**National Institute on Drug Abuse**

# Director's Report

**to the**

**National Advisory Council on Drug Abuse**

**September, 2000**

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**National Institute on Drug Abuse**

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**September, 2000**

# Research Findings

## Basic Research

### Separate Neural Circuits in the Nucleus Accumbens Encode Information About Cocaine Versus Natural Reward

Considerable experimental evidence has implicated the nucleus accumbens as a key brain structure mediating information about the reward value of drugs and other reinforcing stimuli such as food, water, and sexual behaviors. Do drugs activate the same neural circuits regardless of the type of reward, or do separate circuits encode information about different types of rewards? Dr. Regina Carelli and her associates at the University of North Carolina recorded neuronal activity in the n. accumbens of rats as they pressed a lever for either of two natural reinforcers, food and water, or for either food or water paired with intravenous self-administered cocaine. In the rats responding for food or water only, many neurons were phasically active during various phases of the task. Most of the responding neurons showed a similar activity pattern for each of the two natural reinforcers. In contrast, in the n. accumbens of the rats rewarded with water and cocaine, very few of the phasically active neurons responded in a similar way to the two reinforcers, i.e. most cells responded selectively to either water or cocaine, but not both. Similar results were obtained from rats trained with food and cocaine. These findings indicate that in the well-trained animal, cocaine activates a neural circuit in the n. accumbens that is largely separate from the circuit that processes information about food and water reward. These results are consistent with studies showing that selective lesions or pharmacological manipulation of the mesolimbic system can alter cocaine self-administration but will leave operant responding for natural reinforcers relatively unaltered. These results underscore the possibility that pharmacotherapies for cocaine addiction can be developed that leave natural reward systems and consummatory behaviors intact. Carelli, R.M., James, S.G., and Crumling A.J. Evidence that Separate Neural Circuits in the Nucleus Accumbens Encode Cocaine Versus "Natural" (Water and Food) Reward. Journal of Neuroscience, 20, pp. 4255-4266, 2000.

### Morphine-6beta-Glucuronide Antagonist 3-O-Methylnaltrexone Antagonized Heroin and Morphine Self-Administration in Rats

In mice, 3-O-methylnaltrexone, a morphine-6beta-glucuronide antagonist, blocks the analgesic actions of morphine-6beta-glucuronide and heroin at doses that are inactive against morphine. Dr. Pasternak and his colleagues found a similar selectivity in rats. 3-O-methylnaltrexone antagonized the analgesic actions of 6-acetylmorphine in Sprague-Dawley rats and heroin in Wistar rats at doses that were inactive against morphine. Inclusion of a fixed dose of 3-O-methylnaltrexone significantly shifted the analgesic dose-response curves for 6-aceylmorphine and heroin without altering the morphine dose-response curves. In a self-administration model, 3-O-methylnaltrexone treatment significantly increased both heroin and morphine intake during the first hour, suggestive of an antagonist effect. This effect at doses of 3-O-methylnaltrexone that were inactive against morphine analgesia implied a role for the morphine-6beta-glucuronide opioid receptor in the reinforcing properties of heroin and morphine. Walker, J.R., King, M., Izzo, E., Koob, G.F., and Pasternak, G. Antagonism of Heroin and Morphine Self-Administration in Rats by the Morphine-6beta-Glucuronide Antagonist 3-O-Methylnaltrexone. Eur. J. Pharmacology, 383(2), pp. 115-9, 1999.

## Local Administration of Opioid Agonists Attenuates Capsaicin-Induced Thermal Hyperalgesia

Dr. Woods and his research team at the University of Michigan have conducted work characterizing capsaicin-induced thermal hyperalgesia in rats and evaluating the hypothesis that local administration of either mu or kappa opioid agonists (fentanyl and U50,488, respectively) can attenuate capsaicin-induced nociception. Capsaicin dose-dependently produced thermal hyperalgesia in the rat tail-withdrawal assay. Co-administration of either fentanyl or U50,488 with capsaicin attenuated capsaicin-induced hyperalgesia in a dose-dependent manner. This local antinociception was antagonized by small doses of an opioid antagonist, quadazocine, applied to the tail. However, the locally effective doses of quadazocine, when applied to the back near the scapular region did not antagonize either fentanyl or U50,488. It is therefore concluded that activation of peripheral mu or kappa opioid receptors, in this experimental pain model, can attenuate capsaicin-induced thermal hyperalgesia. These data also support the notion that peripheral antinociception can be achieved by the local administration of analgesics into the injured tissue without producing central side effects. Ko, M.C.H., Tuchman, J.E., Johnson, M.D., Wiesenauer, K. and Woods, J.H. Local Administration of Mu or Kappa Opioid Agonists Attenuates Capsaicin-Induced Thermal Hyperalgesia via Peripheral Opioid Receptors in Rats. Psychopharmacology (Berl), 148(2), pp. 180-185, 2000.

## Regulating Cellular Receptors

The delta-opioid receptor is a G-protein coupled receptor that is implicated in the development of morphine tolerance and is found in brain regions associated with reward, motivation, and response to abused drugs. University of California, San Francisco researcher Dr. Mark von Zastrow and his student, Patricia Tsao, are studying the regulation of the delta-opioid receptor and other G-protein coupled receptors on the cellular level. In a recent article, they demonstrated that, when expressed in tissue culture cells, the delta-opioid receptor is down regulated by a novel membrane trafficking mechanism in response to even a brief application of agonist. After agonist-induced endocytosis, the delta-opioid receptor is sorted into a non-recycling pathway, leading to protein degradation. Native delta-opioid receptors expressed in brain tissue exhibit significant agonist-induced down regulation, suggesting that this new membrane trafficking pathway has physiological relevance and may mediate, in part, the long-term actions of agonist drugs. Tsao, P.I. and von Zastrow, M. Type-Specific Sorting of G Protein-Coupled Receptors After Endocytosis. J. Biol. Chem., 275, pp. 11130-11140, 2000.

## Functional Imaging of Cocaine-Induced Brain Activation in Rats

Cocaine exerts a complex set of effects on the central nervous system, in part through stimulation of dopaminergic neurotransmission within brain cortical and subcortical limbic structures. To elucidate the anatomic and temporal patterns of regional brain activation following cocaine administration in rats, Dr. Barry Kosofsky and his colleagues at Massachusetts General Hospital performed functional MRI (fMRI). During the course of brain activation in rats that had never been exposed to drugs, cocaine produced anatomically distinct regional differences. Using a selective antagonist, the researchers demonstrated that the D1 dopamine receptor plays an important role in mediating the cocaine effects seen by fMRI. These data affirm the relevance of the rat model system in the study of the cellular and molecular bases of cocaine-induced brain activation in drug addicts. Marota, J.J.A., Mandeville, J.B., et al. Cocaine Activation Discriminates Dopaminergic Projections by Temporal Response: An fMRI Study in Rat. NeuroImage, 11, pp. 13-23, 2000.

## Neuronal Nicotine Acetylcholine Receptor Populations

In a recent report by Drs. Allan Collins and Michael Marks, a subpopulation of nicotine acetylcholine receptors in mouse brain has been better defined by the use of the ligands epibatidine and a neurotoxin known as alpha-conotoxin MII. Alpha-conotoxin MII, a naturally occurring ligand isolated from the snail, was labeled with iodine-125 for autoradiographic and binding experiments, and used in competition with tritiated and unlabeled cytisine, nicotine, alpha-bungarotoxin, and epibatidine. The distribution of labeled alpha-conotoxin MII was highest in the mouse brain regions of the geniculate nucleus, olivary pretectal nucleus, and in the zonal layer of the superior colliculus. As an antagonist, alpha-conotoxin MII was a weak inhibitor of nicotine and alpha-bungarotoxin, generally believed to bind at alpha4beta2 or alpha7 receptor populations, respectively. The distribution of tritiated epibatidine was determined in various mouse brain regions, many of which are believed to correspond to cytisine-sensitive alpha4beta2 populations. There are, however, other regions to which epibatidine binds even in the presence of excess cytisine (i.e., cytisine-resistant locations) and these could be divided into those that were sensitive and those that were relatively insensitive to alpha-conotoxin MII. Since both of these latter regions were found to contain alpha3 messenger RNA, the tentative assignments for alpha-conotoxin MII binding regions have been proposed as alpha3beta2 and alpha3beta4 subunits of the neuronal acetylcholine receptors. Whiteaeker, P., McIntosh, J.M., Luo,

S., Collins, A.C., Marks, M.J., Molecular Pharmacology, 57, pp. 913-925, 2000.

### In Utero Cocaine Exposure Affects the Respiratory System

Dr. Immanuela Moss and her associates recently reported on the role of endogenous opioid systems, specifically met-enkephalin, in the attenuation of respiration by repeated prenatal cocaine exposure. These investigations were designed to delineate the contribution of met-enkephalin, an endogenous opioid peptide, in the attenuation of cocaine-induced respiratory and arousal responses in six- to seven-day-old and in 20- to 21-day-old piglets. In both age groups, prenatal exposure to cocaine increased met-enkephalin immunoreactivity in the respiratory- and arousal-related medullary regions. These findings support the investigators' hypothesis of a modulatory role of met-enkephalin in the normal development of respiratory control and an involvement of this peptide in the attenuation of respiration by repeated prenatal cocaine exposure. Liu, J-K., Laferriere, A. and Moss, I.R. Brain Research Bulletin. 51, pp. 419-424, 2000.

### Candidates for the Genetic Basis for Individual Differences in Sensitivity to Cocaine-Induced Seizures

Quantitative trait loci (QTL) studies are used to determine the number and chromosomal location of genes involved in complex behaviors that are influenced by more than one gene. Seizures are a well-known but poorly understood consequence of human cocaine abuse, particularly with respect to individual differences in susceptibility. In rodent models, sensitivity to cocaine seizures is strongly influenced by genotype. For example, several studies have reported significant differences between the C57BL/6 (B6) and DBA/2 (D2) inbred mouse strains in their sensitivity to cocaine-induced seizures. These findings prompted Dr. Belknap and his colleagues to undertake a QTL study of cocaine-induced seizures in two populations derived from the C59BL/6 and DBA/2 mouse strains. Three QTLs emerged as significant ($P<0.00005$): one for clonic seizures on chromosome 9 (distal), and two for tonic seizures on chromosomes 14 (proximal to mid) and 15 (distal). Two additional QTLs emerged as suggestive ($P<0.0015$), both associated with clonic seizures on chromosomes 9 (proximal) and 15 (distal). Both QTLs on chromosome 9 were sex-specific, with much larger effects on the phenotype seen in females than in males. The results suggest that different types of seizures have both common and distinct underlying mechanisms, and that there are a variety of factors that may account for individual differences in seizure sensitivity. Some of the QTLs were located in regions of the chromosomes that have been identified as QTLs for other seizure types such as a mouse model of epilepsy. Some of these chromosomal regions are also known to contain nervous system-relevant genes such as those for the dopamine D2 receptor, the serotonin 1B receptor, various glutamate receptors, and ion channel genes. These candidate genes can now be used as the basis of studies on the physiology of cocaine-induced seizures. Hain, H.S., Crabbe J.C., Bergeson, S.E., Belknap, J.K. Cocaine-Induced Seizure Thresholds: Quantitative Trait Loci Detection and Mapping in Two Populations Derived from the C59BL/6 and DBA/2 Mouse Strains. Journal of Pharmacology and Experimental Therapeutics, 293, pp. 180-187, 2000.

### Prenatal Exposure to Cocaine Can Affect the Outcome of Serotonin Receptor Stimulation in the Brains of the Offspring When They Are Tested As Adults

Dopamine normally inhibits the activity of cholinergic neurons in the striatum, and this inhibition is an important aspect of the control of motor activity. However, the activity of the dopamine-containing neurons is regulated by serotonergic activity at the 5HT3 receptor site, the only serotonin receptor of the 17 identified thus far that is an ion channel. The application of a 5HT3 agonist normally limits the release of acetylcholine in a dose-dependent manner. However, prenatal exposure to cocaine alters this relationship in female, but not in male rats. Denise Jackson and her colleagues treated rat mothers with 20 mg/kg of cocaine or saline solution (the control) twice daily from embryonic days 15 to 21 (day of birth). The rats were tested as adults (postnatal days 80-120). Both males and females (at two times in the estrous cycle) that had been treated with saline in utero showed the expected inhibition of cholinergic activity after graded doses of a 5HT3 agonist were applied to the neurons; however, females in diestrus, a relatively quiescent period during the rodent estrous cycle, were much less sensitive to the lower doses of the agonist. This is important because it demonstrates a functional difference in the brains of females given cocaine prenatally; a difference that is apparent in adulthood. The data also suggest that estrogen may modify the response, as animals in the phase of the cycle when estrogen is high did not display this deficit. This result suggests that persistent modification of the dopaminergic system has occurred as the cholinergic output is altered, and suggests that other parts of the mesocorticolimbic dopamine system may be functionally altered, possibly including regions that control motor activity and the perception of reward. Bolanos, C.A., Trksak, G.H., Glatt, S.J. and Jackson, D. Synapse, 36, pp. 1-11, 2000.

### Two Recent Articles Demonstrate That Opioids/Cannabinoids Are Important in Regulating

## the Basic Comunicators (Cytokines and Chemokines) of Immune Function

This basic link of these endogenous 'drug' systems with basic elements of immunity are important in both the understanding of basic immune function as well as in understanding disease (e.g. HIV infection) modulation by abused drugs.

**1) Regulation of Cytokine and Chemokine Receptors by Opioids**
Endogenous and exogenous kappa-opioid agonists have been widely reported to modulate the immune response. Published results of L. Zhang et. al. show that the superantigen-induced proliferative response of thymocytes is inhibited by the selective kappa-opioid agonist (U50,488H). Previous work has established that the kappa-opioid receptor is widely expressed within the thymus; however, little is known about the role of the kappa-opioid receptor in the function of thymocytes. Zhang et. al. measured detectable levels of the cytokines IL-2, IL-4, IL-5, IL-13, and IFN-gamma, and the chemokines, lymphotactin and RANTES, in stimulated thymocyte cultures; however, addition of U50,488H did not alter the expression of these cytokines. Examination of cytokine receptor expression by these thymocytes revealed a significant inhibition in the expression of the transcript For the IL-7 receptor alpha-chain (IL-7R alpha), and these results were confirmed by flow cytometry. Surprisingly, the expression of several other cytokine receptor chains including the common gamma-chain, IL-2R beta, or the IL-2R alpha, IL-4R alpha, and IL-15R alpha chains, was not altered. In contrast to these results, a significant elevation in the expression of the chemokine receptor CCR2 was observed in U50,488H-treated cultures. These results suggest that the kappa-opioid receptor may function to promote cellular migration at the expense of the sensitivity to the growth-promoting/maturation activity of IL-7. Zhang, L and Rogers, T.J. Kappa-Opioid Regulation of Thymocyte IL-7 Receptor and C-C Chemokine Receptor 2 Expression. J. Immunology, 164, pp. 5088-5093, 2000.

**2) Regulation of Cytokine Systems by Cannabinoids**
Regulation of the activator protein-1 (AP-1) complex is very intricate because it involves phosphorylation state, protein-protein, and protein-DNA interactions. In studies by B.L. Faubert et. al., the regulation of AP-1 activity, with emphasis on c-fos and c-jun regulation, was investigated using cannabinol (CBN) in primary mouse splenocytes *In vitroo*. Cannabinoid compounds exhibit immunosuppressive actions that are putatively mediated through Gi-protein coupled receptors that negatively regulate adenylate cyclase. However, recent studies suggest that cannabinoids modulate other signaling cascades. Indeed, CBN inhibited binding to AP-1-containing sites from the interleukin-2 promoter. This inhibition of binding was, in part, due to decreased nuclear expression of c-fos and c-jun. B.L. Faubert et. al. further determined that the effects of CBN were due to posttranslational modifications of these phosphoproteins and showed that CBN inhibited the activation of ERK MAP kinases. Thus, cannabinoid-induced immunosuppression involves disruption of the ERK signaling cascade. Faubert, B.L. and Kaminski, N.E. AP-1 Activity is Negatively Regulated by Cannabinol Through Inhibition of its Protein Components, c-fos and c-jun, J. Leukocyte Biology, 67, pp. 259-266, 2000.

## Cannabinoid Effects on Antigen Processing by Macrophages

Another basic study of immune system processing focuses on how cannabinoids modulate the presentation of antigens to lymphocytes by macrophages. This is an important step in the attack on microorganisms by the immune system. Delta(9)-tetrahydrocannabinol (THC) causes an antigen-dependent defect in the ability of macrophages to activate helper T cells, and this drug-induced impairment is mediated through the peripheral CB2 receptor. Various requirements for the processing of the antigen, lysozyme, were examined by C.B. Hartmann et. al. to determine where along the pathway THC exerts its influence. A THC-exposed macrophage hybridoma inefficiently stimulated interleukin-2 secretion by a helper T cell hybridoma in response to native lysozyme and its reduced form, suggesting that disulfide bond reduction was unaffected. Cell surface expression of major histocompatibility complex class II molecules was normal on THC-exposed macrophages. The drug-exposed macrophages also competently presented a lysozyme peptide to the T cells, indicating that the class II molecules were functional. The proteolytic activity of two thiol cathepsins was unaltered, but aspartyl cathepsin D activity was significantly increased in THC-exposed macrophages. Thus, selective up-regulation of aspartyl cathepsin activity accompanied the deficiency in lysozyme processing and may contribute, at least in part, to the antigen-dependent processing defect in THC-exposed macrophages. Hartmann, C.B., Harrison, M.T., Cabral, G.A., McCoy, K.L. Delta(9)-Tetrahydrocannabinol Selectively Increases Aspartyl Cathepsin D Proteolytic Activity and Impairs Lysozyme Processing by Macrophages. International J. Immunopharmacology, 22, pp. 373-381, 2000.

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# Research Findings

## Behavioral Research

### Environmental Context Modulates Midazolam's Behavioral Effect: Function of High Versus Low Serum Drug Concentration

Dr. John Falk and associates at Rutgers, The State University of New Jersey, have been examining the relationship between pharmacokinetic drug profiles on various behavioral assays and drug effects. With the benzodiazepine derivative midazolam, at any point in time the time course and intensity of effects on operant behavior correspond to the serum concentration of the drug. In the most recent study, under the direction of Dr. Chyan Lau, these investigators imposed delays between the administration of midazolam and the beginning of an operant test session. Some animals experienced the delay in their home cage and another group in the operant test chamber. For long delays (i.e., greater than 60-min), midazolam's effects were less disruptive if the delay was experience in the operant test chamber rather than the home cage. The researchers suggest that environmental manipulations or contextual effects may only be seen with low drug doses, (or, in this case, lower serum drug concentrations) and that at higher doses direct effects of the drug determine behavioral effects. Sun, L., Falk, J.L., Nguyen, K-N., and Lau, C.E. Behavioural Pharmacology, 11, pp. 133-142, 2000.

### Active Versus Passive Drug Administration and the HPA Axis

Recent research has shown that the neurochemical and behavioral effects of cocaine depend upon whether the drug is self-administered, i.e. active administration, or delivered independently of responding, i.e. passive administration. For example, during withdrawal, both neurotransmitter levels and neurotransmitter turnover rates differ for active versus passive cocaine administration. Mortality is higher following passive delivery of cocaine. Research by R. Galici et. al. demonstrates for the first time that active and passively administered cocaine have differential effects on the physiological stress response as measured by plasma corticosterone levels. In the study conducted in the laboratory of Dr. Charles France at Louisiana State University, plasma corticosterone levels in rats were higher following active than following passive cocaine administration. Since cocaine self-administration has been shown by others to be potentiated by the activation of the HPA axis, these results suggest that the stress involved in the self-administration of a drug may contribute to the acquisition, maintenance and reinstatement of self-administration of that drug. Galici, R., Pechnick, R.N., Poland, R.E., and France, C.P. Eur. J. Neurol., 387, pp. 59-62, 2000.

### Conditioned Taste Aversion to Morphine is Related to Corticosterone Response

Drugs of abuse such as the opiates and psychostimulants are readily self-administered in animal behavioral paradigms but also produce a conditioned taste aversion (CTA) suggesting that they may have aversive as well as reinforcing central effects. These self-administered drugs also activate endogenous stress systems through the hypothalamic pituitary axis (HPA) and there are data to indicate that activation enhances both the reinforcing and aversive properties of drugs of abuse. Dr. Felipe Gomez, in collaboration with Drs. Nicole Leo and Patricia Sue Grigson at Penn State College of Medicine, have noted that there are wide inter-subject differences in animals that acquire CTA when a unique taste/solution is paired with morphine. In this procedure, the investigators subsequently assess

intake of a solution (saccharin) previously paired with morphine. Rats with similar baseline corticosterone were separated into two groups, one that showed a strong post-pairing (drug + saccharin) suppression of intake (or an avoidance of saccharin) and one that did not. Both groups received the same number of morphine administrations. Rats showing CTA had greater elevations of plasma corticosterone following saccharin exposure. The researchers suggest that this difference is related to the conditioning or learning process and that saccharin, as a 'conditioned stimulus' takes on the ability to elicit a drug-induced activation of the HPA. Gomez, F., Leo, N.A. and Grigson, P.S. Brain Research, 863, pp. 52-58, 2000.

### Acute Dependence Revealed by Progressive Ratio Procedures with Intra-Cranial Self-Stimulation

Investigators in the laboratory of Dr. Stephen Holtzman at Emory University School of Medicine in Atlanta, Georgia have been studying physical dependence after acute opiate administration. This phenomenon can be demonstrated using sensitive behavioral baselines and the technique of precipitated withdrawal. Thus, rats responding for intra-cranial self-stimulation (ICSS) using an autotitration procedure to assess threshold for reward show a greater suppression of responding for ICSS if they had received naltrexone than if they had received an acute morphine administration. This is interpreted as reflecting a subjective dysphoria during the withdrawal state. A recent study was conducted to extend these findings to a progressive ratio (PR) procedure of ICSS wherein the number of responses an animal is willing to make in order to receive stimulation is taken as the dependent measure. This measure proved incredibly sensitive to detecting precipitated withdrawal, as the $ED_{25}$ for decreasing response rate was 850-fold lower in animals that had received a prior acute morphine treatment. Interestingly, the investigators compared these findings to those for animals treated acutely with benzodiazepines (BZ) and then challenged with a BZ antagonist before the ICSS session. While other measures of operant behavior have revealed signs of precipitated withdrawal from BZs, none were seen using PR ICSS as an indicator. Dr. Holtzman and his colleagues infer that the processes underlying dependence with acute drug administration of these two drug classes may be fundamentally different. Easterling, K.W., Plovnick, R.M. and Holtzman, S.G. Psychopharmacology, 148, pp. 263-271, 2000.

### Laboratory-Based Classical Conditioning of Stimuli Paired with Drugs

Drs. Richard Foltin and Margaret Haney of the New York State Psychiatric Institute and Columbia University have shown that neutral stimuli paired with the administration of smoked cocaine (CS+) versus the administration of a placebo (CS-) acquire emergent stimulus effects, including conditioned reinforcing effects. Eight experienced cocaine smokers were studied over 22 experimental sessions conducted while the subjects resided in a Clinical Research Center. The CS + and CS- were compound stimuli containing visual, olfactory and auditory elements. Pairing cocaine with the CS+ served to increase cocaine's heart rate-increasing effects and ratings of "anxious." Following training trials with CS+ and CS- seven of the eight subjects exhibited preference for the CS+ indicating that the CS+ had acquired conditioning reinforcing effects. During extinction in which the CS+ was presented without cocaine, there was an increase in heart rate, systolic pressure, and ratings of "anxious" and "tired" as well as an increase in craving ("I want cocaine") and a decrease in skin temperature. The CS- produced no behavioral or physiological effects either during training or extinction. This is the first laboratory-based study to show that neutral stimuli paired with the administration of smoked cocaine acquire emergent stimulus effects, including conditioned reinforcing effects. Foltin, R.W., and Haney, M. Conditioned Effects of Environmental Stimuli Paired with Smoked Cocaine in Humans. Psychopharmacology, 149, pp. 24-33, 2000.

### Sex Differences in Language Production in 24-Month-Old Inner City Children Exposed In Utero to Cocaine

Researchers at the Yale Child Study Center compared the language abilities at age 24 months of 47 inner-city children exposed prenatally to cocaine with those of 30 inner-city children not exposed prenatally to cocaine. The sample was recruited prenatally. While both groups of children evidenced some delays in language development, the non-cocaine-exposed children produced more complex language, including longer utterances, a richer vocabulary, and more complex grammatical structure than the cocaine-exposed children were able to do. The effect, however, was largely in girls. Malakoff, M.E., Mayes, L.C., Schottenfeld, R., and Howell, S. Language Production in 24 Month Old Inner City Children Exposed In Utero to Cocaine. Journal of Applied Developmental Psychology, 20, pp. 159-180, 2000.

### Contingent Versus Non-Contingent Cocaine, the HPA Axis, and Sex Differences

Researchers at the University of Michigan Medical School and at Washington University have shown in rhesus monkeys that cocaine-produced increases in cortisol and ACTH release are greater and more dose-dependent when the cocaine (0.01-, 0.03-, 0.1-, and 0.3-mg/kg/injection) is delivered response-contingently than when it is delivered

non-contingently. Under both procedures, the cortisol response was higher in males than in females; there were no sex differences in the ACTH response. A single large dose infusion of cocaine (1 mg/kg) produced a substantially larger ACTH response in males than in females; there were no sex differences in the cortisol response to the large dose. Broadbear, J. H., Winger, W., Cicero, T., and Woods, J.H. Effect of Response Contingent and Non-contingent Cocaine Injection on Hypothalamic-Pituitary-Adrenal Activity in Rhesus Monkeys. Journal of Pharmacology and Experimental Therapeutics, 290, pp. 393-402, 1999.

### Buprenorphine Blocks Mood and Other Effects of Opiates

One of the aims of medicating drug dependent patients with a mu opioid agonist or putting them on antagonist maintenance is to attenuate the effects of illicit opioids such as heroin. This study asked whether buprenorphine, as compared to naltrexone or placebo, attenuates opioid effects at the start and end of treatment. Opioid-experienced volunteers (n = eight) participated in this ten-week, inpatient, double blind, within subject, crossover study. Buprenorphine alone (2 and 8 mg, sublingually) produced dose-related typical agonist effects during induction (i.e., positive mood, respiratory depression, miosis); tolerance developed only to the subjective effects. Buprenorphine at 2 mg partially attenuated the effects of hydromorphone, while nearly complete attenuation was observed with buprenorphine at 8 mg and that lasted up to 72 hours after discontinuation. Naltrexone (25 and 100 mg, PO) produced complete hydromorphone blockade after a single dose. Five days after discontinuation of naltrexone at 100 mg, blockade of the behavioral but not the physiological effects persisted. These data suggest that buprenorphine at 2 mg is a sub-therapeutic maintenance dose; both buprenorphine at 8 mg and naltrexone at 100 mg produce an immediate and efficacious opioid blockade; and adequate protection against illicit opioids may be achieved with less-than-daily dosing. Schuh, K.J., Walsh, S.L., Stitzer, M.L. Psychopharmacology, 145, pp.162-74, 1999.

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# Research Findings

## Treatment Research and Development

### Acute and Protracted Cocaine Abstinence in an Outpatient Population, Effect on Mood, Sleep and Withdrawal Symptoms

Drs. Coffey, Dansky, Carrigan, and Brady at the Medical University of South Carolina evaluated cocaine abstinence over 28 days in a sample of 24 male and female cocaine-dependent outpatients. Abstinence-related symptoms including mood, anxiety, sleep, concentration, and craving were monitored at 2, 5, 10, 14, 21, and 28 days following last cocaine use. Consistent with findings from inpatient studies of cocaine abstinence, linear improvements in negative affect, low cocaine craving, and increases in cognitive skills were reported over the 28 days. Also consistent with inpatient studies of cocaine withdrawal, an aphasic withdrawal syndrome was not observed in this outpatient sample. Unlike inpatient studies, no disturbances in sleep were reported. Coffey, S. Dansky, B., Carrigan, M., Brady, K. Drug and Alcohol Dependence, 59, pp. 277-286, June 2000.

### Gender Differences in Adolescent Drug Abuse: Issues of Comorbidity and Family Functioning

Dr. Gayle Dakof, University of Miami, investigated gender differences in patterns of co-morbidity and family functioning among a sample of 95 youths (42 girls) referred by juvenile justice (80%), education (10%) and social welfare (10%) for substance abuse treatment. Findings indicate that male and female adolescent substance users (13-17 years) entering treatment do differ. The girls not only used drugs and engaged in externalizing behaviors as extensively as did their male counterparts but they also were distinguished by their higher levels of internalizing symptoms and family dysfunction. Dakof, G. Journal of Psychoactive Drugs, 32(1), pp. 25-32, 2000.

### HIV Testing, Drug Use and STD Prevalence Among Juveniles Entering a Rhode Island Correctional Facility

Dr. David Pugatch and colleagues at Brown University surveyed the medical records of 312 incarcerated juveniles (91% boys) to determine the incidence of voluntary HIV testing during their detention stay. Results indicate 69% were tested, 5% reported a history of an STD, 49% used marijuana and 8% used a "hard drug"(e.g., cocaine, heroin and LSD). Results indicate that although adolescents in juvenile detention centers frequently engage in HIV-associated risk-taking behaviors, many youth at high risk for HIV are not being tested. Pugatch, D., Ramratnan, M., Feller, A., Price, D., and Riggs, S. Journal of Correctional Health Care, 6(2), pp. 197-205, 2000.

### Anger Management Group Treatment for Cocaine Dependence: Preliminary Outcomes

Drs. Patrick Reilly and Michael Shopshire at the University of California, San Francisco, conducted a pilot study to examine a manual-guided 12-week cognitive-behavioral anger management group treatment in a sample of 59 men and 32 women who were cocaine dependent and reported frequent and intense episodes of anger. Levels of anger, negative affect, and anger control were measured at baseline, weekly during treatment, and at 3-month post

treatment follow-up. Of the sample, 55% completed the anger management group treatment, 50% remained abstinent from cocaine. The participants increased their ability to control their anger and related negative affect across the 12 months of treatment. Preliminary findings suggest that anger management group treatment may help cocaine-dependent individuals with anger control problems manage their anger. Reilly, P. and Shopshire, M. American Journal of Drug and Alcohol Abuse, 26 (2), pp. 161-177, 2000.

### Prevalence of Attention-Deficit Hyperactivity Disorder and Conduct Disorder Among Substance Abusers

Dr. Schubiner and colleagues at Wayne State University evaluated the prevalence of ADHD and conduct disorder among adults admitted to 2 drug addiction treatment centers. Two hundred and one participants were selected randomly from the 2 treatment sites. Standardized clinical interviews were conducted using the Structured Clinical Interview for DSM-IV, the Addiction Severity Index, and DSM-IV criteria for ADHD. Forty-eight or 24% of the participants met DSM-IV criteria for ADHD. The prevalence of ADHD was 28% in men (30/106) and 19% in women (18/95;NS). Seventy-nine participants (39%) met criteria for conduct disorder, and 34 of these individuals also had ADHD. Over two thirds of those with ADHD in this sample also met criteria for conduct disorder. Individuals with conduct disorder and/or ADHD represent a significant proportion of those seeking treatment for psychoactive substance use disorders. They appear to have greater comorbidity and may benefit from a treatment approach that addresses these comorbidities through medical and behavioral therapies. Schubiner, H., Tzelepis, A., Milberger, S., Lockhart, N., Kruger, M., Kelley, B., Schoener, E. Journal of Clinical Psychiatry, 61(4), pp. 244-251, April, 2000.

### Development of Major Depression After Treatment for Smoking Cessation

Dr. Janice Tsoh and colleagues at the University of California, San Francisco, examined the incidence and predictors of major depression in the 12 months after treatment for smoking cessation. In this study 304 participants (172 women) were recruited from two trials of smoking cessation; both trials provided group cognitive-behavioral mood management, but one group received treatment with nicotine gum and the other received nortriptyline or placebo. The Inventory to Diagnose Depression was administered at follow-up assessments. Among the 304 participants, 14.1% (N=43) reported a major depressive episode within 12 months after the treatment for smoking cessation. The incidence rates across trials were similar. About half (N= 170, 55.9%) of the participants were abstinent from smoking at the end of treatment. Results indicate that history of depression, baseline Beck Depression Inventory score, college education, and age at smoking initiation were significant predictors of major depression after smoking cessation treatment. Patients who achieved abstinence from smoking showed a risk of developing depressive episodes similar to those who failed to achieve abstinence. Patients who had a history of depression were more likely to experience depressive episodes after treatment for smoking cessation. Tsoh, J. Humfleet, G., Munoz, R., Reus, V., Hartz, D., Hall, S. American Journal of Psychiatry, 157(3), pp. 368-374, March 2000.

### Group Therapy for Patients with Bipolar and Substance Dependence: Results of a Pilot Study

This paper reports a behavioral therapy development study of a treatment designed specifically for patients with coexisting bipolar disorder and substance use disorder. The treatment in this study, Integrated Group Therapy (IGT), was developed to integrate therapeutic approaches that are relevant to each disorder. This was an open trial in which patients (N=45) with substance dependence and bipolar disorder received either IGT or monthly assessments, but no experimental treatment. Relative to the control group, patients receiving IGT had significantly better outcomes on the ASI composite score, percentage of months abstinent, and likelihood of achieving 2 or 3 consecutive abstinent months. IGT appears to be a promising treatment for these patients who have traditionally had poor outcomes. A study comparing this treatment with another active psychotherapy treatment is warranted. Weiss, R.D., Griffin, M.L., Greenfield, S.F., Najavits, L.M., Wyner, D., Soto, J.A. and Hennen, J.A. Journal of Clinical Psychiatry, 61, pp. 361-67, 2000.

### Post-Treatment Outcomes of Adolescent Females Referred for Conduct Disorder and Substance Use Disorders

Dr. Elizabeth Whitmore and colleagues, University of Colorado, investigated whether symptoms associated with substance abuse/dependence, conduct disorder and other psychiatric disorders were reduced in adolescents (13-19 years) admitted to a multi-component outpatient drug treatment program. Although the results indicate improvement in three areas (i.e., delinquency and conduct disorder [CD]; attention deficit hyperactivity disorder [ADHD]; educational/vocational status), substance involvement and level of depression did not improve. Unlike results from a concomitant study with boys, no pre-treatment variables predicted post-treatment drug use or conduct outcomes

among the girls. And only two post-treatment factors (peer problems and number of ADHD symptoms) were found related to CD and the substance use disorders outcomes. Whitmore, E.A., Mikulich, S.K., Ehlers, K.M. and Crowley, T.J. Drug and Alcohol Dependence, 59, pp. 131-141, 2000.

### Effectiveness of the Minnesota Model Approach in the Treatment of Adolescent Drug Abusers

Dr. Ken Winters and colleagues at the University of Minnesota assessed adolescents with substance use disorders eligible to enroll in a 12-step drug treatment program. Youths were evaluated 6- and 12-month post-treatment in terms of their drug use outcomes. Three groups of adolescents participated in the study: those (n=101) who completed treatment, those (n=39) who did not, and those (n=66) on a waiting list. Among treatment completers, residential and outpatient samples were also compared. Results indicate completing treatment was associated with far superior outcomes compared to those who did not complete treatment or receive any at all. Percentage of treatment completers reporting abstinence one-year post treatment was 23% compared to 2.6% for non-completers and 3.0% for those on the wait-list. No differences were found between residential and outpatient groups or was gender or age a factor. Winters, K.C., Stinchfield, R.D., Opland, E., Weller, C. and Latimer, W.W. Addiction, 95(4), pp. 601-612, 2000.

### "Recreational" MDMA Use Depletes Serotonin but Not Dopamine

Dr. Stephen J. Kish and colleagues (in Toronto and Washington, DC) performed a neurochemical analysis of an autopsied brain of a 26-year-old male with a nine-year history of acute and chronic MDMA use to determine the neurotoxic effects of the recreational drug MDMA (Ecstasy). The brain was examined and neuropathically compared to neurologically normal subjects. Histopathological analysis disclosed no dopamine related abnormalities in the brains of the control subjects or the MDMA user. The lack of change in the dopaminergic markers (e.g., striatal dopamine, the dopamine transporter and the vesicular monoamine transporter) and in nigral cellularity may explain the lack of anti-Parkinsonian response to dopaminergic therapy in the MDMA user that has been previously reported. In contrast, striatal levels of serotonin and of its metabolite 5-hydroxyindoleactic acid were decreased in the MDMA user by 71-80% of the levels in the normal subjects. Part of this reduction could be the result of toxic damage to striatal serotonin nerve terminals and/or acute reversible depletion of neurotransmitter stores. This study is the first to demonstrate that recreational use of MDMA can cause actual depletion of tissue stores of serotonin that may account for some of the behavioral effects during drug taking and withdrawal but not sufficient release of striatal dopamine. Kish, S.J., Furukawa, Y., Ang, L. and Kalasinsky, K.S. Striatal Serotonin But Not Dopamine is Depleted in Brain of a Human (Ecstasy) User. Neurology, 55(2), pp. 294-296, 2000.

### Stimulant Dependence Affects HIV-Related Neuronal Injury

Since either HIV infection or abuse of CNS stimulants is associated with brain damage and dysfunction, magnetic resonance spectroscopy (MRS) was used to examine the combined effects of HIV infection and stimulant dependence on frontostriatal circuitry. It was hypothesized that HIV-positive/stimulant dependent (HIV+/STIM+) subjects would show increased N-acetylaspartate (NAA), a putative marker of neuronal integrity, compared to the controls (HIV-/STIM-) and HIV+ nonusers (HIV+/STIM-). Elevations in choline (Cho) and myoinositol (MI) were predicted in the HIV+/STIM+ group, reflecting abnormalities in cellular integrity, with smaller increases in HIV+/STIM- and HIV-/STIM+ subjects. Finally, elevated creatine (Cr) was expected in the white matter of the STIM+ groups based on findings from a previous study. Contrary to predictions, results showed no reliable or significant differences in Cho, Cr, or MI across groups. Significant group differences were observed, however, in NAA in the anterior cingulate gyrus ($p < 0.05$), with NAA lowest in HIV+/STIM+, highest in HIV-/STIM-, and at an intermediate level in the HIV+/STIM- and HIV-/STIM+ subjects with levels significantly correlated with measures of neuropsychological functioning ($r$ ranging from -.50 to -38; $p < 0.01$ to $p = 0.05$). Although these data suggest that stimulant dependence does potentiate HIV-related neuronal injury, it cannot be determined at this time if the decrease in neuropsychological functioning is due to dendritic (i.e., reversible) changes or irreversible neuronal death. Taylor, M.J., Alhassoon, O.M. Schweinsburg, B.C. Videen, J.S. Grant, I. MR Spectroscopy in HIV and Stimulant Dependence, Journal of the International Neuropsychological Society, 6, pp. 83-85, 2000.

### Impaired Evaluation of Future Consequences in Drug Abusers

Dr. Steven Grant of the Clinical Neurobiology Branch, DTR&D and colleagues at the Brain Imaging Center examined the performance of drug abusers on a neuropsychological test that requires evaluation of long-term outcomes in the presence of a complex set of mixed reward/punishment contingencies (the Gambling Task). In order to control for generalized deficits related to choice and planning, subjects were also administered the Wisconsin Card Sorting task. Drug abusers performed much more poorly on the Gambling Task than controls, but did not differ from controls on

the Wisconsin Card Sorting Task. The results show that drug abusers are more likely to make maladaptive decisions in the Gambling Task that result in long-term losses exceeding short-term gains, similar to persistent drug use despite long-term adverse consequences. Furthermore, as the Gambling Task was developed to characterize subjects with orbitofrontal lesions, the results suggest that drug abusers may have dysfunction of the orbitofrontal cortex. Grant, S. et al., Drug Abusers Show Impaired Performance in a Laboratory Test of Decision-Making. Neuropsychologia, 38, pp. 1180-1187, 2000.

### Chronic Effects of Marijuana as a Function of Age of First Use

Since a significant degree of brain development occurs during adolescence, males and females with a history of teenage marijuana use received both positive emission tomography (PET) to assess cerebral blood flow (CBF) and magnetic resonance imaging (MRI) scans to evaluate brain volume. Median age of first marijuana use was the variable used to stratify the volunteers into Early (< age 17) or Late (> age 17) use. Primary findings related to age of first use include: 1) those who were identified as Early users had smaller whole brain and percent cortical gray matter and percent white matter volumes compared to those who started use later, suggesting that the mechanism of this effect has more to do with brain development than with atrophy; 2) functionally, males who began use Early, had significantly higher resting CBF compared to the Late males but was not significantly different from females, supporting additional changes in gonadal and pituitary hormones that alter development; these changes, in turn, are related to global CBF and to reduction in gray matter; 3) both males and females who started using marijuana younger were physically smaller in height and weight, with the effects being greater in males. Since THC suppresses the release of prolactin, growth hormone and gonadotropin and because the adolescent growth period for males starts earlier and lasts longer than for females, starting marijuana use early would expose males longer to the adverse effects of reduced growth hormone release. Overall, these findings suggest that exposure to marijuana (and possibly other drugs) at certain critical periods such as during early adolescence, may alter normal patterns of development. Wilson, W., Mathew, R., Turkington, T., Hawk, T., Coleman, R.E., and Provenzale, J. Brain Morphology Changes and Early Marijuana Use: A Magnetic Resonance and Positron Emission Tomography Study. Journal of Addictive Diseases, 19, pp. 1-22, 2000.

### Blood Flow Changes in Substance Abuse and PTSD

PET studies of regional cerebral blood flow during performance of an auditory continuous performance task have been conducted in subjects with PTSD and no substance abuse, substance abuse and no PTSD, PTSD and comorbid alcohol and cocaine abuse, and PTSD and only comorbid alcohol use, and normal control subjects. Although there were no differences in task performance, the PET results indicate that comorbid cocaine use exacerbates the pathophysiological changes in cortical and sub-cortical activity in subjects with PTSD. Cocaine-abusing PTSD subjects have increased regional brain blood flow in brain regions of the amygdala and periacquaductal grey compared to normals. In contrast, cocaine-abusing PTSD subjects have decreased frontal regional blood flow. Cocaine-abusing PTSD subjects have increased regional blood flow in the amygdala compared to cocaine abusers without comorbid PTSD and PTSD patients who only abuse alcohol, indicating that neither cocaine use alone nor PTSD alone is responsible for the elevations in observed blood-flow elevation. These data indicate a clear interaction between cocaine use and PTSD that cannot be explained by other factors. Given the high rate of substance abuse comorbidity in PTSD, these findings are relevant to the diagnosis and treatment of comorbid cocaine abuse in patients with PTSD. Semple, W.E., et al. Higher Brain Blood Flow at Amygdala and Lower Frontal Cortex in PTSD Patients with Comorbid Cocaine and Alcohol Abuse Compared to Normals. Psychiatry: Interpersonal and Biological Processes, 63, pp. 65-74, 2000.

### A Mendelian Genetic Model for Smoking Behavior was Supported in an Analysis of Three-Generation Families

Gary Swan of SRI International conducted a complex segregation analysis in three generation-families to determine the best model for transmission of smoking behavior. This is the first study to date to use three generations for this determination. It was found that the best-fitting model was that of a dominant major gene with low estimated frequency and residual familial correlations. These correlations demonstrate strong influence of mothers (negative) and spouses (positive) toward smoking behavior. However, it should be noted that the sample was selected from those participating in a longitudinal study of aging and health and not selected for smoking behavior per se. Therefore, it is presumed that these results underestimate genetic transmission because heavy-smoking individuals are less likely to volunteer for the study, and many more smokers in the registry may have already died. Nevertheless, these results encourage future linkage studies. Cheng, L.S., Swan, G.E., and Carmelli, D. A Genetic Analysis of Smoking Behavior in Family Members of Older Adult Males. Addiction, 95(3), pp. 427-435, 2000.

## A Genetic Variant Associated with Low Levels of a Dopamine Enzyme (Beta-Hydroxylase) Is also Associated with Cocaine-induced Paranoia

It had been shown that low levels of dopamine beta-hydroxylase (DBH) protein I plasma or cerebrospinal fluid are associated with greater vulnerability to positive psychotic symptoms. The question is whether a gene variant that is associated with that protein would be more prevalent in that circumscribed group of cocaine addicts who endorse paranoia symptoms. There is a gene variant of DBH that associates with plasma activity in European-Americans. Significantly more frequent low DBH-associated Haplotypes ($p < .0003$) was prevalent in cocaine-induced paranoia addicts than in addicts who did not endorse paranoia symptoms. Cubells, J.F., Kranzler, H.R., McCance-Katz E., Anderson G.M., Malison R.T., Price L.H., and Gelernter J. A Haplotype at the DBH Locus, Associated with Low Plasma Dopamine Beta-hydroxylase Activity, Also Associates with Cocaine-induced Paranoia. Molecular Psychiatry, 5(1), pp. 56-63, 2000.

## Various Significant Genetic Influences Are Associated with Transitions between Levels of Use of Illicit Drugs

Using phone interviews of more than 3000 male-male twin pairs conditional probabilities were determined for different illicit drugs between levels of use, from exposure to dependence and addiction. Marijuana had the highest conditional probabilities for the transition from exposure to use, from use to use more than five times, and from use more than five times to regular use. Heroin had a higher rate of transition to regular use than amphetamines, cocaine, psychedelics, or sedatives. Finally, cocaine had the highest conditional probability for transition from regular use to abuse/dependence. Tsuang, M.T., Lyons, M.J., Harley, R.M., Xian, H., Eisen, S., Goldberg, J., True W.R., and Faraone S.V. Genetic and Environmental Influences on Transitions in Drug Use. Behavior Genetics, 29(6), pp. 473-479, 1999.

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**National Institute on Drug Abuse**

**Director's Report to the National Advisory Council on Drug Abuse**

**September, 2000**

# Research Findings

## Research on AIDS and Other Medical Consequences of Drug Abuse

### Substance Use and its Relationship to Depression, Anxiety, and Isolation Among Youth Living with HIV

Reductions from lifetime to recent levels of substance use, the time since HIV diagnosis, physical health symptoms, CD4 counts, emotional distress, and social supports were examined among 227 13 to 24 year old (20% female, 80% male) youth living with HIV (YLH). Substance use pervaded the lives of these youth. Male YLH had used more drugs, more often, and for longer periods than female YLH. However, there had been major reductions in use from lifetime to current reports. Being male, having high emotional distress, and having fewer negative social supports were significantly associated with greater reductions in substance use. There was a trend for the length of time that an individual was seropositive being associated with reductions in substance use. The counterintuitive findings suggest that there must be a re-examination of the role of the social support networks of youth living with HIV, as well as the ways in which emotional distress interact with risk behaviors. Rotheram-Borus, M.J., Murphy, D.A., Swendeman, D., Chao, B., Chabon, B., Zhou, S., Birnbaum, J., and O'Hara, P. Substance Use and its Relationship to Depression, Anxiety, and Isolation Among Youth Living with HIV. International Journal of Behavioral Medicine, 6 (4), pp. 293-311, 1999.

### Disclosure of Serostatus Among Youth Living with HIV

Disclosure of serostatus and predictors of disclosure were examined among youth living with HIV (YLH). Disclosure patterns, sociodemographic characteristics, sexual and substance-use risk history, and current health status were examined among 350 youth living with HIV aged 13-23 years (27% African-American, 38% Latino; 72% male). In this group 35 had AIDS, 108 were symptomatic, and 201 were asymptomatic. Most youth disclosed their serostatus to family (87%); unexpectedly, young men (93%) were more likely to disclose to friends than were young women (79%). Being younger at diagnosis was significantly more associated with disclosure to family; young men disclosed more often to friends. Most youth disclosed to all their sexual partners (69%); higher rates of disclosure to sexual partners were associated with having fewer partners and being African-American. Condom use was significantly associated with disclosure for young women, and tended to be related to disclosure for young men. Although many YLH disclosed their serostatus to their partners, condom use was not increased. Interventions are needed to increase condom use among YLH, as well as to encourage disclosure to partners by the 30% of YLH who do not disclose. Lee, M., Rotheram-Borus, M.J., and O'Hara, P. Disclosure of Serostatus Among Youth Living with HIV. AIDS and Behavior, 3 (1), pp. 33-40, 1999.

### Applications of Ethnography in HIV Epidemiology and Prevention

HIV prevention researchers Clatts and Sotheran have reviewed ways in which ethnography can contribute to public health research targeted to populations of drug-using men having sex with men (DU/MSM). Participant observations were used in specifying the nature and interrelationship between risk practices among DU/MSM. They also show how ethnography can contribute to the process of disentangling the independent effects of age, period, and cohort factors,

a perennial problem in epidemiological research in out-of treatment populations. This kind of information is important in developing targeted prevention messages and services, thereby enhancing both the effectiveness of interventions and the efficiency by which prevention resources are utilized. Clatts, M.C., and Sotheran, J.L. Challenges in Research on Drug and Sexual Risk Practices of Men Who Have Sex with Men: Applications of Ethnography in HIV Epidemiology and Prevention. AIDS and Behavior, 4(2), pp. 169-179, 2000.

### Cost-Effectiveness Analysis of the National AIDS Demonstration Research Project (NADR), 1987-1992

A study was done by Pinkerton and colleagues from the Medical College of Wisconsin to determine if the NADR program was cost-effective. The original goal of the multisite NADR program was to reduce the sexual and drug injection-related HIV risks of out-of-treatment injection drug users and their sex partners. Previous analyses have established that the NADR interventions were effective in changing participants' HIV-related risk behaviors. In this study, savings in averted medical care costs were compared with the cost of implementing a similar intervention program for injection drug users in eight different NADR locations. The results strongly suggest that the NADR interventions were cost-saving overall, and were, at the very least, cost-effective at all eight sites. In the U.S. and other developed countries, investments in HIV-prevention interventions such as NADR, have the potential to save substantial economic resources by averting HIV-related medical care expenses among injection drug users. Pinkerton, S.D., Holtrave, D.R., DiFranceisco, W., Semaan, S., Coyle, S.L., and Johnson-Masotti, A.P. Cost-threshold Analyses of the National AIDS Demonstration Research HIV Prevention Interventions. AIDS, 14(9), pp. 1257-1268, June 16, 2000.

### Focus Group Summaries of High Risk Sexual and Drug-Using Behaviors in Men

The Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research was the basis for 5 sites participating in a research study with a goal of gaining a deeper understanding of the HIV-related risk behaviors and possible intervention strategies for men who have sex with men who are injection drug users and/or crack smokers (referred to as drug-using men who have sex with men or DU/MSM). A Multisite Research Consortium drafted a focus group guide that was led by a facilitator and co-facilitator, at least one of whom was familiar with DU/MSM population in that community. Several common themes emerged from the focus group results across all sites. For DU/MSM, their drug use and drug-related needs are more important determiners of their identity and their behaviors than is their sexual orientation. Many report being alienated or isolated from relationships with others and many of those self-identified as gay report not being part of the local gay community. Participants engage in behaviors which are high risk for HIV, including trading sex for money or drugs, and many report engaging in sex with both men and women. The need for additional services, including services related to HIV prevention and drug treatment, was also identified across sites. The heterogeneity of the DU/MSM community (within and across sites) indicates that a broad range of HIV prevention and other services addressing local needs is required. Rhodes, F., Deren, S., Cottler, L., Siegal, H., Stark, M., and Reich, W. (editors). A Multisite Study of HIV Risks in Drug-Using Men who have Sex with Men: Focus Group Summaries. The University Press, California State University-Long Beach, Long Beach, CA, 2000.

### First Injection and Current Risk Factors for HIV Among New and Long-term Injection Drug Users

The purpose of this study was to estimate HIV seroprevalence and to examine the injection and sexual risk behaviors of a cohort of active new heroin injectors who have initiated injection within the past four years and to compare their risk behaviors with those of long-term heroin injectors who initiated injection prior to January 1, 1985. A stratified network-based sample was used to recruit injection drug users (IDUs) from the streets of Miami-Dade, Florida. New IDUs displayed a significantly lower HIV seroprevalence than long-term injectors (13.3% versus 24.7%). Both new and long-term drug injectors exhibited a high level of current HIV risk behavior. While new injectors were more likely than long-term injectors to practice safer injection behaviors at the initial injection episode, the current risk behaviors of new and long-term injectors are similar. Chitwood, D.D., Sanchez, J., Comerford, M., Page, J.B., McBride, D.C., and Kitner, K.R., First Injection and Current Risk Factors for HIV Among New and Long-term Injection Drug Users. AIDS Care, 12(3), pp. 313-320, 2000.

### HIV Transmission and the Cost Effectiveness of Methadone Maintenance

Dr. Margaret Brandeau of Stanford University and her colleagues recently published the results of a study in which they found that prevention efforts are more effective when they are targeted to individuals who are centrally located in high-risk networks than when they reach individuals on the periphery of such networks. In this respect, if incremental methadone capacity were targeted to injection drug users who are centrally located in networks, then such expansion would likely be more cost effective than if incremental capacity were located on the periphery of such

networks. The paper also concluded that even if methadone maintenance does not lead to a complete or permanent cessation of drug use, it is a cost effective intervention that can play an important role in preventing the spread HIV and improving the length and quality of life for injection drug users and the general population. Zaric, G.S., Barnett, P.G. and Brandeau, M.L. HIV Transmission and the Cost Effectiveness of Methadone Maintenance. American Journal of Public Health, 90(7), pp. 1100-1111, July 2000.

### Zinc Status in Human Immunodeficiency Virus Infection

Baum and colleagues recently presented a summary of data on the role of zinc in immune processes such as T-cell division, maturation, and differentiation; lymphocyte response to mitogens; programmed cell death of lymphoid and myloid origins; gene transcription; and biomembrane function. They report that evidence indicates that adequate amounts of zinc are essential to maintain the integrity of the immune system and that HIV-1 infected individuals are a population particularly susceptible to zinc deficiency. On the other hand, excessive zinc may stimulate HIV-1. The association between zinc deficiency and decreased survival in HIV-1 infected individuals indicates the need to carefully consider therapeutic options. Moreover, with the advent of new antiretroviral therapies that may significantly alter the natural history of HIV/AIDS, the prevalence of zinc deficiency and the potential of interventions in HIV-infected individuals may change dramatically, generating new challenges. Baum, M.K., Shor-Posner, G, and Campa, A. Zinc Status in Human Immunodeficiency Virus Infection. Journal of Nutrition, 130, pp. 1421s-1423, 2000.

### Trends in HIV Risk Behaviors of N.Y. City IDUs Suggest A Declining Phase of the Epidemic

A study was conducted to assess trends in HIV risk behaviors among IDUs in New York City from 1990 to 1997. IDUs were recruited continuously from a large detox treatment program and a storefront in a drug use area, and were interviewed regarding drug use history, HIV risk behaviors, and participation in a syringe exchange program. Trends were assessed for five risk behaviors in the 6-month period before the interview. The 3 injection risk behaviors (any needle sharing; reusing someone else's injection equipment; and sharing at last injection) declined significantly over time at each site ($p<.01$). When data were pooled across the sites, all 5 risk behaviors (the 3 injection risk behaviors plus 2 sex risk behaviors: unsafe sex with a casual partner and unsafe sex with a primary partner) declined significantly over time ($p>.01$). Participation in syringe exchange programs and HIV counseling and testing increased greatly from 1990 to 1997. These findings on trends in HIV risk behaviors among IDUs in New York City indicate a declining phase in the large HIV epidemic. Although the data do not prove that there is a direct causal link between participation in an HIV prevention program and reduced risk behavior, they address the strong possibility. In addition, the findings suggest that it may be possible to reverse large HIV epidemics among persons considered to be at very high risk. DesJarlais, D., Perlis, T., Friedman, S., Chapman, T., et al., Behavioral Risk Reduction in a Declining HIV Epidemic: Injection Drug Users in New York City, 1990-1997. Am J Public Health, 90, pp. 1112-1116, 2000.

### IDUs Participating in Syringe Exchange Programs Are More Likely to Quit Sharing Needles

Between 1992 and 1996, researchers recruited 340 high-risk IDUs who reported sharing syringes. The researchers counseled the subjects and tested them for HIV infection twice each year. At a follow-up interview, 60% of the Ss reported having quit syringe sharing. After adjusting for confounding factors, researchers found that IDUs who began using a syringe exchange program (SEP) were 2.68 times more likely to quit than those not enrolled in a program. Those who were already enrolled and continued in an exchange program were 1.98 times more likely to quit sharing needles than those who did not participate. These findings indicate that use of syringe exchange programs can be an important component in reducing the spread of blood-borne infectious diseases among high-risk IDUs. Although political controversy surrounds SEPs, the data suggest they are among the most effective HIV prevention programs for active IDUs. Bluthenthal, R., Kral, A., Gee, L., Erringer, E. and Edlin, B. The Effect of Syringe Exchange Use on High-Risk Injection Drug Users: A Cohort Study. AIDS, 14, pp. 605-611, 2000.

### Study Explores Differential HIV Risks Among IDUs, Crack Smokers, and IDUs Who Use Crack

This study was designed to assess differences in sex-related risk behaviors between drug injectors who did not smoke crack cocaine, crack smokers who did not inject drugs, and drug users who both injected drugs and smoked crack. Current drug users (i.e. used within the past 30 days) from 22 cities were recruited and assessed. The sample ($n = 26,982$) included 28% who injected only, 42% who smoked crack only, and 30% who both injected and smoked crack. Results showed that active drug users were at risk of HIV infection through sexual transmission: in the 30 day period prior to their interview, 28% reported sex with two or more individuals, 23% had an IDU sex partner, and 24% had exchanged sex for drugs or money. In addition, more than 80% did not use a condom during sex. Crack only smokers and crack smoking injectors were more likely than injectors only to report multiple sex partners and exchanging sex. Because of these high-risk behaviors, condom use was of particular importance. The number of days

of alcohol use and having an IDU sex partner were independently associated with not using a condom. Crack smoking injectors reported the highest average number of days of alcohol consumption and were the most likely to have had an IDU sex partner. Booth, R., Kwiatkowski, C., and Chitwood, D. Sex-Related HIV Risks Behaviors: Differential Risks Among IDUs, Crack Smokers, and IDUs Who Smoke Crack. Drug and Alcohol Dependence, 58(3), pp. 219-226, 2000.

### Street-Recruited Drug Injectors Enter and Remain in Free Methadone Maintenance Treatment

This investigation assessed the treatment entry impact of offering free treatment to street-recruited injecting opioid users, and determined which variables differentiated subjects who entered treatment when it was free, compared to those who entered when they had to pay for treatment. Three hundred and sixty-two out-of-treatment opioid injectors, recruited through street outreach, were randomly assigned to receive or not receive a coupon for 90 days of free substance abuse treatment. Demographics, desire for treatment, drug use and HIV risk behaviors were assessed prior to assignment. Subjects were characterized by frequent and long-term drug use, numerous arrests, a variety of behaviors that placed them at risk for HIV, and ambivalence about entering substance abuse treatment. Offering free treatment led to significantly greater treatment entry (53% vs. 33%) and retention (155 days vs. 83 days). Entry into free treatment was particularly high, compared to those who had to pay for treatment, among persons who had never been in treatment (43% vs. 23%), and those who reported that they did not want to enter treatment (24% vs. 6%). Those who entered free treatment were significantly less likely to have family problems than those who paid for their treatment. Opioid addicts recruited on the street and offered free methadone maintenance treatment are likely to enter and remain in treatment, even if they have never been in treatment before or claim not to want treatment. Different treatment approaches may be necessary if such subjects are motivated more by the removal of financial obstacles than other factors, such as family problems. Kwiatkowski, C., Booth, R., and Lloyd, L. The Effects of Offering Free Treatment to Street-Recruited Injection Opiate Users. Addiction, 95(5), pp. 697-704, 2000.

### Study Reports Needle Exchange Does Not Increase Number of Discarded Needles

Researchers estimated the quantity and geographic distribution of discarded needles on the streets of Baltimore during 2 years after a needle exchange program (NEP) opened. Counts were taken of syringes, drug vials, and bottles before the NEP opened and then at 6 periodic intervals for 2 years after it opened, over 32 randomly sampled city blocks. Two years after the NEP opened, there was a significant decline in the overall quantity of discarded needles relative to that of drug vials and bottles (background trash). There was no difference in the number of discarded needles by distance from the program site. The findings suggest that this NEP did not increase the number or distribution of discarded needles. Doherty, M., Junge, B., Rathouz, P., et al. The Effect of a Needle Exchange Program on Numbers of Discarded Needles. Am J Public Health, 90(6), pp. 936-939, 2000.

### Qualitative Strategies Provide Fuller Understanding of Social Contexts and Risk Behavior

Researchers applied six qualitative methods in combination with traditional epidemiologic survey approaches and laboratory bioassay procedures to examine neighborhood differences in access to sterile syringes among injecting drug users (IDUs) in three northeastern cities. Methods used included neighborhood-based IDU focus groups to construct social maps of local equipment acquisition and drug use sites; ethnographic descriptions of target neighborhoods; IDU diary keeping on drug use and injection equipment acquisition; ethnographic day visits with IDUs in natural settings; interviews with IDUs about syringe acquisition and collection of syringes for laboratory analysis; and focused field observation and processual interviewing during drug injection. By triangulating findings across the six qualitative methods, researchers were able to examine the effects of local contextual factors on the spread of HIV and other blood-borne infections among injecting drug users and develop better approaches for targeting interventions to specific local settings. Singer, M., Stopka, T., Siano, C., Springer, K., Barton, G., et al. The Social Geography of AIDS and Hepatitis Risk: Qualitative Approaches for Assessing Local Differences in Sterile-Syringe Access Among Injection Drug Users. Am J Public Health, 90, pp. 1049-1056, 2000.

### Ethnography May Inform Correlation Between NEP Use and HIV Seroconversion in Montreal

In this article, researchers describe a rapid ethnographic assessment of needle exchange patrons and street youth substance abusers in Montreal in March of 1997 and October of 1998. The ethnographic assessment was designed to collect preliminary participant observation information that could help to explain the disturbing statistical correlation between needle exchange patronage and HIV infection, which was found to occur among IDUs who used the NEP in Montreal from 1989 to 1995. Scenes visited in Montreal were those where cocaine users hustled cocaine and injected the drug. Authors found a disproportionate representation of cocaine injectors among Montreal NEP users, and observed cocaine bingers who injected cocaine repeatedly and rapidly, without regard to whether the syringe was

previously used. They also learned that cocaine injectors primarily asked for wider-gauged syringes compared to the thinner needles requested by heroin users. Injectors explained that the plungers on wider syringes slide more easily so they can flush the cocaine into the bloodstream faster, and supposedly get a more intense initial rush. However, wider-gauged syringes retain a greater volume of blood/biomass after use, which increases the risk of infection to those who reuse them. In addition, since cocaine addicts in Montreal often share bags of cocaine on the run, dissolving the cocaine inside the baggie right on the street, they believe they can draw up more solution faster than their companions with the fast-drawing, wide-gauged syringes. The researchers emphasize the importance of complementing quantitative data with qualitative methods to explain significant statistical associations such as the one reported for Montreal's NEPs, and they argue that NEPs by themselves cannot be expected to stem HIV infection in cities where intravenous cocaine use - characterized by compulsive behavior, craving, and multiple HIV risks - is the drug of choice. Bourgois, P. and Bruneau, J. Needle Exchange, HIV Infection, and the Politics of Science: Confronting Canada's Cocaine Injection Epidemic with Participant Observation. Medical Anthropology, 18, pp. 325-350, 2000.

### Ethnographic Study Yields Significant Insights on Crack Cocaine Injection in Dayton, Ohio

Crack cocaine injection has become increasingly more common among drug injectors. Researchers in Dayton, Ohio sought to understand this emergent phenomenon by conducting in-depth, qualitative interviews and participant observation with a purposive sample of 16 active crack injectors. Participants were recruited with the assistance of three outreach workers. There were 4 African American women, 3 African American men, 6 White men, and 3 White women in the study. The average age was 43.6. Fourteen of the 16 injectors had also smoked crack in the past 30 days and had been doing so for an average of 6.4 years; 50% of the smokers were daily users. The average age of first injection (mostly heroin) was 25.6 years and the average period of crack injection was 3.7 years. Crack injection does not appear to be a rare practice in Dayton. It seems to have become an attractive alternative to injecting powder cocaine because injectors perceive it to produce a more intense high than powder, to be purer than powder cocaine, to produce a more desirable "boost" when dissolved with vinegar, and to be less harmful when dissolved in lemon juice. This ethnographic study provides insights on how crack cocaine has been integrated into drug-injection lifestyles as a smokeable and injectable substance. Ethnographic monitoring can inform our understanding of the rapid transformation of crack cocaine from a drug that was detested by drug injectors to one that was embraced as an acceptable substance to smoke and/or to inject. Carlson, R., Falck, R., and Siegal, H. Crack Cocaine Injection in the Heartland: An Ethnographic Perspective. Medical Anthropology, 18, pp. 305-323, 2000.

### Opiate Inhibition of Chemokine Action

Opiates have been demonstrated to modify immune type cell movement peripherally as well as in the CNS. The simian immunodeficiency virus (SIV)-infected rhesus monkeys are one of the best models for studies related to HIV infection in humans. This group has shown that opiates manifest this action in these monkeys. This is important as a chemokine receptor is key for cell entry of the HIV. In this study, chemotaxis of monkey leukocytes was evaluated using the chemokines interleukin-8 (IL-8) and (RANTES) as the chemoattractants; the effects of various opioid agonists and antagonists on the efficiency of chemotaxis were examined. Opioids were either incubated with monkey leukocytes or added directly to chemokines, and the number of cells migrating toward IL-8 (for neutrophils) or RANTES (for monocytes) was scored. Inhibition of chemotaxis was seen with both assay conditions. Opioids themselves may act as weak chemoattractants for monkey leukocytes; addition of opioid agonists to chemokines appears to reduce the chemoattractant ability of the chemokines. Opioids did not cause the same inhibitory effect on the chemotactic migration of neutrophils when the complement component C5a or the chemotactic peptide N-formyl-MET-LEU-PHE (fMLP) was used as chemoattractant. These studies suggest that the presence of opioids during SIV infection immediately alters chemokine-mediated immune functions. Miyagi, A.U., Chuang, T., Lam, K.M., Kung, H.F., Wang, J.M., Osburn, B.I., and Chuang, R.Y. Opioids Suppress Chemokine-Mediated Migration of Monkey Neutrophils and Monocytes - An Instant Response. Immunopharmology, 47, pp. 53-62, 2000.

### Cannabinoid Suppresses Immunity to Legionella Pneumophila

In an effort to study the effects of cannabinoids on opportunistic infections, a mouse model has been established by this group. They have shown that cannabinoids can enhance the deadly effects of Legionella. Herein, they have more clearly defined that a select population of T cells are involved in this disease and have presented findings clarifying the role of the TH1 population of T cells. In the current study, THC effects on cytokines regulating the development of Th1 cells were examined. BALB/c mice showed significant increases in serum IL-12 and IFN-gamma within hours of infection; however, the levels of these Th1-promoting cytokines as well as resistance to a challenge infection were suppressed by THC. The Th2-promoting cytokine, IL-4, was increased within hours of a Legionella infection and was further increased by THC treatment. These results suggested that THC injection suppressed the cytokine environment promoting Th1 immunity. In additional experiments, THC pretreatment and infection of IL-4 knockout mice showed

that serum IL-12 and IFN-gamma were suppressed equally in both knockout and normal mice. This suggested that the drug-induced increase in IL-4 was not responsible for the decreases in serum IL-12 and IFN-gamma. However, THC treatment was shown to suppress the expression of IL-12 receptor beta 2 mRNA, indicating that, in addition to suppression of IL-12, THC injection suppressed the expression of IL-12 receptors. Finally, the role of cannabinoid receptors in Th1-promoting cytokine suppression was examined. Results with receptor antagonists showed that both cannabinoid receptors 1 and 2 were involved. It is suggested that suppression of Th1 immunity to Legionella is not due to an increase in IL-4 production but to a decrease in IFN-gamma and IL-12. Furthermore, both types of cannabinoid receptors are involved. Klein, T.W., Newton, C.A., Nakachi, N., and Friedman, H. Delta(9)-tetrahydrocannabinol Treatment Suppresses Immunity and early IFN-gamma, IL-12, and IL-12 receptor beta 2 Responses to Legionella Pneumophila Infection. J Immunology, 164, pp. 6461-6466, 2000.

### "Muscle Dysmorphia" in Male Weightlifters: A Case Control Study

In a first ever published controlled study, Pope and his colleagues (McLean Hospital/Harvard) have identified a new diagnostic entity- "Muscle Dysmorphia" among body builders and weightlifters. It is a form of body dysmorphic disorder in which individuals develop a pathological preoccupation with their muscularity. The authors interviewed 24 men (18-30 years old) with muscle dysmorphia and 30 comparison weightlifters, recruited from gymnasiums in the Boston area, using a battery of demographic, psychiatric, and physical measures. Data showed that the men with muscle dysmorphia differed significantly from comparison weightlifters on measures such as body dissatisfaction; eating attitudes; prevalence of anabolic steroids use (45% among muscle dysmorphic men; 6% among comparison weightlifters); and lifetime prevalence of DSM-IV mood, anxiety, and eating disorders. Men with muscle dysmorphia frequently described shame, embarrassment, and impairment of social and occupational functioning in association with their condition. By contrast, ordinary weightlifters displayed little pathology. Indeed, in an a posteriori analysis, the ordinary weightlifters proved closely comparable to a group of male college students recruited as a comparison group in an earlier study. The authors concluded that muscle dysmorphia appears to be a valid diagnostic entity, possibly related to a larger group of disorders, associated with striking and stereotypical features. Men with muscle dysmorphia differ sharply from ordinary weightlifters, most of whom display little psychopathology. Authors recommend research on potential treatment of this syndrome. Olivardia, R., Pope, H.G. and Hudson, A.J. "Muscle Dysmorphia" in Male Weightlifters: A Case Control Study. American Journal of Psychiatry, 157, pp. 1291-1296, 2000.

### Body Image Perception Among Men in Three Countries

In another study, Pope and his colleagues (McLean Hospital/Harvard) tested a hypothesis that men in modern Western societies would desire to have a much leaner and more muscular body than the body they actually had or perceived themselves to have. The investigators measured height, weight, and body fat of college-age men in three countries: Austria (n=54), France (n=65) and the United States (n=81). Using somatomorphic matrix, a computerized test, the men chose (i) the body image that they felt represented their own body, (ii) the body they ideally would like to have, (iii) the body of an average man of their age, and (iv) the male body they believed was preferred by women. The men's actual fat and muscularity was compared with that of the four images chosen. Results showed only slight demographic and physical differences among men from three countries. Importantly, in all three countries, men chose an ideal body that was a mean of about 28 lb more muscular than themselves and estimated that women preferred a male body about 30 lb more muscular than themselves. In a pilot study, however, the authors found that actual women preferred an ordinary male body without added muscle. Pope, H.G., Gruber, A.J. Mangweth, B., deCol, C., Jouvant, R. and Hudson, A.J. Body Image Perception Among Men in Three Countries, American J. Psychiatry, 157, pp. 1297-1301, 2000.

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**National Institute on Drug Abuse**

**Director's Report to the National Advisory Council on Drug Abuse**

**September, 2000**

# Research Findings

## Epidemiology, Etiology and Prevention Research

### Community Epidemiology Work Group

The 48th biannual meeting of the Community Epidemiology Work Group (CEWG), chaired by Mr. Nicholas J. Kozel, DESPR, was held in Baltimore, Maryland on June 13-16, 2000. The CEWG is composed of researchers from 21 metropolitan areas of the United States who meet semiannually to report on patterns and trends of drug abuse in their respective areas; emerging drugs of abuse; vulnerable populations and factors that may place people at risk of drug use and abuse; and, negative health and social consequences. Reports are based on drug abuse indicator data, such as morbidity and mortality information, treatment data and local and State law enforcement data. Additional sources of information include criminal justice, correctional, medical and community health data, local and State survey information and research findings from ethnographic studies.

The following are highlights from the meetings:

### IN THE PAST 6 MONTHS...

**Cocaine** indicators suggest declining or stable trends in most areas.

**Heroin** indicators are mixed. Younger populations continue to initiate use in several cities, and some are shifting from snorting to injecting.

**Marijuana** indicators suggest continued elevated levels, with generally stable or mixed trends in most CEWG sites.

**Methamphetamine** consequences continue to decline in western and central CEWG sites; indicators remain low in the East but may be trending upward.

**"Club drugs,"** especially GHB, GBL, MDMA, and ketamine, continue to spread across the country. MDMA availability is high and increasing in many CEWG areas, and its quality and content often varies widely.

**Cocaine/Crack** - Although some indicators increased slightly in a number of CEWG areas during the last reporting period, most cocaine indicators during this reporting period declined or were stable. Cocaine deaths1 were relatively stable, except in Detroit, where they decreased substantially, and Phoenix, where 1999 deaths outnumbered cumulative deaths for 1993-1998. After increasing in many sites during the last 6-month period, cocaine emergency department (ED) mentions2 decreased significantly in seven cities (Atlanta, Dallas, Chicago, New Orleans, New York, San Francisco, and Washington, DC). Nonsignificant ED decreases were reported in the majority of other cities; only two significant increases were noted (in St. Louis and Baltimore). Cocaine is the primary drug of choice for treatment admissions3 in six CEWG sites, excluding Baltimore where heroin and cocaine admissions are evenly distributed. Cocaine treatment and ED admissions tend to involve relatively older people, and the 35-and-older cohort seems to be increasing in many sites. Mixed trends were found in cocaine-positive urinalysis percentages4 among adult male arrestees, with increases at two sites (Dallas and Washington, DC), declines at three (Chicago, Los Angeles,

Philadelphia), and stable trends at the rest; the drug is now surpassed by marijuana in all but six cities. By contrast, among female arrestees, cocaine is still the most commonly detected drug in all but one city (San Diego); levels increased in four cities (Chicago, Dallas, Minneapolis/St. Paul, and Phoenix) and declined in Los Angeles and Seattle. Speedball (crack combined with heroin) injections continue to be reported in some cities, including Baltimore, Boston, Denver, Miami, New York City, St. Louis, San Francisco, Seattle, and Washington, DC. High purity and greater availability of cocaine hydrochloride (HCl) may be driving the increase in HCl indicators in some sites, including Denver, Miami (among youth), Minneapolis/St. Paul, and Newark, and the decrease in crack indicators in some cities, such as Boston, Denver, Miami (possibly among youth), and Newark.

**Heroin** - Heroin indicators show mixed trends. Heroin mortality figures1 were mixed, with deaths increasing notably in three areas (Detroit, Minneapolis/St. Paul, and Phoenix), declining in two (Miami and Seattle), and stable in two. ED indicators2 were also mixed, with 10 cities showing decreases (2 significant-Miami and Baltimore) and 10 cities showing increases (2 significant-San Francisco and Washington, DC). Heroin is the predominant drug of choice among treatment admissions3 in three reporting sites, excluding Baltimore, where cocaine and heroin admissions are evenly distributed, and Seattle, where heroin and marijuana admissions are even distributed. Opiate-positive urinalysis levels4 among adult males remained relatively low (ranging from 3.4 to 20.1 percent-positive) and stable in most cities, except for Atlanta and Washington, DC, where opiate-positive levels increased, and in Philadelphia and Seattle, where levels declined. Conversely, among adult females, opiate-positive levels increased substantially in six cities (Chicago, Minneapolis/St. Paul, New Orleans, Phoenix, San Diego, and Washington, DC); they declined notably in Detroit. Heroin purity5 ranges from 10.7 percent in Miami to 72 percent in Philadelphia. Purity trended mostly upward or remained stable: increases were particularly steep in five cities (Detroit, Los Angeles, Newark, New Orleans, and Phoenix); a decline was notable in Denver (by 22.4 percentage points). Price trends were mixed. A troubling development is the continued reporting of increases of heroin use among young populations in many CEWG cities, including Atlanta (mostly white youth who snort), Baltimore, Boston (mostly young adults who inject and some high school students who snort), Chicago, Denver (youth who primarily snort or smoke), Detroit (suburban youth), Newark, Seattle (young injectors), and Washington, DC. In Boston, Chicago, Denver, Miami, and Washington, DC, snorting seems to be increasing and is often the initial route of administration for many young, new users; conversely, injecting is on an upward trend in Baltimore (among suburban youth), Boston (among youth), Minneapolis/St. Paul, Newark, New York City, and Seattle (among younger users), and many CEWG ethnographers note that heroin snorters often progress to injecting.

**Marijuana** - After several periods of increasing indicators, marijuana indicators are mixed or stable in most CEWG sites. Marijuana ED mentions2 increased significantly in three cities (Baltimore, Philadelphia, and Phoenix) and nonsignificantly in five others; they declined significantly in five cities (San Diego, San Francisco, New Orleans, Dallas, and Chicago) and declined nonsignificantly or remained level in seven cities. Marijuana is the predominant drug treatment problem3 in two areas (Colorado and Minneapolis/St. Paul), and in Seattle, heroin and marijuana admissions are evenly distributed. Treatment admissions-in particular, clients who use only marijuana-seem to be increasing in many CEWG areas. However, the proportion of marijuana treatment admissions referred by the criminal justice system is very high in most reporting areas when compared with other drug clients. Among adult male arrestees4, marijuana has now surpassed cocaine as the most commonly detected drug in the majority of CEWG cities. Positive findings continue to increase-sharply in six cities (Atlanta, Chicago, Los Angeles, Miami, Phoenix, and Seattle); and levels declined in three (Dallas, Philadelphia, and Washington, DC). Levels also increased or remained stable among female arrestees, except for one notable decline in Seattle. Juvenile arrestee levels exceeded adult marijuana-positive levels at all four sites where juveniles were tested. Marijuana blunts continue to be common in many CEWG areas, including Boston, Chicago (especially among African-American youth), New York City (especially among African-American youth), Washington, DC (especially among youth), and parts of Texas. Marijuana also continues as a delivery medium for other drugs: blunts are often laced with PCP ("3750s") in Chicago and with crack in Chicago, New York City, and parts of Texas. In Texas, marijuana/embalming fluid/PCP combinations are reported, and joints are sometimes dipped in codeine cough syrup. High-quality marijuana is available in most CEWG areas, and potency continues to increase in many.

**Stimulants - Methamphetamine** ("crystal meth," "ice") remains concentrated in the West and, to a lesser extent, in some rural areas elsewhere. In the West, most indicators continued showing the declines reported since 1998. Declining indicators are most likely related to low purity levels in some western and central sites and increased law enforcement attention; however, reports of manufacturers switching from the "cold method" to the "Nazi method" of production may warrant attention. The latter method produces high-purity methamphetamine, which may lead to future increased health consequences. (In San Diego, for example, purity increased in just the past few months.) In the East, methamphetamine indicators remain low, but ethnographic and law enforcement evidence continue to report slight increases in availability, especially in rural areas, among whites, and among youth at clubs, raves, and college parties. Methamphetamine ED mentions2 declined significantly in eight cities (Atlanta, Denver, Dallas, Chicago, New Orleans, Phoenix, San Diego, and San Francisco), decreased nonsignificantly in four cities, and

increased nonsignificantly in only three cities (Philadelphia, St. Louis, and Boston). Methamphetamine remains the number-one primary drug problem among treatment admissions in Honolulu and San Diego3, although in San Diego most methamphetamine indicators continued to decline. Methamphetamine-positive percentages among adult male arrestees4 remained relatively low and stable, except in San Diego, where they declined notably; percentages among adult female arrestees increased notably in San Diego and Seattle and declined notably in Phoenix. In Seattle, youth are reportedly "mega-dosing" on pseudoephedrine, and in Texas, ephedrine abuse seems to be rising, especially among young adults.

**Methylenedioxymethamphetamine** (MDMA) ("ecstasy"), used primarily as a club drug at raves, dance clubs, and college scenes, is reportedly increasing in almost every CEWG city-an increase most likely driven by two factors: high availability due to large shipments from the Netherlands and other European countries; and the perception that it is a relatively harmless drug (known as the "hug drug" in Miami and the "love drug" in Minneapolis/St. Paul). In Boston and New York City, it seems to be spreading outside the club scene to the streets. Being under the influence of MDMA is referred to as "rolling" in cities across the Nation (including Chicago; Miami, where MDMA use is also referred to as "blowing up"; Minneapolis/St. Paul; and Washington, DC). In many cities, MDMA quality varies widely, and it frequently consists of entirely different substances, ranging from caffeine to dextromethorphan (DXM). For example, in Chicago, the ecstasy-like substance paramethoxyamphetamine (PMA) was involved in the deaths of two suburban youths who mistakenly thought the substance was true MDMA. In Washington, DC, where MDMA is taken by a wide range of age groups, some circular tablets are thought to be MDMA plus mescaline, some triangular tablets are thought to be heroin plus MDMA, and "nexus" tablets were verified by the DEA to be LSD plus MDMA. In Phoenix, a large quantity of high-quality MDMA, known as "candy canes" for their red and white stripes, was seized. Some older users in New York City prefer MDMA to cocaine because it lasts longer and is considered safer. Almost all cities reporting 1999 poison center data recorded an increase in MDMA-related calls since 1998. Most MDMA is taken orally in tablet form, but snorting has been reported (in Atlanta and Chicago), as has injecting (in Atlanta) and anal suppository (in Chicago).

**Methylphenidate** (Ritalin) abuse may be increasing. Eight sites reported its abuse, primarily among youth who crush tablets and snort them, including Baltimore (among middle and high school students), Boston (especially in middle- and upper-class communities), Detroit (where one 14-year-old died in 1999 due to prolonged use, and where poison center calls are rising), Minneapolis/St. Paul, Phoenix, and parts of Texas. African-Americans on Chicago's South Side inject it, sometimes with heroin or heroin and cocaine. White injecting drug users (IDUs) in Chicago inject **phenmetrazine** (Preludin).

**Depressants** - Problems associated with rave and club drugs have risen dramatically in 1999. **Gamma-hydroxybutyrate** (GHB, a central nervous system depressant) and two of its precursors, gamma butyrolactone (GBL) and **1,4 butanediol** (1,4 BDL, also called tetramethylene) have been increasingly involved in poisonings, overdoses, drug rapes and other criminal behaviors, or fatalities in nearly every CEWG city and their surrounding suburban and rural areas. These products, obtainable over the Internet and sometimes still sold in health food stores, are available at some gyms, nightclubs, raves, gay male party venues, on college campuses, or on the street. They are commonly mixed with alcohol, which may cause unconsciousness, have a short duration of action, and are not easily detectable on routine hospital toxicology screens. New esters and analogs of GHB continue to appear, even after Federal and State laws removed the sale of these drugs. In 1999, GHB accounted for 32 percent of illicit drug-related poison center calls in Boston-a number larger than that for MDMA. Conversely, in Chicago and San Francisco, GHB use is reportedly low compared with MDMA use, although GHB overdoses seem frequent compared with overdoses related to other club drugs. Even though it may be difficult to distinguish from water, several cities reported law enforcement indicators of GHB, including seizures of large amounts in Minneapolis/St. Paul and Phoenix. Withdrawal, addiction, and treatment indicators are emerging in several areas, including Miami and Minneapolis/St. Paul.

Use of the tranquilizer **ketamine** ("Special K" or "vitamin K"), also available and common in the club, rave, and party scene, is increasingly reported in numerous cities, including Atlanta, Baltimore (where users are predominantly white youth from middle- and upper-socioeconomic backgrounds), Boston (where some white, middle-class youth inject it, it is used as a heroin adulterant, and it may have been involved in some overdose deaths), Chicago (where it is available in powder form), Minneapolis/St. Paul (where injecting is reported), Newark, New York City (where it is available on the street, is either snorted or injected, and is sometimes mistaken for cocaine HCl), Phoenix, San Diego, Texas, and Washington, DC. In Detroit and St. Louis, veterinary break-ins for ketamine have increased in the past year. Clonazepam (Klonopin or Rivotril) and alprazolam (Xanax) use, in various combinations, is reported in Boston, where diverted prescription drug seizures have increased sharply after a recent rash of pharmacy break-ins. Those two drugs have replaced flunitrazepam (Rohypnol) among adolescents in Miami; similarly, in parts of Texas, clonazepam continues to replace flunitrazepam, especially in combination with beer. Flunitrazepam continues to be a problem among treatment admissions in Texas, particularly among young Hispanic males along the Mexican border,

and it has been involved in numerous poison control calls. It also remains available in Atlanta, Minneapolis/St. Paul, and New Orleans. Recent deaths in Seattle have involved concomitant injection of heroin and a depressant, typically diazepam.

**Hallucinogens-Lysergic acid diethylamide (LSD)** ED mentions increased significantly in six cities (Baltimore, Detroit, Minneapolis/St. Paul, Phoenix, and Washington, DC); no significant declines were recorded. In several CEWG areas, LSD used in combination with other club drugs continues to be reported among youth. For example, in south Florida, "rolling and trolling," combining LSD and MDMA, continues. In Texas, MDMA dealers also sell LSD. In Minneapolis/St. Paul for the first time, LSD has been sold on soda crackers, and in Phoenix, it is sold in "Sweet Breath" (a breath freshener) dropper bottles. **Phencyclidine (PCP)** ED mentions were mixed, with two significant increases (in Chicago and Dallas) and two significant declines (in Miami and San Francisco). Among arrestees, PCP-positive findings remained generally stable, except for a decrease in Philadelphia and, following a decade of marked decline, an upturn in Washington, DC. The recent increases in the Dallas PCP indicators (including ADAM, ED, and poison center data) may reflect the use of marijuana cigarettes dipped in embalming fluid containing PCP. PCP continues to be smoked with marijuana in Chicago (known there as "wicky stick" or "donk"), Minneapolis/St. Paul, New York City, and St. Louis. In New York City, it is also sold as a liquid in small shaker bottles; in Phoenix, six deaths in 1999 were related to PCP. Psilocybin mushrooms ("shrooms") and mescaline are common among adolescents and young adults in Boston. Peyote is readily available in Phoenix. In 1999, Texas poison centers reported calls involving the hallucinogenic plants, morning glories.

**Other drugs** - Cough medicines with DXM are commonly abused ("robo tripping") by teens in Boston and Minneapolis/St. Paul, where DXM is reportedly also available as a powder in clear capsules. In Atlanta, inhalants are increasingly used among club goers; in Detroit, nitrous oxide and propane use continues to be reported; in Phoenix, several deaths involving inhalants occurred in 1999, and in Texas, poppers, spray paint, gas, glue, and freon are reportedly abused. Needle exchange personnel in areas surrounding Boston report steroid injection among young male body builders. In Atlanta, law enforcement sources note the potential for abuse of the anabolic steroid clenbuterol (Spiropent) by weight lifters.

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1 Mortality figures are for 1998 versus 1999 projections (based on first-half-year 1999 data) and were available in six reporting areas.

2 Emergency department mentions are for 20 CEWG cities in the Drug Abuse Warning Network (DAWN) of SAMHSA's Office of Applied Studies; comparisons are for 1997 vs 1998 estimates, except for age group comparisons, which are for 1996 vs 1998; changes are noted only when statistically significant at $p<0.05$.

3 Treatment admission figures are primary drug of abuse as a percentage of total admissions; total admissions exclude alcohol-only but include alcohol-in-combination. Comparisons generally are for first-half-1998 vs first-half-1999 data.

4 Arrestee urinalysis data are for the 18 CEWG cities in the National Institute of Justice's Arrestee Drug Abuse Monitoring (ADAM) program; comparisons are for 1998 vs first-half-1999; first-half-1999 data are preliminary; changes are noted only when they are _5 percentage points.

5 Heroin price and purity information are for 19 CEWG cities in the Drug Enforcement Administration (DEA) Domestic Monitor Program (DMP); comparisons are for 1998 vs first-half-1998.

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## Maternal Smoking During Pregnancy and Toddler's Negative Behavior

This study extends previous studies by looking at the effect of the mother's smoking during pregnancy on her toddler's negative behavior. A survey consisting of a structured questionnaire was administered to the mothers of 2-year-old toddlers. Subjects were drawn from a community sample, as part of a larger study of mothers and their children. Participants consisted of 99 toddlers and their mothers taken from a community sample. Fifty-two of the mothers smoked throughout pregnancy, while 47 either stopped smoking during pregnancy or started smoking after childbirth. Measures included assessment of smoking behavior, the mother's personality/behavior, perinatal variables, demographic variables, and aspects of the mother-child relationship. Using logistic regression analyses, maternal smoking during pregnancy was found to be related to negativity in the child, controlling for demographic factors, perinatal factors, maternal personality attributes, and the mother-child relationship. Findings suggest that maternal smoking during pregnancy has an adverse effect on the child's negativity, and that a decrease in maternal smoking during pregnancy might be expected to lead to a decrease in the child's negativity. The relationship of maternal smoking during pregnancy and early childhood negativity to other problem behaviors remains to be explored. Brook,

J.S., Brook, D.W., and Whiteman, M. The Influence of Maternal Smoking During Pregnancy on the Toddler's Negativity. Arch Pediatr Adolesc Med, 154(4), pp. 381-385, 2000.

### Effects of Parent Personality, Upbringing, and Marijuana Use on the Parent-Child Relationship

This study examined predictors of the quality of the parent-child attachment relationship among a sample of 248 young adults with children. In this longitudinal study, data were collected during early adulthood in 1992 and in 1996/1997 via a structured questionnaire. Using logistic regression and multiple regression analyses, the authors assessed the extent to which participants' personality attributes, substance use, and relationships with their mothers predicted the quality of the parent-child bond. Results showed that participants with certain personality attributes (e.g., high sensitivity), less frequent marijuana use, or a close relationship with their mothers had a greater likelihood of having a close parent-child attachment relationship with their own children at a later time. Analyses also showed that the risk of earlier substance use on the parent-child relationship was offset by protective factors in the parents' personality domain. In addition, protective factors in the various parental domains synergistically interacted with a low frequency of marijuana use, relating to a closer parent-child attachment relationship. The findings suggest that certain parenting styles are transmitted across generations and interventions in the personality and drug use domains can help increase the likelihood that parents will form close attachment relationships with their own children. Brook, J.S., Richter, L., and Whiteman, M. Effects of Parent Personality, Upbringing, and Marijuana Use on the Parent-Child Attachment Relationship. J Am Acad Child Adolesc Psychiatry, 39(2), pp. 240-248, 2000.

### Needle Sharing Among HIV+ and HIV- Female Injection Drug Users

This study examined the psychosocial risk and protective factors related to needle-sharing behavior among HIV+ (N = 96) and HIV- (N = 128) female intravenous drug users (IDUs). Participants in this longitudinal study were interviewed individually at two points in time, with a 6-month interval between interviews. The interviewers used a structured questionnaire, which included psychosocial measures and questions about drug and sexual risk behaviors. Data were analyzed using Pearson correlations and hierarchical regression analyses. The findings supported a developmental model in which the psychosocial domains and HIV status predicted T1 (initial) needle-sharing behavior, which in turn was related to T2 (follow-up) needle-sharing behavior. In addition, the relationship between personality and peer risk factors and T2 needle sharing was buffered by family-related protective factors. While HIV-positive status had a direct effect on T1 needle sharing with strangers, its effect was mediated by all of the psychosocial variables in its relation to T1 needle sharing with familiar people. Comparisons of these results were made with a companion study of male IDUs. The results suggest several intervention and treatment approaches that can be implemented at different points in the developmental pathways leading to risky needle-sharing practices among female IDUs. Brook, D.W., Brook, J.S., Richter, L., Masci, J.R., and Roberto, J. Needle Sharing: A Longitudinal Study of Female Injection Drug Users. Am J Drug Alcohol Abuse, 26(2), pp. 263-281, 2000.

### Pathways to Condom Use Among Male Injection Drug Users

This longitudinal study examined the psychosocial risk and protective factors involved in condom use among 265 male IDUs. Subjects were individually interviewed at two points in time using a structured questionnaire, which included psychosocial measures and questions about drug use and condom use. Data were analyzed using Pearson correlations and hierarchical regression analyses. T1 condom use was the most powerful predictor of T2 condom use, with or without control on other variables. T1 family support for condom use, friends' support for condom use, adaptive coping with AIDS or the threat of AIDS, and planning to use condoms were significantly related to T2 condom use. Protective father factors enhanced the effects of other protective psychosocial factors, increasing T2 condom use. The results suggest several approaches for changing risk-taking sexual behavior in male IDUs: enhancing coping abilities, selecting peers who take fewer risks, and planning to use condoms. Brook, D.W., Brook, J.S., Rosenberg, G., Whiteman, M., Masci, J.R., Roberto, J., and de Catalogne, J. Longitudinal Pathways to Condom Use: A Psychosocial Study of Male IDUs. Addict Dis, 19(1), pp. 55-69, 2000.

### Adolescent Personality and Social-Environmental Antecedents to Drug Use in the Late Twenties

This research focused on the interrelation of the parent-child attachment, drug use in the late twenties, unconventionality, friends' drug use, and the young adult's use of drugs. Data were collected from participants at 4 points in time: early adolescence, late adolescence, early 20s, and late 20s. Data were collected from mothers at the 3 points in time that corresponded with the first 3 collections of data from their children. Both the youths and their mothers were individually interviewed. The findings indicated that the effect of parent-child mutual attachment was

mediated through early adolescent personality attributes of greater responsibility, less rebelliousness, and intolerance of deviance. These non-drug-prone personality and behavioral attitudes, in turn, insulated the young adult from affiliating with drug-using peers, and these attitudes were related to less drug use in the early 20s and ultimately in the late 20s. The results suggest that interventions focused on enhancing parent-child mutual attachment should result in a reduction of the risk factors conducive to drug use during the late 20s. The fact that these findings cover a decade and a half, from early adolescence to the late 20s, underscores the significance of placing drug use in a perspective that includes familial and behavioral aspects. Brook, J.S., Whiteman, M., Finch, S., and Cohen, P. Longitudinally Foretelling Drug Use in the Late Twenties: Adolescent Personality and Social-Environmental Antecedents. J Genet Psychol, 161(1), pp. 37-51, 2000.

### Pathways into Prostitution Among Female Jail Detainees and Mental Health Services

To explore the service needs of women in jail, the authors examined three pathways into prostitution: childhood sexual victimization, running away, and drug use. Studies typically have explored only one or two of these pathways, and the relationships among the three points of entry remain unclear. Data on 1,142 female jail detainees were used to examine the effects of childhood sexual victimization, running away, and drug use on entry into prostitution and their differential effects over the life course. Two distinct pathways into prostitution were identified. Running away had a dramatic effect on entry into prostitution in early adolescence, but little effect later in the life course. Childhood sexual victimization, by contrast, nearly doubled the odds of entry into prostitution throughout the lives of women. Although the prevalence of drug use was significantly higher among prostitutes than among non-prostitutes, drug abuse did not explain entry into prostitution. Running away and childhood sexual victimization provide distinct pathways into prostitution. The findings suggest that women wishing to leave prostitution may benefit from different mental health service strategies depending on which pathway to prostitution they experienced. McClanahan, S.F., McClelland, G.M., Abram, K.M., and Teplin, L.A. Pathways into Prostitution Among Female Jail Detainees and their Implications for Mental Health Services. Psychiatr Serv, 50(12), pp. 1606-1613, 1999.

### Risk Factors for Homelessness Among Indigent Urban Adults with No History of Psychotic Illness

This study identified risk factors for homelessness among indigent urban adults without dependent children and with no history of psychotic illness. A match-control study, stratified by sex, of 200 newly homeless men and women and 200 indigent men and women with no history of homelessness was conducted in New York City. Newly homeless case subjects were recruited from shelter assessment centers in New York City. Never-homeless control subjects, selected from public assistance centers, were single adults applying for home relief. Control subjects were matched with case subjects according to ethnicity, age, and sex. Trained interviewers employed standardized research instruments to probe 3 domains of risk factors: Symptom severity and substance use disorder, family support and functioning, and prior use of services. Significant interaction effects by sex were present for symptom severity, heroin use disorder, and prior service use. Greater numbers of the homeless of both sexes lacked a high school diploma and had less income from all sources, including from their families, than of the never homeless. Newly homeless men and women with no history of psychotic illness differed from their never-homeless counterparts in the 3 domains investigated, but socioeconomic factors were also important. Caton, C., Hasin, E., Shrout, P., Opler, L., Hirshfield, M., Dominguez, B., and Felix, A. Risk Factors for Homelessness Among Indigent Urban Adults with No History of Psychotic Illness: A Case-Control Study. American Journal of Public Health, 90, pp. 258-263, 2000.

### Psychopathy among Mexican American Gang Members: A Comparative Study

High-risk Mexican American males were assessed for levels of psychopathy. The Hare Psychopathy Checklist-Screening Version was compared in a random sample of gang members with a matched community sample of violent non-gang members and samples of forensic and psychiatric patients and undergraduate students. More than half of the gang sample was categorized as low, 44% as moderate, and only 4% as high on psychopathy. The gang members had higher scores on the total, affective, and behavioral scores than non-gang members. High scores on adolescent antisocial behavior, poor behavioral control, and lack of remorse were found in both samples. Gang members scored twice as high as non-gang members on lack of empathy. Both samples were lower on psychopathy than the forensics and higher than psychiatric patients and undergraduates. The results provide grounds for early intervention efforts for this high-risk population. Valdez, A., Kaplan, C. and Cordina, E. Pschopathy among Mexican American Gang Members: A Comparative Study. International Journal of Offender Therapy and Comparative Criminology, 44(1), pp. 46-58, 2000.

### Homelessness and Gender in Out-of-Treatment Drug Users

This study examines 5225 out-of-treatment crack users and drug injectors drawn from five different geographic areas

to examine selected factors associated with homelessness. Of these crack users, 27% considered themselves undomiciled, and 60% had previously entered some type of drug treatment. Logistic regression found that substance abusers who were married, female, and persons of color were less likely to be without a home when other variables were controlled. Trading sex for money and perceived chance of getting acquired immunodeficiency syndrome (AIDS) were associated positively with homelessness, while participating in methadone detoxification and methadone maintenance programs seemed to offer some protection from homelessness. Royse, D., Leukefeld, C., Logan, T.K., Dennis, M., Wechsberg, W., Hoffman, J., and Cottler, L. Homelessness and Gender In Out-of-Treatment Drug Users. American Journal of Drug and Alcohol Abuse, 26(2) pp. 283-96, 2000.

### Sexual and Drug Use Behaviors Among Female Crack Users: A Multi-Site Sample

The purpose of this paper was to compare female crack users who report exchanging sex for drugs and/or money with female crack users who did not report exchanging sex for drugs and/or money. A multi-site sample (n = 4667) of female crack users who participated in the National Institute on Drug Abuse (NIDA) AIDS Cooperative Agreement Project from 20 sites were interviewed. Statistical analysis compared two groups on selected variables of interest: women crack users who reported exchanging sex for drugs and/or money (n = 2658) and women crack users who did not report exchanging sex (n = 2009). Results indicated that both groups of women had frequent unprotected sex. However, women who exchanged sex had more sexual partners, had sex more often, used drugs before and during sex more often, and had a higher rate of STDs than women who did not exchange sex. In addition, African-American women, homeless women, and women who reported past substance abuse treatment were about twice as likely to exchange sex. Regional differences were also examined. Logan, T.K. and Leukefeld, C. Sexual and Drug Use Behaviors among Female Crack Users: A Multi-Site Sample. Drug and Alcohol Dependence, 58(3), pp. 237-45, 2000.

### "Drug Dependence" and Death

Illicit drug use and dependence often are associated with premature death, but available evidence comes mainly from clinical samples. Researchers at Johns Hopkins University examined drug-related mortality experience over 14 years in a United States community sample. Following probability sampling, 3,481 adult community household residents were recruited for the 1981 NIMH Baltimore Epidemiologic Catchment Area survey. Follow-up occurred in 1993-1996. Survival analyses were used to estimate median age at death and relative risk of dying in relation to drug use and dependence as assessed in 1981 using the Diagnostic Interview Schedule (DIS). Of 166 respondents who met criteria for a lifetime drug abuse or dependence diagnosis, 11 had died by 1995. Cases categorized by the DIS with "drug dependence" were more likely to have died and to have a younger median age at death ($p < .05$), with and without statistical adjustment for confounding variables. Higher levels of drug involvement also were associated with increased age- adjusted mortality. For example, a greater proportion of surviving cases had met criteria for cannabis disorder only while barbiturate and opiate dependence were more common among the decedents. The evidence favors the hypothesis that DIS-elicited "drug dependence," as well as subthreshold drug use, help to account for premature death in this community sample. Neumark, Y.D., Van Etten, M.L., and Anthony, J.C. "Drug Dependence" and Death: Survival Analysis of the Baltimore ECA Sample from 1981 to 1995. Substance Use & Misuse, 35(3), pp. 313-327, 2000.

### Drug Use Among Welfare Recipients

Another study at Johns Hopkins examined the prevalence of drug use in a nationally representative sample of 1989 recipients and 6840 nonrecipients of four welfare programs. Data from the 1995 National Household Survey on Drug Abuse (NHSDA) were analyzed using the conditional form of multiple logistic regression with matching of respondents on neighborhood of residence. Weighted proportions and variances accounting for the complex sample design of the NHSDA survey were estimated using the Taylor series linearization method. The results indicate that drug use is 50% more common in households with welfare recipients than in neighboring households in which no members received such assistance. Drug use was highest among recipients of multiple programs, particularly those who reported receiving food stamps. These findings provide new and up-to-date evidence of higher drug use among our society's most economically disadvantaged families. They also suggest that legal policies enacted in some states to enforce drug testing and deny welfare benefits to persons testing positive for drugs might have important consequences in addressing drug use in this population, although constitutional issues must be considered. Delva, J., Neumark, Y.D., Furr, C.D.M., and Anthony, J.C. Drug Use Among Welfare Recipients in the United States. American Journal of Drug and Alcohol Abuse, 26(2), pp. 335-342, 2000.

### Temperament and Antisocial Behavior in Sons of Fathers With and Without a History of Substance Abuse

A study using data from the University of Pittsburgh CEDAR sample was conducted to determine the relations

between different dimensions of temperament, and their interactions, with antisocial behavior (ASB) in 351 preadolescent boys with (n=175) or without (n=176) a family history of a substance use disorder (SUD) and to determine whether these relationships are moderated by family history of SUD. Participants were administered the Revised Dimensions of Temperament Survey (DOTS-R) and multiple measures of ASB. Factor analysis reduced the DOTS-R subscales into three factors: Rhythmicity, Behavioral Regulation, and Positive Affectivity. Boys with a family history of SUD demonstrated lower scores on the Behavioral Regulation factor and increased levels of ASB compared to those without a family history of SUD. Results also indicated that above and beyond the effects of age and socioeconomic status, low rhythmicity, low behavioral regulation, and low positive affectivity, as well as some of their higher order interactive effects, are important indicators of different types of ASB and, in some cases, only in boys with a family history of SUD. These findings suggest that ASB and SUD prevention efforts should include components aimed at improving the regulation of behavior, increasing positive affectivity, and improving the rhythmicity of daily eating, sleeping, and other routine behaviors. Giancola, P.R. Temperament and Antisocial Behavior in Preadolescent Boys with or Without a Family History of a Substance Use Disorder. Psychology of Addictive Behaviors, 14(1), pp. 56-68, 2000.

### Psychopathology and Substance-Related Problems During Early Adolescence

Another study with the CEDAR sample examined the chronological and statistical relations among onsets of psychopathology, alcohol and cannabis use, and substance-related problem from late childhood through early adolescence. Boys of fathers with substance use disorder (SUD; high average risk: n = 177) and without SUD (low average risk: n = 203) were compared using survival analysis. Proportional hazard models indicated that antisocial disorders were predicted by risk group (i.e., positive or negative family history of SUD). Antisocial disorders mediated the observed relation between risk group and substance-related problems. Negative affect disorders were predicted by risk group but did not predict substance involvement in early adolescence. Results support a model in which paternal SUD predisposes to increased antisocial and negative affect disorders in boys, and antisocial disorders lead to substance-related problems in early adolescence. Clark, D.B., Parker, A.M., and Lynch, K.G. Psychopathology and Substance-related Problems During Early Adolescence: A Survival Analysis. Journal of Clinical Child Psychology, 28(3), pp. 333-341, 1999.

### Stressful Life Events and Development of Drug Use in Adolescents

In a study of the increase in drug use during early and mid-adolescence, investigators examined the cumulative effects of stressful life experiences over time taking into account possible moderating factors such as sex, income, family attachment, self-esteem, and mastery. Using 4 years of panel data from the Family Health Study (n=651 adolescents ages 11-14 during Year 1), they estimated a hierarchical growth curve model that examined the time-varying effects of stressful life events and peer relations on drug use. Stressful life events were measured by a checklist of 16 items derived from the Junior High Life Experiences Survey and the Family Inventory of Life Events and Life Changes; they included incidents such as death, illness, or accidents among family or friends, changes of school or residence, parental divorce or separation, and family financial problems. The results indicated that experiencing a high number of life events over time is related to a significant "growth" of drug use, even after controlling for "growth" due to age or peer relations. In addition, this relationship is moderated by family attachment; high levels of attachment serve to diminish this growth significantly. Hoffmann, J.P., Cerbone, F.G., and Su, S.S. A Growth Curve Analysis of Stress and Adolescent Drug Use. Substance Use & Misuse, 35(5), pp. 687-716, 2000.

### Effects of Interviewer Characteristics on Telephone Survey Drug Use Responses

Researchers at the University of Illinois at Chicago analyzed data from 3,714 participants in a 1993 Illinois statewide substance abuse treatment needs assessment random-digit-dialing telephone survey to determine the effects of interview characteristics on rates of reporting of drug use. They examined the utility of social attribution and social desirability models for detecting the presence of interviewer effects. The specific outcome variables of interest were reports of lifetime and 18-month composite drug use. Analyses focused on the direct effects of individual interviewer characteristics (to assess social attribution) and a summary measure of interviewer-respondent similarity (to assess social distance). Random effects regression models were used to control for respondent clustering by interviewer. Results were most consistent with a social distance model and suggested that the degree of dissimilarity (social distance) between respondent and interviewer may decrease the probability of respondents reporting substance use behavior. Johnson, T.P., Fendrich, M., Shaligram, C., Garcy, A., and Gillespie, S. An Evaluation of the Effects of Interviewer Characteristics in an RDD Telephone Survey of Drug Use. Journal of Drug Issues, 30(1), pp. 77-101, 2000.

### Natural History of Cigarette Smoking from Adolescence to Adulthood

Previous research on the natural history of smoking has focused on overall group trajectories without considering the possibility of risk subgroup variation, but recent advances in quantitative methods have made it feasible to consider subgroups of trajectories within an overall longitudinal design. Taking advantage of these advances, researchers at Arizona State University used data from a cohort-sequential study of a large community sample (N = 8,556) with measurements spanning ages 11-31 and sought to identify subgroups with varying trajectories of smoking behavior. After removing 2 a priori groups (abstainers and erratics), the investigators empirically identified 4 trajectory groups -- early stable smokers (characterized by smoking onset at age 12-13 and continuation on smoking at subsequent ascertainments), late stable smokers (who typically reach a criterion of weekly smoking around age 18 and remained stable through the course of the study), experimenters (who typically initiated smoking early but had discontinued cigarette use by the age of 20), and quitters (who started smoking at an age between that of the early-stable and late-stable groups and achieved a high level of cigarette use but quit around the age of 25). The study also identified psychosocial variables from adolescence and young adulthood that distinguished among these groups. Chassin, L., Presson, C.C., Pitts, S.C., and Sherman, S.J. The Natural History of Cigarette Smoking from Adolescence to Adulthood in a Midwestern Community Sample: Multiple Trajectories and Their Psychosocial Correlates. Health Psychology, 19(3), pp. 223-231, 2000.

### Early Onset of Substance Use Among African American Children

This research tested predictions from a self-regulation model of factors relevant for early onset of tobacco and alcohol use with a community sample of 889 African American children (mean age = 10.5 years), a population for whom relatively little evidence is available at early ages. Criterion variables were peer substance use, willingness to use substances, and resistance efficacy (intention to refuse substance offers). Structural modeling indicated effects of temperament dimensions were mediated through self-control and risk-taking constructs, which were related to school involvement, life events, and perceived vulnerability to harmful effects of substances. Peer use was predicted by life events, poor self-control, and parent-child conflict; willingness to use substances was predicted by life events, risk taking, and (inversely) parental support; and resistance efficacy was predicted by perceived vulnerability and (inversely) poor self-control. Findings are discussed with reference to theoretical models of early protection and vulnerability processes. Wills, T.A., Gibbons, F.X., Gerrard, M., and Brody, G.H. Protection and Vulnerability Processes Relevant for Early Onset of Substance Use: A Test Among African American Children. Health Psychology, 19(3), pp. 253-263, 2000.

### Predictors of Continued Smoking

To test the hypothesis that high daily cigarette consumption and addiction to smoking are risk factors for the long-term continuation of smoking, a team of researchers from Harvard, the University of Jyvaskyla and the University of Rochester used longitudinal data from 986 male smokers participating in the Normative Aging Study. They entered cigarettes per day, psychological addiction, age, and education into a survival analysis as predictors of continued smoking over a 25- year period. Findings indicate that younger men and those who smoked more cigarettes per day were more likely to remain smokers in the long term. Addiction and education level were not significant predictors of continued smoking. The researchers concluded that heavier smokers are more at risk than lighter smokers for long-term smoking. It is therefore very important to provide smoking cessation treatments for heavy smokers as early as possible after the initiation of smoking. Nordstrom, B.L., Kinnunen, T., Utman, C.H., Krall, E.A., Vokonas, P.S., and Garvey, A.J. Predictors of Continued Smoking Over 25 Years of Follow-up in the Normative Aging Study. American Journal of Public Health, 90(3), pp. 404-406, 2000.

### Use of Case-Crossover Designs and Alternating Logistic Regression in Drug Abuse Studies

Researchers at Johns Hopkins University published two papers on methods for studying illicit drug use. The first deals with the use of the case-crossover design, which was developed to study time-varying exposures that cause transient excess risk of acute health events. It is a variant of case-control and subject-as-own- control research designs, involving use of information about exposure history of each case to estimate the transient effect. This kind of self-control design can help to reduce sampling bias otherwise introduced in the selection of controls, as well as confounding bias that might be derived from enduring individual characteristics, especially personality traits and other long-standing inherited or acquired vulnerabilities. When the subject is used as his or her own control, these personal vulnerabilities are matched. This paper discusses strengths and weaknesses of the case-crossover design and suggests applications of the case-crossover design in epidemiologic studies on suspected hazards of illicit drug use, and in studies of drug use and co-occurring psychiatric disturbances. The authors conclude that the case-crossover design can play a useful role, but it discloses a need to secure fine-grained measurements in epidemiologic research on psychiatric comorbidity. They also argue that this method may be of use to criminologists who study the drugs-crime nexus, to services researchers and clinicians who seek to understand treatment entry and compliance behavior, and to etiologists interested in polydrug use. The second article describes the alternating logistic regression (ALR)

method and places this method in the context of other statistical approaches to the analysis of complex survey data, including the conditional form of logistic regression with matching on neighborhood characteristics. Unlike conditional logistic regression, the ALR method provides for an explicit estimation of the magnitude of clustering of drug use within neighborhoods and within subgroups of the neighborhood defined by male-female or age indicators, with and without covariate adjustments. The application of these ALR methods is illustrated with estimates for the magnitude of clustering of daily marijuana use and weekly marijuana use within neighborhoods of the United States, based on data from the National Household Survey on Drug Abuse samples from 1990 through 1996. (1) Wu, L.T. and Anthony, J.C. The Use of the Case-Crossover Design in Studying Illicit Drug Use. Substance Use & Misuse, 35(6-8), pp. 1035-1050, 2000. (2) Bobashev, G.V. and Anthony, J.C. Use of Alternating Logistic Regression in Studies of Drug-Use Clustering. Substance Use & Misuse, 35(6-8), pp. 1051-1073, 2000.

### Developmental Taxonomy of Marijuana Users

This study applied cluster analysis to a community-based sample of marijuana users followed from adolescence to mid-30's, to create a taxonomy for marijuana use similar to those proposed for alcohol. Four groups with distinguishing characteristics emerged: early onset (age 15)-heavy use; early onset-light use; mid onset (age 16)-heavy use; and late onset (age 19.5)-light use. Of note, early onset of use did not in itself signify risk for later drug dependence; a concurrent psychiatric problem was strongly associated with risk for dependence in the early onset group, and absence of psychopathology distinguished the users who did not progress to heavy use. Association with marijuana-using peers and peer delinquency also distinguished those early users who progressed to heavy use. These findings add to our understanding about the course and risk for marijuana use, and make important distinctions among different typologies. Kandel, D.B., and Chen, K. Types of Marijuana Users by Longitudinal Course. Journal of Studies on Alcohol, 61, pp. 367-378, 2000.

### Genetics of Smoking Initiation vs. Persistence

Using data from three different cultural groups, this study analyzed twin data to assess genetic influences on smoking initiation vs. persistence in several age groups and both sexes. While the contributions of genetics to smoking persistence was very similar among the various age groups and both sexes, findings suggest that the genetic factors accounting for variance in smoking initiation differ from those accounting for smoking persistence. This suggests that future studies seeking to find genes for smoking behavior will need to differentiate between those for initiation and those for persistence, and that identifying genes for persistence may have great public health significance. Madden, P.A. F., Heath, A.C., Pedersen, N.L., Kaprio, J., Koskenvuo, M.J., and Martin, N.G. The Genetics of Smoking Persistence in Men and Women: A Multicultural Study. Behavior Genetics, 29, pp. 423-431, 1999.

### Adolescent Substance Use and Later Health Status

This paper critically reviews the literature on the hypothesized relationship between drug use and physical health status, and uses data from a 20 year follow up of adolescents to examine key mediators in the relationship. There was evidence for a persistent relationship between drug use in adolescence and detrimental adult health status, whether psychological maladjustment was controlled for or treated as an intervening variable. Including adolescent deviance as a mediator reduced the relationship between drug use and later health status to non-significance, and modeling showed adolescent deviance to be a significant intervening construct. Thus, the authors conclude that it is the deviant lifestyle, with effects such as risk-taking, poor diet, and poor medical care, that accounts for the relationship between substance use and adult health status, rather than a unique effect of drug ingestion. Spohn, R.E., and Kaplan, H.B. Adolescent Substance Use and Adult Health Status. Advances in Medical Sociology, 7, pp. 45-65, 2000.

### Adolescent Religiousness and Substance Use

The authors used data from the Mid-Atlantic School Age Twin Study to examine associations between religiousness and substance use. Adolescent religiousness was at least somewhat inversely correlated with drug and alcohol use and with other behavior problems. Religiousness was also related to lower peer conduct problems and drug use, and strongly negatively correlated with sensation seeking, especially in females. From analysis of this twin data, religiousness in adolescents appears to be largely a function of shared environmental factors, with only modest heritability; thus it may prove more important in protecting against initial adolescent use than against more heritable later drug use problems if drugs are initiated. D'Onofrio, B.M., Murrelle, L., Eaves, L.J., McCullough, M.D., Landis, J.L., and Maes, H.H. Adolescent Religiousness and its Influence on Substance Use: Preliminary Findings from the Mid-Atlantic School Age Twin Study. Twin Research, 2, pp. 156-168, 1999.

### Cross-national Comparisons of the Prevalences and Correlates of Mental and Substance Use

## Disorders

Researchers at Harvard University, other U.S. and foreign research institutions and the World Health Organization (WHO) have formed an International Consortium in Psychiatric Epidemiology (ICPE) in order to carry out cross-national comparative studies of the prevalences and correlates of mental disorders. This article describes the findings of surveys in seven countries in North America (Canada and USA), Latin America (Brazil and Mexico), and Europe (Germany, Netherlands, and Turkey), using a version of the WHO Composite International Diagnostic Interview (CIDI) to generate diagnoses. The results are reported using DSM-III-R and DSM-IV criteria without diagnostic hierarchy rules for mental disorders and with hierarchy rules for substance-use disorders. Prevalence estimates varied widely--from >40% lifetime prevalence of any mental disorder in Netherlands and the USA to levels of 12% in Turkey and 20% in Mexico. Comparisons of lifetime versus recent prevalence estimates show that mental disorders were often chronic, although chronicity was consistently higher for anxiety disorders than for mood or substance-use disorders. Retrospective reports suggest that mental disorders typically had early ages of onset, with estimated medians of 15 years for anxiety disorders, 26 years for mood disorders, and 21 years for substance-use disorders. All three classes of disorders were positively related to a number of socioeconomic measures of disadvantage (such as low income and education, unemployed, unmarried). Analysis of retrospective age-of-onset reports suggest that lifetime prevalences had increased in recent cohorts, but the increase was less for anxiety disorders than for mood or substance-use disorders. Delays in seeking professional treatment were widespread, especially among early- onset cases, and only a minority of people with prevailing disorders received any treatment. The authors conclude that there is a need for demonstration projects of early outreach and intervention programs for people with early-onset mental disorders, as well as quality assurance programs to look into the widespread problem of inadequate treatment. Andrade, L., Caraveo-Anduaga, J.J., Berglund, P., Bijl, R., Kessler, R.C., Demler, O., Walters, E., Kylyc, C., Offord, D., Ustun, T.B., and Wittchen, H.U. Cross-national Comparisons of the Prevalences and Correlates of Mental Disorders. Bulletin of the World Health Organization, 78(4), pp. 413-426, 2000.

## Panic Attacks and Suicide

This study investigated the association of panic attacks and suicide attempts in a community-based sample of 13-14-year-old adolescents. The data are from a survey of 1,580 students in an urban public school system located in the mid-Atlantic region of the United States. Logistic regression methods were used to estimate associations between panic attacks and suicidal ideation and suicide attempts. Controlling for demographic factors, major depression, the use of alcohol, and the use of illicit drugs, the authors found that adolescents with panic attacks were three times more likely to have expressed suicidal ideation and approximately two times more likely to have made suicide attempts than were adolescents without panic attacks. This new epidemiologic research adds to the evidence of an association between panic attacks and suicide attempts during the middle years of adolescence. Pilowsky, D.J., Wu, L.T., and Anthony, J., Panic Attacks and Suicide Attempts in Mid-Adolescence. American Journal of Psychiatry, 156, pp. 1545-1549, 1999.

## Weight Gain after Smoking Cessation

Smoking cessation usually results in weight gain. Nicotine gum therapy has been found to reduce weight gain in the first months after cessation, but its long-term effects are not fully known. The present study randomly assigned 608 smokers to receive placebo, 2 or 4 mg nicotine gum. In a follow-up analysis to the short-term weight change results reported in a previous paper, the authors examined the effects of the nicotine gum on weight change for 1 year after cessation among the 921-year abstainers. The authors found that weight change showed some variation with gum dose (active vs. placebo), but that weight change appeared to depend more strongly on the percentage of pre-cessation cotinine levels replaced by the nicotine gum. Participants who replaced higher proportions of their pre-cessation cotinine during the gum therapy period gained less weight during the first year post-cessation than those who replaced less cotinine, with those who replaced greater than 90% of their continue gaining only 1.7 kg by 1 year post-cessation. These findings suggest that future research is warranted to determine whether sufficiently high levels of nicotine replacement can help to permanently reduce cessation-related weight gain. Nordstrom, B.L., Kinnunen, TY. Utman, C.H., and Garvey, A. Long-Term Effects of Nicotine Gum on Weight Gain after Smoking Cessation. Nicotine & Tobacco Research, 1, pp. 259 -268, 1999.

## Perceived Risk of Cocaine Use

This study investigates whether experience with cocaine and the perception of risk associated with cocaine use might tend to cluster within neighborhoods and cities in the US. Population-based data from six years of the National Household Surveys on Drug Abuse public use files were examined. The alternating logistic regressions model was used to quantify the extent of geographic concentration. Perceptions of the harm associated with cocaine use and actual experience with cocaine tend to cluster within neighborhoods; once within-neighborhood concentration is taken

into account, there is little evidence of residual concentration within cities. Petronis, K.R., and Anthony, J. Perceived Risk of Cocaine Use and Experience with Cocaine: Do They Cluster Within US Neighborhoods and Cities? Drug and Alcohol Dependence, 57, pp. 183-192, 2000.

### Initiation of Alcohol and Marijuana Use

Guided by the social development model, this study examined dynamic patterns and predictors of alcohol and marijuana use initiation. The sample was derived from a longitudinal study of 808 youth interviewed annually from 10 to 16 years of age and at 18 years of age. Rate of alcohol initiation rose steeply up to the age of 13 years and then increased more gradually; most participants had initiated by 13 years of age. Marijuana initiation showed a different pattern, with more participants initiating after the age of 13 years. The study showed that: (1) the risk of initiation spans the entire course of adolescent development; (2) young people exposed to others who use substances are at higher risk for early initiation; (3) proactive parents can help delay initiation; and (4) clear family standards and proactive family management are important in delaying alcohol and marijuana use, regardless of how closely bonded a child is to his or her mother. Kosterman R., Hawkins J.D., Guo J., Catalano R.F., and Abbott, R.D. The Dynamics of Alcohol and Marijuana Initiation: Patterns and Predictors of First Use in Adolescence. American Journal of Public Health, 90(3), pp. 360-366, 2000.

### Ethnic and Gender Differences and Similarities in Adolescent Drug Behaviors

This study examined relationships among ethnicity, gender, drug use, and resistance to drug offers in a sample of 2,622 African American, Mexican American, and White American seventh graders. Findings included: first, the adolescents did not possess large or sophisticated repertoires of drug resistance strategies. Second, most offers came from acquaintances in contrast to data on older adolescents where offers generally come from intimate friends. Third, ethnicity had significant effects on use and the offer process. Mexican Americans received more offers, used more drugs, and were more likely to be offered drugs by peers, family members and at parties. European Americans were more likely to receive drug offers from acquaintances and at friends' homes and on the street. African Americans were more likely to receive offers from dating partners and parents, and in the park, and were more likely to resist offers of drugs-using explanations. Fourth, gender significantly affected drug offers and types of offers. Males were more at risk for offers and use at a younger age. Offers of drugs to males were more likely to come from parents or other males, while offers to females were more likely to come from other females or dating partners. Males were also more likely to receive drug offers that appealed to their social standing or self-image whereas females received either simple offers or those that minimize effects. Finally, offers of drugs to males were more likely to be made in public, while those to females were more likely to occur in private. Moon, D.G., Hecht M.L., Jackson, K.M., and Spellers R.E. Ethnic and Gender Differences and Similarities in Adolescent Drug Use and Refusals of Drug Offers. Substance Use and Misuse. 34 (8), pp. 1059-1083, 1999.

### Prediction of Violent Behavior

Using a developmental framework, this study replicates earlier research on risk factors for youth violence and explores the effects of risks for other problem behaviors on violence. Data from the Seattle Social Development Project (SSDP), a prospective study involving a panel of youths followed since 1985 were used. Potential risk factors for violence at age 18 years were measured at ages 10, 14, and 16 years. Risk factors in the individual, family, school, peer and community domains and violence were examined at each age to assess changes in their strength of prediction over time. Attention was also given to the additive strength of increasing numbers of risk factors in the prediction of violence at age 18 years. A final set of analyses explored the extent to which youths were correctly classified as having committed a violent act (or not) at age 18 on the basis of their overall level of risk at ages 10, 14, and 16 years. At each age, risk factors strongly related to later violence were distributed among the five domains. Ten of 15 risk factors measured at age 10 years; 20 of 25 at age 14; and 19 of 21 at age 16 years were significantly predictive of violence at age 18. Many constructs predicted violence from more than one developmental point. Hyperactivity (parent rating), low academic performance, peer delinquency, and availability of drugs in the neighborhood predicted violence from ages 10, 14, and 16 years. Analyses of the additive effects of risk factors revealed that youths exposed to multiple risks were more likely than others to engage in later violence. Youths exposed to more than five risk factors at each age were seven times more likely at age 20, nearly 11 times more likely at age 16 and 10 times more likely at age 14 years to have been violent than youths exposed to fewer than two risk factors at each age. Despite information gained from all significant risk factors, the overall accuracy in predicting which youth would go on to commit violent acts was limited. Herrenkohl, T .I., Maguin, E., Hill, K.G., Hawkins, J.D., Abbott, R.D., and Catalano, R.F. Developmental Risk Factors for Youth Violence. Journal of Adolescent Health, 26(3), pp. 176-186, 2000.

### Peer Behavioral Assessments Predict Later Problems

This study assessed whether peer-ratings of behavioral reputation predicted teacher-rated behavioral adjustment and academic achievement four years later. In a prospective, longitudinal design with a community sample of 213 disruptive and 104 nondisruptive children, peers were asked to assess behavioral reputation. Regression analyses showed that peer ratings of aggressive-disruptive, sensitive-isolated, and social etiquette behaviors were the best predictors of later externalizing and internalizing problems and adaptive skills, respectively. The peer-rated problematic behaviors continued to be related to these outcomes, even when parent and teacher ratings of behavior problems at baseline were included in the equation with peer ratings. However, behavioral reputation was not related to academic achievement. Realmuto, G.M., August, G.J., and Hektner, J.M. Predictive Power of Peer Behavioral Assessment for Subsequent Maladjustment in Community Samples of Disruptive and Nondisruptive Children. Journal of Child Psychology and Psychiatry and Allied Disciplines 41(2), pp. 181-190, 2000.

### Identifying Suicidal Risk Among Potential High School Dropouts

This study examined the validity of the Suicide Risk Screen (SRS) for identifying suicide-risk youths among potential high school dropouts. Five hundred eighty-one potential dropouts, aged 14 to 20 years, participated in a 3-stage case identification protocol. Randomly selected students completed a questionnaire containing the SRS and participated in an assessment interview. Validity measures included Reynolds' Suicide Ideation Questionnaire (SIQ-JR) and two clinical rating scales, the Direct Suicide Risk (DSR) and Clinical Risk Assessment (CRA). Suicide-risk severity was significantly associated with categorization defined by the SRS criteria. Of seven SRS elements, depression, suicidal ideation, and suicide threats predicted all validity measures. Suicide attempts predicted the DSR and CRA, but not Reynolds' SIQ-JR. Drug involvement, though relatively weaker, consistently predicted all validity measures. No additional psychosocial indicators improved the prediction of SIQ-JR or the DSR. Family support, likelihood of dropout, and risky behaviors, however, were additional predictors of the CRA ratings. Thompson, E.A. and Eggert, L.L. Using the Suicide Risk Screen to Identify Suicidal Adolescents Among Potential High School Dropouts. J American Academic Child Adolescent Psychiatry 38 (12), pp. 1506-1514, 1999.

### Using the Community Readiness Model

The stage of readiness of a community for implementing drug abuse prevention programs is a major factor in determining whether the program will be effectively implemented and supported by the community. The Community Readiness Model was developed to meet research needs, (e.g., matching treatment and control communities for an experimental intervention) as well as to provide a tool to help communities mobilize for change. The model defines nine stages of readiness ranging from "no awareness" of the problem to "professionalization" in the response to the problem. Assessment of the stage of readiness is accomplished through key informant interviews, involving questions on six dimensions of community readiness. Fieldwork with communities has resulted in effective strategies for successful implementation efforts at each stage of readiness. Communities that achieve a stage of readiness where focal efforts can be initiated, can then train teams in the use of the community readiness model. These teams can then develop culturally appropriate goals and activities that use local resources to guide the community to more advanced levels of readiness, eventually leading to the long-term sustainability of community efforts. Edwards, R.W., Jumper-Thurman, P., Plested, B.A., Oetting, E.R., and Swanson, L. Community Readiness: Research to Practice. Journal of Community Psychology, 28(3), pp. 291-307, 2000.

### Rural and Minority Communities at Low-levels of Readiness for Drug Prevention Programs

An assessment of community readiness for drug use prevention in rural communities indicated that most rural communities are at relatively low stages of readiness. Minority communities were particularly low in readiness, with only 2% having functioning drug prevention programs. Rural communities at different levels of readiness require different types of programs to increase readiness, i.e., communities at the "no awareness" stage require analysis of the historical and cultural issues that support tolerance of drug use, those at the "denial" and "vague awareness" stages need specific information about local problems, and communities at the "preplanning" and "preparation" stages need information about effective programs, help in identifying resources, and assistance with staff training. In addition, building and maintaining effective programs requires continued evolution of readiness through the stages of "initiation", "stabilization", "confirmation and expansion", and "professionalization". Plested, B., Smitham, D.M., Jumper-Thurman, P., Oetting, E.R., and Edwards, R.W. Readiness for Drug Use Prevention in Rural Minority Communities. Substance Use & Misuse, 34(4-5), pp. 521-544, 1999.

### Results of a Community Intervention to Prevent Adolescent Tobacco Use

This study consisted of an experimental evaluation of a comprehensive community wide program to prevent adolescent tobacco use. Eight pairs of small Oregon communities were randomly assigned to receive a school-based

prevention program or the school-based program plus a community program. The community program included: (a) media advocacy, (b) youth anti-tobacco activities, (c) family communications about tobacco use, and (d) reduction of youth access to tobacco. Effects were assessed through five annual surveys (time 1-5) of seventh through ninth grade students, ages 12-15 years. The main outcome measure used was the prevalence of self-reported smoking and smokeless tobacco use in the week before assessment. The results showed that the community program had significant effects on the prevalence of weekly cigarette use at times 2 and 5 and the effect approached significance at time 4. An effect on the slope of prevalence across time points was evident only when time 2 data points were eliminated from the analysis. The intervention affected the prevalence of smokeless tobacco among grade 9 boys at time 2. There were also significant effects on the slope of alcohol use among ninth graders and the quadratic slope of marijuana for all students. Biglan, A., Ary, D.V., Smolkowski, K., Duncan, T., and Black, C. A Randomized Controlled Trial of a Community Intervention to Prevent Adolescent Tobacco Use. Tobacco Control, 9 (1), pp. 24-32, 2000.

### Institutionalizing Drug Abuse Prevention Through Policy Change

This article summarizes community policies that have been effective in decreasing youth drug use, the contribution of community organization to policy change, and the role of policy change on institutionalizing community-based prevention efforts. Two types of policy change are considered: implementation and regulations. Implementation policies are aimed at institutionalizing prevention programs, usually through raising funds, requiring standard implementation, and creating a formal non-profit organization to implement programs. Regulatory policies include all formal laws, regulations, and ordinances aimed directly at decreasing drug use, for example, regulations which enforce the monitoring of drug-free zones. Results of studies suggest that regulatory policies show the most immediate effect on youth tobacco and alcohol use. However, implementation policies have more potential for long-term effects on use. Community organization appears to stimulate change in both types of policy. As yet unresolved is whether policy change contributes to long-term community prevention efforts. Recent research identified barriers to the translation of evidence-based prevention into practice including: (a) a lack of perceived empowerment by community leaders to continue prevention work; (b) insufficient preparation of community leaders for adoption of evidence-based programs; (c) the tendency to continue using ineffective approaches because of the past investment; and (d) a general perception that no proscribed evidence-based approach can work because each community has its own unique needs. Despite these barriers, several factors that may expedite movement in this direction emerged from case studies: (a) identification of a local "champion" for prevention; (2) development of local resources to sustain prevention; (3) feedback about prevention program effects; and (4) strategic use of supportive mass media. Pentz, M.A. Institutionalizing Community-Based Prevention Through Policy Change. J Community Psychology. 28 (3), pp. 257-270, 2000.

### The Participatory Intervention Model

This article examines the participatory approach for conceptualizing and implementing research-based interventions, the primary aim of which is the development of acceptable and sustainable prevention change efforts. The Participatory Intervention Model (PIM), rooted in participatory action research, provides a mechanism for integrating theory, research, and practice and for promoting involvement of stakeholders. PIM has demonstrated the capacity for promoting intervention acceptability, bridging the gap between research and practice, addressing cultural diversity, fostering partnerships, promoting disciplined reflective practice, and integrating the multiple roles of the school psychologist in international sexual-risk prevention work. Nastasi B.K.,Varjas, K., Schensul, S.L., Silva, K.T., Schensul, J.J., and Ratnayake, P. The Participatory Intervention Model: A Framework for Conceptualizing and Promoting Intervention Acceptability. School Psychology Quarterly. 15 (2), pp. 207-232, 2000.

### Developing Attachment through Prosocial Family Activities

Child attachment to parents has been shown to reduce the likelihood of problem behaviors, such as substance abuse, through enhancing resiliency. Research examining attachment and its relationship to antisocial behavioral outcomes in adolescents has been shaped largely by social control theorists who have theorized that attachment to prosocial others inhibits the expression of antisocial behavioral outcomes. This paper expands the literature by investigating the development of child attachment to parent(s) during the early elementary school years. The social development model posits that consistently applied opportunities for prosocial interactions and involvement with family, praise and recognition by parents, and child social and decision-making skills, predict future level of attachment. Results indicate that level of attachment in grade one or two is the strongest predictor of attachment in grade three or four. In addition, the socializing activities of parents (opportunities and involvement) had a strong positive relationship with rewards, which was a significant predictor of attachment in grade three or four over and above the effects of prior attachment. Only child skill was unrelated to reward. This may be due to the developmental status of the children and parents expectations. Oxford, M.L., Harachi, T.W., Catalano, R.F., Haggerty, K.P., and Abbott, R.D. Early Elementary School-aged Child Attachment to Parents: A Test of Theory and Implications for Prevention. Prevention Science, 1(2),

pp. 61-69, 2000.

### Parenting Skills Program Successful in Changing Behavior

This study explored the effectiveness of using trained, supervised group leaders who were not mental health clinicians to lead an intervention developed for parents of at-risk middle school students. The program was evaluated in a randomized controlled trial in eight small communities. Three hundred three parents were randomly assigned to immediate treatment or a wait-list condition. Latent growth modeling showed that participation in the program led to significant improvements in problem-solving interactions. Parents' over-reactivity and laxness toward their children's behavior were reduced and their feelings toward their children improved significantly as a function of treatment. Parent-reported antisocial behavior was also reduced. Thus, evidence was found for the effectiveness of using non mental health clinicians to aid in behavior change. Irvine, A.B., Biglan, A., Smolkowski, K., Metzler, C.W., and Ary, D.V. The Effectiveness of a Parenting Skills Program for Parents of Middle School Students in Small Communities. Journal of Consulting and Clinical Psychology 67(6), pp. 811-825, 1999.

### Outcomes of a Secondary Preventive Intervention with Aggressive Children

Teacher-identified aggressive children were randomly assigned to one of two treatment conditions, both of which involved college student mentors. The experimental condition (PrimeTime) combined therapeutic mentoring, training in problem-solving skills, and consultation with parents and teachers. The comparison treatment (Standard Mentoring) relied solely on the skills of minimally trained, unsupervised mentors. Both interventions lasted 16 months. The goal was to examine the efficacy of the PrimeTime intervention and the soundness of the model of change. Outcome assessments (at posttreatment and at one-year follow-up) were based on parent-, teacher-, and peer-reports of children's aggression and others' acceptance, as well as on children's self-rated competence and acceptance by others. Outcome analyses revealed small gains for both treatments and provided only partial support for the efficacy of the PrimeTime intervention. Analyses of change processes supported the conceptual model but also identified iatrogenic effects that may have attenuated the therapeutic impact of PrimeTime. The discussion highlights the importance of testing both intervention efficacy and putative mechanisms of change when evaluating newly developed treatment models. Cavell, T.A., and Hughes, J.N. Secondary Prevention as Context for Assessing Change Processes in Aggressive Children. Journal of School Psychology, 38 (3), pp. 199-235, 2000.

### A Manualized Preventive Intervention for Juvenile Offenders

Multi-problem families are often unprepared to provide support for recovering juvenile offenders that can prevent recidivism and associated negative outcomes, including substance abuse. Despite this, juvenile courts often return juvenile offenders to their families during parole, probation, and as an alternative to prosecution. This article provides information on a manual that describes Prosocial Family Therapy (PFT), a method of multisystemic care for juvenile offenders based on theories of risk and protective factors and therapy process. PFT integrates specific parent training techniques and nonspecific family therapy strategies. It includes techniques for reinforcing positive behaviors, skills training in communication, and strategies for motivating behavior change. Additionally, the manual describes how courts, schools, community agencies, and residential treatment centers can provide comprehensive care to juvenile offenders, ensure protocol adherence, and assess clinical significance of results. Blechman, E.A. and Vryan, K.D. Prosocial Family Therapy: A Manualized Preventive Intervention for Juvenile Offenders. Aggression and Violent Behavior 5(4), pp. 343-378, 2000.

### Peer Clique Participation and Social Status in Preadolescence

A method is described to identify peer cliques based on a consensus of group members. It provides quantitative measures of preadolescents' involvement in cliques and their association with peers who often get in trouble. The relationship between peer rejection and participation in peer cliques was of primary interest. Characteristics of peer cliques were assessed for 824 fourth-grade youth as a function of their sociometric status, gender, and aggressiveness. Rejected youth were less central members of their group than were average-status peers; however, aggressive preadolescents were no less centrally involved than their non-aggressive peers. Rejected preadolescents also belonged to smaller cliques and to cliques comprised of other low-status peers. Aggression was the primary factor associated with being a central member of deviant peer cliques. Bagwell, C.L., Coie, J.D., Terry, R.A., and Lochman, J.E. Peer Clique Participation and Social Status in Preadolescence. Merrill-Palmer Quarterly-Journal of Developmental Psychology, 46 (2), pp. 280-305, 2000.

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**National Institute on Drug Abuse**

**Director's Report to the National Advisory Council on Drug Abuse**

**September, 2000**

# Research Findings

## Services Research

### Use of Antiretroviral Therapies by HIV-Infected Persons Receiving Methadone Maintenance

HIV-infected persons receiving methadone maintenance must often seek medical care at a separate site. This study examined the relationship of attitudes and beliefs about antiretroviral therapy (ART) on the decision to initiate ART among those referred off-site. HIV-infected injection drug users (n = 72) were interviewed at three methadone maintenance programs. Of those with CD4 cell counts under 500, 83% reported that they had received ART. Of these persons, 56% had used three-drug combination therapy. Beliefs about the benefits of ART included increased survival (96%), decreased viral load (87%), decreased HIV-related infections (87%), cure for HIV (29%). Physician input, CD4 count, and possible side effects were more important than friends, family, or mass media for patients who had decided to start ART. The off-site referral model for HIV care did not appear to impede access to ART for HIV-infected IDUs in methadone maintenance. Stein, M.D., Urdaneta, M.E., Clarke, J., Maksad, J., Sobota, M., Hanna, L., and Markson L.E. J Addict Dis., 19(1), pp. 85-94, 2000.

### Drug Abuse, Methadone Treatment, and Health Services Use Among Injection Drug Users with AIDS

Health care use by injection drug users (IDUs) with AIDS were analyzed for methadone maintenance treatment (MMT) patients using AIDS surveillance and Medicaid health care claims data. Consistent participation in MMT was associated with a higher probability of antiretroviral use and, among antiretroviral recipients, more consistent use of antiretrovirals. Consistent MMT was more likely among women, whites, and older subjects. For AIDS-infected IDUs, consistent MMT may lower barriers to receipt of appropriate HIV-related health care and reinforce adherence to medical recommendations. Monthly total expenditures and inpatient expenditures were significantly lower for IDUs in MMT than for IDUs with claims indicative of current drug abuse. Sambamoorthi, U., Warner, L.A., Crystal, S., Walkup, J. Drug Alcohol Depend, 60(1), pp. 77-89, 2000.

### Effect of Ongoing Illicit Drug Use on Adherence to Antiretroviral Therapy Among HIV-Infected Methadone Patients

HIV seropositive methadone maintenance patients receiving antiretroviral therapy had HIV RNA testing and were surveyed regarding their adherence to their treatment regimens. Adherence was measured using self-report on 4 questions relating to medication use in the last day and last month and whether the patient took "drug holidays." Over half (52%) of the patients were receiving 2-drug antiretroviral therapy and 48% were receiving triple therapy that included a protease inhibitor. Persons on triple therapy reported higher rates of adherence on all measures and were more likely to have undetectable HIV RNA levels than persons on dual therapy (60% vs. 50%). Ongoing illicit drug injection was the only factor significantly associated with multiple measure nonadherence; however, it was not associated with undetectable HIV RNA level. Levels of nonadherence were comparable to estimates from other chronic diseases. This finding has important implications for patients receiving highly active antiretroviral therapy. Stein, M.D., Rich, J.D., Maksad, J., Chen, M.H., Hu, P., Sobota, M., and Clarke, J. Am J Drug Alcohol Abuse, 26(2),

pp. 195-205, 2000.

### Substance Misuse and Related Infectious Diseases in a Soup Kitchen Population

Representative samples of female (N = 119) and male (N = 100) guests at two inner city soup kitchens were interviewed. By hair analysis, 75% tested positive for cocaine/crack and 25% tested positive for heroin/opiates. Only 25% of guests were in substance dependency treatment. Infectious disease rates were: 16% HIV seropositive, 21% hepatitis B exposure, 6% hepatitis B carrier, and 15% syphilis exposure. Years of injecting drug use and homelessness or marginal housing were associated with HIV infection and hepatitis B exposure. Soup kitchens should be prime locations for outreach to cocaine/crack and heroin users in need of treatment, medical care, and interventions to prevent infectious disease transmission. Magura, S., Nwakeze, P.C., Rosenblum, A., Joseph, H. Subst Use Misuse, 35(4), pp. 551-583, 2000.

### Predictors of Relapse after Treatment for Methamphetamine Use

Using a natural history approach to interview patients treated for methamphetamine use in publicly-funded Los Angeles County programs in 1995-1997, treatment utilization and outcomes as well as relapse to drug use were studied. Results showed that in the 2 to 3 years following treatment, half of the subjects had resumed methamphetamine use, 36% within six months of the end of treatment, and 15% more within seven to 19 months. Shorter time to relapse was predicted by shorter length of treatment, older age of first substance use, involvement in selling methamphetamine, ethnicity (being Hispanic), and a higher number of prior treatment episodes. Brecht, M.L., von Mayrhauser, C., Anglin, M.D. J Psychoactive Drugs, 32(2), pp. 211-220, 2000.

### Illicit Drug Use and Emergency Room Utilization

The relationship between chronic illicit drug use and emergency room (ER) utilization was studied using data from the 1994 National Household Survey on Drug Abuse. A two-stage estimation technique was used to identify chronic drug users (CDUs) and to test for the possibility of endogeneity bias in the estimation of ER utilization. After adjustments for bias, it was estimated that chronic drug use increased the probability of using an ER by more than 30 percent compared to casual users or non-drug-users. McGeary, K.A., French, M.T. Health Serv Res, 35(1), pp. 153-169, 2000.

### Multisystemic Therapy, Monitoring Treatment Fidelity

The importance of insuring the fidelity of implementation of a specific intervention, multisystemic therapy (MST), was examined in relation to patient outcomes in a sample of youth treated for drug abuse. Relations between therapist adherence to MST principles and instrumental and ultimate outcome variables were also examined, as were relations between clinical supervision and therapist adherence. The findings provide modest support for the associations between MST adherence measures and instrumental and ultimate outcomes. Results also show that adherence can be altered when clinical supervision and adherence monitoring procedures are fortified. The modest associations between adherence measures and outcomes argue for further refinement and validation of the MST adherence measure, especially in light of the well-established effectiveness of MST with challenging clinical populations and the increasing dissemination of MST programs. Schoenwald, S.K., Henggeler, S.W., Brondino, M.J., and Rowland, M.D. Fam Process, 39(1), pp. 83-103, 2000.

### Demographic, Individual, and Interpersonal Predictors of Adolescent Alcohol and Marijuana Use Following Treatment

A vulnerability model of adolescent substance abuse treatment outcome provided the basis for investigating demographic, individual, interpersonal, and treatment factors to predict the follow-up use of alcohol and marijuana in a sample of adolescents (N = 225) with psychoactive substance use disorders. Pretreatment levels of sibling substance use and aftercare participation predicted alcohol and marijuana use during the first 6 months posttreatment. Pretreatment levels of deviant behavior also predicted the use of marijuana at 6-month follow-up. Peer substance use at intake and 6-month posttreatment both predicted substance use frequency outcomes at 12-month follow-up. Alcohol and marijuana use frequencies at 6-month follow-up also predicted continued use for these substances throughout the remainder of the 1st posttreatment year. Shorter treatment length and being male were risk factors for alcohol use during the 2nd half of the 1st posttreatment year. Elevated psychological substance dependence at 6-month follow-up was a unique risk factor for subsequent marijuana use. Latimer, W.W., Winters, K.C., Stinchfield, R., and Traver, R.E. Psychol Addict Behav, 14(2), 162-173, 2000.

### The Effectiveness of the Minnesota Model Approach in the Treatment of Adolescent Drug

## Abusers

Outcomes of drug-abusing adolescents treated with a 12-Step "Minnesota Model" approach (inpatient and outpatient) were examined at 6 and 12 months post-treatment among three groups of adolescents: those who completed treatment, those who did not, and those on a waiting list. Subjects were 245 clinic-referred adolescents (12-18 years old) who met at least one DSM-III-R substance dependence disorder. Analyzed from both relative and absolute perspectives, it was found that completing treatment was associated with far superior outcome compared to either not completing or not receiving treatment. In the year after treatment, 53% of treatment completers reported either abstinence or a minor lapse, compared to 15% for the non-completers and 28% for the waiting list group. Favorable drug abuse treatment outcomes were about two to three times more likely if treatment was completed. There were no outcome differences between residential and outpatient groups. Alcohol was the most common drug used during the follow-up period, despite cannabis being the preferred drug at intake. Winters, K.C., Stinchfield, R.D., Opland, E., Weller, C., and Latimer, W.W. Addiction, 95(4), pp. 601-612, 2000.

## Managed Care and Unmet Need for Mental Health and Substance Abuse Care

Unmet needs were analyzed in the 1998 Health Care for the Communities national survey. Need for help with emotional, mental health, alcohol, or drug problems was reported by 1,059 privately insured individuals during the past 12 months. Of those, 12% reported receiving little care or delayed care and 9.5% reported receiving no care. Enrollment in a managed care program did not predict differences in self-reported unmet need. The rate of unmet need associated with no care was lower under managed care, but the rate for less care or delayed care was higher. Sturm, R., and Sherbourne, C.D. Psychiatric Services, 51(2), p. 177, 2000.

## Trends in Psychiatric Care Expenditures and Length of Stay in Industrial Countries

International trends in inpatient psychiatric care and length of stay were examined from 1980 to 1995 using data from the Organization for Economic Cooperation and Development. Psychiatric care as a proportion of total inpatient expenditures was found to have a strong downward trend. The average length of stay for mental health and substance abuse disorders showed a small increase in Australia and Switzerland, while the U.S. and the Netherlands had a small decrease. The international phenomena of decreasing inpatient expenditures for psychiatric disorders may result from treatment advances such as medications that reduce the need for inpatient care. Sturm, R., and Bao, Y. Psychiatric Services, 51(3), p. 295, 2000.

## The Impact of Prior Authorization on Outpatient Utilization in Managed Behavioral Health Plans

The effect of preauthorization on outpatient behavioral health utilization under managed care was examined by comparing plans with similar benefits, but differing in the number of visits authorized. Plans primarily authorizing in increments of 5 visits were compared to plans authorizing in increments of 10 visits. The likelihood of terminating outpatient service between the two groups was analyzed using conditional logistic regression. Results suggest that patients whose treatment is authorized in increments of 5 sessions are nearly 3 times more likely to terminate treatment at exactly the fifth visit than if their treatment is authorized in increments of 10 sessions conditional on being in treatment until the 5th visit. The likelihood of termination peaks in both the 5- and 10-session authorization at the 10th visit, but the difference is not statistically significant. The authorization effect differs by provider type and is weaker among psychiatrists than among nonphysician providers. Liu, X., Sturm, R., and Cuffel, B.J. Med Care Res Rev, 57(2), pp. 182-195, 2000.

## Services Provided During Methadone Treatment, A Gender Comparison

Greater improvement in post-treatment outcomes has been shown in programs that tailor frequency and type of services to unique client needs. Using a sample of 635 clients (199 females and 436 males) admitted to three community-based methadone treatment programs, this study examined gender differences in services needed and provided during the first 3 months of treatment. Results revealed that compared to males, women entered treatment with more psychological symptoms and AIDS/HIV-risky behaviors. They also presented with less criminal activity, less alcohol use, and higher motivation. Counselors addressed psychological and crisis issues more frequently with women, and counseling strategies were more often directed toward developing problem-solving and communication skills. Counselors also made more medical referrals and reported having better rapport with females. Attention to employment issues and HIV/AIDS sexual-risk behaviors did not differ by gender, even though women had more needs in these areas. Rowan-Szal, G.A., Chatham, L.R., Joe, G.W., and Simpson, D.D. Journal of Substance Abuse Treatment, 19(1), pp. 7-14, 2000.

### Abstinent-Contingent Housing and Treatment Retention Among Crack-Cocaine-Dependent Homeless

Attendance in Behavioral Day Treatment was studied with regard to treatment outcome among homeless persons dependent on crack-cocaine. Participants (N = 141) were 72.3% male and 82.7% African American. Days attended, activities attended, and follow-up rates over a 12-month period were positively affected by the more attractive treatment of providing immediate, rent-free, abstinent-contingent housing during a 2-month Behavioral Day Treatment program. Results replicated previous findings that abstinence is a function of treatment attendance and more treatment is associated with greater abstinence. Analytical techniques used in this study allow for the planning, predictability, and measurement of drug abuse treatment success as a function of service utilization. Schumacher, J.E., Usdan, S., Milby, J.B., Wallace, D., and McNamara, C. J of Substance Abuse Treatment, 19(1), pp. 81-88, 2000.

### Depression Among Needle Exchange Program and Methadone Mintenance Cients

The prevalence of major depression was compared in two cohorts of injection drug users in Rhode Island, those enrolled in a methadone maintenance treatment program (MMTP) and those enrolled in a needle exchange program (NEP). Symptomatic and duration criteria for major depression in the last 6 months were identified using the Structured Clinical Interview for DSM-III-R. Among 528 persons interviewed, 54% of those in NEP and 42% of those in MMTP met criteria for major depression. Women (odds ratio [OR] 2.5, 95% confidence interval [CI] 1.7-3.7), persons with alcohol use disorders (OR 1.7, 95% CI 1.1-2.7), and persons without a current partner (OR 1.8, 95% CI 1.2-2.6) were more likely to be depressed. Persons enrolled in MMTP were less likely to be depressed (OR 0.6, 95% CI 0.4-0.8) than NEP. Higher rates of depression were found among NEP attendees than among those enrolled in MMTP. Mental health referrals should be part of the growing number of needle exchanges in the United States. Brienza, R.S., Stein, M.D., Chen, M., Gogineni, A., Sobota, M., Maksad, J., Hu, P., and Clarke, J. J Subst Abuse Treat,18(4), pp. 331-337, 2000.

### Effectiveness of Communication and Relationship Skills Training For Men in Substance Abuse Treatment

Although the importance of gender-sensitive programming for women has been acknowledged, few studies have examined outcomes from male-centered interventions in substance abuse treatment programs. Data were collected from 122 male clients in a court-mandated residential treatment program who participated in a study of a psychoeducational group intervention for men. The intervention (Time Out! For Men) addressed communication skills, sexuality, gender socialization, and intimacy. Participation in the training resulted in significant increases in knowledge and social conformity, along with reductions in attitudes that may be associated with rigid socialization and gender-role conflict. The results provide support for the utility of male targeted programming in substance abuse treatment settings. Bartholomew, N.G., Hiller, M.L., Knight, K., Nucatola, D.C., Simpson, D.D. J Subst Abuse Treat,18(3), pp. 217-225, 2000.

### Chronic Illicit Drug Use, Health Services Utilization and the Cost of Medical Care

Differences in health services utilization and the cost of medical care were studied for chronic drug users (CDUs), chronic injecting drug users (IDUs), and non-drug users (NDUs) in a community-based (out of treatment) sample. Annual differences between CDUs, IDUs, and NDUs were estimated for three measures: number of times admitted to a hospital, number of outpatient visits, and number of emergency room episodes. CDUs and IDUs were found to consume significantly more inpatient and emergency care, but less outpatient services relative to NDUs. Analyses of total health care costs showed that CDUs and IDUs each generated about $1000 in excess services utilization per individual relative to NDUs. This research is the first study to compare differences in health services utilization and cost among out-of-treatment drug users relative to a matched group of non-users in a community-based setting. Strategies are needed that promote more ambulatory care and discourage emergency room and inpatient care among drug users. French, M.T., McGeary, K.A., Chitwood, D.D., and McCoy, C.B. Soc Sci Med, 50(12), pp. 1703-1713, 2000.

### Why Carve Out? Determinants of Behavioral Health Contracting Choice Among Large U.S. Employers

Many U.S. employers have carved substance abuse and mental health services out of their medical plans. Under carve-outs, employers contract directly with specialized vendors, bypassing their general health plans. This study tested hypotheses about why purchasers carve out using data from a survey of America's Fortune 500 firms. Size was the strongest predictor of an employer's decision to carve out behavioral health once other characteristics are

controlled for. Firms that value coordination are less likely to carve out, while those that value special expertise are more likely to carve out. Firms are less likely to carve out enrollees in health maintenance organizations (HMOs) than those in other types of plans. Hodgkin, D., Horgan, C.M., Garnick, D.W., Merrick, E.L., and Goldin, D. J Behav Health Serv Res, 27(2), pp.178-193, 2000.

### Recovery Challenges Among Dually Diagnosed Individuals

Mental health and substance abuse service integration is relatively recent and often poorly implemented despite a high incidence of co-occurring mental and substance abuse disorders, and despite evidence for the benefits of integrated treatment services for dually diagnosed persons. Moreover, service providers and clients often hold divergent views of what constitutes appropriate and feasible treatment goals. This study interviewed an urban sample of dually diagnosed members of self-help groups (N = 310) concerning the challenges confronting them in their recovery, and the interrelations of these issues. The findings suggest that most clients struggle with emotional and socioeconomic issues which bear significantly on their ability to adequately handle other aspects of recovery. Laudet, A.B., Magura, S., Vogel, H.S., and Knight, E. Journal of Substance Abuse Treatment, 18(4), pp. 321-329, 2000.

### Contrasts Between Admitters and Deniers of Drug Use

This study evaluated the agreement between self-reported drug use and urinalysis results in 232 male and 27 female opiate-dependent patients at 2, 7, and 24 months following admission to methadone maintenance treatment. Differences between deniers (those who stated no drug use but whose urinalysis results were positive) and admitters of drug use were compared on psychosocial variables, and degree of Axis I and II psychopathy were examined. Generally, more drug use was acknowledged by self-report than found in urinalyses. Evidence was limited that deniers were consistently different than admitters. However, a significant increase was found for deniers in psychopathy ratings if interview and collateral information was used, compared to use only of interview information. Rutherford, M.J., Cacciola, J.S., Alterman, A.I., McKay, J.R., and Cook, T.G. Journal of Substance Abuse Treatment, 18(4), pp. 343-348, 2000.

### Initiating Abstinence in Cocaine Abusing Dually Diagnosed Homeless Persons

The effectiveness of behavioral day treatment plus abstinence contingent housing and work therapy (DT+) was compared to behavioral day treatment alone (DT). A randomized controlled trial assessed participants at baseline, 2 and 6 months. Participants met criteria for cocaine abuse or dependence, non-psychotic mental disorders, and homelessness. DT+ achieved greater abstinence at 2 and 6 months and more days housed at 6 months than DT. Effectiveness of DT+ was demonstrated, with greatest impacts on abstinence outcomes. Results replicated earlier work demonstrating effectiveness of behavioral day treatment and contingency management as an effective combination for cocaine abusing homeless persons. Milby, J.B., Schumacher, J.E., McNamara, C., Wallace, D., Usdan, S., McGill, T., and Michael, M. Drug and Alcohol Dependence, 60(1), pp. 55-67, 2000.

### Adolescent Amphetamine Users in Treatment, Client Profiles and Treatment Outcomes

The characteristics of adolescent amphetamine users admitted to residential therapeutic community treatment across the eastern United States and Canada 1992-1994 were examined. Amphetamine using adolescents were likely to be white, older, and have parents with higher education and occupational levels than nonusers. However, they also had more psychopathology, more extensive drug use and criminal histories, and engaged in more HIV-risk behaviors than nonusers. Additionally, amphetamine users tend to come from homes where one or both parents used illicit drugs, drank regularly, or had a mental illness, and they often reported histories of childhood maltreatment. At one-year follow-up, being an amphetamine user did not predict differences in treatment outcome after the client's demographic characteristics, overall drug use severity, and treatment completion were taken into account. Hawke, J.M., Jainchill, N., and De Leon, G. J Psychoactive Drugs, 32(1), pp. 95-105, 2000.

### Adolescents in Therapeutic Communities, One-Year Posttreatment Outcomes

One-year post-treatment status was examined for 485 adolescents who had been in residential therapeutic communities (TCs). The majority of the sample had been mandated to treatment by the criminal or juvenile justice system. Most reported marijuana as the main drug of abuse. One year after treatment, there were significant reductions in drug use and criminal activity. The most consistent predictors of positive outcomes were completion of treatment and not associating with deviant peers post-treatment. Jainchill, N., Hawke, J., De Leon, G., Yagelka, J. J Psychoactive Drugs, 32(1), pp. 81-94, 2000.

### Three-year Outcomes of Therapeutic Community Treatment for Drug-involved Offenders in

## Delaware

Dr. Inciardi and his colleagues at the University of Delaware note that researchers have argued for a continuum of primary (in prison), secondary (work release), and tertiary (aftercare) therapeutic community (TC) treatment for drug-involved offenders. Previous work has demonstrated significant reductions in relapse and recidivism for offenders who received primary and secondary TC treatment up to 1 year after leaving work release. However much of the effect declines significantly when the time at risk moves to 3 years after release. Further analyses reveal that program effects remain significant when their continuum model takes into account not simply exposure to the TC program, but, more importantly, program participation, program completion, and aftercare. Their outcome data clearly show that clients who complete secondary treatment do better than those with no treatment or program dropouts, and those who receive aftercare do even better in remaining drug- and arrest-free. Martin, S.S., Butzin, C.A., Saum, C.A., and Inciardi, J.A. Three-year Outcomes of Therapeutic Community Treatment for Drug-involved Offenders in Delaware: From Prison to Work Release to Aftercare. The Prison Journal, 79(3), pp. 294-320, 1999.

## Do Stronger Linkages Promote Client Utilization of Medical and Psychosocial Services in Drug Abuse Treatment?

The relationship between various linkage mechanisms (on-site delivery, external arrangements, case management, and transportation assistance) and utilization of medical and psychosocial services in outpatient drug abuse treatment units was examined using data from a national survey of administrative directors and clinical supervisors in 597 outpatient drug abuse treatment units. Models were created to analyze the correlation of on-site service delivery, external arrangements (joint program/venture or contract), case management, and transportation with patient utilization of eight services: physical examinations, routine medical care, tuberculosis screening, HIV treatment, mental health care, employment counseling, housing assistance, and financial counseling services. On-site service delivery and transportation assistance were significantly associated with higher levels of client utilization of ancillary services. Referral agreements and formal arrangements had no detectable relationship to most service utilization. On-site case management was related to increased clients use of routine medical care, financial counseling, and housing assistance, but off-site case management was not correlated with utilization of most services. Conclusions were that on-site delivery appears to be the most reliable mechanism to link drug abuse treatment clients to ancillary services, while referral agreements and formal external mechanisms offer little detectable advantage over ad hoc referral. On site case management might facilitate utilization of some services, but transportation seems a more important linkage mechanism overall. Friedmann, P.D., D'Aunno, T.A., Jin, L., and Alexander, J.A. HSR, 35(2), pp. 443-466, 2000.

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**National Institute on Drug Abuse**

**Director's Report to the National Advisory Council on Drug Abuse**

**September, 2000**

# Research Findings

## Intramural Research

### Chemistry & Drug Metabolism Section, Clinical Pharmacology & Therapeutics Research Branch

#### Reinforcing and Subjective Effects of Morphine in Human Opioid Abusers: Effect of Dose and Alternative Reinforcer

Although most opioid self-administration research has been conducted with laboratory animals, such research with humans is necessary to answer questions unique to human drug-taking behavior. IRP scientists investigated the influence of morphine dose and an alternative nondrug reinforcer on choice between morphine versus money and examined the relationship between drug-reinforced behavior and subjective euphoria. Five male opioid users participated in the 7-week study. During the first 5 weeks, a single dose of morphine (0, 4, 8, 16, or 32 mg/70 kg) was available each week. On Monday, subjects received an i.m. injection of the dose tested that week. On Tuesday, Thursday, and Friday, subjects could work for morphine or money under a second-order, progressive ratio schedule. For each primary ratio completed on the drug lever, subjects earned 1/9 of the available drug dose, and for each ratio completed on the money lever, subjects earned $1. Total amount of drug earned was administered in a single i.m. injection at the end of the session; money earned was credited to the subject's account. As morphine dose increased, responding for drug increased in an orderly manner and responding for money decreased. During the final phase of the study, the lowest and highest doses that maintained drug responding for each subject were repeated, and the value of the alternative reinforcer was increased to $2 per ratio. This manipulation was associated with decreased drug-maintained responding at the lowest, but not the highest, reinforcing dose of morphine. The progressive ratio, concurrent access procedure may be useful in predicting the outcome of drug abuse treatment interventions that use alternate reinforcement strategies. Heishman, S.J., Schuh, K.J., Schuster, C.R., Henningfield, J.E., and Goldberg, S.R. Psychopharmacology, 148, pp. 272-280, 2000.

### Clinical Pharmacology Section, Clinical Pharmacology & Therapeutics Research Branch

#### Pathological Gambling Among Cocaine-Dependent Outpatients

Pathological gambling has a high-comorbidity rate with drug abuse, but comparatively little is known about their relative order of onset or the influence of gambling on the outcome of addiction treatment. These issues were studied in 313 cocaine-dependent (200 also opiate-dependent) outpatients who participated in clinical trials of medication for treatment of cocaine dependence. Subjects were assessed for pathological gambling (DSM-IIIR criteria) using the Diagnostic Interview Schedule. Treatment outcome was assessed in terms of length of stay (LOS) in treatment and proportion of cocaine-positive urine samples given during treatment. Pathological gambling had a lifetime occurrence rate of 8% and a current (past month) occurrence rate of 4%. Onset of pathological gambling preceded the onset of cocaine dependence in 72% of patients (and the onset of opiate dependence in 44%). Patients diagnosed with pathological gambling (either lifetime or current) did not differ significantly from other patients in LOS in treatment or

proportion of cocaine-positive urine samples. Compared to other patients, those with lifetime pathological gambling were significantly more likely to have tobacco dependence (84% vs 61%) and antisocial personality disorder (56% vs 20%), to be unemployed (80% vs 49%), to have recently engaged in illegal activity for profit (64% vs 40%), and to have spent time incarcerated (64% vs 36%). These findings show that pathological gambling is substantially more prevalent among cocaine-dependent outpatients than in the general population, and support the incorporation of material on pathological gambling into substance abuse treatment. Hall, G.W., Carriero, N.J., Takushi, R.Y., Montoya, I.D., Preston, K.L., and Gorelick, D.A. American Journal of Psychiatry 157, pp. 1127-1133, 2000.

**Coping with Marijuana Quitting and Withdrawal**

There is growing evidence that individuals who stop marijuana use often experience a withdrawal syndrome. However, there is little systematically collected data on how people cope with quit attempts and withdrawal symptoms. This study addressed this issue using data collected retrospectively by self-report questionnaire from 49 physically healthy experienced marijuana smokers (41 men, mean [SD] age 45.3 [8.4] years) who had made at least one serious quit attempt and had no history of intravenous or other illegal smoked drug use. Subjects averaged 23.3 [6.7] years of marijuana use, were currently smoking 2.0 [1.8] joints/day, and had made 3.4 [3.3] quit attempts. The commonest reasons for quitting were to feel in control of their life--71% and concern over health problems--63%. The commonest withdrawal symptoms were marijuana craving--77%, irritability--54%, anxiety--46%, boredom--44%, and difficulty sleeping--42%. Among those using another substance at the time of quitting marijuana use, 59% increased their tobacco use, 58% increased their alcohol use, and 26% increased their coffee use. The most common methods for coping with quitting were getting rid of marijuana supplies (n = 10), encouragement from family (10), stopping association with marijuana-using friends (9), stopping going to places where marijuana was used (9), and encouragement from friends (8). These findings show that marijuana users who report a quit attempt make multiple attempts. A better understanding of the variety of methods used to cope with marijuana quitting, similar to those used with other drugs, may help improve treatment for marijuana abuse. Gorelick, D.A., Dermand, J.C., Nides, M.A., Simmons, M.S., and Tashkin, D.P., Poster, Royal College of Psychiatrists Annual Meeting, Edinburgh, Scotland, July 5, 2000.

**Effect of Mobile Methadone Treatment on Crime in Baltimore Neighborhoods**

Although methadone treatment programs (MTPs) are effective in reducing crime among their patients, their impact on neighborhood crime rates has not been studied. Alternate theories have been proposed: the presence of a MTP could increase crime rates by attracting drug-using individuals, or reduce crime rates by treating opiate abusers who are neighborhood residents. The present study is an ecological analysis of the impact of a mobile methadone treatment program (MMTP) on neighborhood crime. We examined arrest statistics from May 1994 to April 1996 in four Baltimore neighborhoods with MMTPs. In April 1995, the MMTPs in two of the neighborhoods were discontinued. Generalized estimating equations (GEE) were used to determine whether arrest rates changed during the second year (April 1995-April 1996) in the two neighborhoods where the MMTP left (MMTP-l) compared to the two neighborhoods where the MMTP remained (MMTP-r) and to the rest of Baltimore (BALT), after adjusting for baseline arrest rates and socioeconomic status. No significant changes in arrest rates occurred in the MMTP-l neighborhoods. The MMTP-r neighborhoods experienced significant ($p < 0.05$) decreases in arrests: all arrests-- 4.1%, drug-related--5.0%, heroin-related--3.8%, cocaine-related--6.4%. Overall, MMTP-r neighborhoods experienced greater decreases in arrests than the remainder of the city. These findings show that MMTPs may have beneficial effects in their surrounding neighborhood, as well as among their individual patients. Boyd, S., Schroeder, J., and Crape, B. Presentation, College on Problems of Drug Dependence annual meeting, San Juan, P.R., June 17, 2000.

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## Cellular Neurophysiology Section, Cellular Neurobiology Research Branch

**Neuroregenerative Effects of BMP-6 and BMP-7 After Stroke in Rats**

IRP Investigators and others have previously demonstrated that bone morphogenetic protein-7 (BMP-7) has neuroprotective and neuroregenerative effects against brain ischemia. We recently also found that pretreatment with BMP-6 prior to inducing ischemia reduces cerebral infarction, and decreases Caspase-3 immunoreactivity and TUNEL (+) cells in cerebral cortex. These data suggest that BMP-6 may also provide neuroprotection. The purpose of the current study was to compare the neuroregenerative effects of BMP-6 and BMP-7 after ischemia /reperfusion injury, a paradigm with much greater clinical relevance. Adult Sprague-Dawley rats were anesthetized with chloral hydrate. The middle cerebral artery (MCA) was transiently occluded by a filament, inserted through the right internal carotid artery. The filament was removed after 60 min ischemia to allow reperfusion. Animals developed body asymmetry, as shown by the elevated body swing test. BMP-6, BMP-7, or vehicle was injected directly into the lateral ventricle one day after MCA occlusion. Animals receiving BMP-6 or BMP-7 showed a dose-dependent decrease in body asymmetry beginning 6 days after ischemia. Taken together, our data indicate that treatment with BMP-6 or BMP-7 may have

neuroregenerative properties that normalizes motor impairment after ischemia/reperfusion injury. Lin, S.Z., Hoffer, B.J., Kaplan, P., and Wang, Y. Stroke, 30, pp. 126-133, 1999.

**Methamphetamine Exposure Facilitates Ischemic Injury in the Brain**

Previous studies have indicated that both methamphetamine (MA) and ischemia/reperfusion injuries involve reactive oxygen formation and activation of apoptotic mechanisms. It is possible that MA may have synergistic or additive effects with stroke-induced brain damage. The purpose of this study was to investigate if administration of MA *in vivo* will potentiate ischemic brain injury in an animal model. Adult CD-1 mice were treated with MA (10 mg/kg) or saline (i.p., 4 times, each dose two hours apart). Animals were later anesthetized with chloral hydrate and then placed in a stereotaxic frame. A subset of animals received intracerebral administration of GDNF, a protective neurotrophic factor. The right middle cerebral artery (MCA) and bilateral carotids were transiently occluded for 45 minutes. Regional cerebral blood flow was measured by Laser Doppler. Animals were sacrificed for tri-phenyl-tetrazolium chloride (TTC) staining and p53 mRNA Northern blot assay after 24 hours of reperfusion, p53 is a proapoptotic factor. Cortical and striatal glial cell line-derived neurotrophic factor (GDNF) levels were assayed by ELISA. Investigators found that pretreatment with MA increased ischemia-induced cerebral infarction. Ischemia or MA alone enhanced p53 mRNA expression. Moreover, MA potentiated the expression of p53 mRNA in the ischemic mice. MA pretreatment decreased GDNF levels in ischemic striatum. Intracerebral administration of GDNF before ischemia reduced MA - facilitated infarction. These data indicate that MA exacerbates ischemic insults in brain, perhaps through the inhibition of endogenous GDNF-mediated neuroprotective pathways. The data also shows that the mechanism of action of MA may involve an augmentation of apopotosis (programmed cell death) in the critical area surrounding the core of the ischemic lesion. Chiang, Y.H., Lin, S.Z., Su, T.P., Hayashi, T., Tsao, L.I., Borlongan, C.V., and Wang, Y. Society for Neuroscience Annual Meeting Abstracts, Vol 25 (2), page 1851, 1999.

**The Neurobiology of Memory Impairment by Marijuana**

The psychologically active ingredients of marijuana are known as "cannabinoids", and they are typified by the well-known chemical D9-tetrahydocannabinol (THC). Many studies have shown that marijuana can impair learning, memory, and general cognitive function in both humans and experimental animals. There is also very strong evidence that an area of the brain known as the hippocampus is involved in learning new information and in the recall of that information. This study examined the effects of a synthetic cannabinoid drug on communication among nerve cells (neurons) in the hippocampus, and examined the precise physiological mechanisms through which these effects occurred. It was found that the synthetic cannabinoid drug known as WIN 55,212-2 could diminish the release of the inhibitory neurotransmitter GABA from a specific group of neurons in the hippocampus. These effects were found to be dependent on the dose of WIN 55,212-2, and were reversed by a blocker or antagonist (known as SR-141716A) of a specific cannabinoid receptor known as CB1. In order to determine the precise cellular mechanism by which this inhibition of GABA release occurred investigators next examined the role that various ion channels play by blocking them with specific chemicals during application of WIN 55,212-2. They found that when calcium channels were blocked with cadmium chloride the ability of WIN 55,212-2 to inhibit GABA release was eliminated. In addition, they also eliminated the possibility that potassium channels or sodium channels were involved in the effects of this cannabinoid drug. These data provided strong evidence that the effects of WIN 55,212-2, and marijuana, are likely due to the reduction of GABA release through the inhibition of calcium channels by CB1 receptors located on the axon terminals of these neurons. Because GABA release is known to play an important role in synchronizing the activity of large groups of neurons in the hippocampus (which is necessary for normal cognitive function to occur), it is likely that at least part of the ability of marijuana to impair memory and cognitive activity is due to this inhibition of GABA release. Hoffman, A.F. and Lupica, C.R. The Journal of Neuroscience, 20, pp. 2470-2479, 2000.

**The Neurobiology of Marijuana Effects on Brain Drug Reward Circuits**

The nucleus accumbens is a brain structure that plays an important role in the addictive effects of a number of commonly abused drugs, such as cocaine, amphetamine, ethanol and heroin (opioids). Studies using animal models of drug reward have demonstrated that subjects will self administer many of these drugs directly into the nucleus accumbens. Such data indicate that part of the "rewarding" actions of abused drugs is encoded by the direct actions of these drugs on nerve cells (neurons) within this brain region. Since neurons within the nucleus accumbens communicate with a number of different brain areas, including those involved in processes ranging from movement to memory, a disruption of the ongoing communication (termed synaptic transmission) among these neurons has the ability to profoundly alter behavior. By studying the effects of drugs of abuse on synaptic transmission, IRP investigators hope to be able to better understand how these drugs may play a role in disrupting normal brain function. The widespread use and abuse of marijuana has led a number of investigators to attempt to characterize the actions of this drug's active components (termed cannabinoids) in the brain. These studies have shown that cannabinoids interact with specific targets (receptors) on nerve cells, and that these receptors are found in a number of different brain areas, including the nucleus accumbens. In this study, researchers examined the effects of a

synthetic cannabinoid drug called WIN 55,212-2 on synaptic transmission in the nucleus accumbens. It was found that WIN 55,212-2 produced a decrease in the release of an inhibitory neurotransmitter (GABA), but had little effect on the release of an excitatory neurotransmitter (glutamate). These effects were found to be dose-dependent and could be prevented by a synthetic blocker (antagonist) of brain cannabinoid receptors known as SR141716A. Interestingly, it was also found that a synthetic opioid (DAMGO) had the opposite effect of the cannabinoid, since it inhibited glutamate release but did not affect GABA release. These data provide strong evidence that cannabinoids do have direct effects on synaptic transmission in the nucleus accumbens, and that these actions may contribute to the abuse potential of marijuana. The differences between the actions of opioids and cannabinoids in the nucleus accumbens, although not completely understood at this time, may highlight important differences among various classes of abused drugs. Hoffman, A.F. and Lupica, C.R. Society for Neuroscience Annual Meeting Abstracts, New Orleans, LA, November 4-9, 2000.

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## Molecular Neuropsychiatry Section, Cellular Neurobiology Research Branch

### Differential Effects of Cocaine and Cocaine and Alcohol on Neurocognitive Performance

Chronic use of cocaine is associated with persistent decrements in cognitive function that are most pronounced in heavy users. Specific neurobehavioral deficits in areas such as executive function and impulsivity would make it difficult for the cocaine abuser to discontinue using drugs. Because alcohol is often used in conjunction with cocaine, the CNS effects of alcohol when taken with cocaine deserve further investigation. The dose-related effects of cocaine with or without alcohol use on the CNS were investigated by measuring performance on neurobehavioral tests. The authors evaluated the dose-related effects of cocaine and alcohol use on performance in a variety of neuropsychological tests after 1 to 3 days of abstinence and again after 4 weeks of abstinence. Fifty-six chronic cocaine abusers who had used cocaine during the past 24 to 48 hours volunteered to perform a battery of neuropsychological tests on two separate occasions during a period of enforced abstinence. In addition to using cocaine, most of the volunteers consumed alcohol. Approximately half of the participants consumed more than 10 alcohol-containing drinks per week. After controlling for the effects of age, sex, and intelligence on performance, the authors found dose-related associations between neurobehavioral performance and cocaine dose and alcohol dose. When the influences of cocaine and alcohol on neurobehavioral performance were taken separately, cocaine and alcohol each selectively affected performance on different neurobehavioral tests after 1 to 3 days of abstinence, with these effects persisting after 4 weeks of abstinence. The concomitant use of cocaine and alcohol may have additive negative effects on the brain as compared to the use of only one of these two substances. Bolla, K.I., Funderburk, F.R. and Cadet, J.L. Neurology 54, pp. 2285-2292, 2000.

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## Brain Imaging Section, Neuroimaging Research Branch

### 6-[F-18]Fluoro-A-85380, a Novel PET Tracer for nAChRs

A novel positron emission tomography (PET) radiotracer, 6-[F-18]fluoro-3-(2(S)-azetidinyl-methoxy)pyridine (6-[F-18]fluoro-A-85380, 6-[F-18]FA) was synthesized by a no-carrier-added fluorination. *In vitroo* assays of 6-[F-18]FA binding to nicotinic acetylcholine receptors (nAChRs) in rat brain showed that it bound with very high affinity (Kd 28 pM). In PET studies, 6-[F-18]FA specifically labeled central nAChRs in the brain of the Rhesus monkey and demonstrated highest levels of accumulation of radioactivity in brain regions enriched with the alpha4 beta2 subtype of nAChR. 6-[F-18]FA exhibited a target-to-non-target ratio (estimated as radioactivity in the thalamus to that in the cerebellum) of binding in primate brain similar to that previously determined for a labeled analog of epibatidine, [F-18]FPH. In contrast to [F-18]FPH, the novel tracer is expected to exhibit substantially less toxicity. Thus, the novel radioligand, 6-[F-18]FA, appears to be a suitable candidate for imaging nAChRs in human brain. Horti, A.G., Chefer, S.I., Mukhin, A.G., Koren, A.O., Gundisch, D., Links, J.M., Kurian, V., Dannals, R.F., and London, E.D. Life Sciences, 67, pp. 463-469, 2000.

### Tobacco Smoking in Adolescents

This review summarizes what is currently known about tobacco use in children and adolescents. Throughout the tobacco epidemic, long-term nicotine dependence has resulted primarily from the initiation of tobacco use during adolescence, and many adolescents try to quit and fail. Strategies to prevent the onset and treat adolescent tobacco dependence have had limited success. In addition, adolescents do not benefit from the same level of societal support for cessation attempts as adults, and they may be less motivated to quit despite the negative health consequences. Overall, the impact of adolescent smoking cessation clinics has been disappointing due to low participation, high attrition, and low quit rates. This review considers the therapeutic reduction of smoking rates (exposure reduction) as an intermediate therapeutic goal for adolescent individuals who are dependent or dependence-prone, but for whom

initial treatment interventions do not yield complete cessation. Moolchan, E.T., Ernst, M., and Henningfield, J.E. Journal of American Academy of Child and Adolescent Psychiatry, 39, pp. 682-693, 2000.

**Plasma Catecholamines in Lesch-Nyhan Disease**

Noradrenergic dysfunction and abnormality in monoamine oxidase (MAO) enzyme activity have been reported previously in Lesch-Nyhan (LN) disease. This study examines peripheral indices of adrenergic, noradrenergic and MAO function in children and young adults with LN disease (n=11), and healthy subjects (n=9). The LN subjects had significantly higher epinephrine (EPI) levels by 245% ($p<0.00$) and lower 3-methoxy-4-hydroxyphenylglycol (DHPG) levels by 42% ($p<0.00$) compared to the control group. No group differences were noted in NE plasma levels. Cognitive function (IQ tested by Stanford Binet Intelligence Scale) was associated with levels of plasma EPI in the LN group ($r=0.77$, $p=0.009$), but not in the control group. The abnormally high EPI plasma concentrations may indicate another biochemical dysfunction secondary to the absence of the hypoxanthine guanine phosphoribosyl transferase enzyme in LN patients. Such a biochemical deficit is likely to originate from the adrenal medulla, which is the primary site of EPI synthesis. The adrenal medulla may be directly affected by the absence of hypoxanthine guanine phosphoribosyl transferase enzyme, or may receive inappropriately high descending activation input from the brain. The abnormally low DHPG levels, in the context of normal NE levels, indicates low MAO activity, either as a primary deficit, or as secondary adaptive changes to spare NE levels that would otherwise be too low for adequate noradrenergic function. Ernst, M., Zametkin, A.J., Pascualvac, D., Matochik, J.A., Eisenhofer, G., Murphy, D.L., and Cohen, R.M. Neuropsychopharmacology, 22, pp. 320-326, 2000.

**Pictorial Instrument for Child and Adolescent Psychiatry**

The pictorial instrument for child and adolescent psychiatry (PICA-III-R) is presented as part of a comprehensive review of the tools used to diagnose psychiatric disorders in children and adolescents. The development of the PICA-III-R, its content, its initial psychometric properties, and directions for its use are described. The PICA-III-R assesses all DSM-III-R Axis-I psychiatric disorders in children aged 6 to 16 years, categorically (diagnosis present or absent) and dimensionally (range of severity). It comprises 137 pictures organized in modules that cover five diagnostic categories, including disorders of anxiety, mood, psychosis, disruptive behavior, and substance abuse. Its initial psychometric properties are promising with good internal consistency, significant discriminative power for diagnoses, and sensitivity to changes. Despite a large interest expressed by child psychiatrists, further testing has not been possible for practical reasons unrelated to the scientific importance of this work. Although it needs to be modified to follow DSM-IV criteria, the PICA-III-R can be of significant help to child psychiatrists, for clinical as well as research diagnostic purposes. Additionally, it can be used for the assessment of non-English speaking, or hearing/speech impaired children. Ernst, M., Cookus, B.A., and Moravec, B.C. Journal of American Academy of Child and Adolescent Psychiatry, 39, pp. 94-99, 2000.

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## Preclinical Pharmacology Section, Behavioral Neuroscience Research Laboratory

**Butyrylcholinesterase Accelerates Cocaine Metabolism: *In vitroo* and *in vivo* Effects in Non-human Primates and Humans**

Butyrylcholinesterase (BChE) is know to metabolize cocaine in humans. In the present study, IRP investigators determined whether the administration of horse serum-derived BChE would accelerate the metabolism of cocaine. The addition of BChE to squirrel monkey plasma reduced the *In vitroo* half-life of cocaine by over 80%. The administration of BChE to anesthetized squirrel monkeys reduced the *in vivo* peak concentration of cocaine observed. Finally, the addition of BChE to human plasma resulted in a dose-dependent decrease in the *In vitroo* cocaine half-life. Together these results indicate that exogenously administered BChE can accelerate cocaine metabolism in such a way as to potentially lessen the behavioral and toxic effects of cocaine. Therefore, BChE may be useful as a treatment for cocaine addiction and toxicity. Carmona, G.N., Jufer, R.A., Goldberg, S.R., Gorelick, D.A., Greig, N.H., Yu, Q.-S., Cone, E.J. and Schindler, C.W. Drug Metabolism and Disposition, 28, pp. 367-371, 2000.

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## Psychobiology Section, Medications Discovery Research Branch

**Novel Dopamine Uptake Inhibitors as Potential Therapeutics for Cocaine Abuse**

Several analogs of benztropine (BZT) have been characterized as like cocaine in that they occupy the sites in the brain where cocaine produces its potent behavioral effects. However, these compounds do not have all of the behavioral effects of cocaine. If these compounds do not produce effects like cocaine, yet occupy the sites in the brain where cocaine acts, they may serve as antagonists to cocaine and could be useful leads for the discovery of

drugs to treat cocaine abuse. One critical effect of cocaine that is considered important for its liability for abuse is its reinforcing effects - that is, whether a laboratory subject will make a simple response that results in the intravenous infusion of the drug. The present study examined the reinforcing effects of BZT and some of its analogs to determine if they have reinforcing effects. If these compounds have reinforcing effects they are likely to have abuse liability of their own and therefore would not be good candidates for cocaine-abuse therapeutics. Four monkeys were trained to self-administer intravenous injections of cocaine. Once they reliably self-administered cocaine the effects of placebo and various doses of cocaine, BZT and its analogs were assessed. Self-administration was maintained under the FR schedule by cocaine, and to a lesser extent by two analogs of BZT. BZT did not maintain self-administration. This study confirms and extends previous results demonstrating that BZT analogs do not have behavioral effects similar to those of cocaine. Because these compounds compete for the sites in the brain at which cocaine acts, the findings support the suggestion that this group of compounds may provide useful leads for development of pharmacotherapeutic agents for the treatment of drug abuse. Woolverton W.L., Rowlett, J.K., Wilcox, K.M., Paul, I.A., Kline, R.H., Newman, A.H., and Katz, J.L. 3' and 4'-Chloro-substituted Analogs of Benztropine: Intravenous Self-Administration and *In vitroo* Radioligand Binding Studies in Rhesus Monkeys. Psychopharmacology, 147, pp. 426-435, 2000.

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**National Institute on Drug Abuse**

**Director's Report to the National Advisory Council on Drug Abuse**

**September, 2000**

# Program Activities

## New PAs/RFAs

### *NIDA PAs*

On June 27, 2000 NIDA issued a Program Announcement entitled **Molecular Genetics of Drug Addiction Vulnerability (PA-00-115)**. This PA seeks investigator-initiated applications for research projects that identify chromosomal loci and genetic variations in genes that are associated with increased vulnerability to addiction or dependence on stimulants (e.g., cocaine and amphetamine), narcotics (e.g., opiates), nicotine, benzodiazepines, barbiturates, cannabis, hallucinogens, and/or multiple drugs of abuse in human beings.

### *PAs With Other NIH Components*

On June 15, NIDA, in conjunction with a number of other NIH Institutes, issued Program Announcements entitled **Basic and Translational Research in Emotion (R01) (PA-00-105) and Basic and Translational Research in Emotion: Small Grants (PA-00-106).** The purpose of these PAs is to invite research grant applications to expand basic research on the processes and mechanisms involved in the experience and expression of emotion.

On June 27, 2000, NIDA, in conjunction with the National Institute of Mental Health (NIMH) and the National Institute of Child Health and Human Development (NICHD), issued a Program Announcement entitled **Developmental Psychopharmacology (PA-00-114)** soliciting grant applications to study the possible clinically significant effects that various psychotropic medications may have on the brain when administered during the developing phase that spans from birth to early adulthood. The main goal is to generate data that are relevant to the clinical use of psychotherapeutic medications in children and adolescents with respect to safety and/or efficacy within dose ranges, schedules, and routes of administration that are usually employed therapeutically. The ultimate purpose is to increase our knowledge of the safety and effectiveness of psychopharmacological treatments administered to children and adolescents.

On June 29, 2000, NIDA, in conjunction with numerous other NIH components, issued Program Announcements entitled **Innovations in Biomedical Information Science and Technology: Phased Innovation Award (R21/R33) (PA-00-117) and Innovations in Biomedical Information Science and Technology: SBIR/STTR Initiative (PA-00-118).** Through these PAs participating Institutes and Centers of NIH invite applications for innovative research in biomedical information science and technology to promote the progress of biomedical research. There exists an expanding opportunity to speed the progress of biomedical research through the power of computing to manage and analyze data and to model biological processes. The NIH is interested in promoting research and developments in biomedical information science and technology that will support rapid progress in areas of scientific opportunity in biomedical research.

On June 29, 2000, NIDA, in conjunction with numerous other NIH components, issued a Program Announcement entitled **Planning Grants: National Program of Excellence in Biomedical Computing (PRE-NPEBC) (PAR-00-102).** Through this announcement participating components of the NIH invite applications for P20 planning grants

that lead to the establishment of National Programs of Excellence in Biomedical Computing. Subsequent to this PA, a series of solicitations will be issued by participating NIH Institutes and Centers to invite applications for National Programs of Excellence in Biomedical Computing (NPEBC) awards.

On July 25, 2000, NIDA, in conjunction with several other NIH Institutes, issued a Program Announcement entitled **National Research Service Awards for Individual Predoctoral Fellows (PA-00-125).** This is a revision and expansion of PA-99-017 that was published in the NIH Guide on November 19, 1998 and will remain active for three years. This program will provide predoctoral training support for doctoral candidates that have successfully completed their comprehensive examinations or the equivalent by the time of award and will be performing dissertation research and training.

### *RFAs With Other NIH Components*

On May 24, 2000, NIDA and the National Institute of Mental Health (NIMH) issued an RFA entitled **Research on Depression Comorbid With Externalizing Problems in Children (MH-01-002).** The purpose of this RFA is to solicit research grant award applications for research on early identification of depression (Dysthymic Disorder and/or Major Depressive Disorder) comorbid with disruptive behavior problems or disorders (persistent antisocial behavior, attention deficit hyperactivity disorder, oppositional-defiant disorder, and conduct disorder) in children under 12 years of age in pre-school, school, pediatric care, and other settings - and for intervention research designed to treat or prevent these comorbid conditions.

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## Other Program Activities

### Transdisciplinary Tobacco Use Research Centers Update

On June 14, 2000, Dr. Jaylan Turkkan reported to the National Cancer Institute (NCI) National Advisory Board (NCAB) on NIDA's support and activities in nicotine and tobacco use research, including the creation of and progress on the Transdisciplinary Tobacco Use Research Centers (TTURC). On June 29 and 30, 2000 the TTURC Principal Investigators, co-investigators, Mr. Richard Millstein, NIDA Deputy Director and other NIDA staff, NCI staff, staff of the Robert Wood Johnson Foundation and members of the newly appointed Consultation Committee to the TTURCs met for their second retreat, held in Alexandria, Virginia. Consultation Committee Members for the TTURC are: Gary E Swan, Ph.D., SRI International; John "Kim" Worden, Ph.D., University of Vermont; Kathleen T. Brady, M.D., Ph.D., Medical University of South Carolina; Ellen R. Gritz, Ph.D., UT M.D. Anderson Cancer Center; Denis J. Prager, Ph.D., Strategic Consulting Services; Richard R. Clayton, Ph.D., University of Kentucky; Tom Glynn, Ph.D., American Cancer Society; and Michael Goldstein, M.D., Bayer Institute for Communication. The TTURC investigators discussed the potential for cross-center collaborative projects in genetics, cultural research, neuroimaging, cost-effectiveness, and policy-related research in tobacco use. A third retreat is scheduled in San Diego, CA for late January 2001.

### The Methamphetamine Clinical Program

To implement the recommendations of the Methamphetamine Addiction Treatment Think Tank (MATTT) meeting held in January 2000, a process was started to establish a group of sites to conduct clinical trials for methamphetamine dependent patients. Five sites have been selected where the epidemic is currently concentrated, two in the Midwest (Des Moines, Iowa, and Kansas City, Kansas), and the other three are Los Angeles, San Diego, CA, and Honolulu, HI. The first medication study protocol is finalized (bupropion) and was sent to local IRBs for review. This study is projected to start in October 2000. Additionally, selegiline will be studied first in inpatient clinical pharmacology studies at UCLA and UCSF for safety interactions with amphetamine. Following these studies, and if safety is not an issue, selegiline will be advanced to outpatient studies following completion of the bupropion study. Plans are underway to obtain lobeline from a pharmaceutical manufacturer to study its safety profile with amphetamine and ultimately also advance it to outpatient studies.

### Clinical Research Efficacy Screening Trial (CREST-I) Study

On April 26, 2000 a group of outside consultants reviewed the data from each NIDA/VA Medications Development Research Unit (MDRU) in their CREST studies (three medications each and an unmatched placebo). Out of the 15 medications reviewed three medications were shown to give positive signals in these screening pilot studies. Reserpine (an antihypertensive medication) gave the strongest signal while cabergoline (dopamine agonist) and hydergiene (a brain metabolic and blood flow enhancer) gave weak signals. The recommendations of the consultants were to follow up with larger phase II studies on these medications.

### Clinical Research Efficacy Screening Trial (CREST-II) Study

Similar to CREST-I, the second phase of rapid drug screening started following the completion of CREST-I. This second round involves eight different medications. The estimated completion time for these studies is November 2000. The data from these trials will be analyzed and reviewed by consultants by January/February 2001.

### Cocaine Clinical Trials Operations

This network of four academic clinical sites has been established to replace the old MDRU sites to conduct clinical trials for cocaine addiction. These are UCLA, University of Cincinnati, Medical University of South Carolina, and University of Texas at San Antonio. The contract is in place with two other supporting contracts with TRI and KAI for data management. Eight protocols have been submitted for the sites to study, three are phase one interaction studies (Modafnil, Metyrapone, Tolcapone) one phase IIa study (Ondansteron) and two phase IIb studies (resperpine and cabergoline). These studies are projected to start in October 2000.

### GBR 12909

The report from the Phase I (healthy volunteer) study is complete and will be reviewed by consultants in September 2000 in planning for a cocaine interaction study. The study showed 30-40% dopamine transporter occupancy at the 100mg dose level. Based on primate data showing equivalent levels of occupancy at doses reducing cocaine self-administration, this may be clinically meaningful in cocaine treatment.

### NS2359

The final protocol for this safety cocaine interactions study has been submitted to FDA for review and is on line to start in January 2001.

### Methylphenidate in Cocaine Dependant Individuals with Attention Deficit Disorder

An open label feasibility study showed a promising effect of methylphenidate in decreasing cocaine use in this co-morbid subgroup. NIDA has awarded a grant for Dr. Frances Levin to further study methylphenidate in this subgroup in a large double blind study. This study is approximately half way through completion.

### Selegiline

The selegiline IR study has been completed and data are currently being analyzed. The VA Cooperative Studies Program review committee and their central IRB have approved the phase III 300 subject Selegiline Transdermal System study protocol. The protocol was sent out to local investigators for review by local IRBs and was also submitted to FDA for review. This study is projected to start by November 2000.

### Lofexidine for Heroin Withdrawal Study

This phase III multisite study protocol was recently reviewed and approved by the VACSP central IRB, and will be reviewed by the VA CSP review committee. Following this review the protocol will be reviewed by the local sites IRBs as well as the FDA. Projected date to start this study is January 2000.

### Desipramine in Cocaine Dependence

The Clinical/Medical Branch will follow the collective opinion of consultants that NIDA should further evaluate the concept of a desipramine therapeutic window in a phase II study. The protocol is near completion and will be submitted through the Clinical Trials Operations contract mechanism. Projected start date is March 2001.

### Indian Health Research Centers

NIDA has agreed to fund substance abuse related projects that are approved through an RFA to establish Indian Health Research Centers issued through the Indian Health Service and NIGMS. Support for this initiative was recommended by the Native American/Alaska Native Work Group convened by the Special Populations Office. Kathy

Etz, DESPR, Arnold Mills, DESPR, Richard Harrison, OEA and Lula Beatty, SPO, are NIDA staff who are working on the implementation of this activity.

### National Hispanic Science Network on Drug Abuse

The Special Populations Office released an RFC to develop a National Hispanic Science Network on Drug Abuse in June 2000. Award of the contract is expected to be made by November 2000.

### Summer Research with NIDA

For the fourth consecutive year, the Special Populations Office sponsored the Summer Research with NIDA program. Through placements with NIDA extramural investigators, 32 minority high school and undergraduate students were able to gain valuable research experience.

### NIH Summer Internship Program

Scientists at the NIDA IRP selected 11 students to participate in the NIH Summer Internship Program (high school through graduate school). Students spent 8-10 weeks at NIDA working with scientists on various research projects and attending seminars at NIDA and NIH. The internship culminated in the NIH Student Poster Day held at the Clinical Center in Bethesda on August 3, 2000, where more than 300 students presented their research findings. Dr. Stephen Heishman is the NIDA coordinator of the NIH program.

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## NIDA's New and Competing Awards Since April 2000

**Abrams, David B.** --- Miriam Hospital
**Nicotine Dependence: Risk & Recovery Over Generations**

**Al'absi, Mustafa N.** --- University of Minnesota
**Nicotine Withdrawal & Responses To Psychological Stress**

**Amass, Leslie** --- Friends Research Institute, Inc.
**Contingency Management for Real-Life Drug Treatment**

**Ananthan, Subramaniam** --- Southern Research Institute
**Novel Nonpeptide Ligands for the Opioid Receptors**

**Anglin, M. Douglas** --- University of California, Los Angeles
**Drug Abuse Treatment: Process, Outcomes, & Social Policy**

**Atkinson, J. Hampton** --- University of California
**Better Antiretroviral Adherence: HIV+ Amphetamine Users**

**Barker, Eric L.** --- Purdue University
**Molecular Analysis of Endogenous Cannabinoid Transport**

**Battaglia, George** --- Loyola University Chicago
**SSRI Treatment of Prenatal Cocaine-Induced 5HT Deficits**

**Beauvais, Frederick** --- Colorado State University
**Drug Use Among Young Indians: Epidemiology & Prediction**

**Bickel, Warren K.** --- University of Vermont
**Improving Combined Buprenorphine-Behavioral Treatment**

**Billy, John O.** --- Battelle Centers Public Health
**Contextual Effects On Adolescent Drug Involvement**

**Booth, Robert E.** --- University of Colorado
**Intervention To Reduce Injection Drug Use**

**Booze, Rosemarie M.** --- University of Kentucky Medical Center
**HIV/Cocaine Neurotoxicity In Females**

**Cadoret, Remi J.** --- University of Iowa College of Medicine
**Gene-Environment Interaction In Etiology of Drug Abuse**

**Caldwell, Linda L.** --- Pennsylvania State University
**Leisure Education Prevention Program for Junior High**

**Campbell, William B.** --- Medical College of Wisconsin
**Biochemistry of Anandamide, An Endogenous Cannabinoid**

**Catalano, Richard F.** --- University of Washington
**Etiology of Substance Use In Australia/USA**

**Caton, Carol L.** --- NY York State Psychiatric Institute
**Service Needs In Early Psychosis and Drug Use**

**Cepeda-Benito, Antonio** --- Texas A & M University
**Nicotine Tolerance: Associative and Nonassociative**

**Chelonis, John J.** --- University of Arkansas
**Effects of Prenatal Cocaine On Behavioral Plasticity**

**Cherek, Don R.** --- University of Texas Health Sciences Center at Houston
**Drugs of Abuse and Human Aggressive Behavior**

**Chitwood, Dale D.** --- Research & Sponsored Program
**Intervention Among Heroin Sniffers-Prevent IV Drug Use**

**Coussons-Read, Mary E.** --- University of Colorado
**Effects of Morphine on Pulmonary Influenza Infection**

**Covey, Lirio S.** --- New York State Psychiatric Institute
**Maintenance Treatment for Prevention of Smoking Relapse**

**Cunningham, Kathryn A.** --- University of Texas Medical Branch
**Neurobehavioral Pharmacology of Stimulants**

**Cunningham-Williams, Renee M.** --- Washington University
**Issues In Gambling and Comorbid Drug Abuse**

**Dansereau, Donald F.** --- Texas Christian University
**Cognitive Enhancements for Treatment of Probationers**

**Dobs, Adrian S., MD** --- Johns Hopkins University
**Gonadal Hormones on Body Composition, HIV and Drug Use**

**Dovovan, Stephen J.** --- Columbia University of the Health Sciences
**Pharmacology of Addiction Risk Factors**

**Duncan, Terry E.** --- Oregon Research Institute
**Social Context and Adolescent Substance Use Development**

**Edwards, Robert H.** --- University of California, San Francisco
**Presynaptic Mechanisms of Neural Plasticity**

**Ellickson, Phyllis L.** --- RAND
**Consequences of Prior Drug Use for Young Adults**

**Ennett, Susan T.** --- University of North Carolina at Chapel Hill
**The Context of Adolescent Substance Use**

**Erickson, Carlton K.** --- University of Texas at Austin
**Drug Abuse Education for Professionals**

**Fleckenstein, Annette E. Ph.D.** --- University of Utah
**Drug Abuse and Regulatory Enzymes of Biogenic Amines**

**Foltin, Richard W.** --- New York State Psychiatric Institute
**Anorectic Drugs: Abuse & Behavioral Mechanisms of Action**

**Foltin, Richard W.** --- Research Foundation for Mental Hygiene
**Cocaine's Effects Across the Menstrual Cycle**

**Friedman, Alfred S.** --- Belmont Center for Comp Treatment
**Effects of Drug Abuse on Young Black Adult Functioning**

**Friedman, Samuel** --- National Development & Research Institute, Inc.
**Networks, Norms and HIV/STI Risk Among Youth**

**Friedman, Samuel** --- National Development & Research Institute, Inc.
**Community Vulnerability and Responses to IDU-Related HIV**

**Gelernter, Joel E.** --- Yale University School of Medicine
**Genetics of Opioid Dependence**

**Gibb, James W.** --- University of Utah
**Neurochemical Alterations By Designer Drugs**

**Gnegy, Margaret E.** --- University of Michigan Medical School
**Pharmacology of Dopamine Release By Amphetamine**

**Gomez, Felipe, Ph.D.** --- University of Michigan
**Conditioned Corticosterone and Drugs of Abuse**

**Green, Alan I.** --- Massachusetts Mental Health Center
**Cannibus and Schizophrenia: Clozapine Vs Risperidone**

**Greene, Ross W.** --- Massachusetts General Hospital
**Prevention of Substance Abuse In High-Risk ADHD Children**

**Grigson, Patricia S.** --- Pennsylvania State University
**Drugs of Abuse, Reward Comparison, and the Thalamus**

**Gruen, Rand J.** --- New York University Medical Center
**Amphetamine, GABA Transmission, and Behavior**

**Halpern, John H.** --- McLean Hospital
**Cognitive Effects of Substance Use In Native Americans**

**Haney, Margaret** --- New York State Psychiatric Institute
**THC and Marijuana: Effects In Individuals With HIV/AIDS**

**Hauser, Kurt F.** --- University of Kentucky Medical Center
**Opioids and Central Nervous System Vulnerability To HIV**

**Helstrom, Amy W.** --- University of Colorado, Boulder
**A Smoking Intervention For Juvenile Offenders**

**Henriksen, Steven J.** --- Scripps Research Institute
**Methamphetamine and AIDS: Toxic Interactions In Animals**

**Hienz, Robert D.** --- Johns Hopkins University
**Effects of Abused Drugs on Perception: An Animal Model**

**Hienz, Robert D.** --- Johns Hopkins University
**Drug Dependence and HIV/AIDS: A New Biobehavioral Model**

**Hiroi, Noboru** --- Albert Einstein College of Medicine
**Intracellular Molecules of Nicotine Addiction**

**Hone, Robert W.** --- Red Hill Studios
**The Science of Drugs**

**Hough, Lindsay B.** --- Albany Medical College
**Histaminergic Mechanisms of Antinociception**

**Howlett, Allyn C.** --- University of Vermont
**ICRS Symposium on the Cannabinoids**

**Hruby, Victor J.** --- University of Arizona, Tucson
**Novel Non-Peptide Opioid Ligands for Pain**

**Hughes, John R.** --- University of Vermont
**Nicotine Dependence & Tobacco Use Research**

**Hurwitz, Barry E.** --- University of Miami
**Drug Abuse, HIV, Selenium Supplementation, and CVD Risk**

**Iacono, William G.** --- University of Minnesota, Minneapolis
**Twin Study of ADHD, CD, and Substance Abuse**

**Jansson, Lauren M.** --- Johns Hopkins University
**Methadone, Buprenorphine and Fetal Development**

**Johns, Josephine M.** --- University of North Carolina at Chapel Hill
**Cocaine and Maternal Neglect: Intergenerational Effects**

**Kadden, Ronald M.** --- University of Connecticut Health Center
**Contingency Management for Marijuana Dependence**

**Kalivas, Peter W.** --- Medical University of South Carolina
**Cocaine Opioids and Drug Abuse**

**Kandel, Denise B.** --- Columbia University
**Nicotine Dependence Among US Youths**

**Kauer, Julie A.** --- Office of Research Administration
**Glutamate Synapses In Sensitization to Drugs of Abuse**

**Kellam, Sheppard G.** --- Society for Prevention Research
**Society For Prevention Research Annual Conference**

**Knowles, James A.** --- New York State Psychiatric Institute
**Genetic Risk Factors for Nicotine Addiction**

**Kosten, Thomas R.** --- American Academy of Addiction Psychiatry
**11th - 15th Annual Meetings and Symposia**

**Kozikowski, Alan P.** --- Georgetown University Medical School
**Chemical and Pharmacological Studies of Cocaine Analogs**

**Kuhn, Donald M.** --- Wayne State University School of Medicine
**Neurotoxic Amphetamines Radical & 5HT Neurons**

**Lama, Juan, Ph.D.** --- La Jolla Institute for Allergy/Immunology
**Role of CD4 Downmodulation During HIV Infection**

**Lane, Scott D.** --- University of Texas Health Sciences Center at Houston
**Marijuana Effects On Basic Behavioral Mechanisms**

**Lang, Annie** --- Indiana University
**Processing PSAs: Production Pacing, Emotion, and Arousal**

**Lappi, Douglas A.** --- Advanced Targeting Systems
**A Tool to Study the Diverse Behavioral Effects of Galanin**

**Latkin, Carl A.** --- Johns Hopkins University
**The Long-Term Impact of A Network Outreach Intervention**

**Lau, Chyan E.** --- Rutgers University
**Stimulant Abuse Behavior and Pharmacokinetics**

**Levin, Frances R.** --- Columbia University Health Sciences Division
**Treatment of Substance Abuse and Psychiatric Comorbidity**

**Liddle, Howard A.** --- University of Miami
**Adolescent Susbtance Abuse Treatment Conference**

**Lipton, Jack W.** --- Rush-Presbyterian-St. Luke's Medical Center
**Oxidant Stress and Cocaine-Induced Brain Injury In Utero**

**Lundy, Allan C.** --- Thomas Jefferson University
**Accuracy of ASI Reports of Cocaine Use at Follow-Up**

**Mach, Robert H.** --- Wake Forest University School of Medicine
**Development of D3 Antagonists To Treat Cocaine Addiction**

**Mackinnon, David P.** --- Arizona State University
**Analysis of Team-Based Substance Abuse Prevention**

**Madden, Pamela A.** --- Washington University
**The Genetics of Vulnerability to Nicotine Addiction**

**Magura, Stephen Ph.D.** --- National Development & Research Institute, Inc.
**Group Motivational Intervention In Drug Abuse Treatment**

**Makris, Angela** --- University of Kentucky College of Medicine
**The Effects of Modafinil on Food Intake In Humans**

**Marcus, Marsha D., Ph.D.** --- Western Psychiatric Institute & Clinic
**Bupropion and Weight Control for Smoking Cessation**

**Markham, Richard B.** --- Johns Hopkins University
**Drug Abuse and Resistance to Antiretroviral Therapy**

**Markou, Athina** --- Scripps Research Institute
**Neurobiology of Nicotine Reward and Withdrawal**

**Marvizon, Juan-Carlos G.** --- University of California, Los Angeles
**Spinal Neurokinin and Opioid Release In Nociception**

**Matsumoto, Rae R.** --- University of Oklahoma Health Sciences Center
**Sigma Ligands for the Treatment of Cocaine Overdose**

**Mazure, Carolyn M.** --- Yale University
**Yale IWHR Scholar Program On Women and Drug Abuse**

**Mccarson, Kenneth E.** --- University of Kansas Medical Center
**Nociceptive Sensory Regulation of Neurokinin Receptors**

**Mcfarland, Bentson** --- Oregon Health Sciences University
**Drug Courts and Medicaid Managed Behavioral Health Care**

**Meisch, Richard A., MD** --- University of Texas Health Sciences Center
**Polydrug Abuse: Reinforcing Effects of Drug Combinations**

**Moore, Steven D.** --- Center for Image Processing In Education
**Visualizing Addiction: Imaging for Secondary Science Education**

**Morrissey, Joseph P.** --- University of North Carolina at Chapel Hill
**Impacts of Managed Care on Substance Abuse Service Linkages**

**Musto, David F., MD** --- Yale University
**Previous American Drug Experience & Future Perspectives**

**Nader, Michael A.** --- Wake Forest University School of Medicine
**Dopamine D2 Receptors In Primate Models of Cocaine Abuse**

**Napier, T. Celeste, Ph.D.** --- Loyola University
**Opioids and the Physiology of the Ventral Pallidum**

**Nestler, Eric J.** --- University of Texas Southwestern Medical Center
**Neurotrophic Factors and Drugs of Abuse**

**Nunes, Edward V.** --- Research Foundation for Mental Hygiene
**Opiate Dependence: Combined Naltrexone/Behavior Therapy**

**Oetting, Eugene R.** --- Senior Research Administrator, Sponsored Programs
**The Tri-Ethnic Center For Prevention Research**

**Page, J. B.** --- University of Miami
**HIV Infection Potential /IDU-Related Injection Materials**

**Perkins, Kenneth A.** --- University of Pittsburgh
**Sex Differences In Nicotine Reinforcement: Human/Animal**

**Petry, Nancy M.** --- University of Connecticut Health Center
**Vouchers Vs. Prizes: Contingency Management**

**Polich, John M.** --- The Scripps Research Institute
**Marijuana CNS Effects In Low- And High Risk--Supplement**

**Rajadhyaksha, Anjali M.** --- Massachusetts General Hospital
**Amphetamine-Mediated Phosphorylation and Gene Expression**

**Reggio, Patrici H.** --- Kennesaw State University
**Molecular Determinants for Cannabinoid Activity**

**Reith, Maarten E.** --- University of Illinois College of Medicine
**Dopamine Transporters and Ions, Substrates, Blockers**

**Ridenour, Ty A.** --- Washington University
**Drug Use Liability: Investigating Competing Models**

**Robles, Rafaela R.** --- Universidad Central Del Caribe
**Puerto Rico Drug Abuse Research Development Program**

**Robles-Sotelo, Elias** --- University of Arkansas
**Delay Discounting & Impulsiveness In Methadone Patients**

**Roddy, Juliette K.** --- Office of Research & Sponsored Programs
**An Economic Analysis of Cigarette Smoking**

**Ruth, James A.** --- University of Colorado Health Sciences Center
**Mechanisms of Drug Deposition In Hair**

**Salvemini, Daniela** --- Metaphore Pharmaceuticals, Inc.
**Superoxide Dismutase Mimetics for Management of Pain**

**Santisteban, Daniel** --- University of Miami
**Developing A Culturally Rooted Adolescent Family Therapy**

**Sherman, Steven J.** --- Indiana University
**Social Psychological Factors In Teen and Adult Smoking**

**Simon, Eric J.** --- New York University School of Medicine
**31st Annual International Narcotics Research Conference**

**Smith, Mark** --- Davidson College
**Age-Related Differences In Opioid Sensitivity**

**Smith, Miles P.** --- Zebra Pharmaceuticals, Inc.
**Polypharmacophore Model for Treatment of Cocaine Abuse**

**Snyder, Solomon H.** --- Johns Hopkins University School of Medicine
**Neurotransmitter Receptors**

**Sparber, Sheldon B.** --- University of Minnesota
**Prenatal Cocaine-Acute & Delayed Functional Toxicity**

**Spielberg, Freya** --- Harborview Medical Center
**Counseling Strategies to Reduce HIV Risk Among IDU**

**Stephan, Megan M.** --- Yale University School of Medicine
**Functions of Membrane Spans In the Serotonin Transporter**

**Stewart, David G.** --- Children's Hospital & Regional Medical Center
**Ready: School-Based Substance Abuse Intervention**

**Strauss, Shiela M.** --- National Development & Research Institute, Inc.
**HVC Service Innovations In Drug Treatment Programs**

**Tallarida, Ronald J.** --- Temple University School of Medicine
**Synergism and Medications Development for Drug Abuse**

**Taylor, Ethan W.** --- University of Georgia
**Selenoproteins, Nf-Kb, And HIV Disease In IV Drug Users**

**Todorovic, Slobodan M.** --- Washington University
**Multiple Classes Of Ca2+ Channels - Sensory Transmission**

**Toll, Lawrence R.** --- SRI International
**Biochemical Studies of Opiate Efficacies**

**Tompkins, Christopher** --- Brandeis University
**Development of Case Rates For Substance Abusers**

**Trussell, Laurence O., Ph.D.** --- OHRC & Vollum Institute
**Gordon Conference on Synaptic Transmission**

**Tsoh, Janice Y.** --- University of California, San Francisco
**Treating Chinese Smokers With Interactive Expert Systems**

**Van Haaren, Frans** --- University of Florida
**Impulsivity: Precursor to and Sequel of Toxicant Exposure**

**Vaughan, Mary S.** --- University of Iowa
**Gender Differences In Health Services Utilization**

**Vlahov, David** --- New York Academy of Medicine
**Evaluating Supervised HAART In Late Stage HIV In IDUs**

**Waldron, Holly B.** --- University of New Mexico
**Drug Use & HIV Risk: Treatment of Hispanic & Anglo Youth**

**Webster-Stratton, Carolyn H.** --- University of Washington
**Preventing Conduct Problems, Promoting Social Competence**

**Weiss, Friedbert** --- Scripps Research Institute
**Novel Methods to Explore Mechanisms of Cocaine Abuse**

**Wessendorf, Martin W.** --- University of Minnesota, Minneapolis
**Brainstem Circuits In Opiate Analgesia**

**Williams, John T.** --- Oregon Health Sciences University
**Cocaine: Effects on Single Neurons**

**Wolf, Marina E.** --- Chicago Medical School
**Glutamate Transmission and Amphetamine Sensitization**

**Worley, Paul F.** --- Johns Hopkins University School of Medicine
**Analysis of A Novel Cocaine-Induced IEG**

**Wu, Li T.** --- Research Triangle Institute
**Substance Use & Dependence Problems Among the Uninsured**

**Xian, Hong** --- Washington University
**Smoking Cessation: The Role of Withdrawal & Dependence**

**Yamamoto, Bryan K.** --- Case Western Reserve University
**Methamphetamine Toxicity and Corticostriatal Glutamate**

**Yantis, Steven G.** --- Johns Hopkins University
**Brain Mechanisms of Attentional Control Revealed By fMRI**

**Zhang, Heping** --- Yale University School of Medicine
**Statistical Methods for Correlated Substance Use Data**

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[ Office of the Director][Report Index][Next Report Section]

**National Institute on Drug Abuse**

**Director's Report to the National Advisory Council on Drug Abuse**

**September, 2000**

# Extramural Policy and Review Activities

## Review Meetings

During this council cycle, the Office of Extramural Affairs arranged and managed 21 review meetings for grant applications and 9 meetings for contract proposal reviews. In addition, the Office managed the concept reviews of 24 contract concepts.

The reviews for NIDA's chartered committees were held, which include NIDA-E (Treatment Review Committee), NIDA-F (Health Services Review Committee), NIDA-L (Medications Development Committee), and NIDA-K (Training Committee). Four Special Emphasis panels were also held to review applications in conflict with the chartered committees. Five Special Emphasis Panels were constituted for reviews of specific mechanisms: program projects (two committees), centers (including site visits), Minority Institutions Drug Abuse Research Development Program R24s, and conference grants. Eight of the review meetings were for seven RFAs, as follows:

| | |
|---|---|
| DA-00-002 | National Drug Abuse Treatment Clinical Trials Network (two meetings held, along with nine site visits) |
| DA-00-003 | Micro-Array Based Research on Drug Abuse |
| DA-00-004 | The Next Generation of Drug Abuse Prevention Research |
| DA-00-005 | Basic Behavioral, Cognitive, and Neurological Research: Applications to HIV/AIDS and Drug Abuse |
| DA-00-006 | Viral Hepatitis and HIV in Drug and Alcohol Users |
| DA-00-007 | HIV Therapy for Drug Users: Access, Adherence, Effectiveness |
| DA-00-008 | Centers for Drug Abuse and AIDS Research Core Grants |

The Contracts Review Branch reviewed twenty-three concepts for the SBIR Contracts program, all of which were approved. A concept for a National Hispanic Science Network on Drug Abuse was also reviewed and approved. The following nine contract reviews were also completed:

| | |
|---|---|
| N01 DA-0-1101 | Bridging the Disconnect |
| N01DA-0-1102 | Policy Planning and Support Services |
| N01DA-0-7707 | Production and Analysis of Cannabis |

| | |
|---|---|
| N43DA-0-7708 | Development of Placebo Marijuana Cigarettes |
| N01DA-0-8805 | Cardiovascular and Safety Evaluations of Potential Medications to Reduce Drug Use |
| N01DA-0-8806 | Screening for Cocaine Pharmacotherapies Using the Rat Self-Administration Test |
| N01DA-0-8807 | Pharmacokinetics of Psychoactive Drugs |
| N01DA-0-8808 | CTN Administrative Coordinating Center |
| N01DA-0-9901 | Brain Bank |

## Extramural Staff Development

The Office of Extramural Affairs Symposium Series, which provides an opportunity for training and staff interchanges on topics related to extramural administration, brought Dr. Jean Paddock, Associate Director for Program Evaluation, Center for Scientific Review (CSR), to the May meeting. Dr. Paddock was invited in response to NIDA program staff's request to have a symposium session address recent changes in CSR practices. July and August meetings used case studies to address day-to-day challenges in administering scientific activities. Dr. William C. Grace, Deputy Director, OEA, coordinates the series.

## Extramural Outreach

Dr. Khursheed Asghar, Chief, Basic Sciences Review Branch, OEA, made a presentation at the International Cannabinoid Research Society meeting in Hunt Valley, MD in June 2000. His topic was "NIDA Training and Career Development Programs for Young Investigators".

Dr. Mark Swieter, SRA in the Basic Sciences Review Branch, OEA, provided a talk entitled, "The NIH Grant Application Review Process," to a meeting of Social Work researchers at Howard University in Washington, DC in May 2000.

At the NIDA/NIMH sponsored meeting, "Assessing the Impact of Childhood Interventions on Subsequent Drug Abuse," which was held in Washington, DC in May 2000 Dr. Swieter presented "Research and Career Development Opportunities Supported by NIDA."

At the CPDD meeting in June 2000, Dr. Teri Levitin, Director, OEA, and Dr. Swieter participated in activities designed to inform the extramural community about peer review and career development. Dr. Levitin organized a symposium on career development in which Dr. Swieter was one of the speakers. Dr. Swieter also participated in a grant writing workshop, which he co-organized with Drs. Timothy Condon and Cindy Miner, OSPC.

Dr. Teri Levitin spoke to the Native American Research and Scholars Work Group Meeting about NIH and NIDA peer review in May 2000.

Mr. Richard Harrison, Chief, Contracts Review Branch, OEA, represented NIDA at Washington, DC events marking the "Journey of the Sacred Hoop," a nationwide walk organized by Native Americans to address substance abuse and violence. A number of tribes as well as governmental, and non-governmental organizations participated. Of particular note was Mr. Harrison's participation in a closing ceremony honoring Elders in the Sobriety Movement.

## Scientific Meetings

In conjunction with the NIDA-E Treatment Review Committee, Dr. Kay Nimit, SRA in the Clinical, Epidemiological, and Applied Sciences Review Branch, OEA, organized a presentation, "NIDA's Stage Model of Behavioral Therapies Research: Getting Started and Moving on From Stage I". Bruce J. Rounsaville, M.D., was the featured speaker. This event occurred on June 29, 2000.

Dr. Marina Volkov, SRA in the Clinical, Epidemiological, and Applies Sciences Review Branch, OEA, helped organize a lecture series at the American Psychological Association's annual meeting in August 2000. The lecture series, entitled "Vulnerability to Drug Addiction," was done under the auspices of NIDA's Behavioral Sciences Working Group as part of special events organized by Dr. Jaylan Turkkan, Dr. Minda Lynch, and others in the working group.

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**National Institute on Drug Abuse**

**Director's Report to the National Advisory Council on Drug Abuse**

**September, 2000**

# Congressional Affairs

(Prepared August 1, 2000)

## FY 2001 Funding NIH/NIDA

On July 25, 2000, The House and Senate conferees began work on H.R. 4577, the Labor, HHS, Education and Related Agencies Appropriation bill, which includes funding for NIH. The conference concluded on July 27, 2000, with a report to be filed in September. Early reports indicate that the agreement would provide NIH a $2.7 billion increase over funding levels for FY 2000.

The House passed HR 4577 on June 14, 2000, after several days of debate, by a vote of 217-214. The House approved the funding levels recommended by the House Appropriations Committee when it passed the bill May 24, 2000, including a $1 billion increase for NIH. The measure passed the Senate on June 30, 2000 by a 52-43 vote. The Senate bill included a $20.5 billion budget for NIH, a $2.7 billion increase.

## FY 2001 House Appropriations Report Language for NIDA

The Committee provides $788,201,000 for the National Institute on Drug Abuse (NIDA), which is $100,825,000 above the fiscal year 2000 comparable level, and $62,734,000 above the Administration request; however, due to limited funding within the allocation, funding increases in the bill are constrained to the amount proposed in the Administration request.

**Mission:** NIDA-supported science addresses questions about drug abuse and addiction, which range from its causes and consequences to its prevention and treatment. NIDA research explores how drugs of abuse affect the brain and behavior and develops effective prevention and treatment strategies; the Institute works to ensure the transfer of scientific data to policy makers, practitioners, and the public.

**Centers for Drug Abuse Research and Treatment:** The Committee commends NIDA for its strategy of developing and establishing centers for drug abuse research and treatment around the country. Consideration should be given to locating one or more centers in areas where drug trafficking, the production of illegal drugs such as methamphetamine, and drug abuse, is more prevalent.

**Clinical Trials:** The Committee commends NIDA for launching the National Drug Abuse Treatment Clinical Trials Network. By providing a national research infrastructure to test and disseminate new and improved behavioral and pharmacological treatments in real-life treatment settings the Institute is improving the quality of drug treatment across the country.

**Neuroimaging and Drug Abuse:** The sophisticated research questions now being probed by NIDA-supported researchers requires advanced state-of-the-art technologies. The Committee commends NIDA for applying the rapidly developing neuroimaging technologies to research in drug abuse treatment and prevention to gain a better understanding of the human brain's underlying circuitry and mechanisms. NIDA is encouraged to expand these research efforts.

## FY 2001 Senate Appropriations Report Language for NIDA

The Committee recommends an appropriation of $790,038,000 for NIDA. This is $64,571,000 more than the budget request and $102,662,000 more than the fiscal year 2000 appropriation. The comparable numbers for the budget estimate include funds to be transferred from the Office of AIDS Research.

**Mission:** Created in 1974, NIDA supports about 85 percent of the world's biomedical research in the area of drug abuse and addiction. The Committee commends NIDA for demonstrating through research that drug use is a preventable behavior and addiction is a treatable disease. NIDA's basic research plays a fundamental role in furthering knowledge about the ways in which drugs act on the brain to produce dependence, and contributes to understanding how the brain works. In addition, NIDA research identifies the most effective pharmacological and behavioral drug abuse treatments. NIDA conducts research on the nature and extent of drug abuse in the United States and monitors drug abuse trends nationwide to provide information for planning both prevention and treatment services. An important component of NIDA's mission is also to study the outcomes, effectiveness, and cost benefits of drug abuse services delivered in a variety of settings.

**Behavioral Sciences:** The Committee understands that behavioral intervention is a critical, and sometimes only, component of drug addiction treatment. The Committee continues to support NIDA's expansion of its behavioral science portfolio and views NIDA as a model of how to approach its behavioral science and public health responsibilities.

**Children & Adolescents:** Recognizing the devastating impact of drug addiction on children and youth, the Committee commends NIDA's children and adolescent research initiative. The Committee urges NIDA to continue to support its research portfolio in areas of co-occurring mental disorders, developmental consequences, prenatal exposure, genetic vulnerability, and environmental risk factors.

**Clinical Trials:** The Committee is pleased with NIDA's continuing progress in developing behavioral and pharmacological drug abuse treatments, and supports NIDA's initiative to establish a national drug abuse treatment clinical trials network. The Committee commends NIDA's leadership in forging strong partnerships with treatment researchers and community-based treatment providers to assure that new treatments are tested and incorporated into ongoing drug treatment programs.

**Emerging Drug Problems:** The Committee is pleased that NIDA has launched a new Club Drug Research and Dissemination Initiative. Given the emergence of club drugs, such as ecstasy, methamphetamine, GHB, and ketamine, the Committee is encouraged by NIDA's proactive efforts to curtail these emerging drug problems and urges NIDA to continue its efforts to develop an even broader array of effective new prevention and treatment approaches to focus on these emerging drug challenges.

**Genetic Vulnerability:** The Committee understands that both genes and environment influence drug abuse and addiction. The relationship between the two is complex, requiring continued research in areas of behavioral genetics, psychiatric and epidemiological genetics, molecular genetics, and population genetics. The Committee encourages NIDA to continue to pursue this area of drug and addiction research.

**Medications Development:** The Committee encourages NIDA to study the development of anti-addiction medications, to clarify the neurological and behavioral benefits of the use of pharmacological agents, and develop an understanding of how best to use these medications.

**Methamphetamine:** The Committee is very disturbed by the explosion in methamphetamine abuse across the nation. The problem is especially acute in Iowa and other Mid-western states. The Committee again urges NIDA to expand its research on improved methods of prevention and treatment of methamphetamine abuse.

**National Drug Abuse Clinical Trials Network:** The Committee commends NIDA's leadership in continuing to recognize the importance of behavioral and social science research, and is especially pleased that this is reflected in the recent NIDA reorganization, which elevates behavioral research in both the Division of Neuroscience and Behavioral Research and the Division of Treatment Research and Development. The Committee believes NIDA could consider evaluating these promising behavioral treatments in clinical trials through its new National Drug Abuse Clinical Trials Network.

**Neuroscience:** The Committee recognizes that basic neuroscience provides a foundation for NIDA's research portfolio. Basic neuroscience research has advanced the field's understanding of drug abuse and addiction. The Committee urges NIDA to continue its efforts to develop new areas of neuroscience research.

**New Genes & Drug Abuse:** The Committee supports research efforts to identify many of the genes that may play a

role in addiction. Seizing upon these opportunities could lead to a more complete picture of the disease of addiction.

**Nicotine Research:** The Committee recognizes that the consequences of nicotine addiction are substantial to adults, children, and adolescents, and commends NIDA's support of research yielding effective replacement therapies and behavioral interventions. The Committee encourages NIDA to continue to support research on the prevention and behavioral and pharmacological treatment of nicotine addiction. The Committee supports NIDA's ongoing research in the basic sciences, behavioral and medical treatments, genetic vulnerability, and epidemiology of nicotine use and abuse.

**Trans-disciplinary Tobacco Research Centers:** The use of tobacco products remains one of the nation's deadliest addictions. The Committee strongly supports NIDA's continuing efforts to address this major public health problem through its comprehensive research portfolio. The Committee is pleased that NIDA has teamed with the National Cancer Institute and an outside foundation to establish the Trans-disciplinary Tobacco Use Research Center (TTURC). This multifaceted approach should lead to an increased understanding of how nicotine acts in the brain and body and lead to new strategies for treating nicotine addiction and preventing tobacco use, particularly by teens and younger children.

**Vulnerability To Addiction Initiative:** The Committee commends NIDA for launching its ''Vulnerability to Drug Addiction Initiative'' and encourages NIDA to support research to identify genes associated with drug abuse and addiction. Increasing our understanding of why some people are vulnerable to drug abuse and addiction while others are not, will speed progress in treating and preventing these critical problems.

## Congressional Briefings and Hearings

**May 8** - At their request, Dr. Timothy P. Condon, Associate Director, NIDA, briefed the majority staff of the Senate Judiciary Committee about current research on steroid abuse. Dr. Condon described what anabolic steroids are, how they are taken, possible public health consequences, trends in use, and provided an overview of NIDA's Anabolic Steroid Initiative.

**June 13** - At the request of the Senate Caucus on International Narcotics Control (Sen. Charles Grassley, R-IA, Chair), Dr. Timothy P. Condon, Associate Director, NIDA, briefed a bi-partisan group of Senate staff on what is known about ecstasy and current research efforts underway.

**July 11** - The House Government Reform Subcommittee on Criminal Justice, Drug Policy and Human Resources (Rep. John Mica, R-FL, Chair) held a hearing on "Evaluating the National Youth Anti-Drug Media Campaign." Witnesses included Barry McCaffrey, Director, Office of National Drug Control Policy. Also asked to testify were NIDA contractors, David Maklan, Ph.D., Vice President, Westat, Inc. and Robert Hornik, Ph.D., Professor, Annenberg School for Communication.

**July 25** - The Senate Caucus on International Narcotics Control (Sen. Charles Grassley, R-IA, Chair) held a hearing on "Ecstasy: Underestimating the Threat," to examine the rising trend of use and trafficking patterns of the club drug ecstasy. The Caucus requested that NIDA submit a statement for the record addressing scientific research on the medical and social consequences of the drug along with the implications this research has for the nation's drug policy. Dr. Donald Vereen, Deputy Director, ONDCP, submitted the statement on behalf of NIDA. Also testifying were witnesses from the Department of State, U.S. Customs, and DEA.

## BILLS OF INTEREST

**HR2634**, the **"Drug Addiction Treatment Act,"** passed the House on Wednesday, July 19, 2000, by a vote of 412-1. The bill was introduced by Rep. Tom Bliley, R-VA, on July 29, 1999. The measure would allow qualified physicians to prescribe certain anti-addiction medications in an office setting, including buprenorphine and buprenorphine/naloxone, medications for opiate addiction developed under a CRADA between NIDA and Reckitt & Colman Pharmaceuticals, Inc. In a statement before the House Commerce Subcommittee on Health and Environment in July 1999, NIDA Director, Dr. Alan Leshner, said "Medications such as buprenorphine and buprenorphine combined with naloxone have been found to be safe and efficacious as a treatment for opiate dependence.... In research settings, buprenorphine products have been found to be medications that will be well tolerated by addicts and have low value and desirability for sale on the street. These factors make this medication a prime candidate to be administered in less traditional environments, thus expanding access to populations who do not have access to methadone programs or are unsuited to them, such as adolescents." A similar provision passed the Senate in November 1999 as part of the "Methamphetamine Anti-Proliferation Act," S 486 (Ashcroft-MO).

**HR 2987**, the **"Methamphetamine Anti-Proliferation Act of 1999,"** was introduced September 30, 1999, by

Rep. Chris Cannon (R-UT). The bill was referred to the Committee on Commerce and to the Committee on the Judiciary. On July 25, 2000, full Committee consideration and markup was held by the House Judiciary Committee. The Committee voted to report the bill as amended in the nature of a substitute. As reported, the bill contains a provision similar to HR2634.

**HR4923**, the **"Community Renewal and New Markets Act of 2000,"** introduced by Rep. Watts, (R-OK), on July 24, 2000, passed the House. The bill includes language about faith-based treatment for substance abuse. Related bills: S1594 (Kerry, D-MA) which incorporates language similar to S2779, the "American Community Renewal and New Markets Act," which the Senate sought to add as an amendment to the estate tax bill (HR8).

**HConRes 371** - Adopted by the House on July 24, 2000, the measure aims to raise awareness of the prevalence of drug and alcohol abuse in the U.S. September is National Alcohol and Drug Addiction Recovery Month which recognizes individuals who have undergone successful treatment and those who have dedicated their lives to helping people recover from addiction. The sponsor, Rep. Jim Ramstad, (R-MN), said he especially wants to draw attention to drug and alcohol use among youth.

**S2527**, the **"Drug Treatment and Research Enhancement Act"** was introduced on May 9, 2000, by Sen. Charles Grassley (R-IA), Chairman, Senate Caucus on International Narcotics Control, to reinforce the national drug control effort. The bill provides additional resources to anti-drug coalitions and parent groups, amends the PHSA to authorize grants to non-governmental organizations to help professionals participate in coalitions and identify and help youth affected by family substance abuse, and strengthens research efforts concerning how to better treat addiction. Section 5 amends the PHSA to establish a National Drug Abuse Treatment Clinical Trials Network and provides an authorization of appropriations for such a Network to conduct large-scale drug abuse treatment studies in community settings using broadly diverse patient populations. The bill also encourages NIH to work with private industry to promote research into pharmacological options that could be used in support of drug treatment efforts.

**S2612**, the **"Ecstasy Anti-Proliferation Act of 2000,"** was introduced May 23, 2000, by Sen. Bob Graham (D-FL) to combat ecstasy trafficking, distribution, and abuse in the U.S., and for other purposes. In part, the bill urges that greater emphasis be placed on education of young people and of state and local law enforcement agencies. It also encourages adequate funding for NIDA to accomplish the following: identify those most vulnerable to using ecstasy and develop science-based prevention approaches; understand how ecstasy produces its toxic effects and how to reverse neurotoxic damage; develop treatments, including new medications and behavioral treatment approaches; better understand the effects that ecstasy has on developing children and adolescents; and translate research findings into useful tools and ensure their effective dissemination. The bill was referred to the Committee on the Judiciary.

**S2779**, the **"American Community Renewal and New Markets Empowerment Act,"** a bill to provide for the designation of renewal communities and to provide tax incentives and tax credits, was introduced by Sen. Santorum, (R-PA), on June 22, 2000. In part, the bill would amend authorities of the Substance Abuse and Mental Health Services Administration (SAMHSA) under Title V of the PHSA. It also contains provisions relating to standards for substance abuse treatment professionals and includes under Title IV (Faith Based Substance Abuse Treatment), language concerning educational qualifications for counselors and other personnel in drug treatment programs.

**S2868**, the **"Children's Public Health Act of 2000,"** was introduced on July 13, 2000, by Senator William Frist (R-TN). The bill would amend the PHSA with respect to children's health. Provisions address several areas of pediatric research including traumatic brain injury, asthma, oral health, autism, and rare diseases. Title II - Maternal and Infant Health, Sec 399L, contains provisions relating to CDC concerning research on prenatal smoking, alcohol, and illegal drug use. Title II, Sec 399N - Prevention Research to Ensure Safe Motherhood, authorizes the Secretary, HHS, acting through CDC, to "carry out activities to expand research relating to ...preventing smoking, alcohol and illegal drug usage before, during, and after pregnancy." Title IV - Pediatric Research, Sec. 421. Long-Term Child Development Study would authorize NICHD to conduct a national longitudinal study of environmental influences on children's health.

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# International Activities

Scientists from 17 countries participated in the fifth NIDA International Forum, **Building International Research on Drug Abuse: Drug Abuse Treatment in the New Millennium,** convened from June 15-17, 2000, in San Juan, Puerto Rico, immediately before the Annual Scientific Meeting of the College on Problems of Drug Dependence. Throughout the NIDA forum, participants discussed the implications for drug abuse treatment of advances in basic science, epidemiology and prevention, and pharmacological and behavioral treatment research. In addition to 20 oral research presentations, 18 scientists presented their research results during poster sessions. Presenters from NIDA included Dr. Frank Vocci and Dr. Betty Tai, DTR&D, who discussed the basic science of addiction and the Clinical Trials Network respectively (see Summer 2000 INVEST Letter for more detail about the meeting).

NIDA sponsored a one-day pre-conference on May 30, 2000, as part of the **Third U.S.-Mexico Bi-national Drug Demand Reduction Conference,** to focus on the recommendations of the research work groups from the two previous bi-national conferences and to define potential collaborative research projects. The morning session included research information sessions by Mexican and United States drug abuse scientists, followed by afternoon work groups on epidemiology and prevention, drug abuse treatment, and basic science. Meeting recommendations for building the bi-national research cooperation included: 1) access to a bi-national website and/or listserv; 2) research pre-conference again in 2001 with scientific presentations that feature U.S.-Mexico collaborations; and 3) establish a program of research cooperation. Key presenters at the meeting included Dr. Mary Jane Kreek, Rockefeller University; Dr. Silvia Cruz, former INVEST Fellow and Researcher for CINVESTAV; Dr. Richard Needle, CAMCODA; Ms. Haydee Rosovsky, Mexican National Council Against Addiction (CONADIC); Dr. Judith Brook, Mt. Sinai School of Medicine; and Dr. Luciana Ramos, Mexican Institute of Psychiatry. On June 1, 2000, Dr. Timothy P. Condon, Associate Director, NIDA, presented at the conference plenary session: "Challenges and Opportunities in Drug Demand Reduction: What We Have Learned from Research".

Dr. Timothy P. Condon, Associate Director, NIDA, accompanied General Barry McCaffrey and others to China and Thailand for the **Southeast Asia Regional Counternarcotics Conference** to promote regional information sharing, provide regional updates on heroin and methamphetamine trafficking, provide U.S. policy guidance, promote regional team building and to examine the "road ahead". Dr. Condon delivered a presentation entitled "Challenges and Opportunities in Drug Demand Reduction," in Bangkok, Thailand on June 16, 2000.

On July 21, 2000, NIDA hosted a delegation from Hong Kong led by Mrs. Clarie Lo, Commissioner for Narcotics, and including Mr. Ng Kam Wing, Hong Kong Police Force Narcotics Bureau, and Mr. Benjamin Weber of the Department of State. Drs. Alan Leshner, Director, NIDA; Timothy Condon, Associate Director, NIDA; Frank Vocci, DTR&D; and Patricia Needle, OSPC, presented an overview of NIDA research findings related to U.S. trends in drug use, particularly methamphetamine and club drugs; and the Clinical Trials Network. The meeting concluded with discussion of areas of potential cooperation, and exchange of research and program information.

Three researchers have been awarded NIDA Hubert H. Humphrey Drug Abuse Research Fellowships for 2000-2001: Dr. Olga Vassioutina, Russia; Dr. Vedran Mardesic, Croatia; and Ms. Elvia Amesty de Torres, Venezuela. The competitive, 10-month Fellowships are sponsored by NIDA in cooperation with the U.S. Department of State, the Institute of International Education, and The Johns Hopkins University. Through a combination of academic courses and professional experience, Fellows learn about NIDA-supported drug abuse research and the application of research

to the development of prevention programs, treatment protocols, and government policy.

Two scientists have been selected as INVEST Research Fellows for 2000-2001: Dr. Henrik Druid, Sweden, and Dr. Chuang Liu, China. During his Fellowship, Dr. Druid will study the neurochemical mechanisms involved in the deaths of chronic cocaine abusers in order to provide a more comprehensive understanding of the causes and risk factors of sudden death. He hopes to conduct similar studies with methamphetamine abusers upon his return to Sweden. He will spend his Fellowship working with Dr. Deborah C. Mash, University of Miami School of Medicine. Dr. Liu's INVEST Fellowship research will employ functional magnetic resonance imaging to determine the neuroanatomical sites activated during cue-induced nicotine craving and to examine the effective mechanisms underlying the craving response in humans. The study results may then be used to develop behavioral and pharmacological interventions for nicotine abuse. Dr. Liu will spend his Fellowship working with Dr. Elliott A. Stein, Medical College of Wisconsin, Milwaukee.

Dr. James Colliver, DESPR, and Dr. Charles Sharp, DNBR, met with Dr. Kultegin Ogel of the Bakirkoy State Hospital in Istanbul, Turkey, regarding collection of data on adolescents' abuse of inhalants. Dr. Ogel's visit was part of his CPDD Traveling Fellowship. While at NIDA, Dr. Ogel also discussed plans for a forthcoming Turkey-U.S. bi-national meeting with Dr. Patricia Needle.

Moira O'Brien, DESPR, served as U.S. representative to the **Council of Europe's 30th Meeting of the Group of Experts in Epidemiology of Drug Problems (Pompidou Group),** May 22-23, 2000, Strasbourg, France, and gave a presentation on, "Drug Abuse Trends in the U.S. and NIDA Activities."

On July 24, 2000, Dr. Patricia Needle, Director, International Program, OSPC and Dr. Elizabeth Robertson, DESPR, met with Mr. Lkhaasuren Azbayar, Executive Director of the Mongolian Association to Protect the Population from Narcotics. They presented an overview of NIDA's international work and the current status of prevention research. The Mongolian Association is seeking support for training drug abuse professionals to address this emerging problem in their country.

Drs. Elizabeth Robertson, DESPR, Vince Smeriglio, CAMCODA, and Patricia Needle, in conjunction with Silvia Kniel of the Fogarty International Center, met with a delegation from Kazakhstan on May 19, 2000. Research findings on drug abuse and HIV prevention and the medical consequences of drug abuse were discussed.

Ms. Daphne Nelson, Director of Projects at the National Council on Drug Abuse of Jamaica, visited NIDA on May 9, 2000. Dr. Elizabeth Robertson presented information on research-based drug abuse prevention programs for schools and communities. Dr. Patricia Needle shared information on NIDA's research program, information dissemination, and fellowship programs.

Dr. Frank Vocci, Director, DTR&D, attended a workshop on Illicit Opiate Addiction held May 31 to June 3, 2000 where he presented a review of "Current Medication and Treatment Developments for the Treatment of Opiate Addiction in the US: A View from NIDA" in Toronto, Canada.

Dr. Frank Vocci was invited by the Amsterdam congress to be the leading speaker at a conference on the Pharmacotherapy of Opiate Addiction held June 7-8, 2000. Dr. Vocci presented the evidence-based research as to the efficacy and cost effectiveness of methadone as a treatment for opiate addiction.

Dr. Peter Hartsock served on the organizing committee of the **8th International Conference on AIDS, Cancer, and Related Problems,** St. Petersburg, Russia, May 2000. This conference was supported by the Russian Ministry of Science, the NIH Fogarty International Center and other organizations and included participation by the President of the International AIDS Society and NIDA grantees from Yale University and Johns Hopkins University among others. Additionally, Dr. Hartsock co-organized and co-chaired the conference's special session on drug abuse and AIDS. Dr. Hartsock also met with the Russian Military Medical Academy in St. Petersburg, Russia in May 2000 to discuss plans for a special conference dealing with AIDS at the Academy in 2001.

Prior to the 13th International AIDS Meeting in Durban, South Africa, a consortium of international organizations sponsored the third annual **Global Research Network (GRN) Meeting on HIV Prevention in Drug-Using Populations.** NIDA had a pivotal role in creating the GRN and in supporting its continuation. The agenda for this meeting, held on July 5-7, 2000, was designed to facilitate the global diffusion and application of research-based principles on effective HIV prevention strategies for populations of injecting and non-injecting drug users around the world. The objectives of the meeting included exchanging empirically-based quantitative and qualitative research data on drug users and HIV prevention; to promote the global diffusion and application of empirically-based research findings on drug users and HIV prevention; to increase cross-national, regional and country research and international collaborations; to discuss HIV prevention among users of drugs in different countries, with a focus on Africa; and to explore other health conditions and consequences of drug use. NIDA was one of 11 co-sponsoring

organizations hosting the meeting, attended by 80 HIV prevention researchers, policy makers, practitioners, and service providers (representing approximately 30 countries, worldwide). Dr. Henry Francis, Dr. Richard Needle, Helen Cesari, and Elizabeth Lambert of CAMCODA were members of the planning committee.

NIDA (CAMCODA, DESPR, and the Special Populations Office) co-sponsored a meeting entitled **"Substance Abuse, Crime, Violence and HIV/AIDS as Consequences of Poverty: Prevention, Intervention and Treatment in the U.S. and South Africa,"** that was held in Cape Town, South Africa, July 1-5, 2000. The meeting was convened by the Center for Drug Abuse Research at Howard University, the Department of Corrections and the Medical Research Council of South Africa. The purpose of the meeting was to bring together leading black researchers and practitioners from the U.S. and South Africa to present relevant research and devise a plan to develop common strategies for addressing the common problem of poverty and its devastating consequences. The meeting was attended by several high ranking elected South African officials, academicians and health officials, as well as faculty from U.S. institutions and staff from sponsoring agencies. The meeting was organized such that each day focused on one topic reflected in the meeting title. Dr. Alan Leshner gave a keynote address and the following staff made presentations and facilitated small group discussions: Dr. Lula Beatty, OD, Dr. Leslie Cooper, DESPR, Dr. Dionne Jones, CAMCODA, and Mr. Arnold Mills, DESPR.

Mr. Richard Millstein, NIDA Deputy Director, accompanied by Dr. Patricia Needle and Dr. Stephen Zukin, DTR&D, met with Drs. Ghodse and Schaepe, Secretary and Vice Secretary of the International Narcotics Control Board, in a wide ranging discussion of recent NIDA research findings on drugs of abuse, with a focus on new opiate medications, GHB and Ritalin, July 24, 2000.

Dr. Rebekah Rasooly, DNBR, attended the Second International Meeting on Microarray Data Standards, Annotations, Ontologies and Databases at the Deutsches Krebsforschungszentrum (DKFZ)--the German Cancer Research Center and the European Molecular Biology Laboratory (EMBL) held in May 2000 in Heidelberg, Germany. The purpose of the meeting was to continue international efforts to standardize data reporting from genetic microarrays, an important new type of experimentation.

NIDA postdoctoral fellow Dr. Ricardo Gomez-Flores, working on a project on cellular and molecular mechanisms of opioid action with his sponsor, Dr. Richard J. Weber, has become the first participant in a collaboration of the University of Illinois with the Universidad Autonoma de Nuevo Leon (UANL) in Monterrey, Mexico.

Dr. Betty Tai, DTR&D, presented an overview of the Clinical Trials Network at the NIDA International Forum held on June 17, 2000, in San Juan, Puerto Rico.

Dr. David Gorelick, IRP, helped organize and co-chaired a symposium on "Ethical Issues in Clinical Psychiatric Research" at the World Psychiatric Association international congress in Paris, France, June 27, 2000. He also presented a paper on "Ethical Issues in Substance Abuse Research" at the symposium.

Dr. David Gorelick, IRP, helped organize and co-chaired a symposium on "Functional Neuroimaging in Psychiatry" at the World Psychiatric Association international congress in Paris, France, June 28, 2000. He also presented a paper on "Brain Mu-Opiate Receptor Function in Cocaine Addicts" at the symposium.

Dr. David Gorelick, IRP, presented two posters at the Royal College of Psychiatrists annual meeting in Edinburgh, Scotland, July 5, 2000: "Coping with Marijuana Quitting and Withdrawal" and "Brain Mu-Opiate Receptor Binding in Chronic Cocaine Users."

Dr. David Gorelick, IRP, presented a seminar on "Coping with Marijuana Quitting and Withdrawal" at the National Addiction Centre, Institute of Psychiatry, London, England, July 7, 2000.

Dr. David Gorelick, IRP, presented a poster on "Brain Mu-Opiate Receptor Function in Cocaine Addicts" at the Collegium International Neuropsychopharmacologicum biennial meeting in Brussels, Belgium, July 12, 2000.

Dr. Stephen Heishman, IRP, organized and chaired a symposium entitled, "Clinical Issues in Cannabis Use" at the World Psychiatric Association International Congress in Paris, France, June 27, 2000. He also presented a paper, "Cannabis Craving: Assessment and Quantification," at the symposium.

Dr. Monique Ernst, IRP, chaired the symposium entitled "Functional Neuroimaging in Psychiatry" and participated in the "Ethical Issues in Clinical Psychiatric Research" at the International Jubilee Congress entitled "From Clinical Practice to Research: Rethinking Psychiatry", June 26-30, 2000, Paris, France.

Dr. George Uhl presented "Molecular Mechanisms of Cocaine Action: Single and Multiple Transporter Knockouts" at the College on Problems of Drug Dependence meeting in San Juan, Puerto Rico, June 18-22, 2000.

Scott Hall, IRP, presented "Dopamine and Vesicular Monoamine Transporter2: Roles in Cocaine and Amphetamine Actions," at the Collegium Internationale Neuro-Psychopharmacologicum meeting in Brussels in July 2000.

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# Meetings/Conferences

NIDA hosted a meeting on May 9, 2000, **"Bringing It All Together: Drug Use, HIV, and Hepatitis,"** in Baltimore, MD with the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment, and the Centers for Disease Control and Prevention. At the meeting, NIDA released a Community Drug Alert Bulletin on Hepatitis C designed to provide information to the public and health professionals on the intertwined problems of substance abuse and diseases such as HIV/AIDS and Hepatitis C.

NIDA's Division of Epidemiology, Services and Prevention Research sponsored the **Community Epidemiology Work Group (CEWG)**, which met in Baltimore on June 13-16, 2000, to discuss current and emerging patterns and trends in drug abuse. The CEWG, established by NIDA in 1976, is a network of researchers and public health officials from 20 major U.S. metropolitan areas and the state of Texas. The group meets twice a year to discuss current patterns and trends of drug abuse. Mr. Richard Millstein moderated the session at which NIDA Divisions presented on their activities and discussed collaborative, expanded activities with the 21 CEWG reporters.

More than 1,000 researchers met in Puerto Rico at the annual **College on Problems of Drug Dependence (CPDD)** to discuss the latest studies on drug dependence and abuse. The international aspects of drug abuse were discussed at a meeting convened by NIDA on June 16-17, 2000. The 62nd annual meeting of the CPDD was held June 17-23, 2000, and featured the latest news on drug dependence and abuse as it relates to adolescents, gender differences, technological advancements, and treatment.

On May 31st and June 1st, 2000, Drs. Tony Simon, CAMCODA, Vince Smeriglio, CAMCODA, and Joe Frascella, DTR&D, hosted the NIDA meeting, **"Neuroimaging of Brain & Behavioral Development Following Early Drug Exposure".** The main goal of this meeting was to explore the value of combining the two emerging scientific fields of pediatric neuroimaging and the assessment of early exposure to drugs of abuse. In order to most effectively advance new work in this area almost 100 researchers from the drug abuse field were invited and attended. Three "foundational" papers were presented by Diana Dow-Edwards, Linda Mayes and Adele Diamond, outlining key issues concerning the effects of drugs such as cocaine and methamphetamine on the developing fetus. Barry Kosofsky highlighted themes emerging from those talks that were relevant to neuroimaging imaging techniques. Then Jay Giedd, Linda Chang, Peter Basser, Susan Bookheimer and Dennis Molfese presented talks on the relevance of a specific imaging method to pediatric drug exposure research. On the second morning, four discussants, (Monique Ernst, Peter Fried, James Olds and Bruce Rosen) presented interpretive summaries and then played the role of organizing, facilitating and directing interaction between the non-speaker attendees and the speakers, and between different non-speakers (since they represented a broad range of considerable expertise). The meeting engendered tremendous enthusiasm for this novel and timely brand of research and new collaborations as well as grant proposals have already resulted. There is also a full videotaped record of the meeting which can be viewed online using the RealPlayer at: http://videocast.nih.gov/PastEvents.asp

A symposium entitled **"Drug Addiction Treatment for Women: Does Gender Matter,?"** was co-chaired by Dr. Cora Lee Wetherington, NIDA's Women's Health Coordinator, and Dr. Betty Tai, Director of NIDA's Clinical Trials Network, at the June 2000 meeting of the College on Problems of Drug Dependence (CPDD) held in San Juan, Puerto Rico. Speakers were Drs. Cora Lee Wetherington, Kenneth Perkins (University of Pittsburgh), Karla Moras (University of Pennsylvania), Kathleen Brady (Medical University of South Carolina), and Hendree Jones (Johns Hopkins

University). The symposium was co-sponsored by NIDA's Women and Gender Research Group and NIDA's Treatment Workgroup.

Dr. Minda Lynch, BSRB, DNBR, was the discussant for a symposium at the Society for Prevention Science annual convention in Montreal, Quebec, held in June 2000. The symposium, entitled **"The Role of Experience-Dependent Plasticity in Psychopathology: Implications for Prevention,"** explored the malleable nature of developmental trajectories to positive or deleterious behavioral outcomes. The discussion focused on environmental influences across classes of variables, e.g., maternal nurturing, enrichment versus social isolation, and stress, and how the identification of variables conferring protective influences may be optimized in preclinical investigations.

Drs. David Shurtleff, Susan Volman, Herb Weingartner and Karen Skinner of DNBR organized and chaired a NIDA sponsored workshop held May 30-31, 2000 on **"Computational Models: Applications to Drug Abuse,"** to explore how computational and theoretical modeling could be used in drug abuse research. Workshop participants included researchers studying the neurobiology and behavior of drug abuse and researchers using computational modeling techniques in a variety of other applications. The participants saw a great potential for collaborations that would apply computational methodology to areas of importance for a scientific understanding of drug abuse and addiction, such as neural modulation, cellular homeostasis, learning and memory, decision-making and economics, and behavioral flexibility.

NIDA and NIMH cosponsored a conference entitled **"Assessing the Impact of Childhood Interventions on Subsequent Drug Abuse"** to develop research on the impact of mental health treatments for childhood psychopathologies on later risk for drug abuse. The meeting was developed by NIDA's Origins and Pathways Work Group, chaired by Dr. Meyer Glantz, DESPR. It was attended by over 150 researchers from around the country and was held May 23-24, 2000 in Washington, D.C. Special funding was provided so that 14 young scholars could attend. The primary purpose of the meeting was to encourage those already engaged in trials of mental health interventions for childhood psychopathologies to incorporate a focus on substance abuse outcomes and to encourage researchers involved with prevention research to consider a special focus on children and adolescents with psychopathology related vulnerabilities to drug abuse. Background papers were commissioned and these materials along with the excellent presentations by panels of experts provided the attendees with resources and encouragement to develop research in this important but understudied area. Papers based on the meeting will be published, probably in a special journal section. Dr. Meyer Glantz chaired the meeting with topic sections chaired by Drs. Naimah Weinberg, DESPR, James Colliver, DESPR, Elizabeth Robertson, DESPR, and Vincent Smeriglio, CAMCODA. Dr. Kathleen Etz, DESPR, chaired the Young Scholars program and Dr. Lynda Erinoff, DESPR, served as logistics coordinator. Mr. Richard Millstein, NIDA Deputy Director and DESPR Acting Director, presented welcoming remarks.

Mr. Richard A. Millstein, NIDA Deputy Director and Acting Director, DESPR, is a member of the Expert Panel advising the Robert Wood Johnson funded ImpacTeen Illicit Drug Abuse project. In this capacity, on August 1, 2000, he met with Dr. Duane McBride, project director, to plan for enhanced NIDA activity relating to the project.

On August 30-31, 2000 NIDA's Division of Epidemiology, Services and Prevention Research and Division of Treatment Research and Development held a meeting entitled **New Directions in Therapeutic Community Research**, in conjunction with the World Conference of Therapeutic Communities in San Francisco, CA. The purpose of this meeting was to inform NIDA regarding the direction future therapeutic communities (TC) research should be going and included presentations, open forum panel discussions, and breakout sessions.

Drs. David Shurtleff , DNBR and Steven Grant, DTR&D participated in a NIDA-sponsored symposium at the year 2000 meeting of the College on Problems of Drug Dependence (CPDD) entitled **"Antecedents, Consequences, and Treatment of Drug Abuse: A Cognitive Science Perspective."**

Drs. Minda Lynch and Susan Volman, DNBR organized and co-chaired a workshop at the Society of Biological Psychiatry's annual convention in Chicago, Illinois in May 2000. The workshop, sponsored by NIDA's cognitive workgroup, was entitled **"Frontal Cortical Function and Drug Abuse."** Participants explored recent directions using multidisciplinary approaches for studying the role of frontal cortical function (e.g., inhibition, working memory, impulse control, self-monitoring, reward anticipation, obsessive behavior, incentive motivation learning, and attentive mechanisms) in behaviors believed to be important for understanding drug addiction.

Drs. Minda Lynch, Lucinda Miner, Mark Swieter and David Shurtleff co-chaired a daylong **"Career Development Workshop"** in Washington, D.C. on August 3, 2000 as a pre-convention activity for the American Psychological Association annual meeting. This event was sponsored by NIDA's Behavioral Science Working Group and recruited 50 junior investigators from graduate programs throughout the United States to learn about contemporary issues in drug abuse research and attend a grants writing workshop. Presentations were given from drug abuse scientists actively involved in cutting-edge research representing prevention interventions, treatment strategies, gender and pregnancy

issues, genetic influences, special populations and AIDS, club drug use, field studies, neurobiological factors and co-morbidity.

The Behavioral Science Working Group, in collaboration with the Science Directorate of the American Psychological Association (APA) and the Science Divisions of APA hosted a series of eight invited lectures around the theme of **"Vulnerability to Drug Abuse"** during the APA convention (August 4-6, 2000) held in Washington D.C. The invited speakers and their topics were Drs. JosŽ Szapocznik, Ecological Developmental Approach to Vulnerability; Ralph Tarter, Etiology of Substance Abuse: From Individual Differences to Different Individuals; Kathleen Merikangas, The Search for Genes for Drug Abuse: Promises and Pitfalls; John Falk, Environmental Sources of Vulnerability to Drug Abuse; Marilyn E. Carroll, Vulnerability to Drug Abuse: How It Can Be Avoided or Accelerated; Nicholas E. Goeders, Role of Stress in the Motivation for Drug Abuse-Preclinical Models; Howard B. Moss, Behavioral Undercontrol and Family Liability for Substance Abuse; and Alan I. Leshner, Vulnerability to Drug Abuse and Addiction: A Quintessential Biobehavioral Issue.

Drs. Jerry Frankenheim and Minda Lynch organized a day-long international colloquium entitled **"All About GHB"** sponsored by NIDA's Neuroscience Consortium in its "Cutting Edge" series, in Rockville, MD, on June 27, 2000. Gamma-hydroxybutyrate (GHB, also known as "liquid ecstasy," "grievous bodily harm," or "Georgia home boy") recently emerged in the medical literature and lay press as a prominent drug of abuse and a drug used in rape. The organizers, and Drs. Timothy P. Condon, NIDA Associate Director, and Stephen R. Zukin, Associate Director, DTRD, introduced and co-chaired the meeting. Eminent researchers described GHB's trafficking, illicit use, dangers, and caring for patients under its influence; biochemistry, behavioral and neuropharmacology and toxicology, metabolism, and pharmacokinetics; physiological functions, and disorders involving this endogenous compound (e.g. petit mal epilepsy); and therapeutic potential (e.g. in narcolepsy and alcoholism).

The **"NIDA DTR&D Preclinical Workshop on Cocaine Medication Discovery and Development"** was held on the evening of June 20, 2000 during the Annual CPDD Scientific Meeting in San Juan, Puerto Rico. Dr. David McCann organized and chaired the workshop, which included presentations on Estimates of Market Size (Dr. Frank Vocci), Early Safety Assessment with Small Compound Quantities (Dr. James Terrill), In Silico Estimations of Safety and Chemical/Pharmacokinetic Properties (Dr. Richard Kline), "Hot" Receptor Targets (Dr. Jane Acri), and a Status Update on the Search for a "Dopamine-Sparing Cocaine Antagonist" (Dr. Nathan Appel). The workshop was well attended and received enthusiastically by chemists and pharmacologists working in the field of medication discovery.

NIDA co-sponsored and worked with ONDCP in the design, planning and organizing the **U.S./Mexico Drug Abuse Demand Reduction Conference** that took place in Phoenix, Arizona on May 30-31, 2000.

On July 15, 2000, in collaboration with CSAT, HRSA and OMH, NIDA and the Interamerican College of Physicians and Surgeons held a conference for primary care physicians entitled **"Substance Abuse in Primary Care Settings: Treating Hispanic Patients"** in Miami, Florida.

NIDA's Special Populations Office sponsored the workshop **"Opiate Substance Abuse: Potential for HIV Associated Complications,"** in Rosemont, Illinois, June 26-28, 2000. The three-day workshop offered minority and female scholars opportunities to learn about current NIDA-supported research in the field and to see demonstrations of the latest techniques in computer-assisted microscopic image analysis. A portion of the workshop was devoted to the NIH research grants process. The workshop was chaired by Pamela Goodlow, Special Populations Office, Dr. Joseph Frascella, Division of Treatment Research and Development, and Dr. George Stefano, State University of New York at Old Westbury.

On May 15-16, 2000, the Special Populations Office convened the first meeting of the **NIDA Native American Researchers and Scholars Work Group** at the Neuroscience Center.

On July 27-28, 2000, Lula Beatty co-planned and co-chaired a **CSAT/NIDA meeting** held in Rockville, MD on increasing minority participation in clinical/treatment research. At the meeting participants advised NIDA on how to increase researchers of color involved in treatment and clinical research. Presentations were made by Drs. Alan Leshner, Lucinda Miner, Eric Moolchan, Betty Tai, and Lula Beatty. Recommendations from the group were made to Dr. Tim Condon.

The Special Populations Office planned and supported activities of the **Diversity 2000 Program**, Office of Ethnic Minority Affairs, American Psychological Association at the annual convention of the association held in August, 2000 in Washington, DC. Dr. Lula Beatty presented a session on careers in drug abuse research for psychology students. In addition, a former minority supplement recipient who is active with Johns Hopkins' summer research program for high school and undergraduate students sponsored by NIDA presented a session for students participating in the Diversity 2000 project. Further, Diversity 2000 participants visited the NIDA established Center for Drug Abuse Research, Howard University, and discussed graduate education and research careers.

A **CTN National Steering Committee Meeting** was held May 23-24, 2000, in Hartford, CT. Dr. Thomas Kirk, Commissioner of the Connecticut Department of Addiction Services, gave a welcoming address. This meeting focused on updating the progress on first three protocol implementation teams and procedures for submitting the second round of new protocol concepts. Dr. Nancy Petry held a panel discussion with treatment providers and previous study participants in her motivational incentives trials.

A **CTN Quality Assurance Sub-Committee Meeting** was held on June 8-9, 2000, in Bethesda, MD. A second Quality Assurance Sub-Committee was held in Philadelphia, PA, on July 7, 2000.

A **CTN National Steering Committee Meeting** was held on July 19-20, 2000, in Portland, Oregon. The two-day meeting focused on implementation plans for the first seven protocols and status reports from various subcommittees.

A **CTN National Training Meeting** was held on July 21, 2000, in Portland, Oregon. The meeting was a "train the trainer" session with materials distributed on Good Clinical Practice, Science and the CTN, and tips and tricks for training various audiences.

On July 12, 2000, a meeting was held to discuss the standardization of urine tests for CTN protocols. Dr. J. Michael Walsh was invited to present information on the current availability of types of urine test cups, sensitivity for illicit drugs to be tested, and issues on the pros and cons of on-site versus central drug testing.

On July 13, 2000, a **CTN Protocol Review Board** met to review the first six protocols to be implemented among the community addiction treatment programs this fall. The panel consisted of six member experts from the NIH community, academia, and the pharmaceutical industry.

A **NIDA Ad Hoc Oversight Board Meeting**, chaired by Dr. Alan Leshner, was held on August 23, 2000 to review the second round of protocol concepts for the CTN.

Dr. Timothy P. Condon, Associate Director, NIDA, gave an update on NIDA's new Anabolic Steroid and Club Drug initiatives at the American Medical Association National Coalition on Adolescent Health in Washington, D.C. on May 5, 2000.

Drs. Timothy P. Condon, Associate Director, NIDA and Jack Stein, Deputy Director, OSPC, gave an update on NIDA Initiatives at a National Leadership Forum Meeting in Washington, D.C. on May 19, 2000.

Dr. Timothy P. Condon, Associate Director, NIDA, made a presentation at the plenary session titled "Challenges and Opportunities in Drug Demand Reduction: What We Have Learned from Research," at the U.S.-Mexico High Level Contact Group: Third Bi-National Drug Demand Reduction Conference in Phoenix, Arizona on June 1, 2000.

Dr. Timothy P. Condon, Associate Director, NIDA, presented Dr. Michael Picucci with the National Institute on Drug Abuse Leadership in Research Award for Outstanding Leadership in Applying Research on Drug Abuse and Addiction at the National Association of Alcoholism and Drug Abuse Counselors' 24th Annual Conference on Addiction Treatment on June 28, 2000 in Denver, Colorado.

Dr. Timothy P. Condon, Associate Director, NIDA, served on the screening jury and presented an award at The Face of Drugs Awards, sponsored by the Partnership for a Drug-Free America and the Palm Springs International Short Film Festival on August 4, 2000 in Palm Springs, California.

Dr. Timothy P. Condon, Associate Director, NIDA, presented and moderated the session "U.S. National Institute on Drug Abuse Research on How Smoking Changes the Brain: Big Findings, Big Opportunities," at the 11th World Congress on Tobacco OR Health in Chicago, Illinois on August 8, 2000.

Dr. Timothy P. Condon, Associate Director, NIDA, made a presentation "Club Drugs in the LGBT Community," at the 18th Annual Conference of the Gay and Lesbian Medical Association in Vancouver, Canada on August 10, 2000.

Dr. Jack Stein, OSPC, presented "Understanding Drug Abuse: What Science Says" at the Pennsylvania 10th Annual Prevention Conference, State College, PA on April 12-13, 2000.

Dr. Jack Stein, OSPC, presented "What's New at NIDA?" at the Ohio Annual Summer Institute of Addiction Studies, Columbus, OH on July 21, 2000.

Dr. Jack Stein, OSPC, presented "Update on Drug Addiction Research" at the South Florida Hispanic Physician Training Seminar, Miami, FL on July 15, 2000.

Dr. Jack Stein, OSPC, presented "Research Opportunities with Sexual Minority Populations" at the Annual Meeting of the American Psychological Association, Washington, D.C. on August 4, 2000.

Dr. Cindy Miner, OSPC, presented an update of NIDA's Club Drug Initiative at the June 9, 2000 meeting of the National Consortium for Child and Adolescent Mental Health Services held in Washington, D.C.

Dr. Cindy Miner, OSPC, organized and participated in the "NIDA Grant Writing Workshop" at the annual meeting of the College on Problems of Drug Dependence held in San Juan Puerto Rico, June 20, 2000. Drs. Mark Swieter, OEA, and David Shurtleff, DNBR, also participated in the workshop.

Dr. Cindy Miner, OSPC, participated in a panel discussion on club drugs at the Gay Men's Health Summit, held in Boulder, Colorado, July 20-23, 2000.

Drs. Cindy Miner, OSPC, Mark Swieter, OEA, and David Shurtleff, DNBR, organized and participated in a grant-writing tutorial at the annual meeting of the American Psychological Association held in Washington, D.C., August 3, 2000.

Angela M. Martinelli, RN, DNSC, OSPC, presented "NIDA Funding and Training Opportunities" at the American Psychiatric Association Annual Meeting, Chicago, IL.

Dr. Angela Martinelli, OSPC, discussed funding opportunities at the International Cannabinoid Research Society meeting held in Baltimore, MD on June 24, 2000, and at the NIDA Grant Writing Workshop held at Fordham University, School of Social Work, NY in July, 2000.

Dr. Lula Beatty, Director, Special Populations Office, served on the planning committee for the Student National Medical Association and Student Health Fair activities sponsored by NIH and held on June 3-4, 2000. She attended the health fair and met with students and others at NIDA's exhibit table.

Dr. Lula Beatty attended the CPDD meeting in Puerto Rico in June 2000 where she participated in the underrepresented populations committee activities.

Dr. Lula Beatty met with participants in the Extramural Associates Program, OD, NIH, on June 23, 2000. She presented an overview of NIDA programs and discussed their interest and plans for drug abuse research.

Ana Anders, Senior Advisor on Special Populations, was invited to participate as NIDA's representative in SAMHSA's (CSAT) "Changing the Conversation", a National Plan to Improve Substance Abuse Treatment.

Ana Anders worked with the NIH Office on Minority Health for the placement of four (4) Hispanic interns, through the Hispanic Association of Colleges and Universities (HACU). The four interns spent the summer at NIDA, and worked in their area of scientific interest. The main objective was to provide the interns the exposure to scientific research that would ignite their interest in the drug abuse research field.

Ana Anders convened a NIDA Internal "Asian American and Pacific Islander NIDA Research Workgroup" (AAPI) whose mission is to establish and maintain the Expert Panel of AAPI and to provide expertise and guidance to the NIDA - AAPI Initiative.

Ana Anders participated in outreach and meetings with the Executive Director of the National Council of La Raza, and the Executive Director of the National Latino Lesbian, Gay, Bisexual and Transgender Organization.

On June 29, 2000, Flair Lindsey, Special Populations Office, presented a poster on NIDA programs centered on youth and adolescents and NIDA funding opportunities at the Head Start Research Conference.

Dr. Frank Vocci, Director, DTR&D, was the co-chair of the NIDA Symposium "Treating the Multiple Drug Abuser: Science-Based Approaches" at the American Society of Addiction Medicine (ASAM) and addressed the opening ceremony of the 31st Annual Medical Scientific conference on April 14, 2000 in Chicago, IL.

Dr. Frank Vocci attended the American Psychiatric Association Conference on May 15-16, 2000 in Chicago and presented on "Buprenorphine Treatment: Research and Practice." While at the conference, Dr. Vocci addressed the APA Council on Addiction Psychiatry on the Medications Development Program.

Dr. Vocci summarized the status of the opiate and cocaine treatment development programs to the CPDD Board of Directors on June 17, 2000 in Puerto Rico.

Dr. Frank Vocci presented at a NIDA international satellite symposium on The Impact of Basic Research on Drug Abuse Treatment at CPDD. His presentation was entitled: " New Development in the Neurobiology of Drug Abuse" on June 16, 2000.

Dr. Frank Vocci was a co-chair and discussant at a June 19, 2000 workshop at the CPDD meeting. The workshop was entitled: "Where 'STOP?' meets 'GO!'" (And Guess Who Wins?) Treatment Implications of Inhibitory Deficits for Addiction & Relapse.

Dr. Betty Tai presented an overview of the CTN at the HAFCI 2000 Conference on Research to Practice, San Francisco, CA.

Debra Grossman, DTR&D, participated in a meeting of investigators conducting research on tobacco use among youth in Lakewood, Co on June 8-9, 2000.

Dr. Elizabeth Rahdert, DTR&D, presented a poster entitled '"rogress Report on the Development of an HIV/STD Risk-of-Future-Exposure Screen for Drug Using Adolescents" at the 62nd Annual Scientific Meeting of the College on Problems of Drug Dependence, June 17-22, 2000, in San Juan, Puerto Rico.

Dr. Elizabeth Rahdert, DTR&D, organized and chaired the symposium, "Family-Focused Therapies for Adolescent Drug Abuse: Research and Practice," at the 108th Annual Convention of the American Psychological Association, August 4-8, 2000, in Washington, DC.

Dr. Elizabeth Rahdert, Ph.D., DTR&D, presented a workshop entitled "Adolescent Assessment and Use of the Problem Oriented Screening Instrument for Teenagers (POSIT)," at the Mid-Atlantic Regional Adolescent Conference, September 11-12, 2000, in Charlottesville, VA.

On May 16, 2000, Dr. Dorynne Czechowicz, BTDB/DTR&D, represented NIDA at a Young Investigators Forum at the American Psychiatric Association meeting in Chicago, Illinois.

Dr. Dorynne Czechowicz, BTDB, DTR&D, and Carol Cushing, CTN, DTR&D, represented NIDA at a seminar, Women and Clinical Research: Breaking Through the Barriers to Recruitment and Retention, sponsored by the Society for Women's Health Research. This meeting was held on May 18, 2000 in New Orleans, LA.

Dr. Lisa Onken, BTDB, DTR&D organized and chaired a symposium, "Innovations in Behavioral Therapies for Drug Addiction." NIDA Council Member Dr. G. Alan Marlatt, and NIDA grantees Drs. Kathleen Carroll, Steve Higgins, and Rick Rawson participated in the symposium. The symposium was held on August 5, 2000 at the American Psychological Association Annual Meeting in Washington, DC.

Dr. Lisa Onken, BTDB, DTR&D organized a panel, "A Behavioral Treatment Research Perspective on Therapeutic Community Research," for the NIDA meeting, "New Directions in Therapeutic Community Research," held in San Francisco, CA on August 30-31, 2000.

Dr. Steven Grant of the Clinical Neurobiology Branch, DTR&D co-chaired a symposium with Dr. David Shurtleff, DNBR entitled "Antecedents, Consequences and Treatment of Drug Abuse: a Cognitive Science Perspective" at the annual meeting of the College on Problems of Drug Dependence, San Juan, Puerto Rico, June 18, 2000.

Dr. Steven Grant presented a talk entitled "Brain Activity Differentiates Drug Abusers and Controls During Gambling Task Performance .....' As If '" at the symposium "Where 'STOP?' meets 'GO!' (and Guess Who Wins?): Treatment Implications of Inhibitory Deficits for Addiction and Relapse " at the annual meeting of the College on Problems of Drug Dependence, San Juan, Puerto Rico, June 19, 2000.

Dr. Steven Grant gave a seminar entitled "Brain Activity Differentiates Drug Abusers and Controls During Gambling Task Performance .....' As If '" at the Treatment Research Center, University of Pennsylvania, on July 17, 2000.

Dr. Steven Grant represented NIDA at the Summer Training Institute for Cognitive Neuroscience at Dartmouth College, Hanover, NH on July 2 - July 8, 2000. The topic of the Summer Institute was Cognitive Development and Self-Regulation, and included a day of presentations on addiction and drug abuse.

Dr. Ro Nemeth-Coslett of the Clinical Neurobiology Branch, DTR&D represented NIDA and participated in the National NeuroAIDS Tissue Consortium meetings and Steering Committee meetings.

Dr. Joseph Frascella, Chief of the Clinical Neurobiology Branch, DTR&D participated in the Special Populations Research Development Seminar Series: Opiate Substance Abuse: Potential for HIV-Associated Complications and gave presentations on the Neurobiology of Addiction and the Grant Process in Rosemont, Illinois, June 27, 2000.

Dr. Joseph Frascella participated in the NIDA/American Psychological Association Early Careers Workshop and the special scientific track on Vulnerability to Drug Addiction Lecture; he chaired an invited address session by Ralph Tarter, Ph.D. on Etiology of Substance Abuse: From Individual Differences to Different Individuals, Washington, D.C.,

August 3 - 6, 2000.

Dr. Jack Blaine, DTR&D, chaired a Workshop on Translating Substance Abuse Treatment Research to Practice: Innovative Trial Designs at the 40th Annual NCDEU Meeting on May 30, 2000. He also made a presentation during the workshop on the NIDA National Drug Abuse Treatment Clinical Trials Network. Ann Montgomery, RN, MA made a presentation on the LAAM study and Bob Walsh, RAC made a presentation on the Buprenorphine Best Practice study. Dr. Barbara Mason presented her data on the large acamprosate trial in alcohol dependence. Dr. Frank Vocci served as a discussant with Dr. Celia Winchell from FDA.

Dr. Jacques Normand served as a member of the Planning Board for the Surgeon General's Report on Youth Violence and participated in the Board's meeting held in Washington, DC on June 28-29, 2000.

Dr. James Colliver, DESPR, has become NIDA's representative to the Federal Interagency Forum on Child and Family Statistics and also serves on the reports committee of that organization. He represented NIDA at the Forum's meeting on June 23, 2000 and has provided information regarding Monitoring the Future findings for use in the Forum's America's Children: Key National Indicators of Well Being 2000.

Dr. Leslie Cooper, DESPR, participated in the NIH Extramural Associates Program Advisory Board Retreat in St. Michaels, MD, July 16 -18, 2000.

Moira O'Brien, DESPR, served as NIDA representative on the NIH Planning Committee for the Office of Behavioral and Social Sciences sponsored conference, Toward Higher Levels of Analysis: Progress and Promise in Research on the Social and Cultural Dimensions of Health, which was held in Bethesda, MD, June 27-28, 2000. Ms. O'Brien also moderated a conference panel session on, "Etiology: Interpersonal Processes" and served as the NIH representative during a research agenda setting session on the topic of "Etiology Research" in follow up to the Conference on June 29, 2000.

Moira O'Brien, DESPR, served on the planning committee for the 2001 Department of Defense Survey of Health Related Behaviors Among Military Personnel and participated in meetings on June 22 and July 20, 2000.

On July 26, 2000, Dr. Elizabeth Robertson briefed the Secretary's Youth Substance Abuse Prevention Initiative on NIDA's prevention programs. Dr. Bill Bukoski, DEPSR, and Beverly Jackson, OSPC were invited to the meeting as observers.

Drs. Kathy Etz and Elizabeth Robertson, PRB, DESPR chaired a symposium entitled Family-based Preventive Interventions for Drug Abuse: Factors Influencing Program Outcomes and Future Directions at the annual meeting of the Society for Prevention Research, Montreal, Canada in June. Symposium speakers included Drs. Richard Spoth, Kate Kavanaugh, Susan Ennett, Karl Bauman and Richard Catalano. In addition, Drs. Robertson, Etz, Eve Reider, and Larry Seitz, PRB, DESPR, presented a discussion session entitled New Directions in Prevention Research at the National Institute on Drug Abuse. All four also participated in a Round Table session sponsored by the Early Career Preventionist Network.

On July 25, 2000, Drs. Elizabeth Robertson, Kathy Etz, Eve Reider, and Jacques Normand, DESPR met with researchers from three universities at the Johns Hopkins University School of Public Health Prevention Research Center. NIDA staff presented information on new direction in prevention and community research. Researchers from Johns Hopkins University, Morgan State University, and George Washington University presented information on their current research and future plans.

On April 24-25, 2000, Susan David, DESPR, convened a meeting of NIDA-supported Prevention & Communications Research grantees to present an overview of their research progress, and provide insights and recommendations for planners of the ONDCP National Youth Anti-Drug Media Campaign. The research, which ranges from the communications laboratory to multi-community field trials, are testing behavior change theories, message strategies, and individual differences that can improve knowledge about the use of the media to prevent substance abuse.

Ms. Susan David, DESPR, presented NIDA's prevention funding priorities on a panel at the International Communications Association (ICA) meeting, June 1-5, 2000, in Acapulco, Mexico. In addition, Ms. David met with several communications grantees who presented papers at the conference. Plans are underway for the May 2001 ICA conference in Washington, DC, which will feature a NIDA symposium on drug abuse communications research.

Ms. Susan David, DESPR, gave a presentation on NIDA prevention research to the National Mental Health Coalition in Alexandria, VA, on June 13, 2000. This group represents the concerns of national mental health organizations, and were interested in how NIDA prevention research intersects with mental health promotion and early intervention research for youth.

Ms. Susan David, DESPR, gave a presentation on community prevention research on June 27, 2000 as part of a panel at a National Community Empowerment Conference, sponsored by the Departments of Housing and Urban Development and Labor, in Columbus, OH.

Dr. Eve Reider, DESPR, represented NIDA at the Federal Interagency Work Group on Child Abuse and Neglect meeting on April 18, 2000 at Loews L'Enfant Plaza Hotel in Washington, D.C.

Dr. Eve Reider, DESPR, represented NIDA at the Science and Ecology of Early Development (SEED) meeting on May 1, 2000 at the Humphrey Building in Washington, D.C.

Dr. Eve Reider, DESPR, represented NIDA at an interagency planning meeting for the Surgeon General's Conference on Children's Mental Health on July 14, 2000 at the Humphrey Building in Washington, D.C.

Dr. Larry Seitz, PRB, DESPR, presented an overview of "Principles of Prevention" to a group of Montgomery County, Maryland teachers and school staff who were attending a substance abuse workshop sponsored by the Montgomery County Public Schools' Safe and Drug Free Institute on June 20, 2000.

Dr. Larry Seitz, PRB, DESPR, represented the Institute at the recent monthly POPOF (Project Officers and Program Officials Forum) Meeting held on June 29, 2000. The agenda included: (1) a presentation by Dr. Belinda Seto regarding "Data and Safety Monitoring Boards, Phase I and Phase II", and (2) IMPAC II priorities for program staff.

Dr. Elizabeth Robertson participated in two events at the American Psychological Association meeting in Washington, DC, on August 5, 2000: a panel on Future of Addiction Prevention and Treatment: Funding Agency's Perspective, and a funding breakfast to meet prospective grantees. Ms. Susan David participated in a panel on Behavioral and Social Science Contributions to Public Health on August 7, 2000 entitled Evaluating the National Youth Anti-Drug Media Campaign. Dr. Kathy Etz chaired a session on vulnerability to drug abuse.

Dr. William J. Bukoski, DESPR, served (for the third consecutive year) as the program chair for the Eighth Annual Meeting of the Society for Prevention Research. This year's conference was held in Montreal, Canada, June 1-3, 2000.

Dr. William J. Bukoski, DESPR, served as co-chair and moderator for a plenary session at the Eighth Annual Meeting of the Society for Prevention Research titled: "Stress and Vulnerability: Implications for Prevention," that was held June 1, 2000 in Montreal, Canada.

On May 31, 2000, Dr. William J. Bukoski, DESPR, and William Cartwright, Ph.D., DESPR, co-chaired and presented on "Research Grant Opportunities: Economic Analyses in Prevention and Treatment," at the Eighth Annual Meeting of the Society for Prevention Research, Montreal, Canada.

On July 19, 2000, Dr. William J. Bukoski, DESPR, represented NIDA at the Prevention Coordination Meeting sponsored by the Deputy Director for Demand Reduction, White House Office of National Drug Control Policy.

Dr. Bennett Fletcher, SRB, DESPR, presented on "NIDA Services Research" at the AHSR Conference, Los Angeles, June 25, 2000.

Dr. Bennett Fletcher, SRB, DESPR, presented the DATOS findings in a "Science for the Staff" seminar at NIDA, July 11, 2000.

Drs. Bennett Fletcher, William Cartwright, and Jerry Flanzer, SRB, DESPR presented the health services research program to researchers at the National Development and Research Institutes, Inc., on August 3, 2000.

Dr. William Cartwright, SRB, DESPR, chaired a session at the Fifth Workshop on "Costs and Assessment in Psychiatry: The Value of Psychiatry - Economic and Health Policy Implications," University of Chicago, May 10-12, 2000.

Dr. William Cartwright, SRB, DESPR, presented on "Economics Research in Drug Abuse Prevention at NIDA," at the Society of Prevention, Montreal, Canada, May 31, 2000.

Dr. Jerry Flanzer, SRB, DESPR, presented on "NIDA Services Research" at the Services Research Roundtable, American Psychiatric Association, May 17, 2000, in Chicago, IL.

Dr. Jerry Flanzer, SRB, DESPR, presented on "NIDA Services Research" at the Summit on "Social Work and the Neurobiology of Addictions," June 11-13, 2000, Austin, Texas.

Dr. Jerry Flanzer, SRB, DESPR, conducted a panel on "Adolescents Drug Abuse Treatment: Current Research Programs and Practices" at the AHSR Conference, Los Angeles, June 24, 2000.

Dr. Jerry Flanzer, SRB, DESPR, conducted a workshop series, "Funding Opportunities for Social Work Research," at Howard University (May 22-24, 2000), San Jose State University (June 21-23, 2000), and Fordham University (July 12-14, 2000). The first workshop was co-led with Dr. Peter Delany.

Dr. Thomas Hilton, SRB, DESPR, led a panel on the Clinical Trials Network at the AHSR Conference, Los Angeles, CA on June 27, 2000.

Dr. Roy Wise was invited to present "Mechanisms of Drug Reward: Dopamine and Beyond" at the Harvard Symposium on The Neurobiology of Addiction, Cambridge, MA held May 5-6, 2000.

Dr. Svetlana Chefer presented "Characterization of 2-[F-18]fluro-A-85380 Binding *in vivo* by Positron Emission Tomography" at the Neuroreceptor Mapping Meeting held June 9-11, 2000, in New York, New York.

Dr. Svetlana Chefer presented "2-[F-18]Fluoro-A-85380: A Novel Positron Emission Tomography Ligand for Nicotinic Acetylcholine Receptors" at the Mathematics and Engineering Techniques in Medicine and Biological Sciences Meeting, June 26-29, 2000, Las Vegas, Nevada.

Dr. Alexey Mukhin presented "Radiohalogenated Analogs of A-85380: Potential Ligands for Mapping alpha 4 beta2 Nicotinic Receptors in Human Brain" at the Neuroreceptor Mapping Meeting, June 9-11, 2000, New York, New York.

Dr. Alexey Mukhin presented "Radiohalogenated Analogs of A-85380 as Potential Ligands for *in vivo* Monitoring of alpha4 beta2 Nicotinic Receptor Alteration in Alzheimer's Disease" at the Mathematics and Engineering Techniques in Medicine and Biological Sciences Meeting, June 26-29, 2000, Las Vegas, Nevada.

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# Media and Education Activities

## Awards

NIDA's Treatment Solutions Video won the **2nd Place Silver Screen Award in the International Film and Video Festival** in the category of Medicine, Health: Current Issues. The 33rd annual awards competition received over 1,600 entries from 30 countries.

NIDA's *Principles of Drug Addiction Treatment* received an **Award for Publication Excellence in the APEX 2000 12th Annual Competition for Communications Professionals** sponsored by Communications Concepts, Springfield, VA. The awards are based on excellence in graphic design, editorial content, and the ability to achieve overall communications excellence. NIDA competed against some 4,900 entries.

NIDA's *Mind over Matter* website was rated "Spectacular!" and awarded five stars in the March 2000 syndicated newspaper column **"Surfing the Net with Kids"** by Barbara J. Feldman. The column appears in many papers nationally, including San Diego Union-Tribune, Indianapolis Star News, Richmond Times-Dispatch, Contra Costa Times, and Winston-Salem Journal.

NIDA's *Principles of Drug Abuse Treatment* website was awarded the **Star Rating from the Awesome Library**. Sites included in the Awesome Library are among the top 5% of sites in the field of K-12 education.

## Press Releases

April 14, 2000 - **NIDA Announces Multimedia Public Education Initiative Aimed at Reversing Rise in Use of Anabolic Steroids by Teens.** NIDA's partners in the initiative include the National Collegiate Athletic Association, American College of Sports Medicine, American Academy of Pediatrics, National Association of School Nurses, National Federation of High Schools, International Students in Action, and Dr. Drew Pinsky, host of MTV's Loveline and drDrew.com. In addition to launching a new website - https://www.drugabuse.gov/drugs-abuse/steroids-anabolic - NIDA is distributing 250,000 copies of a Community Drug Alert Bulletin about anabolic steroids and 150,000 copies of an updated report that explains what research has shown about anabolic steroids and their effects as well as approaches to prevent the use of these drugs. Some 500,000 postcards with messages about the harmful effects of steroids were distributed in nearly a thousand locations nationwide. As a result of this event, coverage appeared in *USA Today, Time, HealthAtoZ.com, Your Health Daily, Fox News, The Oregonian, San Antonio Express-News, Associated Press, Reuters Health, CBS HealthWatch, Keeping Well,* and *Alcohol and Drug Abuse Weekly.*

May 2, 2000 - **Drug Use, HIV/AIDS and Hepatitis C: A Public Health Emergency.** The media advisory announced the meeting, "Bringing It All Together: Drug Use, HIV, and Hepatitis," hosted by NIDA, the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment, and the Centers for Disease Control and Prevention in Baltimore on May 9, 2000. At this meeting, NIDA released a Community Drug Alert Bulletin on Hepatitis C designed to provide information to the public and health professionals on the intertwined problems of substance abuse and diseases such as HIV/AIDS and Hepatitis C. As a result of this event, coverage appeared in *Yahoo! News.*

June 8, 2000 - **Urban Researchers Who Track Drug Use Will Meet in Baltimore, June 13-16: Their Frontline Reports Offer Early Warning of National Trends.** This save-the-date announced the 48th meeting of the Community Epidemiology Work Group (CEWG). NIDA sponsors the CEWG, which met in Baltimore to discuss current and emerging patterns and trends in drug abuse. The CEWG, established by NIDA in 1976, is a network of researchers and public health officials from 20 major U.S. metropolitan areas and the state of Texas. The group meets twice a year to discuss current patterns and trends of drug abuse. As a result of this event, coverage appeared on *Fox News.*

June 14, 2000 - **Study Shows a Combination of Antabuse and Buprenorphine May Be Effective in Treating Those Addicted to Cocaine.** A study in the Spring 2000 issue of Biological Psychiatry reported that combining buprenorphine, an alternative to methadone for treating opiate addiction, with disulfiram (marketed as Antabuse and used in treating alcoholism) was more effective than buprenorphine alone in reducing cocaine use in persons with this dual addiction. Coverage of this publication appeared in *USA Today, The Los Angeles Times, Alcohol and Drug Abuse Weekly, Join Together Online, Yahoo! News,* and *Reuters Health.*

June 15, 2000 - **Researchers Announce Latest Findings on Drug Dependence and Abuse.** This media advisory announced that the College on Problems of Drug Dependence (CPDD) was holding its annual meeting of more than 1,000 researchers worldwide to announce the latest findings on drug abuse related to adolescents, gender differences, technology, and treatment. The meeting was held from June 17-23, 2000, in San Juan, Puerto Rico. As a result of this event, coverage appeared in *HHS-HEO News.*

June 20, 2000 - **Study Finds Marijuana Ingredient Promotes Tumor Growth, Impairs Anti-Tumor Defenses.** Researchers reported in the July 2000 issue of the Journal of Immunology that tetrahydrocannabinol (THC), the major psychoactive component of marijuana, can promote tumor growth by impairing the body's anti-tumor immunity system. While previous research has shown that THC can lower resistance to both bacterial and viral infections, this is the first time that its possible tumor-promoting activity has been reported. Coverage of this publication appeared in *USA Today, CNN.com, ITN.com (UK),* and *Join Together Online.*

June 22, 2000 - **All About GHB: Scientific Meeting to Focus on Research about Date Rape Drug.** This media advisory announced the scientific meeting convened by NIDA on June 27, 2000, in Rockville, MD, to focus on research about the drug GHB (gamma-hydroxybutyrate). The drug, which has sedative effects, has been associated with sexual assaults in cities across the country. The meeting facilitated scientific dialogue about the following: GHB use, pharmacology and toxicology; the roles of endogenous GHB in the normal brain and in neurological disorders; and the therapeutic potential of GHB. As a result of this event, coverage appeared in *WebMD,* and *USA Today.*

June 26, 2000 - **Cocaine and Alcohol Combined Are More Damaging to Mental Ability Than Either Drug Alone.** Scientists found that cocaine abuse coupled with use of alcohol leads to more impulsive decision-making and to poorer performance on tests of learning and memory than does use of either cocaine or alcohol alone. The negative effects on the ability to think clearly persist for at least a month after the substance use stops, according to an article about the study in the June 27 issue of Neurology. Coverage of this publication appeared in *ScienceDaily Magazine, EurekAlert!,* and *Join Together Online.*

June 30, 2000 - **Conferences in South Africa to Focus on the Role of Drug Use in HIV Transmission.** Prior to the 13th International AIDS Meeting in Durban, South Africa, researchers met in three separate forums to discuss the role of drug use in the transmission of HIV/AIDS. On July 5-7, 2000, a consortium of international organizations sponsored the third annual Global Research Network (GRN) Meeting on HIV Prevention in Drug-Using Populations. NIDA had a pivotal role in creating the GRN and in supporting its continuation. The agenda for this meeting was designed to facilitate the global diffusion and application of research-based principles on effective HIV prevention strategies for populations of injecting and non-injecting drug users around the world.

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## Opinion Pieces/Letters

April 2000, *Society for Research on Nicotine and Tobacco (SRNT) Newsletter* - Article adapted from keynote speech for the 6th Annual Meeting of SRNT - "NIDA Director's Message: 'We Want You to Do More'"

May/June 2000, *Primary Care Practice* - Article by Alan I. Leshner - "The Disease of Addiction"

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## Articles of Interest

March 23, *New York Times* - Interview of Alan I. Leshner - "New Campus High: Illicit Prescription Drugs"

April 2000, *Connection (Association for Health Services Research)* - Interview of M. Patricia Needle - "International Trends in Drug Abuse Services Research"

April 2, 2000, *Sun-Sentinel (Fort Lauderdale, FL)* - Interview of Timothy P. Condon - "Teens Find 'Club Drugs' Anywhere; Accessibility Makes Them a Chief Threat"

April 12-13, *CBS HealthWatch, ABC News, HealthScout, The Washington Post, The Associated Press, CNN,* and *MSNBC* - Interviews with Alan I. Leshner and Jacques Normand - Re: Brook, J.S., Brook, D.W., and Whiteman M. "The Influence of Maternal Smoking During Pregnancy on the Toddler's Negativity," Arch Pediatr Adolesc Med 154, Apr 2000, pp 381-5.

April 19, 2000, *USA Today* - Interview of Alan I. Leshner - "Feds Crack Down on Ecstasy"

April 21, 2000, *Psychiatric News* - Interview of Alan I. Leshner - "NIDA Drug-Treatment Guide a Hit with Addiction Experts"

April 21, 2000, *The Chronicle of Higher Education* - Interview of Alan I. Leshner and Frank Vocci - "In the Nation's Battle Against Drug Abuse, Scholars Have More Insight Than Influence"

April 26, 2000, *salon.com* - Interview of Alan I. Leshner - "Immunized Against Addiction"

May 3, 2000, *JAMA* - Interview of Alan I. Leshner - "NIDA Seeking Data on Effect of Fetal Exposure to Methamphetamine"

May 5, 2000, *Psychiatric News* - Interviews of Alan I. Leshner - "Innovative NIDA Program Tests New Treatment Methods" and "NIDA Moves Proactively on Growing 'Club Drug' Menace"

May 5, 2000, *Join Together Online* - Interview of Nicholas Kozel - "Researchers Provide 'Heads-Up' on Emerging Drug Trends"

May 7, 2000, *The Atlanta Journal and Constitution* - Interview of Alan I. Leshner - "Substance Abuse: Having to Grasp for Treatment"

May 16, 2000, *London (AP)* - Interview of Alan I. Leshner - "Study: Ecstasy Drug May Dull Mind"

May 21, 2000, *Chicago Tribune (Family Adviser)* - Interview of Alan I. Leshner - "Ways to Tell If a Child Is Using Drugs"

May 31, 2000, *USA Today* - Interview of Alan I. Leshner - "Heroin's New Fix and Why It Matters to You"

June 2000, *New Scientist* - Interview of Frank Vocci - "What Do You Do for Kicks?"

June 5, 2000, *Time* - Interview of Alan I. Leshner - " The Lure of Ecstasy"

June 20, 2000, *Health Oasis (Mayo Clinic)* - Interview of Stephen Zukin - "Date-Rape Drugs: Keep an Eye on That Drink"

June 23, 2000, *The Detroit News* - Interview of Nicholas Kozel - "Drug Users Flood Hospitals"

June 23, 2000, *APBnews.com* - Interview of Timothy P. Condon - "Meth Infants Called the New 'Crack Babies:' Doctors See Spike as Drug's Popularity Rises"

June 24, 2000, *The New York Times* - Interview of Alan I. Leshner - "Seeing Drugs as a Choice"

June 28, 2000, *USA Today* - Interview of Jerry Frankenheim - "Time Out on Ecstasy"

July 2000, *NASW News* - Interview of Peter Delany - "Grants Facilitate Drug Abuse Research"

July 12, 2000, *Village Voice* - Interview of Frank Vocci - "New Vaccines May Drug-Proof Kids: Injecting Big Brother"

July 13-14, 2000, *CBS HealthWatch, Newsday* - Interviews with James Colliver-Re: America's Children: Key National Indicators of Well - Being 2000 (issued by NICHD)

August 2000, *YM Magazine* - Interview of Alan I. Leshner - "Poisoned at the Party"

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## NIDA Exhibits Program

Meetings where NIDA exhibited publications and program announcements over the past several months are as follows:

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| May 31-June 2, 2000 | Third Bi-National Drug Demand Reduction Conference |
| June 1-3, 2000 | National Association of Drug Court Professionals |
| June 3-7, 2000 | National Association of State Alcohol and Drug Abuse Directors |
| June 3, 2000 | NIH Health Fair |
| June 8-11, 2000 | American Psychological Society |
| June 14-18, 2000 | The Nation's Voice on Mental Illness |
| June 17-22, 2000 | 62nd Annual Scientific Meeting of the College on Problems of Drug Dependence |
| June 23-28, 2000 | American Nurses Association Biennial Convention and Exposition |
| June 24-27, 2000 | 104th Annual National Congress of Parents and Teachers Association |
| June 28-July 1, 2000 | 24th Annual Meeting of the National Association of Alcoholism and Drug Abuse Counselors |
| July 1-5, 2000 | National Council of La Raza Annual Conference |
| July 12-15, 2000 | 23rd Annual Association on Higher Education and Disability |
| July 19-21, 2000 | National Association of Hispanic Nurses |
| August 1-2, 2000 | DEA Conference |
| August 4-8, 2000 | American Psychological Association |
| August 6-11, 2000 | The World Congress on Tobacco OR Health |

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# Planned Meetings

NIDA, the World Health Organization, and the National Inhalant Prevention Coalition will co-sponsor an international meeting, **"Street Children and Drug Abuse: Social and Health Consequences,"** on September 17-19, 2000, in Los Angeles, CA, to examine the connections between street kids, violence, and drug abuse. At this meeting, NIDA will launch an updated research report that will discuss recent studies on the use of inhalants among adolescents in the United States, with the goal of alerting the public to the widespread use of inhalants and the dangers inherent in such use.

November 1-2, 2000. NIDA, the University of California, Los Angeles, the Los Angeles County Alcohol and Drug Program Administration, and the Robert Wood Johnson Foundation will co-sponsor a conference, **"Blending Clinical Practice and Research to Enhance Drug Addiction Treatment"** in Los Angeles, CA, to disseminate research-based information on drug abuse and addiction. Researchers and practitioners will examine ways to enhance ongoing efforts to ensure that research is incorporated into practice settings.

**"The Science of the Placebo: Toward an Interdisciplinary Research Agenda,"** will be held November 19-21, 2000 in Natcher Auditorium, NIH, Bethesda, MD. NIDA is a co-sponsor in this trans-NIH meeting and Dr. Lisa Onken is a member of the Executive Committee that is organizing this conference.

**National CTN Steering Committee Meetings** are planned for the follow dates and locations: September 19-20, 2000, in Philadelphia, PA; and October 30, 2000, in Los Angeles, California.

A second **CTN Kick-Off Meeting** is planned for October 31, 2000, in Los Angeles, CA, for the second group of new grantee awards for the CTN RFA.

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# Publications

**Research Report Series: Methamphetamine Abuse and Addiction (Spanish)**
**NIH Pub. No.: 00-4811**
This Research Report Series provides scientific information on various topics; this report focuses on methamphetamine abuse. It will describe methamphetamine and related drug and analogues (e.g., MDMA); how it enters the body; current epidemiological data regarding its abuse; and the short-term and long-term effects of abuse, with an emphasis upon how it affects the brain.

**Preventing Drug Use Among Children and Adolescents (Spanish)**
**NIH Pub. No.: 00-4785**
This guide is designed to provide important research-based concepts and information to further efforts to develop and carry out effective drug abuse prevention programs. The answers were developed in consultation with prevention scientists. This guide presents an overview of the research on the origins and pathways of drug abuse, the basic principles derived from effective drug abuse prevention research results to the prevention of drug use among young people.

**National Survey Results from the Monitoring the Future Study, 1975-1999, Volume I: Secondary School Students**
**NIH Pub. No.: 00-4802**
The annual report provides information about the prevalence of drug use among American secondary students (specifically 8th, 10th, and 12th graders). The trends are used for understanding the changing drug abuse problems and for formulating the appropriate intervention (prevention/treatment) policies.

**National Survey Results from the Monitoring the Future Study, 1975-1999, Volume II: College and Young Adults**
**NIH Pub. No.: 00-4803**
The annual report provides information about the trends in use by populations based on gender, college plans, region of the country, population density, race/ethnicity, and parents' education. The trends are useful for understanding the changing drug abuse problems and for formulating the appropriate intervention (prevention/treatment) policies.

**The NIDA Community-Based Outreach Model: A Manual to Reduce Risk of HIV and Other Blood-Borne Infections in Drug Users**
**NIH Pub. No.: 4812**
This publication provides community-based organizations, prevention program planners, and service providers with a practical, step-by-step manual for planning, developing, and implementing effective HIV outreach/prevention programs for not-in-treatment drug users in their communities. It describes NIDA's Outreach-Based HIV/AIDS Risk Reduction Model, which is based on a synthesis of findings and best practices from two national multi-site intervention programs supported by NIDA (The National AIDS Demonstration Research Program {NADR} and the Cooperative Agreement {CA} for HIV/AIDS Community-Based Outreach/Intervention Research Program), as well as from several smaller evaluations of outreach-based HIV prevention strategies.

## NIDA NOTES

### NIDA NOTES, Volume 15, No. 2
**NIH Pub. No.: 00-3478**

This issue's lead story reports on evidence that genes influence cigarette smoking. Other research reported in this issue includes the following: a study showing that ketamine, PCP, and alcohol trigger widespread cell death in the brains of rats; and a study developing a potential antibody for PCP overdose and abuse. In the Director's Column, Dr. Leshner describes the Institute's strategic plan from the present to the year 2005. Other articles review NIDA's annual constituent conference and a number of other outreach forums the Institute has undertaken in recent months.

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## Other Publications

Wise, R.A. Addiction Becomes a Brain Disease. Neuron, 26, pp. 27-33, 2000.

Heishman, S.J., Schuh, K.J., Schuster, C.R., Henningfield, J.E., and Goldberg, S.R. Reinforcing and Subjective Effects of Morphine in Human Opioid Abusers: Effect of Dose and Alternative Reinforcer. Psychopharmacology, 148, pp. 272-280, 2000.

Rothman, R.B., Gorelick, D.A., Heishman, S.J., Eichmiller, P.R., Hill, B.H., Norbeck, J., and Liberto, J.G. An Open-label Study of a Functional Opioid Kappa Antagonist in the Treatment of Opioid Dependence. Journal of Substance Abuse Treatment, 18, pp. 277-281, 2000.

Jones, H.E., Johnson, R.E., Fudala, P.J., Henningfield, J.E., and Heishman, S.J. Nalmefene: Blockade of Intravenous Morphine Challenge Effects in Opioid Abusing Humans. Drug and Alcohol Dependence, 60, pp. 29-37, 2000.

Katz, J.L., Izenwasser, S., Kline, R.H., Allen, A.C., and Newman, A.H. Novel 3-diphenyl- methoxytropane Analogs: Selective Dopamine Uptake Inhibitors with Behavioral Effects Distinct from those of Cocaine. Journal of Pharmacology and Experimental Therapeutics, 288, pp. 302-315, 1999.

Tolliver, B.K., Newman, A.H., Katz, J.L., Ho, L.B., Fox, L.M., Hsu, K., Jr., and Berger, P.S. Behavioral and Neurochemical Effects of Dopamine Transporter Ligands Alone and in Combination with Cocaine: Characterization of 4-chlorobenztropine *in vivo*. Journal of Pharmacology and Experimental Therapeutics, 289, pp. 110-122, 1999.

Katz, J.L., Kopajtic, T.A., Myers, K., Mitkus, R., and Chider, M. The Behavioral Effects of Cocaine: Interactions with D1 Dopaminergic Antagonists and Partial Agonists in Mice and Squirrel Monkeys. Journal of Pharmacology and Experimental Therapeutics, 291, pp. 265-279, 1999.

Katz, J.L., Izenwasser, S., and Terry, P. Relationships Among Dopamine Transporter Affinities and Cocaine-like Discriminative Stimulus Effects. Psychopharmacology, 148, pp. 90-98, 2000.

Woolverton W.L., Rowlett, J.K., Wilcox, K.M., Paul, I.A., Kline, R.H., Newman, A.H., and Katz, J.L. 3' and 4'-Chloro-substituted Analogs of Benztropine: Intravenous Self-administration and *In vitroo* Radioligand Binding Studies in Rhesus Monkeys. Psychopharmacology, 147, pp. 426-435, 2000.

A new NIDA publication, "Approaches to Drug Abuse Counseling," has been released. This publication was edited by Drs. John Boren, Lisa Onken, and Kathleen Carroll: The volume describes a variety of counseling approaches used across the country. The approaches are described according to a common format so that each counseling approach can be easily compared to the others. The document gives the reader a greater understanding of the variety of drug abuse counseling approaches used today in both research and "real-world" settings.

The first quarterly news update for the CTN was approved in March. The quarterly report was distributed at the May Steering Committee Meeting in Hartford, CT.

The informational brochure entitled "What Is the CTN?" was approved and copies were distributed to all participants at the May Meeting in Hartford, CT.

An informational brochure entitled "What Is a Clinical Trial?" was written and approved. Copies of the brochure were distributed at the Portland, Oregon, Steering Committee Meeting on July 19-21, 2000.

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# Staff Highlights

## Honors and Awards

**Ms. Carol Sneeringer**, IRP, received the NIH Director's Award in June 2000: "In recognition of outstanding contributions in support of the mission of the Intramural Research Program of the National Institute on Drug Abuse".

**Dr. Jaylan S. Turkkan**, DNBR, received two NIH Director's Awards in June 2000. These were: from NIDA: "For superb leadership, resourcefulness and innovative approaches to the investigations of new ways to combat tobacco use and nicotine addiction;" and from NCI: Group award, The Transdisciplinary Tobacco Use Research Centers Implementation Group: "For creating and implementing the TTURC Program, a model for collaborative research and public/private partnerships".

**The Buprenorphine Development Team** received the HHS Secretary's Distinguished Award for their outstanding performance in development of Buprenorphine products as treatment agents for opiate dependence.

**Dr. Elizabeth Rahdert**, DTR&D, received the Division of Family Psychology Distinguished Service to Family Psychology Award, August 4, 2000, at the 108th Annual Convention of the American Psychological Association held in Washington DC.

**Dr. Jack Blaine and Dr. Lisa Onken**, DTR&D each received a Distinguished Friend to Behavioral Therapy Award from the American Academy of Behavioral Therapy (AABT) as special recognition for their work in spearheading and fostering the growth of efficacious behavioral treatments for drug abuse, as well as concomitant disorders. The AABT will present the awards to Drs. Blaine and Onken at their annual meeting on November 17, 2000 in New Orleans, LA.

**CDR Peter J. Delany**, D.S.W., received the year 2000 Public Health Service Social Worker of the Year Award on June 10, 2000. He was recognized by RADM Kenneth Moritsugu, Deputy Surgeon General for his "Outstanding leadership in promotion of critical public health research and commitment to public health social work services." Dr. Delany is currently the Acting Deputy Director of the Division of Epidemiology, Services and Prevention Research.

**William J. Bukoski**, Ph.D., DESPR, received a special recognition award from The Metropolitan Washington Council of Governments for ten years of outstanding service in drug abuse prevention science that directly benefited prevention practitioners in the Washington, D.C. metropolitan area.

**Dr. Jerry Flanzer**, DESPR, was appointed for a two year term as the Chair of the National Steering Committee of the Alcohol, Tobacco and Drug Section of the National Association for Social Workers. Dr. Flanzer also earned the status of Life Fellow of the American Orthopsychiatric Association (2000).

**Dr. Peter Hartsock**, CAMCODA, was awarded a special commendation from the Russian Association Against HIV/AIDS at the 8th International Conference on AIDS, Cancer, and Related Problems, St. Petersburg, Russia, May 2000. The commendation was presented to Dr. Hartsock "to acknowledge his invaluable contribution towards building cooperative relations between the Russian Federation and the United States of America in HIV prevention among Injecting Drug Users" and reflects 20 years of cooperation-building efforts.

**Dr. Jonathan L. Katz**, IRP, was invited to serve as a member of the Executive Committee of the Division for Behavioral Pharmacology and as a Program Committee Member, American Society for Pharmacology and Experimental Therapeutics.

**Dr. Jonathan L. Katz**, IRP, was invited to serve as chair of the Liaison Committee for Drug Testing and Evaluation, of the College on Problems of Drug Dependence.

**Dr. Jonathan L. Katz**, IRP, was elected to a two-year term as President of the Behavioral Pharmacology Society.

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## Staff Changes

**Dr. Lucinda Miner** has been selected for the position of Chief, Science Policy Branch, OSPC. She received her Ph.D. from the University of Colorado in 1986. She started at NIDA in 1992 to work in the Intramural Research Program in Baltimore. While at the IRP, NIDA, she helped to establish the Molecular Genetics Section and worked closely with Dr. George Uhl to develop their transgenic mouse facilities. She joined the Science Policy Branch in 1996 to serve as the Deputy Research Training Coordinator. In that capacity, she has helped to increase the visibility of NIDA's research training programs and has assisted numerous young investigators in their efforts to launch their research careers. In 1999, she was promoted to Deputy Chief of the Science Policy Branch and has been serving as the Acting Director for the last several months.

**Garveyette Brown** joined the Public Information Branch of OSPC as a Program Assistant in June 2000. Formerly, Ms. Brown taught second and third graders in the D.C. Public Schools as well as Baltimore City Public Schools. Prior to her teaching career, Ms. Brown was a Communications Industry Analyst at the Federal Communications Commission, where she was instrumental in processing and granting many station licenses for AM/TV stations as well as mobile phones. Ms. Brown has also been a secretary for a congressman and a senator. She has a B.S. degree in Elementary Education from Bowie State University.

**Dr. Naresh Chand** joined the Medications Discovery & Toxicology Branch of DTR&D as a Health Scientist Administrator on August 28, 2000. Prior to joining NIDA, Dr. Chand spent 20 years in the pharmaceutical industry. He served as Director of the Department of Pharmacology at Wallace Laboratories and as Associate Director of Drug Safety Evaluation at Otsuka America Pharmaceuticals. Dr. Chand will oversee a portion of the Division's growing workload in the area of preclinical safety assessment and will assume full responsibility for shaping and directing a preclinical program focused on cardiovascular drug interaction studies.

**Dr. Mary Ann Chutuape** came to the CTN office of DTR&D as a Special Expert in June 2000. Prior to joining NIDA, Dr. Chutuape was Project Director for a NIDA-funded substance abuse treatment research clinic at Johns Hopkins University School of Medicine, where she was appointed as an Assistant Professor in the Department of Psychiatry. Her research focused on behavioral and pharmacotherapy clinical trials for opioid dependence. Dr. Chutuape received her Ph.D. in Behavioral Sciences from the University of Chicago.

**Katia Delrahim** joined the CTN Office of DTR&D in July 2000 as a summer intern. She is a fourth year Biological Anthropology student at the University of California, San Diego. She is planning a career in the medical profession, and will be with the CTN until the end of August.

**Donna Inman** joined NIDA's Division of Treatment Research and Development as a Clinical Trials Specialist on August 27, 2000. Before coming to NIDA, Ms. Inman was a Project Specialist with the FDA's Center for Drug Evaluation and Research (CDER).

**Anne Jarrett** joined NIDA in July 2000 as the Secretary to the Associate Director. Previously, she was the Executive Assistant to the President of American Councils for International Education, a non-profit educational organization that deals with student and teacher exchanges between the U.S. and the former Soviet Union. Prior to this she was an assistant to the Public Affairs Manager at Resources for the Future, an environmental think tank with a focus on economics. She developed and maintained a database of congressional staff, in addition to writing occasional press releases.

**Catherine Law** joined NIDA in July 2000 as a science writer and editor in OSPC's Science Policy Branch. She has a Bachelor of Science degree in Chemistry from Kent State University (1993) and a Master of Technical and Scientific Communication degree from Miami University (1998). She began working at NIH in 1996 as a Graduate Health Communications Intern in the National Cancer Institute's Mass Media Branch. In 1997, she moved to NCI's Office of Science Planning and Assessment (OSPA) as a Technology Transfer Fellow and was hired as a permanent staff member in 1999. She was a member of OSPA's Science Policy and Planning Team, which prepares NCI's annual Bypass Budget and handles a variety of other science policy and planning projects.

**Dr. E. Douglas Kramer** recently joined the Clinical Trials Network (CTN) office of DTR&D. He came from FDA's Center for Drug Evaluation and Research where he was extensively involved in the review of pharmacotherapies for addictive disorders. Dr. Kramer received his medical degree and residency training in pathology at Columbia University in New York.

**Dr. Cecelia Lee McNamara** recently joined the Clinical Trials Network Office of DTR&D as a Health Scientist Administrator. Cecelia received her doctorate in clinical psychology from the University of New Mexico where she received training in behavioral treatments for substance abuse. As a post-doctoral fellow at the University of Alabama at Birmingham with Jesse Milby, Ph.D. and Joe Schumacher, Ph.D, she managed a NIDA sponsored R01 evaluating a contingency management intervention with homeless, dually-diagnosed cocaine users. Most recently she worked as an Assistant Professor at the UAB School of Medicine.

**Dr. Paul Schnur** recently joined the Behavioral Sciences Research Branch, DNBR as a Health Scientist Administrator. Dr. Schnur is an experimental psychologist with interests in the neuropsychopharmacology of drug abuse. He has done both animal and human research and has published in the areas of classical conditioning, selective attention, memory, and behavioral pharmacology. Dr. Schnur brings his interests in cognitive psychology to NIDA and expects to assume some responsibility for new initiatives that integrate cognitive and behavioral science approaches to understanding drug abuse. Dr. Schnur earned his Ph.D. at Indiana University and completed NIDA supported post-doctoral training at Brown University's Center for Alcohol and Addiction Studies. He spent fourteen years at the University of Southern Colorado where he investigated biphasic effects of opiates on locomotor activity, conditioned tolerance/withdrawal and conditioned dopamine release in the n. accumbens. Prior to joining NIDA, Dr. Schnur served as Chairperson of the Department of Psychology at Indiana University South Bend.

**Bryan Necciai**, CAMCODA, formerly a temporary Office Automation clerk, converted to Secretary (OA) on June 18, 2000.

**Moira O'Brien**, DESPR, transferred from the Epidemiology Research Branch, DESPR, to the Community Research Branch, DESPR.

**Mr. Arthur Hughes**, Chief of the Epidemiology Research Branch, DESPR, left NIDA in June to join the Office of Applied Studies, SAMHSA, where he will work on the National Household Survey on Drug Abuse. Dr. James Colliver is serving as Acting Chief of ERB.

**Gwen Jones** left OSPC in August 2000 to accept a position as a program support assistant with the Food and Drug Administration (FDA); she will be working in the Office of the Commissioner, Office of International and Constituent Relations, Office of Women's Health.

**Dr. Corina S. Pic** left NIDA at the end of May 2000 after serving as an Intramural Research Training Associate (IRTA) Fellow in the Teen Tobacco Addiction Treatment Research Clinic. Dr. Pic went to the University of Maryland to begin her residency program in child psychiatry.

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**National Institute on Drug Abuse**

**Director's Report to the National Advisory Council on Drug Abuse**

**September, 2000**

# Grantee Honors

**Dr. Robert L. Balster** received the first College on Problems of Drug Dependence (CPDD) "Mentorship Award" at the annual convention in San Juan, Puerto Rico in June 2000. Dr. Balster was honored for making substantial contributions to the field of drug abuse research, not only for his active role in preclinical investigation but also for training 13 doctoral and 15 postdoctoral trainees over the past three decades in the Department of Pharmacology and Toxicology at the Medical College of Virginia in Richmond where he served as the department's Director of Graduate Training.

**Dr. Heidi Resnick** was promoted to Full Professor at the Medical University of South Carolina and was also appointed to serve as a reviewer on the internal University Research Council review board.

**Dr. Tony Biglan** has been selected as a Fellow at the Center for Advanced Study in the Behavioral Sciences, Stanford, California, from September 2000 to March 2001. He will be working with other scholars on the prevention of youth problem behaviors.

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