responded to mood-related emergencies, however, with clinically appropriate interventions.

During the 20-week trial, recipients of both therapies reduced their alcohol and illicit drug use as assessed by urine toxicology and self-reports (see table). The IGT group showed greater reductions, and those in the group who achieved a month-

PEOPLE WITH BIPOLAR DISORDER REDUCE SUBSTANCE USE MORE WITH INTEGRATED GROUP THERAPY

	IGT *	Drug Counseling
Average days of substance use per month		
Before group therapy	10.2	13.3
During group therapy	5.3	10.0
During the 3 months after group therapy	6.0	12.0
Average days of alcohol use per month		
Before group therapy	9.3	7.8
During group therapy	4.4	6.5
During the 3 months after group therapy	4.5	7.8
Average days of illicit drug use per month		
Before group therapy	6.7	9.7
During group therapy	2.1	5.2
During the 3 months after group therapy	3.4	6.5
*Integrated Group Therapy		

Community-Friendly Version of Integrated Group Therapy Shows Promise

Although their research demonstrated that integrated group therapy (IGT) can foster recovery in abusers with bipolar disorder, a group of Massachusetts scientists recognized barriers that might prevent community programs from adopting the treatment. Now, they report that during a 12-week study, patients who received a modified IGT therapy, designed especially for delivery in community addiction treatment programs, were nearly twice as likely as those in standard drug counseling to attain 1 month of abstinence from illicit drugs and alcohol and nearly three times as likely to abstain for the entire period.

Dr. Roger D. Weiss, professor of psychiatry at Harvard Medical School and chief of the Division of Alcohol and Drug Abuse at McLean Hospital in Belmont, Massachusetts, and colleagues made three major changes in their IGT treatment:

- To increase the likelihood of insurance reimbursement, they decreased therapy from 20 to 12 group sessions.
- Rather than using counselors with experience in both substance abuse and psychiatric disorder treatment, the modified IGT program was delivered by addiction counselors who had received general information on bipolar disorder and the cognitive-behavioral therapeutic approach but who had little experience in these areas.
- Rather than participating as a single group for a pre-defined 12-week period, patients could join ongoing group therapy at any time, which is the usual practice in most community treatment programs.

All of the new study's 61 participants were taking mood-stabilizing medications. They were randomly assigned to one of two treatment groups and further divided into groups of six to eight members led by clinicians who provided either the modified IGT or standard, manual-based substance abuse counseling.

Both treatments helped patients reduce their days of substance use. Comparing results from the month before treatment began to the last month of treatment, drug use dropped from 18.6 days to 4.4 days in the modified IGT group and from 17.9 days to 6.5 days in the group receiving standard drug counseling. Of the patients who received modified IGT, 71 percent attained at least 1 month of abstinence from both drugs and alcohol during treatment, compared with 40 percent of those in standard group drug counseling. Modified-IGT patients also achieved their first month of abstinence sooner than those in group drug counseling. Moreover, 36 percent of the men and women who participated in modified IGT were abstinent throughout all 3 months of treatment, compared with only 13 percent of the patients in standard counseling.

About 70 percent of patients reported depression, mania, or a mixture of the two during treatment. Patients receiving modified IGT, however, were more than twice as likely as those in group drug counseling to be abstinent and to report no mood disorder episode during the final month of treatment.

"If the findings are borne out in future studies with larger numbers of patients, community addiction treatment programs could benefit from adding modified IGT to mood-stabilizing pharmacotherapies for people with co-occurring substance abuse and bipolar disorders," says Dr. Lisa Onken, chief of NIDA's Behavioral and Integrated Treatment Branch. "This approach might not only improve outcomes in this difficult-to-treat group but also do so in a community-friendly way," she adds.

SOURCE

Weiss, R.D., et al. A "community-friendly" version of integrated group therapy for patients with bipolar disorder and substance dependence: A randomized controlled trial. *Drug and Alcohol Dependence* 104(3):212-219, 2009.

long period of abstinence did so earlier than participants in the standard counseling group. In the 3 months following the therapy, substance use remained lower in the IGT group but returned to baseline levels in the standard counseling group.

Alcohol use dropped more than illicit drug use in both groups. This result may reflect the greater severity of the patients'

alcohol problems. "There was more room for improvement and perhaps greater motivation among patients to address their drinking," Dr. Weiss says.

Although IGT focuses on mood disorders as well as substance abuse, IGT group members experienced mood disorder episodes as frequently during and after treatment as they had before. In fact, they also

received higher scores on two measures of mood symptoms than did members of the drug counseling groups. "It is unclear whether this reflects true mood differences or an increased awareness among IGT participants of mood symptoms more subtle than those that cause a bipolar episode," Dr. Weiss says. He notes that IGT encourages early recognition of mood

changes, and he suggests that reduced substance use may temporarily worsen mood in people with bipolar disorder.

APPRECIATION AND ENGAGEMENT

According to Dr. Weiss, the participants in the IGT group appreciated having a treatment program tailored to their needs. “Many of our people had bounced back and forth between specialty programs for substance abuse and bipolar disorder, and in each program they felt that only some of their issues were being addressed,” Dr. Weiss says.

Twelve study participants dropped out of therapy. When Dr. Weiss and colleagues analyzed the characteristics of these 12

dropouts, they were surprised to find that 11 were smokers. (Of the 49 participants who completed the study, 24 were smokers.) The researchers say that smokers with bipolar disorder may represent a subgroup that requires special efforts to engage in substance abuse treatment.

“IGT shows a lot of promise,” says Dr. Lisa Onken, chief of NIDA’s Behavioral and Integrative Treatment Branch. “Before Dr. Weiss and his colleagues began their work, we had many questions about how to treat people with bipolar and substance abuse disorders. The finding that IGT reduces days of substance use disorder indicates that this program is a meaningful step in the right direction.

“In addition, because IGT is group therapy, it’s more likely to be used in community drug treatment centers, providing more individuals with comorbid bipolar and substance use disorders access to an evidence-based treatment that was designed specifically for their needs,” Dr. Onken adds. ■

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VOUCHERS

[Continued from page 10]

tained abstinence for 9.7 weeks of their pregnancy, on average, compared with 2.0 weeks in the control group. Forty-one percent of the VBRT women but only 10 percent of the control group were abstinent at their last assessment before giving birth. Twenty-four percent of women in the VBRT group sustained abstinence throughout the entire third trimester of pregnancy, compared with only 3 percent of women in the control group. The clinic’s outlay for vouchers to the women in the VBRT group averaged \$461 per participant and ranged from \$0 to \$1,180.

MORE ROBUST FETAL GROWTH

The researchers obtained ultrasound measurements in the 30th and 34th weeks of 57 women’s pregnancies to ascertain whether VBRT also promoted fetal growth. While previous studies found correlations between smoking abstinence, greater fetal growth, and higher neonatal birth weight, experimental evidence of the relationship has been considered weak.

The ultrasound results showed greater fetal growth in the 29 women in the VBRT group, compared with the 28 women in

the control group. “It’s known that smoking retards fetal growth, but demonstrating that a treatment actually increases growth is pretty rare,” says Dr. Higgins.

“These findings are quite exciting, providing promising preliminary evidence of an association between higher abstinence rates in the third trimester and greater fetal growth,” says Debra Grossman of NIDA’s Division of Clinical Neuroscience and Behavioral Research. “In addition to the health benefits observed, VBRT may also provide cost savings, given the high medical costs for infants associated with maternal smoking.”

Although the success rate for this intervention was high relative to conventional therapies, Dr. Higgins notes that 59 percent of the women who received VBRT continued to smoke throughout their pregnancies. The researchers are currently testing whether offering greater rewards at the start of the intervention or making changes in the voucher schedule could help more women quit. “Based on what we know from our research and that of other researchers in the field, the amount of the reward for changing behavior matters a lot,” says Dr. Heil.

Dr. Higgins notes that there is not

likely to be a one-size-fits-all approach to quitting smoking during pregnancy. “We anticipate needing an array of interventions tailored to these women,” he says.

The impressive increase in abstinence among women in the VBRT group during pregnancy dropped by 24 weeks postpartum: 8 percent remained abstinent, compared with 3 percent of the control group. However, an earlier study by these investigators using the same conditions showed a bigger disparity: 27 percent of women in the VBRT group remained abstinent at 24 weeks postpartum compared with none in the control group.

Although abstinence may have been short-lived, VBRT benefits were substantial, especially in terms of fetal health. “Even if the effects only lasted while the intervention was in place, that would be a good thing for these women and their babies,” Dr. Higgins concludes. ■

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Dr. Phil Skolnick Now Leads NIDA's Medications Development Efforts



Dr. Phil Skolnick has joined NIDA as director of the Division of Pharmacotherapies and Medical Consequences of Drug Abuse. Dr. Skolnick, who has extensive experience in corporate and academic drug research, will lead a NIDA team that stimulates and conducts all phases of medications development and supports

clinical trial infrastructure.

"We are delighted to have Dr. Skolnick join our team of scientists looking for solutions to the management of drug addiction," says NIDA Director Dr. Nora D. Volkow. "His many remarkable years of innovation and leadership in both public and private research arenas will strengthen our complex medications development process and enhance our search for pharmacotherapeutic and immunological treatment agents."

Prior to joining NIDA, Dr. Skolnick was a research professor of psychiatry at New York University Langone Medical Center. He served as Chief Scientific Officer at DOV Pharmaceutical, Inc., from 2001 to 2009 and led the discovery and development of compounds that may ultimately help treat a variety of neuropsychiatric disorders. Dr. Skolnick's appointment marks a return to the National Institutes of Health, which he first joined in 1972 as a staff fellow and in which he later held various leadership positions in neurobiology and neuroscience. Dr. Skolnick left government service in 1997 when he accepted a position in the private sector at Eli Lilly.

"I am delighted to return to the NIH community, which was a wonderful professional home for 25 years," says Dr. Skolnick. "My new position at NIDA will enable me to take what I have learned in the private sector about medications development and apply it to the challenging field of drug abuse and addiction."

How-To Guides Provide Tips for Publishing Addiction-Related Articles

Students and practitioners of addiction science who are interested in publishing their studies in scholarly journals can find tips for doing so in a book and online tutorial developed by the International Society of Addiction Journal Editors (ISAJE). The book and related tutorial are targeted to graduate students,

postdoctoral fellows, young investigators, and others who are new to publishing.

The tutorial, partly funded by NIDA and the World Health Organization, is accessible at www.parint.org/tutorial.cfm. Each of its 10 modules is based on one or more chapters from the book, *Publishing Addiction Science: A Guide for the Perplexed, 2nd Edition*. Chapter topics range from how to choose a journal to how to avoid the "seven deadly sins of scientific publishing." One chapter, devoted to the special challenges faced by researchers from developing and non-English-speaking countries, discusses ways these researchers can improve their chances of publishing in English-language journals and determine when the public interest is best served by publishing in their local languages.

The book can be read or downloaded at no charge from www.parint.org/isajewebsite/isajebook2.htm. Hard copies of the book can be ordered from Multi-Science Publishing Company, Ltd., 5 Wates Way, Brentwood, Essex CM15 9TB, United Kingdom; fax: +44(0)1277 223453; www.multi-science.co.uk/addiction-science.htm. ISAJE is a London-based international organization devoted to improving the quality of publishing in addiction and related sciences, particularly in the areas of publication ethics and research integrity.

James A. Inciardi (1939–2009)

Dr. James A. Inciardi, founder and co-director of the Center for Drug and Alcohol Studies and professor of sociology and criminal justice at the University of Delaware, died on November 23 after a long battle with cancer. A pioneer of drug abuse and criminal justice research, Dr. Inciardi's research influenced policy and program development in these fields.

Before receiving his doctorate in sociology in 1973, Dr. Inciardi worked as a jazz drummer and a New York City parole officer. As a researcher, he conducted seminal studies on the link between drug abuse and criminal activity and developed therapeutic interventions for criminal offenders—work that formed a treatment model now used internationally. His research on the connection between drug abuse and HIV infection and transmission, and later on interventions for people at high risk of the infection, led to programs in probation and community settings. Until his death, Dr. Inciardi continued working on studies of prescription drug abuse, approaches to case management for vulnerable women, and a new ethnography of drug abuse in Brazil. He published over 500 articles, chapters, books, and monographs and was a fellow of the American Society of Criminology.

Reality Videos Bring NIDA Scientists to Web Site for Teens

In fast-moving, 2-minute video clips on NIDA's Web site for teens, NIDA staff scientists pause in the midst of various recreational activities to speak about the dangers of drug abuse. In NIDA's version of reality television, accessible at teens.drugabuse.gov/new_media/video.php:

- **Dr. Redonna Chandler** and **Dr. Gaya Dowling**, while shooting pool, react to a cloud of cigarette smoke left behind by a poolroom patron. Dr. Chandler asks the viewer, "Did you know that nicotine is one of the most widely used addictive drugs?" A title card pops up displaying the information that 60 percent of smokers report starting before age 18. "That's scary because teens respond differently to nicotine than adults do," Dr. Dowling says as she sets up a shot. "And that's why it could be harder for you to quit," she adds, driving the eight ball into the pocket. The two scientists continue to provide information in the course of their play and conversation.
- **Dr. Ruben Baler**, attired in sweats, works out at a gym. "Steroids can weaken your body's ability to defend against germs and diseases," Dr. Baler tells the viewer as he lifts and lowers a barbell. "The fact is that, after a while, people on steroids can become aggressive or even depressed . . . but that's not all. If you're a guy, steroids can lower your testosterone levels, reduce your sperm count, and even shrink your testicles." He winces in pain at the thought. This video is presented in both English and Spanish.
- **Dr. Joe Frascella**, while perusing snack bar offerings in a movie theater, contrasts the depiction of marijuana in many films with the drug's real dangers. Taking his seat, he tallies the drug's potential adverse effects, including addiction.
- **Dr. Cindy Miner** and **Dr. Joni Rutter** duel as pitcher and batter on a softball field. A beanball prompts discussion of the value of painkillers when prescribed by a doctor versus their potential consequences when taken otherwise.

The site also features longer videos of NIDA Director Dr. Nora D. Volkow answering students' drug-related queries at a Harlem, New York, high school and responding to questions from their parents about how and when to talk with kids about drugs.

The NIDA for Teens Web site (teens.drugabuse.gov) is designed to appeal to youth between ages 11 and 15 and to be useful to teachers and parents. Visitors can choose from many features and activities, including:

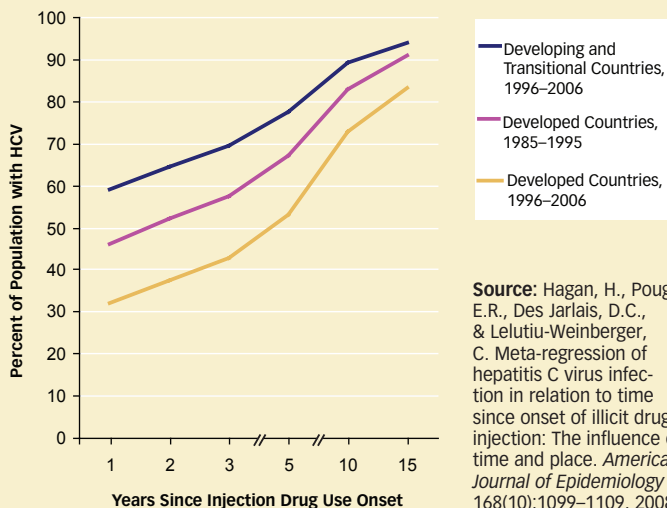
ONLINE VIDEOS INFORM STUDENTS AND PARENTS ABOUT DRUG ABUSE In the "New Media" section of NIDA's Web site for teens, Dr. Ruben Baler of NIDA's Office of Science Policy and Communications speaks to teens as he works out (top frame), and Harlem students and their parents pose questions to NIDA Director Dr. Nora D. Volkow (bottom frame).



- Detailed answers to frequently asked questions about how common drugs of abuse affect the brain and body.
- Stories from teens who have experienced or witnessed the devastating effects of drugs and addiction.
- Word games and multimedia activities that test knowledge of drug abuse and addiction.

Teens can download freebies from the site as well, such as sticker designs, T-shirt iron-ons, and computer icons. The site also provides links to Facebook, other social networking sites, and NIDA's home page, www.drugabuse.gov. In addition, teachers will find downloadable quizzes to test their students' knowledge of drugs and their effects.

Injection Drug Users Acquire Hepatitis C Infection Later in Developed Countries



Source: Hagan, H., Pouget, E.R., Des Jarlais, D.C., & 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. *American Journal of Epidemiology* 168(10):1099-1109, 2008.

The typical time from onset of injection drug use to infection with hepatitis C virus (HCV) in developed countries has lengthened, according to a recent analysis. In the decade 1985 to 1995, nearly 70 percent of injection drug users acquired the virus within 5 years of starting to inject, and about 90 percent were infected after 15 years. In the following decade, only 50 percent were infected 5 years after their initial injections, and less than 85 percent at 15 years. This lengthening time to infection corresponds with the expansion of prevention efforts in developed countries, suggesting that expanded access to drug treatment and programs such as needle exchanges are having an effect on HCV transmission.

In developing and transitional countries, where public health resources are more limited, the onset of HCV infection was more rapid among people who began injecting illegal drugs between 1996 and 2006 than in developed countries even a decade before. Percentages are projections based on data from 72 studies conducted as part of the HCV Synthesis Project, a NIDA-funded effort to summarize research on HCV prevalence around the world.

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