
National Institute on Drug Abuse
Director's Report
to the
National Advisory Council on Drug Abuse
September, 1999

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****September, 1999**

Research Findings

Basic Research

Gene Therapy Provides Potential New Treatment for Chronic Pain

Dr. David Yeomans of the University of Illinois and his colleagues describe a potential new chronic pain control method that uses a novel genetic therapeutic approach. These researchers applied to the skin of mice a recombinant herpes simplex virus that contained specially programmed complementary DNA (cDNA) that held the gene that produces the precursor to the opiates that stop pain. This virus then traveled up the nerve to a part of the brain that is involved in sensing pain (i.e. the spinal dorsal horn). Models of chronic pain failed to elicit a pain response in the virus-treated mice. In addition, after the virus treatment these mice appeared normal in their response to acute pain. These findings demonstrate that it is possible to specifically block chronic pain in mice using gene therapy with few side effects. This research raises hopes that gene therapy may be useful in the treatment of chronic pain in humans. Wilson, S.P., Yeomans, D.C., Bender, M.A., Lu, Y., Goins, W.F., and Glorioso, J.C. *Proceedings of the National Academy of Science*, 96(6), pp. 3211-3216, 1999.

G-Protein-Coupled Receptor Heterodimerization Modulates Receptor Function

The opioid system modulates physiological processes such as analgesia, stress, the immune response, and neuroendocrine function. Pharmacological and molecular cloning studies have identified three opioid-receptor types, delta, kappa and mu, that mediate these diverse effects. Structural and biochemical studies with a variety of G-protein coupled receptors (GPCRs) indicate that a number of them exist as homodimers (i.e. pairs of the same protein). Relatively few studies have examined heterodimerization (i.e. pairs of different proteins) between these receptors. NIDA grantees Bryen Jordan and Lakshmi Devi have recently published a paper in *Nature* in which they found biochemical and pharmacological evidence for two fully functional opioid receptors, kappa and delta, to heterodimerize and generate a new receptor. The agonist binding properties of the heterodimer are distinct from the properties of either of the receptors. The heterodimer synergistically binds highly selective agonists leading to potentiation of signal transduction. Heterodimerization of GPCRs represents a novel mechanism that could modulate receptor function. These findings on heterodimerization between two fully functional GPCRs improve our understanding of the complex regulation of GPCR function. Heterodimerization also points to additional targets for the development of drug therapies. Jordan, B.A. and Devi, L.A. *Nature*, 399, pp. 697-700, 1999.

Anandamide Transport

The mechanism of action of the endogenous cannabinoid ligand anandamide continues to be actively studied. Drs. Daniele Piomelli and Alexandros Makriyannis reported their evidence for the existence of an anandamide transporter

capable of carrying labeled anandamide into human astrocytoma cells where it is then rapidly hydrolyzed. The transport process is analogous to the process for prostaglandin E2 and unsaturated fatty acids. In the case of anandamide, the process is rapid, temperature dependent, sodium ion independent, and exhibits "saturation" kinetics with a reported K_m and V_{max} . A sampling of prostaglandins, tetra- and trienoic acids, biogenic amines, and amino acids, capable of inhibiting membrane transporters, did not affect the cellular accumulation of tritiated anandamide. Inhibition of transport was demonstrated by N-(4-hydroxyphenyl)-arachidonamide, known as AM 404, and to a lesser extent by its 3-hydroxyphenyl congener. The results of examining a large number of substrates related to anandamide suggest that one or more cis double bonds in the anandamide "tail" are necessary for recognition, as well as a secondary amide function with a "head" group substituted by a polar hydroxalkyl or hydroxyaryl group. The investigators have also shown that tritiated anandamide, AM 404, and the endogenous compound arachidonylglycerol have comparable transport rates as measured by the decrease in radioactivity from the cellular medium over time. Several analogs lacking one, two, three, or all four of the cis double bonds in anandamide are transported relatively slowly or not at all. It has been suggested that one set of structural features may be needed for recognition by the transporter and another set for the actual transport. The development of transport inhibitors for anandamide has the potential utility of prolonging its antinociceptive effects by inhibiting its rapid inactivation due to transport and hydrolysis. Piomelli, D., Beltramo, M., Glasnapp, S., Lin, S.Y., Goutopoulos, A., Xie, X.-Q., Makriyannis, A. *Proceedings of the National Academy of Sciences*, 96, pp. 5802-5805, 1999.

Rewarding Effects of Drugs of Abuse and Neurotrophic Factors

The rewarding effects of drugs of abuse such as cocaine and morphine are mediated by the activation of dopamine neurons that make synaptic connections with neurons in the nucleus accumbens. Previous work by Dr. Eric Nestler and his colleagues at Yale University showed that the administration of brain derived neurotrophic factor (BDNF), a neurotrophin that supports the survival of dopamine neurons, prevents many of the biochemical and morphological changes associated with chronically administered cocaine and morphine. Injection of BDNF directly into the brain region known as the ventral tegmental area (VTA) blocks the induction of the rate-limited enzyme, tyrosine hydroxylase, in the synthesis of the neurotransmitter dopamine (DA). In addition, BDNF blocked the increase in protein kinase A (PKA) in the nucleus accumbens (Nac) produced by chronic morphine or cocaine administrations. In addition, BDNF prevents morphine from reducing the size of cell bodies in the DA neurons. Dr. Nestler suggests that BDNF prevents cocaine and morphine induced biochemical and morphological changes in the DA system through a converging biochemical pathway. If BDNF regulates the cellular signaling pathways activated by cocaine, then BDNF should alter behavioral responses to cocaine. To test this hypothesis, Dr. Nestler examined the effect of BDNF on locomotor activity and conditioned reward to cocaine. Conditioned rewards are cues that have become rewarding and provide incentive to seek a drug by virtue of being paired with the drug. The pairing of these discrete cues with cocaine could be an important mechanism involved in drug craving and relapse in addicts.

Injections of BDNF into the VTA or Nac enhanced both locomotor activity and the development of locomotor sensitization to cocaine. Mice expressing half as much endogenous BDNF showed delayed development of locomotor sensitization. Furthermore, intra-Nac injections of BDNF enhanced the ability of a stimulus to act as a conditioned reward to cocaine for up to a month following BDNF infusion. Dr. Nestler suggests that BDNF enhances the behavioral responses to cocaine by increasing dopamine transmission in response to cocaine. The delay in locomotor sensitization to cocaine in the BDNF heterozygous mutant mice also suggests that signaling pathways regulated by BDNF are required for long-term adaptation to cocaine. Horger, B.A., Iyasere, C.A., Berhow, M.T., Messer, C.J., Nestler, E.J., Taylor, J.R. *Journal of Neuroscience*, 19(10), pp. 4110-4122, 1999.

Orphanin FQ and Hypothalamic-Pituitary Axis

Orphanin FQ (OFQ) is a novel heptadecapeptide whose structure resembles that of dynorphin A1-17. Its receptor shares appreciable homology with m-, d-, and k- opioid receptors, and is highly expressed in the hypothalamus. A recent article by Dr. Martin Kelly and his group demonstrates that OFQ activates a receptor that is not opioid in nature but is coupled to an inwardly-rectifying K^+ channel, leading to an inhibition of b-endorphin neurons, and dopamine neurosecretory cells within the arcuate nucleus of the mediobasal hypothalamus. Collectively, these findings suggest that OFQ is not only an antiopioid peptide, but that it also modulates the hypothalamic-pituitary axis. Wagner, E.J., Ronnekleiv, O.K., Grandy, D.K., and Kelly, M.J. *Neuroendocrinology*, 67, pp. 73-82, 1998.

Identification and Characterization of Three New Alternatively Spliced m-Opioid Receptor Isoforms

Using genomic cloning in mice, Drs. Gavril Pasternak and Ying-Xian Pan and their research team at the Memorial Sloan-Kettering Cancer Center have identified four new m-opioid receptor (MOR)-1 exons, indicating that the gene now contains at least nine exons spanning more than 200 kilobases. Replacement of exon 4 by combinations of the new exons yields three new receptors. When expressed in Chinese hamster ovary (CHO) cells, all three variants displayed high affinity for m-opioid ligands, but k and d drugs were inactive. However, there were subtle, but significant, differences in the binding profiles of the three opioid receptor variants among themselves and from MOR-1. Immunohistochemically, the major variant, MOR-1C, displayed a regional distribution quite distinct from that of MOR-1. Region-specific processing also was seen at the mRNA level. Antisense probes designed to block each of the four new exons revealed that they were all involved in morphine analgesia. Together with two other variants generated from alternative splicing of exon 4, there are now six distinct MOR-1 receptors. The continued discovery of new opioid receptor isoforms with subtle but distinct differences in binding profiles, regional distribution, and region-specific processing and of their involvement in morphine analgesia suggests that these opioid receptor subtypes are pharmacologically relevant receptors. These findings are significant in that they provide new targets for designing analgesics that may be more effective with fewer undesirable side effects. Pan, Y-X, Xu, J., Bolan, E., Abbadie, C., Chang, A., Zuckerman, A., Rossi, G., and Pasternak, G.W. *Molecular Pharmacology*, 56, pp. 1-8, 1999.

Endomorphin-2 is an Endogenous Opioid in Primary Sensory Afferent Fibers

Drs. Sheryl B. Martin-Schild and James E. Zadina and their research group at Tulane University and Veterans Affairs Medical Center presented evidence that the recently discovered endogenous mu-opioid selective agonist, endomorphin-2, is localized in primary sensory afferents. Endomorphin-2-like immunoreactivity was found to be colocalized in a subset of substance P (a primary peptide neurotransmitter involved in the transmission of painful stimuli)- and mu opiate receptor-containing fibers in the superficial laminae of the spinal cord and spinal trigeminal nucleus. Disruption of primary sensory afferents by mechanical or chemical methods virtually abolished endomorphin-2-like immunoreactivity in the dorsal horn. These results indicate that endomorphin-2 is present in primary afferent fibers where it can serve as the endogenous ligand for pre- and post-synaptic mu receptors and as a major modulator of pain perception. Martin-Schild, S.B., Gerall, A.A., Kastin, A. J., and Zadina, J.E. *Peptides*, 19(10), pp. 1783-1789, 1998.

Endogenously Formed Cannabinoids Control Synaptic Potentiation in Rat Hippocampus

Dr. Paul Schweitzer is studying the involvement of the endogenous cannabinoid anandamide system in brain neural synaptic activity and plasticity in the rat. It is known that administered cannabinoids impair learning and memory and that in the laboratory, superfusion of cannabinoid agonists in the hippocampus prevents long-term potentiation (LTP) of neuronal activity, a putative mechanism for learning and memory. Dr. Schweitzer hypothesized that if endogenously formed cannabinoids prevent or attenuate the potentiation process, a cannabinoid receptor antagonist would increase LTP. However, he did not observe increased LTP in the presence of a cannabinoid antagonist. He reasoned that the widely used LTP paradigm, which he also was using, was too extreme, such that the LTP could not be further increased under these conditions (a "ceiling" effect). To test this idea, Dr. Schweitzer used two moderate stimulation paradigms believed to be more relevant to physiological conditions. He found that LTP was enhanced in the presence of the cannabinoid antagonist in both of the moderate stimulation paradigms, indicating that endogenously formed cannabinoids control the enhancement of synaptic activity in the hippocampus. These results suggest that the endogenous cannabinoid system may serve as a "brake" to limit the level of potentiation and modulate synaptic neuronal activity in normal brain functioning. Schweitzer, P. *International Cannabis Research Society Abstracts*, p. 38, 1998.

Blockade of NMDA Receptors by Drugs of Abuse Causes Neurons to Die in the Infant Rat Brain

Several abused, addicting drugs [ethanol, phencyclidine (PCP, "angel dust"), ketamine (special K), and nitrous oxide] characteristically block the NMDA (N-methyl-D-aspartate) receptor in the brain. Since the proper development of this receptor and its activation by glutamate are essential for the formation of these synapses in the developing brain, the effects of these drugs on the fetal brain is an important area of study. Dr. John W. Olney, and his group examined the effect in rats of NMDA receptor blockade on the developing brain using dizocilpine, a specific NMDA receptor blocker. Blockade of NMDA glutamate receptors for four hours or more during early neonatal development triggered widespread neuronal death in the developing rat brain. Especially affected were layer II of parietal, frontal, and cingulate cortices, and laterodorsal thalamus. The mechanism of cell death was shown to be apoptosis, also known as

the process of programmed cell death. Apoptosis is a process that occurs naturally during normal development of the brain; the brief exposure to dizocilpine magnified this process up to 40-fold. PCP and ketamine each triggered the same apoptotic response as dizocilpine. These findings may have relevance to human neurodevelopmental disorders caused by prenatal or postnatal exposure to drugs that block NMDA receptors. If peak vulnerability of the human forebrain to the pro-apoptotic action of NMDA antagonists corresponds to the developmental events in the rat, the window of vulnerability for humans would include the entire third trimester of pregnancy. Understanding the mechanisms underlying brain damage in the offspring of drug-abusing mothers may lead to strategies for preventing and treating this disorder. Ikonomidou, C., Bosch, F., Miksa, M., Bittigau, P., Vřckler, J., Dikranian, K., Tenkova, T.I., Stefovská, V., Turski, L., and Olney, J.W. *Science*, 283, pp. 70-74, 1999.

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Research Findings

Behavioral Research

Laboratory Measurement of Adaptive Behavior Change in Humans with a History of Substance Dependence

Dr. Scott Lane and colleagues at the University of Texas Health Science Center examined components of behavioral adaptation to changes in environmental conditions in human subjects with and without a history of substance dependence. Over a two-day period, volunteers were rewarded for changing their patterns of response. On the first day, they earned monetary rewards for producing high response rates. However, on the second day they were required to wait ten seconds between each response, producing low response rates. Volunteers meeting DSM-IV criteria for past substance dependence and having histories of substance dependence longer than ten years adjusted poorly to the required transition in responding, exhibiting high rates of responding on both days. Because of their inability to change to a slower response rate, subjects with long substance abuse histories earned few if any monetary rewards on the second day. These results were unrelated to age, attention, impulsiveness, or general intellectual aptitude and suggest a deficiency in adaptive behavior change. Whether this deficiency predated or was a consequence of drug abuse is unclear. Lane, S.D., Cherek, D.R., Dougherty, D.M., and Moeller, F.G. *Drug and Alcohol Dependence*, 51, pp. 239-252, 1998.

Luteinizing Hormone-Releasing Hormone Affects Plasma Cocaine Levels in Rhesus Monkeys

Considerable evidence points to the role of the brain neurotransmitter dopamine in the reinforcing effects of cocaine. Cocaine binds to the dopamine transporter, thus blocking the reuptake of dopamine and resulting in increased levels of dopamine at the synapse between neurons in the brain. Harvard researchers Drs. Jack Mendelson, Nancy Mello, and Stevens Negus noted structural similarities between the dopamine transporter and luteinizing hormone (LH), a gonadotropin hormone released by the anterior pituitary. They hypothesized that LH bound to cocaine and thereby decreased cocaine levels. They report that when they administered synthetic LH-releasing hormone (LHRH) to male and female rhesus monkeys prior to the administration of cocaine, LH secretion significantly increased and peak plasma levels of cocaine significantly decreased in both males and females. In males, but not females, there was an inverse relationship between levels of LHRH-stimulated LH immediately prior to cocaine injection and peak plasma cocaine levels two minutes following cocaine injection. There were also gender differences in the levels of LH required, 70ng/ml in males versus 45 ng/ml in females, to decrease plasma cocaine levels. This research raises the possibility of developing LH or an LH-like molecule as medications that will bind to cocaine for use in the treatment of cocaine addiction. Mendelson, J.H., Mello, N.K., and Negus, S. *Journal of Pharmacology and Experimental Therapeutics*, 289, pp. 791-799, 1999.

Cocaine Pharmacokinetics in Male and Female Rhesus Monkeys and in Humans

Several studies, both animal and human, have shown greater cocaine toxicity in males than in females. There has been little research focus however, on the study of sex differences in pharmacokinetics and the relation it may have to cocaine's greater toxicity in males. In the course of their research on the effects of luteinizing hormone-releasing hormone on plasma cocaine levels in rhesus monkeys (see above), Dr. Jack Mendelson and colleagues compared the pharmacokinetics of plasma cocaine in males and females following the intravenous administration of 0.8 mg/kg cocaine. Females were tested during the follicular phase of the menstrual cycle, six to eight days after the onset of menstruation. Pharmacokinetic analyses indicated that although females had significantly lower plasma cocaine levels than males ten minutes after injection, males and females did not differ in peak levels of cocaine, time to reach peak levels of cocaine in plasma, the elimination half life, or the area under the curve. These findings in rhesus monkeys are consistent with results obtained by Dr. Mendelson and Dr. Nancy Mello and their colleagues following intravenous cocaine administration (0.2 and 0.4 mg/kg) in humans. No sex differences in peak plasma cocaine levels, elimination half-life, or area of the curve were observed, nor were sex differences observed in cardiovascular effects on heart rate and blood pressure or in the subjective report of feeling "high." In females, both the pharmacokinetic and pharmacodynamic measures were similar in the follicular and mid-luteal phases of the cycle. The single significant difference observed in the pharmacokinetic parameters was that the time to reach peak plasma levels was significantly lower in the follicular phase women (four minutes) than in the luteal phase women (6.7 minutes) or in males (eight minutes). The authors conclude that pharmacokinetic factors alone do not account for sex differences observed in cocaine toxicity and they recommend exploring neuroendocrine and other factors. Mendelson, J.H., Mello, N.K., and Negus, S. *Journal of Pharmacology and Experimental Therapeutics*, 289, pp. 791-799, 1999. Mendelson, J.H., Mello, N.K., Sholar, M.B., Siegel, A.J., Kaufman, M.J., Levin, J.M., Renshaw, P.F., and Cohen, B.M. *Neuropsychopharmacology*, 21, pp. 294-303, 1999.

Female Rats Acquire Self-Administration of Cocaine and Heroin Faster than Male Rats

Animal studies of the locomotor response to psychostimulants have shown greater responsivity in female as compared to male rats. Studies of the self-administration of drugs including cocaine, caffeine, alcohol, morphine, and fentanyl have shown higher levels of intake in females than males. Less research attention, however, has been paid to sex differences in the acquisition of drug self-administration. Drs. Wendy Lynch and Marilyn Carroll at the University of Minnesota report significantly faster acquisition of intravenous cocaine and heroin self-administration for female as compared to male rats. Females acquired cocaine self-administration in a mean of 7.57 sessions as compared to 16.67 sessions for males. Females acquired heroin self-administration in a mean of 8.7 sessions as compared to 13 sessions for males. For cocaine, but not heroin, significantly more females than males met the acquisition criterion within the 30-day maximum. Seventy percent of the females, but only 30 percent of the males met the acquisition criterion for cocaine self-administration. For heroin self-administration, 90 percent of the females and 91.7 percent of the males met the criterion. Following the acquisition of drug self-administration, the level of self-administered cocaine and heroin was higher in females than in males, but was significant only for cocaine. Lynch, W.J. and Carroll, M.E. *Psychopharmacology*, 144, pp. 77-82, 1999.

New Techniques for Measuring Inhalant Effects in Animals

Dr. Robert Balster at the Medical College of Virginia has been investigating the effects of inhaled solvents for the past twenty years using animal models that incorporate multiple behavioral assessments. These are compounds that are found in typical household products and have been demonstrated to have abuse potential in humans. Typically, pharmacological investigations with behavioral endpoints are useful for establishing dose-response relationships, and for determining thresholds and dosing midpoints for behavioral effects. However, dose-orderly effects on complex responses in operant behavioral paradigms have been difficult to establish for compounds administered via the inhalation route. Recently, Dr. Balster has developed a novel "adjusting" procedure for delivering compounds in the inhalation chamber to mice. Animals are trained to press a lever for milk as solvent concentrations in the chamber are altered every five minutes, dependent upon the rate of lever press responding for milk. Using this procedure, Dr. Balster was able to show concentration-dependent decreases in lever pressing and established a subthreshold and minimal concentrations that affect this behavior. This new approach for adjusting exposures to solvents will be useful in the rapid assessment of compounds that are potentially behaviorally disruptive and allow for determining "near threshold" levels of exposure in an animal model. Bowen, S.E., Hamilton, J., and Balster, R.E. *Neurotoxicology and Teratology*, 2, pp. 169-180, 1998.

Cannabinoid History Determines Cannabinoid Response

Previous studies have revealed that drug history affects the subsequent responsivity to psychotropic drugs. Dr. Harriet de Wit at the University of Chicago found this to be the case for the subjective effects of oral tetrahydrocannabinol (THC) in humans. Dr. de Wit assessed self-reported measures from several scales following oral THC administration in subjects who differed in the extent of their prior marijuana exposure. She found that the groups differed in their self-reports of "feel" drug effects, "high", and "like", but that these differences depended on the dose of oral THC administered. At the 7.5-mg dose level, infrequent users showed no increases on any of these measures, whereas habitual users showed increased scores on all three scales. At a higher dose of 15 mg, only the infrequent users reported sedation and decreases in the "like" scale. Interestingly, no differences in either heart rate or performance cannabinoid effects were noted between subject populations. These varying profiles of subjective effects for users differing in their prior marijuana exposure suggests that conditioning and expectancies may play a role in the ability to detect THC effects seen in frequent marijuana users. Furthermore, frequent users may develop tolerance to unpleasant subjective drug effects independent of the drug's cardiovascular effects. Kirk, J.M., and de Wit, H. *Pharmacology, Biochemistry and Behavior*, 63, pp. 137-142, 1999.

Relapse to Drug Use: It's Not Enough to Discriminate the Drug's Effects

Experimenter-induced stress has been observed to enhance the acquisition of drug self-administration and to prompt a return to drug-seeking behavior in animal models of relapse. Dr. Nick Goeders at the Louisiana State University Medical Center in Shreveport, Louisiana recently reported that footshock-induced reinstatement of responding for cocaine during extinction could be blocked by ketoconazole, an antimycotic drug that inhibits adrenocorticosteroid synthesis and antagonizes glucocorticoid receptors. This and many other previous observations implicate the activation of central corticosterone systems in relapse. It has further been suggested that the "internal state" produced by a stressor may mimic components of the subjective drug experience. In support of this hypothesis, Dr. Goeders also found that footshock generalized to the cocaine cue in drug discrimination procedures with the rat. However, unlike the effects of ketoconazole on footshock-induced reinstatement, the glucocorticoid antagonist was without effect on the ability of footshock to engender cocaine appropriate responding in the drug discrimination task. From these findings, Dr. Goeders concluded that, in these animal models, reproduction of cocaine's discriminative properties alone, may be insufficient for prompting a return to drug-seeking behavior. Mantsch, J.R., and Goeders, N.E. *Psychopharmacology*, 142, pp. 399-407, 1999.

Antagonism by MK-801 and Conditioned Place Preference

This study examined if conditioned place preference preparation is useful in studying the appetitive quality of novelty, whether IV cocaine would condition an increase in preference, and the role of the N-methyl-D-aspartate (NMDA) receptor in this paradigm. In 3 separate experiments with 95 male rats, repeated access to novel objects in one of 2 distinct environments conditioned an increase in preference for the novelty-paired environment. A conditioned increase in preference was found whether novel objects were paired with a randomly chosen environment or with the less preferred of 2 environments (conditioned against a preference). This enhanced preference did not depend on the control group employed. IV infusions of cocaine produced an increase in preference using the procedures employed with novel objects. Pretreatment with the NMDA receptor antagonist MK-801 blocked acquisition of the enhanced place preference conditioned by access to novel objects without decreasing time spent with objects or inducing a place aversion in controls. Bevins, R.A. and Bardo, M.T. *Conditioned Increase in Place Preference by Access to Novel Objects*. *Behavioral Brain Research*, 99, pp. 53-60, 1999.

Dopamine Receptors and Individual Differences in Amphetamine Self-Administration

This study examined the effect DA antagonists have on single-trial conditioned place preference (CPP) produced by acute intravenous amphetamine in rats. In the first of three studies, amphetamine (0.1-3.0 mg/kg) was given in one specific compartment of a CPP chamber. Relative to sham controls amphetamine produced a dose-related increase in both activity and CPP. The second study showed that pretreatment with either SCH-22309 (0.025 and 0.25 mg/kg) or eticlopride (0.2 and 2.0 mg/kg) completely blocked both activity and CPP. Finally, single-trial amphetamine CPP did not predict subsequent self-administration of IV amphetamine (10-50 ug/infusion) using either a schedule of continuous reinforcement (CRF) or partial reinforcement progressive ratio (PR), which demonstrates that single-trial CPP and self-administration are dissociable effects of IV amphetamine. Bardo, M.T., Valone, J.M. and Bevis, R.A. *Locomotion and Conditioned Place Preference Produced by Acute Intravenous Amphetamine: Role of Dopamine*

Receptors and Individual Differences in Amphetamine Self-Administration. *Psychopharmacology*, 143, pp. 39-46, 1999.

Predictor of Amphetamine Conditioned Place Preference

A study was conducted to assess whether the activity observed when rats are exposed to an inescapable novel environment may reflect escape behavior due to stress. A new test, the playground maze, designed to evaluate approach to novelty in a free choice situation was used to predict individual responses to amphetamine (1.0 or 3.0 mg/kg). The playground maze was used to categorize rats as either high or low novelty seekers. Results indicate that individual differences in novelty seeking did not predict amphetamine-induced changes in locomotion activity following either single or repeated injections. However, the high novelty seekers showed greater amphetamine-conditioned place preference than low novelty seekers. Klebaur, J.E. and Bardo M. T. Individual Differences in Novelty Seeking on the Playground Maze Predict Amphetamine Conditioned Place Preference. *Pharmacology, Biochemistry and Behavior*, pp. 1-6, 1999.

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Research Findings

Clinical and Services Research

Therapeutic Alliance and Psychiatric Severity as Predictors of Completion of Treatment For Opioid Dependence

Information about patient characteristics and scores on the subscales of the Addiction Severity Index (ASI) were obtained for 114 patients at intake to a buprenorphine treatment program lasting 3-4 months. The strength of the therapeutic alliance was assessed by the Helping Alliance Questionnaire (HAQ). Patients with fewer psychiatric symptoms were more likely to complete treatment. Among patients with moderate to severe psychiatric symptoms, the strength of the therapeutic alliance was a significant predictor of treatment completion. The findings underscore the importance of early identification of opioid-dependent patients with moderate to severe levels of psychopathology. In this patient subgroup, a strong therapeutic alliance may be an essential condition for successful treatment. Petry, N. and Bickel, W. *Psychiatric Services*, 50 (2), pp. 219-227, February 1999.

Technology Transfer of Network Therapy to Community-Based Addictions Counselors

In this study Network Therapy, a drug addiction treatment that utilizes peer and family support, was disseminated to a cohort of addiction counselors located in an outpatient community-based addiction treatment center. Training methods included a didactic seminar, role-playing, use of videotaped illustrations, and clinical case supervision. The trained counselors then implemented the Network Therapy with a sample of cocaine-abusing patients; the Network Therapy patients were compared by chart review to a cohort of cocaine abusers who received treatment as usual. The two groups were similar in demographics and in the amount of standard treatment that they received. However, the Network Therapy patients had significantly fewer positive urinalyses than the standard treatment patients, though they were not significantly different in terms of treatment retention, however. These preliminary findings demonstrated the feasibility of training addiction counselors and transporting the Network Behavioral Therapy approach to counselors in a community-based treatment program. Keller, D., and Galanter, M. *Journal of Substance Abuse Treatment*, 16(2), pp. 183-189, March 1999.

Relative Potency of LAAM and Methadone in Humans Under Acute Dosing Conditions

This study compared the effects of acute doses of LAAM and methadone and also examined the ability of naloxone to reverse their effects. Five occasional opioid users received once weekly doses of either placebo, LAAM, or methadone (15, 30, or 60 mg/70 kg orally) in agonist exposure sessions and then received naloxone (1 mg/70kg intramuscularly) 24, 72, and 144 hours after agonist exposure. Subject-rated, observer-rated, and physiological

measures were assessed regularly. Comparisons of physiological and subjective measures in agonist exposure sessions indicate that LAAM is not less potent than methadone under acute dosing conditions. For some measures LAAM was significantly more potent. Three subjects were withdrawn from the study due to greater than anticipated and clinically relevant respiratory depression after receiving 60 mg of LAAM. Acute agonist effects suggest that LAAM may be more potent than methadone and more potent than current labeling indicates. An accurate LAAM: methadone relative potency estimate will aid determination of adequate doses for opioid dependent patients inducted onto LAAM and for methadone maintenance patients who choose to switch to more convenient 3x weekly LAAM. Eissenberg, T., Stitzer, M., Bigelow, G., Buchhalter, A., and Walsh, S. J. of *Pharmacology and Experimental Therapeutics*, 289, pp. 936-945, 1999.

Factors Associated with Lapses to Heroin Use During Methadone Maintenance

This prospective, observational study investigated factors predicting a lapse to heroin use in 74 heroin-abstinent methadone maintenance patients. After baseline data collection, participants were assessed twice per week for 7 weeks and again at 6 months after baseline. Proportional hazards regression and logistic regression were used to investigate the effects of study predictors on heroin use. A goal of absolute heroin abstinence consistently predicted a lower risk of a lapse, whereas marijuana use was associated with a greater risk. Stress did not appear to be a predictor of a lapse in this study. The findings suggest that factors influencing lapses are similar across drug treatment populations and the role of stress in precipitating relapse remains unresolved. Wasserman, D., Weinstein, M., Havassy, B., and Hall, S. *Alcohol and Drug Dependence*, Vol. 1, pp. 1-10, January 1999.

Identifying Methadone Maintenance Clients at Risk for Poor Treatment Response: Pretreatment and Early Progress Indicators

This study evaluated whether early treatment response predicts treatment response 6 and 9 months later. New admissions to methadone maintenance treatment (n=59) were divided into outcome groups based on treatment retention and ongoing drug use as revealed by urinalysis results 6 and 9 months after admission. Regression analyses revealed that two early (week 2) performance measures, counseling attendance and opioid abstinence, could be used to correctly classify the outcomes of more than 80% of the sample. Of the 20 participants who neither submitted an opiate-negative sample during week 2 of treatment nor attended at least 2 scheduled counseling sessions by that time, not one achieved a superior 6-month outcome. The odds of having a superior treatment outcome increased considerably for those who submitted two opiate negative urine samples and attended two counseling sessions by the second week of treatment. These findings suggest that determining patient performance early in treatment may be used to guide subsequent treatment planning and may facilitate better patient-treatment matching. Morral, A., Belding, M., and Iguchi, M. *Drug and Alcohol Dependence* 55, pp. 25-33, 1999.

History of Alcohol or Drug Problems, Current Use of Alcohol or Marijuana, As Predictors of Success in Quitting Smoking

This study examined the relationship of alcohol/drug use history and current alcohol and marijuana use with success in smoking cessation treatment in a smoking clinic population. Of the 199 smokers who participated, 23% reported a history of alcohol or drug use problems; 12.6% reported a history of drug treatment; 78.7% reported alcohol use, and 21.3% reported marijuana use during treatment. The results indicate that a history of alcohol or drug problems does not predict smoking cessation success. However, current alcohol use, even at low levels, appears to increase the likelihood of treatment failure. In this study neither use of marijuana at baseline nor during treatment predicted outcome, which appears to be inconsistent with the limited research available indicating a negative effect of marijuana use on outcome. Differences in local cultural norms, frequency, and rate of marijuana use, and community attitudes regarding marijuana use may have influenced this finding. Humfleet, G., Munoz, R., Sees, K., Reus, V., and Hall, S. *Addictive Behaviors*, Vol. 24(1), pp. 149-154, 1999.

Contingent Reinforcement Sustains Post-Detoxification Abstinence for Multiple Drugs: A Preliminary Study with Methadone Patients

This study examined the efficacy of a urinalysis-based contingency management program for preventing relapse to abused drugs following a brief residential detoxification. Fourteen methadone maintenance patients who were chronic

benzodiazepine users were enrolled in a 7-day inpatient benzodiazepine detoxification and randomly assigned to receive Contingency Management (N=7) or Standard Care (N=7) therapy upon return to outpatient methadone treatment. In the Contingency Management condition, a methadone take-home dose or \$25 (patient's choice) could be earned for each urine submitted that was free of opiates, cocaine, and benzodiazepines. Preliminary findings from this study suggest that abstinence-based contingency management is a promising approach for preventing relapse to multiple drug abuse in a subgroup of methadone maintenance patients when abstinence has been initiated through brief detoxification treatment. Chutuape, M., Silverman, K., and Stitzer, M. *Drug and Alcohol Dependence*, 54, pp. 69-81, 1999.

Relationship of ADHD, Depression and Non-Tobacco Substance Use Disorders to Nicotine Dependence in Substance-Dependent Delinquents

In a study of 367 male and female behaviorally disordered juvenile delinquents, 13 - 19 years old, Dr. Riggs and colleagues, Department of Psychiatry, University of Colorado School of Medicine, found that attention deficit hyperactivity disorder (ADHD) and major depression significantly contributed to the severity of nicotine dependence in adolescents diagnosed with a non-tobacco substance use disorder (SUD). ADHD was associated with earlier onset of regular smoking in males, and the severity of non-tobacco SUD was related to nicotine dependence severity in both boys and girls. Riggs, P.D., Mikulich, S.K., Whitmore, E.A., and Crowley, T.J. *Drug and Alcohol Dependence*, 54, pp. 195-205, 1999.

Effects of Naltrexone on Alcohol and Cocaine Use in Dually Addicted Patients

Drs. Oslin, Pettinati, Volpicelli and colleagues from the Center for the Study of Addictions, Department of Psychiatry, University of Pennsylvania, reported the results of a small-scale study evaluating the efficacy of naltrexone in treating alcohol and cocaine dependent patients. Of 15 patients (mean age 36 years; 87% African American males) enrolled in the 12-week, open medication trial, 7 did not complete the study. Of the remaining 8, seven patients were rated as much or very much improved for alcohol and cocaine use, with two subjects achieving complete abstinence from both alcohol and cocaine for the 12-week period. Oslin, D.W., Pettinati, H.M., Volpicelli, J.R., Wolf, A.L., Kampman, K. and O'Brien, C. *Journal of Substance Abuse Treatment*, 16(2), pp.163-167, 1999.

An Efficient Tool for Screening for Maladaptive Family Functioning in Adolescent Drug Abusers: The Problem Oriented Screening Instrument for Teenagers (POSIT)

Dr. Santisteban and colleagues from the Center for Family Studies, University of Miami School of Medicine, reported results of a study that examined the validity of the NIDA-developed POSIT questionnaire's 11-item Family functioning (problem area) scale in terms of degree to which the scale provides useful information regarding family functioning when the POSIT is administered to youths with behavior problems. Study participants were 135 boys and girls referred for drug treatment. Family functional status was determined by use of the general scale of the Family Assessment Measure (FAM) and the family scale of the Adolescent Drug Abuse Diagnosis (ADAD). Results indicate POSIT Family area problem scores can classify families correctly in terms of their functioning. Santisteban, D.A., Tejeda, M., Dominicis, C. and Szapocznik, J. *American Journal of Drug and Alcohol Abuse*, 25(2), pp. 197-206, 1999.

Drug Abuse Counseling Shows Promise for Cocaine Dependence

The National Institute on Drug Abuse Collaborative Cocaine Treatment Study was a large multi-site investigation consisting of NIDA scientists, a Coordinating Center at the University of Pennsylvania, and four clinical sites at the following locations: University of Pennsylvania; Brookside Hospital in Nashua, NH; McLean Hospital and Massachusetts General Hospital; and University of Pittsburgh's Western Psychiatric Institute and Clinic. The purpose of this study was to evaluate four behavioral treatments for cocaine-dependent patients. All patients enrolled in the study received Group Drug Counseling (GDC). The three other treatment conditions consisted of a combination of Group Drug Counseling plus Individual Drug Counseling (IDC), Cognitive Therapy, or Supportive-Expressive Psychotherapy. A major finding from this study indicates that while all groups improved, patients that received the combination of Individual and Group Drug Counseling showed the greatest reduction in frequency of drug use. The combination of GDC and IDC shown to be successful in reducing drug use in this study, was an intensive, manual-guided therapy delivered by carefully selected, experienced counselors. In contrast, drug counseling performed in the

community may vary widely in intensity, quality and type of interventions. However, this approach shows promise for the treatment of cocaine dependence. Crits-Christoph, P., Siqueland, L., Blaine, J., Frank, A., Luborsky, L., Onken, L.S., Muenz, L.R., Thase, M.E., Weiss, R.D., Gastfriend, D.R., Woody, G.E., Barber, J.P., Butler, S.F., Daley, D., Salloum, I., Bishop, S., Najavits, L.M., Lis, J., Mercer, D., Griffin, M.L., Moras, K. and Beck A.T. Psychosocial Treatments for Cocaine Dependence. Archives of General Psychiatry, 56, pp. 493-502, 1999.

Cocaine Stimulates the Human Cardiovascular System via a Central Mechanism of Action

Cocaine is thought to stimulate the cardiovascular system by blocking the peripheral norepinephrine reuptake. Now Victor and his colleagues' research shows that cocaine also stimulates central sympathetic outflow. This central sympathetic activation appears to be targeted not only to the cutaneous circulation promoting peripheral vasoconstriction but also to the heart promoting tachycardia. The investigators measured blood pressure, heart rate, and skin sympathetic nerve activity in 14 healthy volunteers before, during and for 90 minutes after intranasal cocaine (2 mg/kg, n=7) or lidocaine (2 mg/kg, n=7). Cocaine caused >3-fold increase in skin sympathetic nerve activity and this was accompanied by decreased skin blood flow, increased skin vascular resistance, and increased heart rate. Intranasal lidocaine caused only a small transient increase in SNA due to local nasal irritation. In 11 additional subjects, cocaine-induced increase in heart rate was eliminated by beta-blockade (propranolol) but was unaffected by muscarinic receptor blockade (atropine), indicating sympathetic mediation of cocaine effects. Vongpatanasin, W., Mansour, Y., Chavoshan, B., Arbique, D., and Victor, R.G. Circulation, 100, pp. 497-502, 1999.

Inhibitory Control Involves the Right Side of the Brain

Dr. Elliot Stein and his colleagues at the Milwaukee College of Medicine used an advanced brain imaging technique, event-related functional magnetic resonance imaging (fMRI), to determine what parts of the brain are active when a normal person withholds a pre-potent response in a laboratory task. Past attempts to determine what areas of the brain are associated with behavioral inhibition have been hampered by the inability to separate brain activity associated with correct withholding responses from brain activity associated with incorrect responses. With event-related fMRI, brain activity can be imaged during a single behavioral response trial. It was expected that the ventral portions of the frontal lobe of the brain would be activated when a person successfully withheld a response to the second target letter. Contrary to this expectation, response inhibition was most strongly associated with activation of brain regions distributed across the right hemisphere, including areas in the dorsal prefrontal cortex, frontal limbic areas, and the parietal lobe. As relapse of drug-taking after a period of abstinence can be seen as a failure to inhibit drug-seeking and drug-taking, these results suggest the possibility that dysfunction in these brain areas contributes to the difficulty drug abusers have in refraining from drug use. Garavan et al., Proc Natl. Acad. Sci., 96, pp. 8301-8306, 1999.

Association of Methylphenidate-Induced Craving with Changes in Brain Metabolism in Cocaine Abusers

Dr. Nora Volkow and colleagues previously have shown that decreases in dopamine D2 receptors in cocaine abusers were associated with decreased metabolic activity in the prefrontal cortex, cingulate gyrus, and orbitofrontal cortex. Because it was also shown that the orbitofrontal cortex and the striatum had increased metabolic activity in active cocaine abusers reporting intense craving, it was postulated that during cocaine intoxication, the increase in dopamine facilitates activation of these brain regions, which in turn, leads to craving and subsequent impulsive and compulsive drug-taking, characteristic of the addicted individual. To test this hypothesis, the effects of two sequential doses of methylphenidate (a drug very similar to cocaine) on regional glucose metabolism in detoxified cocaine abusers was measured using positron emission tomography (PET). Results showed that methylphenidate induced variable changes in brain metabolism. Subjects with higher D2 measures tended to have increased metabolism, whereas subjects with lower D2 measures tended to have decreased metabolism. Methylphenidate's effects were significant for increases in metabolism in the superior cingulate, right thalamus, and cerebellum. Methylphenidate-induced changes in the right orbitofrontal cortex and right striatum were associated with craving, and those changes in the prefrontal cortex were associated with mood. Given these results, this study indicates that dopamine enhancement is not sufficient to increase metabolism in the frontal regions. Activation of the right orbitofrontal cortex and right striatum, which are regions found to be abnormal in compulsive disorders, in subjects reporting craving may be one of the mechanisms underlying compulsive drug administration in addicted persons. The finding of a predominant correlation of craving with the right brain regions and not left suggests laterality of reinforcing responses. Volkow, N.D. et al., Association of Methylphenidate-Induced Craving with Changes in Right Striato-

orbitofrontal Metabolism in Cocaine Abusers: Implications in Addiction. *Am. J. Psychiatry*, 156, pp. 19-26, 1999.

Brain Dopamine Receptor Levels Predict Reinforcing Responses to Drugs in Humans

The dopamine system is involved in the reinforcing properties of all drugs of abuse. It has been hypothesized that low levels of dopamine D2 receptors may predispose individuals to use drugs in order to compensate for the decrease in activation of 'reward' circuits stimulated by this receptor system. Using PET neuroimaging techniques, Dr. Nora Volkow and colleagues at the Brookhaven National Laboratory and SUNY-Stony Brook have correlated concentrations of brain dopamine D2 receptors to measures of subjective responses to the drug methylphenidate (a psychostimulant drug that acts like cocaine in that it blocks brain dopamine transporters, thereby amplifying dopamine's effect in the brain). Using [¹¹C]raclopride, a molecule that specifically attaches to D2 dopamine receptors to indicate concentrations of receptor sites, it was shown that those individuals with relatively lower levels of brain dopamine D2 receptors found the drug methylphenidate to elicit "pleasant" effects, whereas those individuals with relatively higher levels of brain D2 dopamine receptors found the drug methylphenidate to be "unpleasant." Most cocaine abusers report methylphenidate as pleasant, and individuals that reported methylphenidate as pleasant had D2 dopamine levels similar to those previously shown for cocaine abusers. These results are highly suggestive of a dopamine D2 involvement in the perception of reinforcing effects of psychostimulant drugs and are consistent with findings in animals that D2 dopamine receptors mediate the reinforcing responses to drugs. The findings in this study are the first evidence in humans revealing a direct association between D2 dopamine receptor levels in brain and the reinforcing effects of psychostimulants. These data have significant implications for individual differences in drug liking and may represent a critical component in the neurobiological basis for drug abuse and addiction vulnerability. Volkow, N.D. et al., *Brain Dopamine D2 Receptor Levels Predict Reinforcing Responses to Psychostimulants in Humans*. *American Journal of Psychiatry*, September 1999.

Treatment Outcome Prediction Based in Quantitative EEG Profiles

Dr. Leslie Prichep at the New York University School of Medicine and Nathan S. Kline Institute for Psychiatric Research and her colleagues have investigated the existence of outcome-related neurophysiological subtypes within a population of abstinent cocaine-dependent adults. This group has demonstrated a distinctive quantitative EEG (QEEG) profile in abstinent cocaine abusers showing abnormalities in specific wave activity that persists up to six months. In this study, a group of 35 adult, abstinent, male, cocaine abusers were evaluated, and two neurophysiological subtypes were identified: Cluster 1 characterized by significant deficits of delta and theta activity, significant excess of alpha activity and more normal amounts of beta activity, and Cluster 2 characterized by deficits of delta, more normal amounts of theta and anterior excess of alpha and beta activity. No significant relationship was found between QEEG subtype and length of exposure to cocaine, time since last use, demographic characteristics, or comorbid clinical features of depression and anxiety for either cluster. A significant relationship, however, was shown between QEEG subtype grouping and length of stay in treatment; Cluster 2 individuals remained in treatment significantly longer (approximately 62 weeks) than Cluster 1 individuals (approximately 18 weeks). These data point to a possible neurobiological marker or predictor of treatment outcome. Prichep, L.S. et al., *Prediction of Treatment Outcome in Cocaine Dependent Males Using Quantitative EEG*. *Drug and Alcohol Dependence*, 54, pp. 35-43, 1999.

Increases in Provoked Aggression during Marijuana Withdrawal

Dr. Harrison Pope, Jr. of McLean Hospital/Harvard Medical School and associates found that during withdrawal from long-term marijuana use there is an increase in aggressive responding in a laboratory task. Little is known about aggressive behavior associated with extended abstinence from marijuana as most studies in the literature have addressed the effects of acute marijuana administration on aggression. Long-term marijuana users (> 10 years) were tested immediately prior to stopping marijuana use and repeatedly up to 28 days of abstinence (verified by daily urines). Subjects were tested on a computerized task in which they had the choice of pushing one button to accumulate points and pushing a second button to subtract points from an opponent. The subjects were informed that they were competing with other subjects, but in fact were playing against the computer. Aggressive behavior was defined as responding on the point subtraction button. Aggressive behavior was provoked by subtracting points from the subject on a random basis, which would be attributed to actions of the fictitious opponent. Furthermore, aggressive behavior was encouraged by providing a provocation-free interval if the subject engaged in responding on the button that resulted in points being subtracted by the fictitious opponent. Aggressive responding increased markedly on the third day of abstinence and peaked on the seventh day of abstinence. Aggressive responding returned to baseline by the 28th day of abstinence. There was no change in non-aggressive responding during the

entire abstinence period. The increase in aggressive responding paralleled increases in scores on the Hamilton Depression and Anxiety Scales. The results suggest that increased susceptibility to aggressive responses to provocation may be a component of an abstinence syndrome associated with chronic marijuana use. Kouri, E.M., Pope, H.G., Lukas, S.E., *Psychopharmacology*, 143, pp. 302-308, 1999.

Abnormalities in Human Post-Mortem Striatal Dopaminergic Terminal Markers

Dr. Karley Little and associates at the University of Michigan assayed dopamine transporter binding and vesicular monoamine transporter binding in post-mortem tissue from cocaine-using subjects and matched controls. The vesicular monoamine transporter binding assayed with (+)-[3H]dihydrotrabenazine (DTBZ) was used to distinguish alterations in binding associated adaptive changes in the dopamine transporter from changes in the number of dopamine terminals. The investigators report that cocaine abusers exhibited abnormally high levels of WIN 35428 binding to the dopamine transporter in striatal tissue from cocaine users relative to controls. On the other hand, DTBZ binding was lower in cocaine users compared to controls. The results indicate that cocaine users exhibit upregulation of the dopamine transporter with concomitant reductions in the apparent number of dopamine terminals. Little, K.Y. et al., *American Journal of Psychiatry*, 156, pp. 238-245, 1999.

Attention Deficit Disorder and Substance Abuse

Timothy Wilens, M.D. and his colleagues at Harvard Medical School have shown that boys with attention deficit hyperactivity disorder (ADHD) who are treated with stimulants such as Ritalin are 84 percent less likely to abuse drugs and alcohol when they get older. Research showed that 75 percent of the non-medicated ADHD boys had at least one substance use disorder, compared to 25 percent of the medicated ADHD boys and 18 percent of the boys without ADHD. Researchers calculated that treating ADHD with stimulants was associated with an 84 percent reduction in risk of developing a substance use disorder. Rather than being concerned that boys with ADHD might be prescribed stimulant medication, scientists are now concerned when they are not. Appropriate treatment of ADHD appears to be quite helpful in preventing the later emergence of substance abuse in these vulnerable individuals with ADHD. The use of interventions in childhood to prevent the later emergence of substance abuse is a promising avenue for future research investigations. Biederman et al., *Pediatrics*, Vol 104(2), August 1999.

Susceptibility Genes Identified for Further Study in Possible Linkage for Nicotine Dependence

It has been clear from twin and other studies that there is a significant genetic component for smoking. However, as yet no gene has been identified as related to either smoking initiation or dependence on nicotine. Now, Straub, Kendler and colleagues have identified several suggestive regions on 6 chromosomes that may have critical genes. These were determined by a whole genome scan using 451 markers in 343 genotyped individuals (308 of whom were nicotine dependent). Regions yielding a large lod score of linkage were examined more closely in the original and in a second sample. The results pointed to regions on Chromosomes 2,4, 10, 16, 17, and 18 that merit further study. It is cautioned that although these results are suggestive, further study may show the linkage to be due to chance. Straub, R.E. et al., *Molecular Psychiatry*, 4, pp. 129-144, 1999.

On-Site Primary Care and Mental Health Services in Outpatient Drug Abuse Treatment Units

Providing primary care and mental health services to substance abuse clients has been shown to improve retention and substance abuse outcomes. This article examines the relationship between the organizational features of 597 outpatient drug abuse treatment units and the degree to which they provide on-site primary care and mental health services. In two-stage models, Joint Commission on Accreditation of Healthcare Organizations-certified and methadone programs delivered more on-site primary care services. Units affiliated with mental health centers provided more on-site mental health services but less direct medical care. Units with dual-diagnosis clients provided more on-site mental health but fewer on-site HIV/AIDS treatment services. These findings suggest that organizational features influence the degree to which health services are incorporated into drug abuse treatment. Fully integrated care might be an unattainable ideal for many such organizations, but quality improvement across the treatment system might increase the reliability of clients' access to health services. Friedmann, P., Alexander, J., Jin, L., D'Aunno, T. *Journal of Behavioral Health Services & Research*, Vol. 26 (1), February, pp. 80-94, 1999.

Modified Therapeutic Community for Mentally Ill Chemical Abusers: Outcomes and Costs

Several studies have established that the personal and social consequences of substance abuse are extensive and costly. These consequences are frequently compounded by mental illness. Although interventions that target mentally ill chemical abusers (MICAs) present several challenges, the potential benefits of successful interventions are significant. This article presents outcomes and costs of a modified therapeutic community (TC) intervention for homeless MICAs. Outcomes at follow-up are compared with those for a control group of homeless MICAs receiving standard services in a "treatment-as-usual" (TAU) condition. Annual economic costs for the modified TC and the average weekly cost of treating a single client are estimated. Treatment and other health service costs at 12 months postbaseline are compared for modified TC and TAU clients. The results of this study indicate that, suitably modified, the TC approach is an effective treatment alternative for homeless MICAs, with the potential to be highly cost-effective relative to standard services. French, M.T., Sacks, S., De Leon, G., Staines, G., and McKendrick, K. *Evaluation Health Professional*, 22(1), pp. 60-85, March 1999.

Program Quality Effects on Patient Outcomes During Methadone Maintenance: A Study of 17 Clinics

This study was designed to replicate Ball and Ross' benchmark research, which was the first to identify a set of program quality factors for methadone maintenance programs and relate them to patient outcomes. Ball and Ross' treatment domain variables were measured in a new and larger sample of methadone clinics, and eight candidate program quality factors were derived. Both studies found that program factors defined by more frequent counseling contacts, higher director involvement with treatment, and more director experience were associated with lower drug use by patients during treatment. Several patient and counselor characteristics also were associated with drug use outcomes. Magura, S., Nwakeze, P.C., Kang, S.Y., and Demsky, S. *Substance Use and Misuse*, 34(9), pp. 1299-1324, July 1999.

Effects of Culturally Congruent Intervention on Cognitive Factors Related to Drug-Use Recovery

This paper describes a culturally congruent intervention to promote recovery from illegal drug use among African Americans and reports initial outcomes. The intervention was based on the transtheoretical stages-of-change model and on techniques of focused dyadic counseling and motivational interviewing. Subjects were randomly assigned to the culturally congruent intervention or to a control condition. Each condition featured a single counseling session during which drug-related and other needs were assessed and appropriate referrals offered. Posttest data indicated that subjects in the culturally congruent condition were more involved in the counseling session, more willing to self-disclose, more motivated to seek help for drug use associated problems, and higher for preparation for change. Longshore, D., Grills, C., Annon, K. *Substance Use and Misuse*, 34(9), pp. 1223-1241, July 1999.

Matching Clients' Needs with Drug Treatment Services

This study reports results of a study that investigated whether matching drug treatment services with client needs improved outcomes for a sample of 171 clients who participated in community-based drug treatment programs. Clients were initially assessed on multiple problem areas (alcohol use, drug use, medical, psychological, family/social, legal, employment, housing) and on areas of special needs or stated preferences for services (e.g., transportation, child care, language). A 6-month follow-up interview reassessed clients' problems/needs in all areas and collected information on the services received. The results showed that some services significantly improved client outcome for those who had expressed needs for such services. Notably, services meeting the need for vocational training, child care, transportation and housing showed beneficial effects. A higher level of needs and services matching (defined either by the ratio of services received to services desired, or by the total level of met versus unmet needs in the eight problem areas) significantly predicted longer treatment retention. *Journal of Substance Abuse Treatment*, 16(4), pp. 299-305, June 1999.

Predicting Posttreatment Cocaine Abstinence for First-Time Admissions and Treatment Repeaters

This study examined client and program characteristics that predict posttreatment cocaine abstinence among cocaine abusers (n=507) with different treatment histories. Client and program data were collected as part of the recently

completed nationwide Drug Abuse Treatment Outcome Study (DATOS). Cocaine abusers (n=507) treated in 18 residential programs were interviewed at intake and 1-year follow-up. Program directors provided program level data. Results indicate that no prior treatment and longer retention in DATOS programs were positive predictors of posttreatment abstinence. The interactive effect of these two variables was also significantly positive. Programs that offered legal services and included recovering staff increased their clients' likelihood of cocaine abstinence. Crack use at both the client and program level predicted negative impact. None of the program variables assessed differentially affected the outcomes of first-timers and repeaters. Although treatment repeaters were difficult to treat, their likelihood of achieving abstinence was similar to first timers if they were retained in treatment for a sufficient time. Both repeaters and first-timers responded similarly to the treatment program characteristics examined. Hser, Y.I., Joshi, V., Anglin, M.D., and Fletcher, B. *American Journal of Public Health*, 89 (5), pp. 666-671, May 1999.

Sequences of Powder Cocaine and Crack Use Among Arrestees in Los Angeles County

This paper examines the sequence or progression of use between powder cocaine and crack using arrestee data collected from county jails in Los Angeles County. Four sequences are identified and examined each in terms of user characteristics, history of use, dependence, contact with the criminal justice system, and concomitant use of other drugs. Findings confirm some already established observations, but also offer new knowledge on powder cocaine and crack abuse. For instance, powder cocaine-initiated users are more likely to progress to crack than to restrict their use to powder cocaine only, whereas crack-initiated users tend more often to use crack only than to progress to powder cocaine. This study provides additional support to the notion that powder cocaine and crack, when used interchangeably, can interact and reinforce each other, resulting in a higher level of use and dependence on both forms of the substance. In addition to contributing to the understanding of powder cocaine and crack use among criminal offenders, in particular, and across the adult population, in general, this article sheds light on prevention, treatment, and social control policies of both cocaine abuse and overall illicit drug use. Shaw, V.N., Hser, Y.I., Anglin, M.D., and Boyle, K. *American Journal of Drug and Alcohol Abuse*, 25(1), pp. 47-66, February 1999.

Interaction Effects of Client and Treatment Program Characteristic on Retention: An Exploratory Analysis Using Hierarchical Linear Models

This study examined the interaction effects of treatment program and client characteristics on client retention in treatment for drug users. Program characteristics included services provision, funding source, staff-client gender congruence, and client characteristics included gender, age at admission, and drug use level prior to admission. The same model was applied separately to residential methadone maintenance and outpatient drug-free programs. Data were obtained from 59 treatment programs and 3,764 patients who had discharge records. A noteworthy significant interaction effect was the program's funding source and patient's gender on treatment retention in the outpatient drug-free modality. Female clients stayed in the programs that accepted only public funding for shorter periods than in programs that accepted both public and private funding. Male patients remained in treatment an average of 25.3 fewer days than female patients in programs that only accepted public funds, but stayed about the same time as females if the programs received mixed funding. Chou, C., Hser, Y., & Anglin, M.D. *Substance Use & Misuse*, 33(11), pp. 2281-2301, 1998.

Managed Care and Technical Efficiency in Outpatient Substance Abuse Treatment Units

This study examined the extent to which managed care participation was associated with technical efficiency in outpatient substance abuse treatment organizations as well as the contribution of specific managed care practices and other organizational, financial, and environmental attributes to technical efficiency in these organizations. Technical efficiency is a mechanism by which cost savings may be gained or lost under managed care. As used here it is the use of specific input resources (e.g. staff hours and expenses) to provide specific outputs (e.g. therapy hours). Managed care was defined as a set of public or private programs designed to control access to care, types of care delivered, or the amount and/or costs of care. Data are from a nationally representative sample survey of substance abuse treatment organizations conducted in 1995 (n=618). Overall, analyses indicate that managed care participation is not significantly related to the level of efficiency. Only one managed care oversight procedure, the imposition of sanctions by managed care firms, was significantly associated with relative efficiency of these provider organizations. However, several organizational factors were associated with the relative level of efficiency, including hospital affiliation, mental health center affiliation, JCAHA accreditation, receipt of lump sum revenues, methadone treatment modality, percent clients unemployed, and percent clients who abuse multiple drugs. Alexander, J., Wheeler, J., Nahra, T., and Lemak, C. *Journal of Behavioral Health Services and Research*, 25(4), November 1998.

Changes in Methadone Treatment Practices: Results from a Panel Study, 1988-1995

This paper examines the extent to which key methadone treatment practices (dose levels, treatment duration, and client influence in dose decisions) changed from 1988 to 1995 using panel data from a random national sample of methadone maintenance units. Results from studies conducted in the late 1980's and early 1990's showed that most methadone treatment units did not use the most effective treatment practices. Results reported in this paper indicate that treatment practices concerning dose level, client influence in dose decisions, and treatment duration improved significantly in the most recent period. However, the average dose level of 59 mg/d is still below the level found to be optimally effective and average treatment duration increased only one month. Several characteristics of client (race, age) and treatment units (staff, ownership, geographic location) are associated with effective treatment practices. D'Aunno, T., Folz-Murphy, N., and Lin, X. *American Journal of Drug and Alcohol Abuse*, June 1999.

Health Care Need and Utilization: A Preliminary Comparison of Injection Drug Users, Other Illicit Drug Users, and Nonusers

This paper investigates the relationship between chronic drug use and the health care system. Data from 536 African-American, Hispanic, and non-Hispanic White men and women were analyzed to determine independent risk factors for three outcome variables: 1) Need for health care treatment, 2) Utilization of health care treatment, and 3) Failure to receive needed treatment. Nine independent demographic, health, and drug-use history variables were assessed in logistic regression models. Analysis of the data shows that chronic drug users were more likely in the past year to need health care treatment, were as likely to receive some health care treatment, and were more likely not to receive needed treatment than were nonusers. Chitwood, D.D., McBride, D.C., French, M.T., and Comerford, M. *Substance Use and Misuse*, 34(4-5), pp. 727-746, March-April 1999.

Cost of Employee Assistance Programs: Comparison of National Estimates from 1993 and 1995

The cost and financing of mental health services is gaining increasing importance with the spread of managed care and cost-cutting measures throughout the health care system. The delivery of mental health services through structured employee assistance programs (EAPs) could be undermined by revised health insurance contracts and cutbacks in employer-provided benefits at the workplace. This study uses two recently completed national surveys of EAPs to estimate the costs of providing EAP services during 1993 and 1995. EAP costs are determined by program type, worksite size, industry, and region. In addition, information on program services is reported to determine the most common types and categories of services and whether service delivery changes have occurred between 1993 and 1995. The results of this study will be useful to EAP managers, mental health administrators, and mental health services researchers who are interested in the delivery and costs of EAP services. French, M.T., Zarkin, G.A., Bray, J.W., Hartwell, T.D. *Journal of Behavioral Health Services Research*, 26(1), pp. 95-103, February 1999.

Characteristics of Women-Only and Mixed-Gender Drug Abuse Treatment Programs

Specialized substance abuse treatment programs have been developed for women within the past two decades. This article presents the results of a secondary analysis of a regional database of drug abuse treatment programs that compared the characteristics of women-only (WO) and mixed-gender (MG) programs across three treatment modalities. In general, WO programs differed from MG programs in their policies regarding fees, sources of payment, special populations served, services offered, and treatment capacity, process, and duration. The differences in program characteristics reflect broader societal gender differences, including women's generally lower economic status and primary responsibility for child-rearing. Grella, C.E., Polinsky, M.L., Hser, Y.I., Perry, S.M. *Journal of Substance Abuse Treatment*. 17(1-2), pp. 37-44, July-September 1999.

Women in Residential Drug Treatment: Differences by Program Type and Pregnancy

This study compared the characteristics of 4,117 women treated in publicly funded residential drug treatment programs in Los Angeles County between 1987 and 1994 by pregnancy status and program gender composition, that is, women-only and mixed-gender programs. A logistic regression analysis determined the predictors of program completion. Women in women-only programs were more likely than women in mixed-gender programs to be

pregnant, homeless, or on probation; to use methamphetamines; to use alcohol; and have prior drug treatment. Pregnant women were younger, more likely to be homeless, had fewer years of drug use, were more often referred by other service providers, and were less likely to have injected drugs or have prior drug treatment than non-pregnant women. Although women in women-only programs had more problems, they spent more time in treatment and were more than twice as likely to complete treatment as compared with women in mixed-gender programs. Grella, C.E. *Journal of Health Care for the Poor and Underserved*, 10(2), pp. 216-229, May 1999.

A National Evaluation of Treatment Outcomes for Cocaine Dependence

This national study focused on posttreatment outcomes of community treatments of cocaine dependence. Relapse to weekly (or more frequent) cocaine use in the first year after discharge from 3 major treatment modalities was examined in relation to patient problem severity at admission to the treatment program and length of stay. Cocaine-dependent patients (N = 1605) from 11 cities located throughout the United States were studied using a naturalistic, nonexperimental evaluation design. They were sequentially admitted from November 1991 to December 1993 to 55 community-based treatment programs in the national Drug Abuse Treatment Outcome Studies (DATOS). Included were 542 patients admitted to 19 long-term residential programs, 458 patients admitted to 24 outpatient drug-free programs, and 605 patients admitted to 12 short-term inpatient programs. Of the 1605 patients, 377 (23.5%) reported weekly cocaine use in the year following treatment (dropping from 73.1% in the year before admission). An additional 18.0% had returned to another drug treatment program. Higher severity of patient problems at program intake and shorter stays in treatment (<90 days) were related to higher cocaine relapse rates. Patients with the most severe problems were more likely to enter long-term residential programs, and better outcomes were reported by those treated 90 days or longer. These findings suggest that dimensions of psychosocial problem severity and length of stay are, therefore, important considerations in the treatment of cocaine dependence. Cocaine relapse rates for patients with few problems at program intake were most favorable across all treatment conditions, but better outcomes for patients with medium- to high-level problems were dependent on longer treatment stays. Simpson, D.D., Joe, G.W., Fletcher, B.W., Hubbard, R.L., and Anglin, M.D. *Archives of General Psychiatry*, 56(6), pp. 507-514, June 1999.

A Cost-Effectiveness and Cost-Benefit Analysis of Contingency Contracting-Enhanced Methadone Detoxification Treatment

The researchers examined treatment costs in an ongoing study in which 102 opioid-addicted patients had been randomly assigned to either 180-day methadone detoxification or the same treatment enhanced with contingency contracting. In the latter condition, study participants received regular reinforcers contingent on negative urine toxicology screens and breath analyses for a range of drugs and alcohol. Both conditions involved psychosocial treatment, and all participants were stabilized to a daily methadone dose of approximately 80 mg during the first 4 months, followed by a 2-month taper. Individuals participating in the enhanced condition were more likely to provide continuously drug-free urine samples and alcohol-free breath samples during the final month of treatment than were participants in the control condition. Cost of treatment was calculated individually for each participant based on actual services received. First, unit cost for each service was determined, including adjusted staff salaries for direct treatment and opportunity cost of facilities utilized during service delivery. Next, each patient's use of services during the first 120 days of the study was valued and then added the cost of methadone, laboratory work, and contingent reinforcers. A subsample (n = 45) also provided data on health care utilization during treatment, which we valued using standard Medicare unit costs. The marginal cost of enhancing the standard treatment with contingency contracting was approximately 8%. An incremental cost of \$17.27 produced an additional 1% increase in the number of participants providing continuously substance-free urine and breath samples during month 4 of the study. For every additional dollar spent on treatment, a \$4.87 health care cost offset was realized; however, this difference was statistically insignificant due to extreme variances and small subsample size. Hartz, D.T., Meek, P., Piotrowski, N.A., Tusel, D.J., Henke, C.J., Delucchi, K., Sees, K., Hall, S.M. *American Journal of Drug and Alcohol Abuse*, 25(2), pp. 207-218, May 1999.

Continuing Care for Cocaine Dependence: Comprehensive 2-Year Outcomes

This report presents 2-year outcome data from an outpatient continuing care study in which cocaine-dependent patients (N = 132) were randomly assigned to either standard group counseling (STD) or individualized relapse prevention (RP). Data on cocaine outcomes during the 6-month treatment phase of the study were presented in an earlier report. In the present report, a continuing care condition main effect was obtained on only 1 of 8 outcome

variables examined. However, patients who endorsed a goal of absolute abstinence on entering continuing care had better cocaine use outcomes in RP than in STD, whereas the opposite was true for those with less stringent abstinence goals. In addition, patients with current cocaine or alcohol dependence on entering continuing care who received RP had better cocaine use outcomes in Months 1-6 and better alcohol use outcomes in Months 13-24 than those in STD. McKay, J.R., Alterman, A.I., Cacciola, J.S., O'Brien, C.P., Koppenhaver, J.M., Shepard, D.S. *J Consult Clin Psychol*, 67(3), pp. 420-427, June 1999.

How Expensive are Unlimited Substance Abuse Benefits under Managed Care?

Substance abuse (SA) care has been excluded from recent federal and state legislation mandating equal benefits for mental health and medical care ("parity"), largely because of cost concerns. This article studies how many patients are affected by SA coverage limits and the likely implications of limits on insurance payments, using 1996-97 claims from 25 managed care plans with unlimited SA benefits. Findings suggest that changing even stringent limits on annual SA benefits has a small absolute effect on overall insurance costs under managed care, even though a large percentage of SA patients are affected. Removing an annual limit of \$10,000 per year on SA care is estimated to increase insurance payments by about 6 cents per member per year, removing a limit of \$1,000 increases payments by about \$3.40. As long as care is comprehensively managed, "parity" for SA in employer-sponsored health plans is not very costly. Sturm, R., Zhang, W., and Schoenbaum, M. *Journal of Behavioral Health Services Research*, 26(2), pp. 203-210, May 1999.

The DSM-IV Criteria for Adolescent Alcohol and Cannabis Use Disorders

The aims of this study are to compare DSM-IV criteria for alcohol and cannabis use disorders with its predecessor, DSM-III-R, and to examine the validity of the new criteria in an adolescent drug clinic sample. During evaluation, a sample of 772 adolescents (63% boys, 77% white) were administered a structured interview of diagnostic symptoms and additional problem severity measures. Independent staff ratings of problem severity and treatment referral were collected as well. Compared to its predecessor, DSM-III-R, application of the DSM-IV criteria for alcohol and cannabis users resulted in more abuse assignments and fewer dependence assignments. The shift in assignments appeared to be largely due to a lowering of the abuse threshold, rather than to a tightening of the dependence criteria. The external validity data generally supported the DSM-IV abuse and dependence distinction in adolescents, and the newer criteria were as valid as the older criteria. In contrast to DSM-III-R, the DSM-IV system yields more abuse cases and fewer dependence cases among adolescent alcohol and cannabis abusers. Validity evidence for the new criteria are defensible, yet the findings are seen as a starting point for discussing the need for tailoring substance use disorder criteria for adolescents. Winters, K.C., Latimer, W., and Stinchfield, R.D. *J Stud Alcohol*, 60(3), pp. 337-344, May 1999.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****September, 1999**

Research Findings

AIDS Research

Micronutrients and Survival among HIV-Infected Children

New insights on the role of nutrition in improving survival among individuals with HIV have been gained from studies on micronutrient deficiencies among drug abusers with HIV infection. Baum and her colleagues at the University of Miami School of Medicine have found that low levels of selenium may be related to decreased survival of HIV-infected children. The study population consisted of 24 children who were exposed perinatally to HIV and who were symptomatic. They were recruited between October and December 1990 from the Jackson Memorial Pediatric Immunology Clinic, Miami, and were observed for 5 years. The children were assessed for their immune status by their CD4 cell count; and nutritional status by serum albumin level and plasma levels of trace elements (iron, zinc, selenium). Twelve children died of HIV-related causes. Cox multivariate analyses showed that only CD4 cell count below 200 (RR=7.05, CI=1.87-26.5, $p<0.004$), and low levels of selenium (RR=5.96, CI=1.32-26.8, $p<0.02$) were significantly and independently related to mortality. Among the children who died, those with low selenium levels (<85 ug/l) died at a younger age, suggesting more rapid disease progression. These data in children concur with the Baum's earlier findings of increased mortality with low levels of selenium in HIV infected adults. Campa, A., Shor-Posner, G., Indacochea, F., Zhang, G., Lai, H., Asthana, D., Scott, G., and Baum, M. Mortality Risk in Selenium-Deficient HIV-Positive Children. *Journal of Acquired Immune Deficiency and Human Retrovirology*, 20, pp. 508-513, 1999.

Highly Active Antiretroviral Therapy in a Large Urban Clinic: Risk Factors for Virologic Failure and Adverse Drug Reactions

In a retrospective cohort study, Lucas and his colleagues from Johns Hopkins University School of Medicine identified demographic, behavioral, and clinical features that correlated with failure to suppress viral load outside of the clinical trial setting. In clinical trials, highly active antiretroviral therapy (HAART) reduces HIV-1 viral load to undetectable levels (500 copies/ml or less) in 60% to 90% of patients. The researchers' hypothesis was that the virologic response to HAART would be less efficient among unselected patients in an inner-city clinic than among patients enrolled in clinical trials. The study population was composed of 273 protease inhibitor-na•ve patients who began taking a protease inhibitor regimen containing at least one other antiretroviral drug to which the patient had not previously been exposed. Levels of HIV-1 RNA were undetectable in 42% of the cohort at 1 to 90 days, 44% at 3 to 7 months, and 37% at 7 to 14 months. Missed clinic visits was the most important factor associated with failure to suppress the HIV-1 viral load. Other factors associated with failure to suppress viral load were nonwhite ethnicity, age 40 years or younger, injection drug use, lower baseline CD4 lymphocyte count, and higher baseline viral load. Lucas, G.M., Chaisson, R.E., Moore, R.D. *Ann Int Med*, 131, pp. 222-229, 1999.

Comparison of Clinical Manifestations of HIV Infections Among Women by Risk Group, CD4 Cell Count, and HIV-1 Plasma Viral Load

This cross-sectional analysis was conducted on data available for 724 HIV infected women. The women were participants of the HIV Epidemiology Research Study (HERS), a multi-center prospective study of HIV infection in women. In this study the authors compared the prevalence of HIV-related symptoms, physical examination findings and hematologic variables among women whose risk for HIV was injection drug use (n=387) since 1985 as opposed to sexual contact (n=337). The researchers also evaluated the influence of HIV plasma viral load and CD4 cell count on clinical manifestations according to risk. In analyses adjusting for CD4 cell level alone and for plasma viral load combined with CD4 cell level, injection drug users (IDUs) were more likely to report: recent memory loss and weight loss, but not recent episodes of genital herpes. IDUs were also more likely to have enlarged livers, a body mass index (BMI) less than 24, and low hematocrit (<34%) and platelet count (<150,000/ml). After adjusting for CD4 cell count and risk group, high and medium HIV-1 plasma viral load levels were associated with the presence of oral leukoplakia on examination, and only the highest level of plasma viral load was associated with recent histories of fever and thrush, oral hairy leukoplakia, pseudomembranous candidiasis, and BMI less than 24 on examination, and low hematocrit. This study demonstrated some differences in frequency of signs, symptoms and laboratory values between risk groups, but this may be due to effects of injections drug use rather than HIV infection. The fact that the difference in signs and symptoms found associated with increasing levels of viral load was not different across risk groups indicates a more direct association of these findings with HIV infection. Rompalo, A.M., Astemborski, J., Schoenbaum, E., Schuman, P., Carpenter, C. Holmberg, S.D., Warren, D.L., Farzadegan, H., Vlahov, D., Smith, D.K. *JAIDS & HR* 20(5), pp. 448-454, 1999.

Gender Differences at Admission and Follow-Up in a Sample of Methadone Maintenance Clients

Although one-third of clients enrolled in methadone treatment (MMT) in the United States are female, few studies have looked at gender differences at admission and follow-up. An understanding of these differences can lead to improved treatment strategies. The investigation reported is based on data collected as part of the Drug Abuse Treatment and AIDS-Risk Reduction (DATAR) project. Using interview data from 435 opioid dependent clients (31% female) collected at admission and approximately one year after discharge, females were found to have more dysfunctional families of origin and greater prior and current psychological and medical problems. Both genders showed significant improvement from admission to follow-up in terms of reduced drug use, criminal activity and HIV/AIDS-risky behaviors. In some areas such as improved family relationships and improved psychosocial status, females seemed to benefit more from treatment than did the males. In addition, females were more likely to seek further help for both drug misuse and psychological problems subsequent to discharge. Chatham, L.R., Hiller, M.L., Rowan-Sal, G.A., Joe, G.W., and Simpson D.D. *Substance Use & Misuse*, June 1999, 34(8), pp. 1137-1165, 1999.

Cocaine Use and High Risk Sexual Behavior Among STD Clinic Patients

This study examined the effect of cocaine use and other correlates on participation in high-risk sexual behavior among STD clinic patients. This was a cross-sectional study of 1,490 consecutive patients attending three Los Angeles County STD clinics between 1992 and 1994. Male patients number 892 and females, 598. Analyses found high-risk sexual activity was associated with being male and being of younger age. Among women, high-risk sexual behavior was associated with crack cocaine use and a perceived need for help. Among the men in the study, ethnicity (being black) and having an arrest history were associated with high-risk behavior. The present study confirmed findings from other studies that showed an association between cocaine use and high-risk sexual practices among STD clinic patients and identified several important gender differences that may be considered in planning AIDS and drug prevention programs. These gender differences also suggest that programs might employ different outreach and intervention strategies for women and men. Hser, Y., Chou, C., Hoffman, V., and Anglin, M.D. *Sexually Transmitted Diseases*, 26(2), February 1999.

An Institutional Analysis of HIV Prevention Efforts by the Nation's Outpatient Drug Abuse Treatment Units

This paper examines the use of human immunodeficiency virus (HIV) prevention practices by the nation's outpatient substance abuse treatment units during the period 1988 to 1995. Using an institutional perspective that argues that organizations adopt new practices not only for technical reasons, but also because external factors actively promote

or model the use of particular practices, the researchers examine the extent to which treatment units use several practices to prevent HIV infection among their clients and among drug-users not in treatment. Results from random-effects regression analyses of national survey data show that treatment units significantly increased their use of HIV prevention practices during the study period. Both the number of units engaged in the prevention efforts and the intensity of their efforts increased. Those efforts included HIV testing and counseling with clients and outreach to intravenous drug users not in treatment. Further, the results show that treatment units' use of prevention practices was related to clients' risks for HIV infection, unit resources available to support these practices, and organizational support for the practices. D'Aunno, T., Vaughn, T., and McElroy, P. *Journal of Health and Social Behavior*, Vol. 40, pp. 175-192, 1999.

Relationship Between Substance Use During Adolescence and HIV Risk Behavior Among Young Adults

Young men (N=400) and women (N= 552) 19-21 years of age, some with, some without college experience represented a targeted sample of 2,071 who completed a questionnaire while in the sixth grade in 1987-88. Questionnaires to assess current substance use and sex behavior were mailed to the study participants. Early substance use (as reported in the 1987-88 questionnaire) placed study participants in one of three categories: Frequent users (n=148), experimental users (n=603), or abstainers (n=200). ANOVA with post hoc analyses was used. Results indicate that frequent users of both genders were younger than experimenters and female experimenters were younger than female abstainers at first intercourse. There was a significant interaction between gender and educational level and a significant main effect for number of sexual partners with college experience serving as a protective factor. Overall, the results of the study support the hypothesis that substance use at an early age is related to earlier initiation of sexual activity. Staton, M., Leukefeld, C., et al. *Risky Sex Behavior and Substance Use Among Young Adults*. *Health & Social Work*, 24 (2), 1999.

HIV Risk is Higher for Puerto Rican Drug Users Compared to Other Hispanic Subgroups

Researchers estimated and compared the HIV risks among three Hispanic subpopulations (N= 3,660) chronic drug users who participated in NIDA's Cooperative Agreement intervention study on drug use. Interview data were collected regarding drug use and sexual behavior. HIV risk was estimated using information about individuals' HIV-relevant behaviors, the social context (i.e., city) in which such behaviors occur, and published estimates of HIV transmission for various risk behaviors. Multiple linear regression analysis was used to investigate differences in estimated HIV risk between Puerto Rican, Mexican-American, and Mexican drug users, accounting for sociodemographic factors, sexual preference, and geographic region. Puerto Ricans were found to have significantly greater estimated overall HIV risk, estimated injection risk, and in general, significantly greater estimated sexual risk than Mexican Americans and Mexicans. No significant differences were found among any of the subgroups for estimated risk from having unprotected high-risk sex. These findings suggest that Puerto Ricans who use drugs experience a higher risk of HIV infection than other Hispanic drug users.

Research is needed to identify which economic, social, and cultural components account for this increased risk. Montoya, I., Bell, D., Richard, A., Carlson, J., et al. *Estimated HIV Risk Among Hispanics in a National Sample of Drug Users*. *J AIDS Hum Retroviol*, 21, pp. 42-50, 1999.

Risk Network Cohesion is Dynamically Linked to Infectious Disease Transmission

In this study, researchers sought to relate dynamic changes in risk-network (sex and/or injecting drug) structure to observe STD/HIV transmission. They analyzed macro- and micro-structural elements in two heterosexual networks, augmented by ethnographic observations. In a Colorado cohort of injecting drug users (N = 595), measures of subgroup formation and of density of activity showed a decrease of network cohesion over time; only one HIV transmission was observed in three years. In a group of adolescent heterosexuals in Georgia (N = 99), the reverse process (increase in structural cohesion) was associated with efficient syphilis transmission: 10 cases were observed. Changes in personal risk behaviors over time were modest. STD/HIV transmission patterns were associated with intensification or diminution of network cohesion. Network and ethnographic data suggest that enhanced connectivity facilitates transmission while segmentation impedes it, suggesting opportunities for interventions. These data also emphasize the need to re-evaluate purely behavioral explanations of STD/HIV transmission. Potterat, J., Rothenberg, R., Muth, S.Q. *Network Structural Dynamics and Infectious Disease Propagation*. *Int J STD AIDS*, 10(3), pp. 182-185, 1999.

"Shotgunning" is Linked to Both Sexual Risk Behaviors and Risks of Infection

A series of ethnographic observations were conducted to characterize more fully the practice of "shot gunning," an illicit drug smoking practice in which smoked drugs are exhaled or blown by one user into the mouth of another user. Inhalation drug use such as this is implicated in the transmission of a variety of pathogens by the respiratory route. In addition, crack smoking has been associated with an increased risk of HIV infection, particularly through the exchange of sex for drugs. This study also sought to characterize the range of behaviors associated with the shot gunning drug use practice, and the settings and contexts in which the practice occurs. Shot gunning is a form of drug use that is closely linked to high risk sexual behaviors. It is associated with the potential for both direct and indirect risk of disease transmission by sexual, blood-borne and respiratory routes, making the development and evaluation of comprehensive risk reduction interventions essential. Perlman, D., Henman, A., Kochems, L., Paone, D., et al. Doing a Shotgun: A Drug Use Practice and Its Relationship to Sexual Behaviors and Infection Risk. *Soc Sci Med*, 48(10), pp. 1441-1448, 1999.

Forgetting is a Factor in Incomplete Reporting of Sexual and Drug Use Partners

Partner notification and social network studies of infectious disease often involve interviewing people to elicit their sexual and/or drug injection partners. Incomplete reporting of partners in these contexts would significantly hamper efforts to understand and control the spread of sexually transmitted diseases, HIV, and other infections. There are many reasons why individuals might not name their partners in interviews. This study provides a comprehensive assessment of forgetting as a cause of incomplete reporting of sexual and injection partners. One hundred fifty-six persons in Seattle, Washington, at presumed high risk for HIV recalled their sexual and/or injection partners in two interviews separated by 1 week or 3 months. Repeated, nonspecific prompting elicited, on average, 10% of all partners recalled in an interview. Subjects displayed substantial forgetting of partners across partner types, recall periods, and four independent measurement approaches, with up to 72% of partners forgotten. The number of partners recalled and subjective assessment of forgetting are moderate to good predictors of the number of partners forgotten. Recalled and forgotten partners do not differ dramatically on any of several partner variables. Forgetting is a primary factor in the incomplete reporting of sexual and injection partners. Interviewers should prompt repeatedly to maximize recall of partners. Re-interviewing is currently the best method available for identifying partners as completely as possible and should be focused on individuals who report many partners and/or sense they have other partners they cannot recall. Brewer D., Garrett S., and Kulasingam S. Forgetting as a Cause of Incomplete Reporting of Sexual and Drug Injection Partners. *Sex Transm Dis*, 26(3), pp. 166-76, 1999.

Simulation Estimates HIV Transmission Probabilities In a Network of Cocaine Injectors

In a simulation study, researchers addressed the applicability of various network measures for the analysis of a disease transmission network. A simulation was conducted to estimate HIV transmission probabilities within an empirical network of cocaine injectors. The results of the simulation were then used as a criterion to evaluate network measures of disease vulnerability and infectivity. For the type of disease transmission studied, the analysis showed that relatively simple network measures can be adequate to the measurement of vulnerability to disease and infectivity. Vulnerability (the probability of being infected) and infectivity (the probability that an important or prominent network member or "actor" will infect others) are of most concern in the consideration of HIV transmission networks. The findings will help investigators in understanding disease processes and particularly, the dynamic propagation of HIV in drug use and sexual risk networks. Bell, D., Atkinson, J., and Carlson, J. Centrality Measures for Disease Transmission Networks. *Social Networks*, 21, pp. 1-21, 1999.

How Tucson IDUs Appropriate and Internalize HIV Prevention Concepts

In this study, researchers illuminate how social categorizations, concepts, and procedures that are a valuable part of HIV prevention efforts are reportedly enacted by IDUs within certain social contexts. The categories and concepts circulated by AIDS prevention programs have a direct if not always apparent influence on the regulation of relations within IDU social networks. Ideas regarding risk groups, safer sex, and HIV test results are actualized in specific interactions and often serve to structure the patterns of relationships IDUs share with specific people around them. Ultimately, this study points to some of the parameters governing the regulation of relationships among people by illustrating how macro-communications are enacted in micro-contexts. Estrada, A. and G. Quintero. Redefining

Categories of Risk and Identity: The Appropriation of AIDS Prevention Information and Constructions of Risk. In Elwood, W. (ed.) Power in the Blood: A Handbook of AIDS, Politics, and Communication. Mahwah, N.J.: Lawrence Erlbaum Associates, 1999.

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National Institute on Drug Abuse

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

September, 1999

Research Findings

Epidemiology, Etiology, and Prevention Research

In the Past 6 Months

- Despite the leveling epidemic, consequences of cocaine use have increased among aging users in some cities; increases among younger age groups in some indicators in several areas have been reported recently.
- New heroin use among young populations continues to be reported in several cities; in general, prices continue to decline as purity increases.
- Marijuana indicators continue to escalate across the country.
- Use of "Club drugs," especially GHB and MDMA, continue to be reported across the country.
- Despite its appearance in midwestern and southern rural areas, abuse of methamphetamine remains a predominantly western problem; however, indicators suggest declines in some areas.

The 46th meeting of the **Community Epidemiology Work Group (CEWG)** was held in Vancouver, British Columbia, Canada on June 8-11, 1999.

The CEWG, established by NIDA in 1976 is a network of researchers from 21 U.S. metropolitan areas and selected foreign countries which meets semiannually to report surveillance data and discuss the current epidemiology of drug abuse. The following are highlights of the 46th meeting:

- **Cocaine** - Cocaine remains the Nation's dominant drug problem, driven mainly by aging users who continue to experience adverse consequences. Recent indicators show a mixed picture. Mortality figures increased in six cities (Chicago, Detroit, Honolulu, Phoenix, San Francisco, and Seattle) and declined or remained stable in four (Miami, Minneapolis/St. Paul, Philadelphia, and San Diego). Emergency department (ED) mentions increased significantly in four cities (Atlanta, Dallas, Philadelphia, and Washington, DC) and declined significantly in one (San Francisco). The largest shift was a 46-percent increase in Dallas. Nonsignificant increases were reported in the majority of the other cities. Among treatment admissions, cocaine (including crack) is now the foremost primary drug of abuse (excluding alcohol-only but including alcohol-in-combination) in only 8 of the 21 CEWG areas. Among adult arrestees, cocaine-positive urinalysis percentages declined in the majority of cities, especially among males in Chicago, New York City, and St. Louis, and among females in St. Louis; percentages increased, however, for males in Philadelphia and Detroit and for females in Houston. Increases generally corresponded to increases in self-reported powder cocaine use and declines in self-reported crack use. Among younger age groups, recent slight increases in some indicators have been reported: ED mentions in Dallas, Denver, and Phoenix; treatment admissions in Los Angeles; school survey data of Texas border youth; and arrestee urinalysis data in Atlanta, Los Angeles, New Orleans, Phoenix, and San Antonio. Changing sales strategies in some cities, such as New York, are

masking cocaine activity that would normally appear on law enforcement indicators.

- Heroin** - Heroin indicators show mixed trends. Mortality figures¹ increased in seven cities (Chicago, Detroit, Miami, Minneapolis/St. Paul, Phoenix, San Francisco, and Seattle) and declined in three (Honolulu, Philadelphia, and San Diego). Heroin ED rates² per 100,000 population increased significantly in six cities (Atlanta, Denver, Miami, Newark, New Orleans, and Washington, DC) and nonsignificantly in another six cities; conversely, rates declined significantly in San Francisco and nonsignificantly in seven other cities. During that same time period, heroin as a percentage of total ED mentions remained generally stable, except for increases in Newark and Chicago. Heroin is now the predominant primary drug problem (excluding alcohol-only, but including alcohol-in-combination) in 8 of the 21 CEWG areas: Baltimore, Boston, Detroit, Los Angeles, Newark, New York, Phoenix, and San Francisco. Opiate-positive screens among arrestees³ remained relatively low and generally stable; they often involved polydrug use. Heroin purity increased⁴ in nearly every city, while prices generally declined. Purity increases were particularly large in Detroit, New Orleans, and Philadelphia. Younger populations are increasingly initiating heroin use in several cities, including New York, where street informants indicate a steady increase in young buyers. In Boston and other Massachusetts areas, new and younger users are reportedly progressing from snorting to injecting. A Chicago study identified a high percentage of suburban youth, particularly young women, who are injectors. Suburban heroin activity is also reported around the Baltimore area, both among youth and young professionals.
- Marijuana** - Marijuana now accounts for more than 10 percent of total ED mentions in 12 cities (Atlanta, Boston, Chicago, Dallas, Detroit, Los Angeles, Miami, New Orleans, Philadelphia, St. Louis, San Diego, and Washington, DC), up from just 6 cities a year earlier--the result of increases² in 7 cities; no significant declines were noted. Marijuana is the predominant primary drug treatment problem in three cities (Denver, Seattle, and Minneapolis/St. Paul). Treatment percentages decreased in New Orleans, Newark, Chicago, and Seattle and increased in San Diego. Among adult male arrestees, marijuana-positive findings were equal to or exceeded cocaine-positives in 10 cities; percentages declined substantially in 2 cities and increased in 13. In many cities, marijuana use appears to be increasing among youth, as is reflected in the percentages of juvenile arrestees testing positive for the drug: in six of the seven CEWG sites where ADAM tests juveniles, the percentage testing positive for marijuana was substantially greater than in the adult population. In Boston, cannabis is reportedly as available as alcohol, and use among adolescents is common, approaching that of cigarettes among older students. Blunt usage continues to grow or retain popularity in Chicago, Minneapolis/St. Paul, New York City, Philadelphia, and Seattle. Marijuana is combined with crack in Chicago ("primos" or "diablitos"), Philadelphia ("turbo"), and Houston (where it is a declining fad among young people); with PCP in Chicago ("wicky sticks" or "donk"), Minneapolis/St. Paul ("happy stick"), New York, Philadelphia ("loveboat" or "wet"), and St. Louis; with formaldehyde in Minneapolis/St. Paul and Seattle; with PCP plus formaldehyde in Houston ("fry," "amp," "water-water"); and with psilocybin mushrooms in Minneapolis/St. Paul. Marijuana combinations are not frequently reported in Denver, but the drug reported to be used to come down from or temper excited highs.
- Stimulants** - Despite its appearance in midwestern and southern rural areas, methamphetamine remains concentrated in the West. However, indicators suggest some declines in that region. Available mortality figures¹ show methamphetamine-related deaths declined in four cities (Honolulu, Philadelphia, San Diego, and Seattle) and increased in three (Minneapolis/St. Paul, Phoenix, and San Francisco). Following increases in 1997, methamphetamine ED mentions² declined significantly in six cities (Denver, Los Angeles, Minneapolis/St. Paul, Phoenix, San Francisco, and Seattle) and increased only in Dallas. Methamphetamine remains the number-one primary drug treatment problem in San Diego and Honolulu. Methamphetamine-positive percentages among arrestees³ remained stable across most sites, except for San Diego, where levels declined notably. Methamphetamine users are heterogeneous, consisting of many small subgroups, as suggested by ethnographic data in Atlanta. Furthermore, use patterns and contexts vary widely, depending on population, location, and history of use, as suggested by ethnographic research in Seattle. Injecting remains the predominant route of administration in several areas, including San Francisco and Denver; however, it has been declining somewhat while snorting or smoking have been increasing. Mexico remains the source of methamphetamine for many areas; however, local clandestine methamphetamine labs also proliferate in several areas, including parts of Arizona, Minnesota, Texas, and Washington State.
- Methylenedioxymethamphetamine (MDMA)** - ("ecstasy," "blue lips," "blue kisses," "white dove," "E," and "XTC") availability is reported, primarily as a club drug at "raves" and dance parties, in Atlanta, Austin, Boston, Chicago, Dallas, Detroit, Houston, Miami, St. Louis, Seattle, and Washington, DC. Young cohorts of users have been identified in several of those cities. Reports of increases in indicators of use of the drug continue in Boston and throughout Massachusetts. Though it is not readily available in Newark, it is becoming trendy on college campuses across New Jersey. In New Orleans, the drug is less available than crystal methamphetamine. In Austin, where it is often crushed and re-pressed with methamphetamine, psilocybin mushrooms, or LSD, three types of

MDMA are available: "liquid ecstasy"; "chocolate sprinkles," a heroin-based white pill with brown spots popular in the topless bar scene and in gay bars; and a nickel-sized wafer form. MDMA is used with methamphetamine, LSD, and marijuana in Washington, DC, where law enforcement officers recently noted increased trafficking. Methylenedioxy-amphet-amine (MDA) is reportedly available in St. Louis. Methylphenidate (Ritalin) is readily obtainable in Boston, Chicago, Detroit, and Minneapolis/St. Paul. It is crushed and snorted in Detroit and Minneapolis/St. Paul, and it is mixed with heroin instead of cocaine and injected as a "speedball" in Chicago. Phenmetrazine (Preludin) is also reportedly injected in Chicago. Despite concern about sibutramine (Meridia), a new weight loss drug, there were no reports of diversion or abuse.

- **Depressants** - Gamma-hydroxy butyrate (GHB), a central nervous system depressant, continues to be reported across the country, with recipes for its manufacture easily accessible on the Internet. GHB has been increasingly involved in poisonings, overdoses, date rapes, and fatalities in Boston, Denver, Los Angeles, South Florida, San Diego, Seattle, and parts of Arizona and Texas. It is available at gyms, nightclubs, raves, gay male party venues, or on college campuses in Atlanta, Baltimore, Boston, Chicago, Denver, Detroit, Los Angeles, Miami, Minneapolis/St. Paul, Newark, New Orleans, San Diego, San Francisco, Seattle, and parts of Arizona and Texas. GHB is available in several forms: clear liquid, white powder, tablets, and capsules. It is used in combination with ketamine or MDMA in Detroit; alcohol in South Florida and New Orleans; and alcohol and ketamine in a "G and B" in Minneapolis. Gamma butyrolactone (GBL) is contained in commercial products (Blue Nitro, Renew-Trient, and ReVivarin); it metabolizes into GHB and produces clinical symptoms identical to GHB. The drug was responsible for overdoses, poisonings, and hospitalizations in Detroit, South Florida, Minneapolis, Newark, and in Texas, where it was also responsible for a death.

Another club drug, ketamine ("Special K" or "vitamin K") is reported in cities such as Baltimore, Boston, Detroit, Miami, Minneapolis/St. Paul, Newark, New Orleans, New York City, and San Diego. It is injected intramuscularly by young, white, middle-class needle exchange clients in Boston; converted into a white powder and snorted in Minnesota; injected, smoked, or mixed in beverages in New Orleans; and boiled down to crystal form and snorted as an alternative to cocaine in New York City. Ketamine has been responsible for deaths in New Orleans and San Diego.

Clonazepam (Klonopin or Rivotril) was recently mentioned in hospital emergencies in New York City; in Texas, it is used by juveniles in combination with beer, just as flunitrazepam (Rohypnol) has been used. Alprazolam (Xanax, or "sticks"), along with clonazepam, has replaced flunitrazepam among adolescents in Miami, where "xanax candy bars" have caused several medical emergencies. In New York City, it is the most sought-after diverted prescription pharmaceutical and has almost replaced diazepam on the street. Diazepam is the most readily available and frequently used pharmaceutical depressant on the street in Chicago; it is the leading psychoactive prescription drug in New York City ED mentions; and is injected with heroin in Seattle. Flunitrazepam is common in Atlanta, popular among hard-core heroin and cocaine users in Los Angeles, continues to be abused in New Orleans, and is beginning to emerge in treatment indicators among youth along the Texas-Mexico border. In New Jersey, flunitrazepam no longer appears to be a problem. Trazedone (Desyrel) has been involved in numerous poisonings and one death in Detroit.

Depressants are used in Chicago in combination with a variety of drugs including heroin, cocaine, methamphetamine, or alcohol. In Miami, the use of diverted Schedule III and IV medications associated with concomitant upper and downer abuse appears on the rise, with "rolling and trolling" the rage among the "young and unknowing." Benzodiazepines are used in Phoenix to reduce "the edge" from cocaine or methamphetamine.

- **Hallucinogens** - Ethnographic, ED, law enforcement, and survey data suggest continued low-level abuse of lysergic acid diethylamide (LSD) and phencyclidine (PCP). Hallucinogen use appears to be increasing in Massachusetts, where lifetime use among students has been rising since 1994. In Chicago, primary hallucinogen admissions are increasing; LSD use in New Orleans is reportedly on the rise; the drug has sporadically reappeared in St. Louis-area high schools and rural areas. A new form of LSD appearing as a hard plastic translucent bubble pack with colors of light blue or red was reported in Detroit. In Texas, blotter acid is available on sugar cubes and triangular window panes, in a gel tab form called "jelly bean" that is popular in clubs, and in liquid form that is becoming more common around university and club scenes.

PCP use appears to be increasing in Chicago, where it is sprayed on a tobaccolike substance ("mint leaf" or "love leaf"), used as a dip on cigarettes ("sherm sticks"), or mixed with marijuana ("wicky stick" or "donk"). It appeared in 1997 ED mentions for the first time this decade in Minneapolis; a resurgence of manufacturing, mostly by African-American street gangs, is noted in Los Angeles. PCP-related ED mentions are declining in New York City, where it is available as a powder sprinkled on green mint leaves or on marijuana and as a liquid in small shaker bottles. It continues to be used as a dip on marijuana joints in St. Louis. Psilocybin mushrooms ("shrooms") were reported by Minneapolis law enforcement agencies.

- **Other Drugs** - Dextromethorphan (DXM) abuse is reported by teens in Boston, apparently encouraged by mentions on the Internet. In addition to the readily available store-bought liquid, DXM is available in Minneapolis as a white powder packaged in clear, unmarked capsules. Use of ephedrine, nitrous oxide, and other inhalants (including propane) is reported in Detroit. One accidental death in Minnesota was attributed to inhalation of an industrial solvent, and inhalant abuse has declined among students in grades 6, 9, and 12 since 1995. Toluene "huffing" is reportedly common among white males in their preteens or early teens in Philadelphia; in Texas, use of inhalants such as liquid or spray paint and correction fluid is increasing among school students. Khat seizures continue in Detroit; khat first appeared in Minnesota in 1997, and interceptions have increased in recent years.

1. Mortality figures are for 1997 versus 1998 and were available in 10 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 first half 1997 versus preliminary estimates for first half 1998; changes are noted only when statistically significant at $p < 0.05$.
3. 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 1997 versus 1998; changes are noted only when they are ≥ 5 percentage points.
4. Heroin price and purity information are from the Drug Enforcement Administration (DEA) Domestic Monitor Program; comparisons are for 1997 versus 1998.

Adolescent Substance Abuse and Psychiatric Comorbidity: Timing and Gender

This study used state of the art evaluation methods to assess a large population based sample longitudinally, relating the development of drug abuse to pre-existing psychiatric disorder, other risk factors, and sex. Boys, but not girls, who later developed dependence or abuse began substance use at earlier ages. Disruptive behavior disorders and depression were both associated with higher rates and earlier onset of substance use and abuse in both sexes, while anxiety predicted later onset of smoking. Family history of drug problems was the strongest correlate of early onset. Boys and girls showed much similarity in the course of early drug use and abuse, and in associated psychopathology. This study is notable for the size of the sample and the sophistication of the methodology and analyses, enabling new observations about development and gender in regard to onset of substance use problems. Costello, E.J., Erkanli, A., Federman, E., and Angold, A. The Development of Psychiatric Comorbidity with Substance Abuse in Adolescents: Effects of Timing and Sex. *Journal of Clinical Child Psychology*, 28, pp. 298-311, 1999.

Juvenile Substance Abuse, Delinquency, and Internalizing Problems

Longitudinal data from the Pittsburgh Youth Study on boys ages 7 to 18 were analyzed to examine the co-occurrence of persistent substance use with other problem behaviors, including attention deficit hyperactivity disorder, delinquency, and internalizing problems such as depression and anxiety. Developmental differences were found. Among preadolescents, those who continued to use drugs tended to be persistent delinquents, and half this group displayed persistent internalizing problems as well. Among adolescents, a third persisted in drug use without manifesting other problems. Substance use was least common among those with persistent internalizing problems only. While delinquency and internalizing problems predicted persistent drug use in preadolescents, and persistent delinquency predicted substance use in adolescents, ADHD was not a predictor of persistent substance use or delinquency. This study adds important findings to the literature on comorbidity and prediction of substance use problems in youth. Loeber, R., Stouthamer-Loeber, M., and White, H.R. Developmental Aspects of Delinquency and Internalizing Problems and Their Association with Persistent Juvenile Substance Use Between Ages 7 and 18. *Journal of Clinical Child Psychology*, 28, pp. 322-332, 1999.

Maternal Smoking During Pregnancy And Offspring Psychopathology

Data from a longitudinal study of depressed probands and normal controls were used to replicate findings from several other reports of an association between maternal smoking during pregnancy and attention deficit hyperactivity disorder, conduct disorder, and substance abuse in offspring. Among offspring of mothers who reported smoking 10 or more cigarettes per day during pregnancy, boys showed a significantly increased risk of early onset conduct disorder, and girls a significant increase in adolescent drug dependence. Controlling for several relevant

factors such as maternal substance abuse and parental diagnosis did not alter the findings. Thus, findings from several other studies were supported, underscoring concerns about the potential impact of prenatal exposure to maternal smoking. Weissman, M.M., Warner, V., Wickramaratne, P.J., Kandel, D.B. Maternal Smoking During Pregnancy and Psychopathology in Offspring Followed to Adulthood. *Journal of the American Academy of Child and Adolescent Psychiatry*, 38, pp. 892-899, 1999.

Association between Maternal Smoking During Pregnancy and Attention Deficit Hyper-activity Disorder

This study extends previous findings regarding maternal smoking and ADHD in offspring, by studying the siblings of probands in a high-risk (ADHD) sample. Maternal smoking during pregnancy was associated with over four times the risk of ADHD in offspring (OR 4.4) even when controlling for parental ADHD, parental IQ, and socioeconomic status. These findings replicate those of these authors and others. If confirmed in other populations and using other methods, these findings have implications for the need for prevention and smoking cessation programs for women of child-bearing age. Milberger, S., Biederman, J., Faraone, S.V., and Jones, J. Further Evidence Of An Association Between Maternal Smoking During Pregnancy And Attention Deficit Hyperactivity Disorder: Findings From A High-Risk Sample Of Siblings. *Journal of Clinical Child Psychology*, 27, pp. 352-358, 1998.

Deviance Training

Aggregating high-risk youth into groups can increase their substance use involvement and delinquency. Two random assignment studies are reviewed that reveal three-year and 30-year negative effects. These effects are most likely secondary to using high-risk peer groups to intervene. Analysis of videotaped interactions in the three-year outcome study and archival data in the 30-year study suggests that interest in and verbal and non-verbal expressions of deviancy within the group may increase investment in a delinquent lifestyle. "Deviance training" is defined as contingent positive reactions to rule breaking discussions. This study suggests a need for caution in using interventions that aggregate high-risk children in prevention and treatment. Dishion, T.J., McCord, J., and Poulin, F. Iatrogenic Effects that Aggregate High Risk Youth. *American Psychologist*, Vol. 54, September 1999. Deviance Training Among Anti-Social Boys One of the key risk factors in the etiology of adolescent problem behavior is association with deviant peers. This study examined the early adolescent friendships of 206 Oregon Youth Study boys who were recruited into the study at ages 9-10 from schools in neighborhoods with high rates of delinquency. Data were collected again at ages 13-14 and 15-16. Results suggest that boys identified as anti-social in childhood showed poor-quality friendships at ages 13 -14 and were the most vulnerable to subsequent peer influences in the following two years. Boys with both poor-quality friendships and a high level of delinquency at age 13-14 escalated in delinquent behavior in the subsequent two years. This study suggests that problem behavior in early adolescence, on occasion, functions to initiate and establish friendships. This process of deviancy training is highly related to an adolescent metamorphosis, in that early patterns of antisocial behavior turn into drug abuse and other forms of problem behavior. Poulin, F., Dishion, T.J., and Hass, E. The Peer Influence Paradox: Friendship Quality and Deviance Training Within Male Adolescent Friendships. *Merrill-Palmer Quarterly*, 45(1), pp. 42-61, 1999.

Many Problem Behaviors Form Single Construct

This study explored whether multiple problem behaviors form a single construct and whether the developmental model of antisocial behavior (Patterson and colleagues) generalizes to the development of other problem behaviors. Longitudinal data obtained from 204 adolescents and parents support a single construct for problem behavior comprised of youth antisocial behavior, high-risk sexual behavior, academic failure and substance use. Further, the data support the developmental model of antisocial behavior. That is, families experiencing high levels of conflict are more likely to have adolescents who engage in an array of problem behaviors at a two-year follow-up. This relationship was mediated by low levels of parent-child involvement, poor parental monitoring, and association by the adolescent with deviant peers. Ary, D.V., Duncan, T. E., Duncan, S.C., and Hops, H. Adolescent Problem Behavior: The Influence of Parents and Peers. *Behavior Research and Therapy*, 37, pp. 217-230, 1999.

Family Processes and Deviant Peers Related to Wide Array of Problem Behaviors

This study used structural equation modeling to evaluate a model of family and peer influence on problem behaviors using longitudinal data obtained from 523 adolescents. The study found that families with high levels of conflict were

less likely to have high levels of parent-child involvement. Such family conditions resulted in less adequate parental monitoring of adolescent behavior, making associations with deviant peers more likely. In turn, a lack of parental monitoring and association with deviant peers accounted for 46% of the variance in engagement in a variety of problem behaviors including substance use, antisocial behavior, academic failure, and risky sexual behavior. Although association with deviant peers was the most proximal social influence on problem behavior, parental monitoring and family factors (conflict and involvement) were key parenting practices that influenced this development process. Ary, D.V., Duncan, T.E., Biglan, A., Metzler, C. W., Noell, J. W., and Smolkowski, K. Development of Adolescent Problem Behavior. *Journal of Abnormal Child Psychology*, 27, pp. 141-150, 1999.

Association Between Hyperactivity and Executive Cognitive Functioning in Childhood and Substance Use in Early Adolescence

To determine whether deficient executive cognitive functioning (ECF) in association with high behavioral activity level increases the liability to substance abuse, researchers at the Center for Education and Drug Abuse Treatment (CEDAR) compared a high-risk (HR) group having fathers with a lifetime DSM-III-R diagnosis of a psychoactive substance use disorder with a low-average-risk (LAR) group whose fathers had neither psychoactive substance use disorder nor another adult Axis I psychiatric disorder. ECF and behavioral activity were measured using neuropsychological tests, activity monitor, diagnostic interview, and informant ratings when the subjects were 10 to 12 years of age. Alcohol, tobacco, and cannabis use were measured at 2-year follow-up. Findings indicate that at baseline the HR group had a significantly higher behavioral activity level and exhibited poorer performance on ECF tests than the LAR group. By early adolescence, HR subjects had a higher lifetime rate of tobacco and cannabis use and earlier age at onset of cannabis use. ECF capacity, but not behavioral activity level, predicted tobacco and cannabis use, total number of drugs ever tried, and severity of drug involvement. ECF accounted for additional variance beyond the effects of conduct problems on these outcomes. Whereas behavioral activity and ECF capacity in late childhood distinguishes HR from LAR youth, childhood ECF capacity is the more salient predictor of drug use in early adolescence. Aytaclar, S., Tarter, R.E., Kirisci, L., and Lu, S. *Journal of the American Academy of Child and Adolescent Psychiatry*, 38(2), pp. 172-178, 1999.

Changing Patterns of Drug Use Among U.S. Military Recruits Before and After Enlistment

The U.S. armed forces adopted "zero tolerance" policies concerning illicit drug use in 1980 and later developed policies to discourage tobacco and alcohol abuse. This article examines drug use among young active-duty recruits both before and after enlistment compared with non-military age-mates, and documents historical shifts in such drug use across 2 decades. Analyses employed longitudinal panel data from 20 nationally representative samples of high school seniors (cohorts of 1976-1995), each surveyed just before graduation and again within 2 years. Separate analyses for men (n = 12,082) and women (n = 15,345) contrasted those who entered military service, college, and civilian employment. Illicit drug use declined more among young military recruits than among their civilian counterparts. Analyses of male recruits at multiple time periods showed (1) declines in the prevalence of marijuana use and cocaine use after the initiation of routine military drug testing and (2) lower proportions of smokers of half a pack or more of cigarettes per day who entered service after the initiation of tobacco bans during basic training. Recent military drug policies appear to deter illicit drug use among enlistees and discourage some smokers from enlisting. Bachman, J.G., Freedman-Doan, P., O'Malley, P.M., Johnston, L.D., and Segal, D.R., *American Journal of Public Health*, 89(5), pp. 672-677, 1999.

Cigarette Smoking Among U.S. High School Seniors

This study identified high school seniors at low, moderate, and high risk for cigarette use to examine changes in the prevalence of daily smoking within risk groups from 1976 to 1995. Data were taken from the Monitoring the Future Project's national surveys of high school seniors. Risk classification was based on grade-point average, truancy, nights out per week, and religious commitment. Logistic regression models were used to estimate trends for all seniors and separately for White (n = 244,221), African American (n = 41,005), and Hispanic (n = 18,457) male and female subgroups. Risk group distribution (low = 45%, moderate = 30%, high = 25%) changed little over time. Between 1976 and 1990, greater absolute declines in smoking occurred among high-risk students (17 percentage points) than among low-risk students (6 percentage points). Particularly large declines occurred among high-risk African Americans and Hispanics. Smoking increased in all risk groups in the 1990s. Among high school seniors, a large part of the overall change in smoking occurred among high-risk youth. Policies and programs to reduce smoking among youth must have broad appeal, especially to those at the higher end of the risk spectrum. An, L.C., O'Malley,

P.M., Schulenberg, J.E., Bachman, J.G., and Johnston, L.D. American Journal of Public Health, 89(5), pp. 699-705, 1999.

Investigation of Family Associations Between ADHD And Substance Use Disorders

This paper reports on findings using the family study method to test hypotheses regarding familial associations between attention deficit hyperactivity disorder (ADHD) and substance use disorders (SUD). The risk for ADHD did not differ by SUD family status, and the risk for SUD did not differ by ADHD family status, but each disorder was associated with a significantly increased risk for that disorder in family members. These findings are consistent with independent transmission of ADHD and SUD in families. However, the probands are young adolescents, and follow up is needed to see if an association emerges as they pass through the age of risk for SUD. Milberger, S., Faraone, S.V., Biederman, J., Chu, M.P., Wilens, T. Familial Risk Analysis of the Association Between Attention Deficit Hyperactivity Disorder and Psychoactive Substance Use Disorders. Archives of Pediatric and Adolescent Medicine, 152, pp. 945-951, 1998.

Initial Drug Opportunities and Transitions to First Use

Researchers at Johns Hopkins University examined initial opportunities to try selected drugs and transitions from first opportunity to first use of those drugs. Target drugs were marijuana, cocaine, heroin, and hallucinogens. Investigators examined sex and race-ethnicity differences in estimates of having a drug opportunity, and in the probability of progressing from having an opportunity to try a drug to actually using the drug. Self-report interview data collected for the National Household Surveys on Drug Abuse (NHSDA) from 1979 to 1994 were analyzed. Results showed that an estimated 51% of US residents have had an opportunity to try marijuana; comparative estimates for cocaine, hallucinogens, and heroin are 23, 14, and 5%, respectively. Among those who eventually used each drug, the vast majority made the transition from first opportunity to first use within 1 year. Males were more likely than females to have opportunities to try these drugs, but were not more likely than females to progress to actual use once an opportunity occurred. Time trends indicate recent increases from 1990 to 1994 in the estimated probability of using an illicit drug once an opportunity occurs, particularly for hallucinogens. This study sheds light on the epidemiology of the earliest stages of drug involvement in the USA. Van Etten, M.L., and Anthony, J.C. Comparative Epidemiology of Initial Drug Opportunities and Transitions to First Use: Marijuana, Cocaine, Hallucinogens and Heroin. Drug and Alcohol Dependence, 54(2), pp. 117-125, 1999.

Salivary Cortisol Responses in Prepubertal Boys: The Effects of Parental Substance Abuse and Association with Drug Use Behavior During Adolescence

Using male index cases from the CEDAR sample, researchers extended earlier observation of decreased cortisol reactivity to an anticipated stressor in sons of fathers with a substance use disorder (SUD), examined whether salivary cortisol underresponsivity in these high-risk prepubertal boys is an adaptation to the stress associated with having a father with a current SUD, and tested whether prepubertal cortisol underreactivity might be associated with subsequent drug use behavior during adolescence. Preadolescent salivary cortisol responses were examined in the context of risk-group status, paternal substance abuse offsets, and subsequent adolescent drug use behavior. The results confirmed a decreased salivary cortisol response to an anticipated stressor among sons of SUD fathers. Lower anticipatory cortisol levels were found for boys whose fathers had a current SUD or an SUD that ended between the boys' 3rd to 6th birthdays than for sons of control fathers. Lower preadolescent anticipatory cortisol responses also were associated with regular monthly cigarette smoking and regular monthly marijuana use during adolescence. The investigators concluded that cortisol hyporeactivity as an adaptation to chronic stress may be a key component of the intergenerational transmission of substance abuse liability. Moss, H.B., Vanyukov, M., Yao J.K., and Kirillova, G.P. Biological Psychiatry, 45(10), pp. 1293-1299, 1999.

Inhalant Use and Delinquent Behavior Among Adolescents

To evaluate the association between inhalant use and delinquent or criminal behavior, an analysis of a large statewide sample survey of high school students was conducted. Five groups were identified based on reported drug use: inhalant experimenters, other drug experimenters, inhalant users, other drug users and non-users. Inhalant users were compared with other drug users and inhalant experimenters with other drug experimenters on measures of problem behavior. Over 13,000 students in grades 7-12 participated in the 1993 survey on drug use. Three

measures of problem behavior were included: drinking and drug-taking, "trouble behavior", and minor criminal activity. Among upper (9-12) grade level students only, both inhalant users and inhalant experimenters reported more minor criminal activity than other drug users and other drug experimenters, respectively. A similar trend was noted for trouble behavior. The same was not found for drinking and drug-taking behavior. The findings suggest that inhalant use is categorically different from other drug use, and that it has more in common with general delinquency than with general drug use. Prevention and treatment strategies should take this into consideration. Mackesy-Amiti, M.E. and Fendrich, M. *Addiction*, 94(4), pp. 555-564, 1999.

Adolescent Drug Use and Adult Drug Problems in Women

The authors studied effects of variables assessed in adolescence on problems from drug use in adulthood in a community sample of women. One focus of this 13-year longitudinal study was moderators, which were hypothesized to exacerbate, or attenuate, the effects of early drug consumption on later drug problems. Potential moderators were sensation seeking, social conformity, academic orientation, parental support, depression, and drug problems in parents. Direct and mediating effects of these variables, as well as of drug consumption, were also evaluated. Results showed that most of the significant effects involved sensation seeking and social conformity. In addition, adolescent drug use significantly predicted adult polydrug problems. The effects of sensation seeking are consistent with the view that this variable reflects a sensitivity to drug use, which makes it more likely that drug use gets translated into drug abuse. Stacy, A.W., and Newcomb, M.D. *Experimental and Clinical Psychopharmacology*, 7(2), pp. 160-173, 1999.

Substance Use Established by Ages 14-15 Can Be Predicted by Academic and Social Behavior Displayed at Ages 7-9

This study examined early school-based academic and social variables with concurrent family conflict in predicting adolescent alcohol and other drug use. Children (N=335) were assessed initially in grades 2-4 on academic-related and social behavior variables using teacher ratings and rankings, peer nominations and ratings and direct observation of playground and classroom behavior. They were reassessed in grades 9-10, using interviews and questionnaires to determine the initiation and sequence of their use of alcohol, tobacco, marijuana and other hard drugs. In analyses done independently for males and females, lifetime abstainers were compared with adolescents who had used: (1) only alcohol; (2) alcohol and tobacco; (3) alcohol, tobacco and marijuana; and (4) all three plus other hard drugs. The drug classifications represent a normative-deviant continuum of adolescent drug use. Constructs were developed for early academic and social predictors as well as concurrent family conflict. Results showed more wide-ranging academic and social difficulties during elementary school for children falling at the more deviant end of the drug use continuum. For girls, the concurrent home environment appeared to moderate the effect of early academic and social variables. In effects, substance use established by ages 14-15 could be predicted by academic and social behavior displayed at ages 7-9. Hops, H., Davis, B., and Lewin, L.M. *The Development of Alcohol and Other Substance Use: A Gender Study of Family and Peer Context*. *Journal of Studies on Alcohol*, pp. 22-31, Supplement, 13 March 1999.

High Rate of Coexisting Psychiatric Disorders among Adolescents with Substance Use Disorders in the Community

To investigate the extent to which adolescents in the community with current substance use disorders (SUD) experience co-occurring psychiatric disorders, diagnostic data were obtained from probability samples of 401 children and adolescents, aged 14 to 17 years, and their mothers/caretakers, who participated in the Methods for the Epidemiology of Child and Adolescent Mental Disorders (MECA) Study. Results indicate the rates of mood and disruptive behavior disorders are much higher among adolescents with current SUD than among adolescents without SUD. Comparison with adult samples suggests that the rates of current comorbidity of SUD with psychiatric disorders are the same among adolescents as adults, and lower for lifetime disruptive disorders/antisocial personality disorder among adolescents than adults. The high rate of coexisting psychiatric disorders among adolescents with SUD in the community needs to be taken into account in prevention and treatment programs.. Kandel, D.B., Johnson, J.G., Bird, H.R., Weissman, M.M., Goodman, S.H., Lahey, B.B., Regier, D.A., and Schwab-Stone, M.E. *Psychiatric Comorbidity among Adolescents with Substance Use Disorders: Findings from the MECA Study*. *Journal of the American Academy of Child and Adolescent Psychiatry*, 38(6), pp. 693-699, 1999.

Flunitrazepam Becoming Health Concern to Sexually Active Young Women in Southwestern U.S.

Flunitrazepam [Rohypnol"] is a short-acting benzodiazepine with general properties similar to those of diazepam. In a cross-sectional survey to determine prevalence, patterns, correlates and physical effects of voluntary flunitrazepam use in a sample of sexually active adolescent and young women 14 to 26 years of age (N=904) using university-based ambulatory reproductive health clinics, lifetime use was reported by 5.9% (n = 53) of subjects, with frequency of use ranging from 1 to 40 times. Flunitrazepam was taken most often with alcohol (74%), and 49% took this substance with other illicit drugs. Logistic regression analyses controlling for age and race/ethnicity found that users were significantly more likely than were nonusers to report lifetime use of marijuana (odds ratio [OR] = 3.6) or LSD (OR = 5.2), having a peer or partner who used flunitrazepam (OR = 21.7), pressure to use flunitrazepam when out with friends (OR = 2.7), and a mother who had at least a high school education (OR = 2.6). Finally, 10% of voluntary users reported experiencing subsequent physical or sexual victimization. Voluntary use of flunitrazepam is becoming a health concern to sexually active young women who reside in the southwestern United States. Young women who have used LSD or marijuana in the past or who have a peer or partner who used this drug appear to be at the greatest risk. Rickert, V.I., Wiemann, C.M., Berenson, A.B. Prevalence, Patterns, and Correlates of Voluntary Flunitrazepam Use. *Pediatrics* 103(1), pp. E61-E65, 1999.

Estimation of the Prevalence of Substance Use Problems Among Nurses Using Capture-Recapture Methods

This study estimated the lifetime prevalence of substance use problems among registered nurses using capture-recapture methods with two separate items indicating a history of substance use problems from the same questionnaire. Capture-recapture methods yielded an estimate of 6.4% of nurses with a history of substance use problems, a 22% increase in the estimate from the data as collected. Among respondents indicating no history of problems, a substantial number reported substance use behavior that was as high as those in the reported problem group, suggesting that the estimate of additional unreported cases (from capture-recapture) is plausible. This estimate provides valuable information for planning preventive initiatives for nurses, and the methodology should invite further consideration of multiple measures of a variable as sources to estimate prevalence using capture-recapture methods. Trinkoff, A., Zhou, Q. and Storr, C. *Journal of Drug Issues*, 29(1), pp. 187-198, 1999.

Prospective Study of Tobacco Smoking and Substance Dependencies Among Samples of ADHD and Non-ADHD Participants

This study focused on a group of young adults who as children had attention deficit/hyperactivity disorder (ADHD) and are at high risk for heavy use of licit and illicit substances. The study participants were part of a longitudinal study of the life histories of 492 children, one third who were identified as hyperactive in 1974 and whose childhood symptom ratings and medical histories were used to establish the Diagnostic and Statistical Manual of Mental Disorders (3rd edition, revised; DSM-III-R) ADHD diagnoses. The objectives of the study centered on describing (a) developmental history of tobacco use among ADHD and non-ADHD participants in a longitudinal sample, (b) the characteristic adult patterns of tobacco use from early adolescence through early adulthood, and (c) the relationship between ADHD status and tobacco and substance dependence outcomes. Adult data were obtained for 81% of the original 492 participants. Lifetime and current tobacco use were assessed from child, adolescent, and adult data, yielding eight measures of smoking status. The study showed that participants with and without ADHD did not differ in age of initiation to smoking, but there was a significant difference in the age smoking regularly began. By age 17, 46% of all participants with ADHD, as contrasted with 24% of the age-mate controls, reported smoking cigarettes daily. In adulthood, the proportion of participants with ADHD who were current smokers (42%) continued to exceed that of the age -mate controls. They were significantly different lifetime tobacco dependence rates - 40% compared to 19% for age mate controls. The rates for cocaine dependence were 21% for participants with ADHD and 10% for age mate controls. The rates for stimulants were 20% for participants with ADHD and 11% for age mate controls. Results were interpreted to support a possible link between ADHD treatment histories, and levels of tobacco smoking and tobacco dependence in adulthood. Lambert, N. and Hartsough, C. *Journal of Learning Disabilities* 31(6) pp. 533-544, 1998.

Cloninger's Constructs Related to Substance Use Level and Problems in Late Adolescence

Cloninger's constructs of novelty seeking, harm avoidance, task-reward dependence, and social reward dependence have been related to smoking and alcohol use in adolescence and adulthood. A study at Yeshiva University tested the role of these constructs as mediators related to substance use level and substance use problems. Participants were

1,225 adolescents with average age of 15.5 years. Structural modeling showed indirect effects for novelty seeking, harm avoidance, and task reward dependence, mediated through self-control; harm avoidance also had an inverse direct path to substance use level. Social reward dependence had a positive direct path to coping motives for substance use. Good self-control had inverse paths to negative life events and deviant peer affiliations; poor self-control had positive paths to negative life events and coping motives; and risk taking had positive paths to coping motives and peer affiliations. These findings suggest that substance abuse prevention programs should incorporate components focusing on beliefs about the functions of substance use and that treatment programs for substance abusers should include self-control training that targets behavior patterns such as anger proneness and impulsive responding. Wills, T.A., Sandy, J.M., and Shinar, O. Cloninger's Constructs Related to Substance Use Level and Problems in Late Adolescence: A Mediational Model Based on Self-Control and Coping Motives. *Experimental and Clinical Psychopharmacology*, 7(2), pp. 122-134, 1999.

Drinking and Driving Among U.S. High School Seniors

This article reports the prevalence of, and trends in, driving after drinking and riding in a car with a driver who has been drinking among American high school seniors, based on data from more than a decade (1984-1997) of annual national surveys. Logistic regression was used to assess the effects of demographic factors (gender, region of country, population density, parental education and race/ethnicity) and selected "lifestyle" factors (religious commitment, high school grades, truancy, illicit drug use, evenings out per week, and miles driven per week). Rates of adolescent driving after drinking and riding with a driver who had been drinking declined significantly from the mid-1980s to the early or mid-1990s, but the declines have not continued in recent years. Rates of driving or riding after drinking were higher among high school seniors who are male, White, living in the western and northeastern regions of the United States, and living in rural areas. Truancy, number of evenings out, and illicit drug use all related significantly positively with the dependent variables, whereas grade point average and religious commitment had a negative relationship. Miles driven per week related positively to driving after drinking. O'Malley, P.M., and Johnston L.D. *American Journal of Public Health*, 89(5), pp. 678-684, 1999.

Family History of Substance Use Disorder Moderates Relation between Cognitive Distortions and Aggressive Behavior and Aggressive Behavior and Drug Use for Adolescent Boys

The purpose of this study was to determine whether the relations between (a) cognitive distortions and aggressive behavior, (b) cognitive distortions and drug use, and (c) aggressive behavior and drug use are moderated by a family history of a substance use disorder (SUD) in adolescent boys. Participants were 165 boys aged 15-17 years with (FH+; N=75) and without (FH-; N=90) a family history of SUD. Results indicated that a family history of SUD moderated the relation between cognitive distortions and aggressive behavior and the relation between aggressive behavior and drug use. Family history of SUD did not moderate the relation between cognitive distortions and drug use; however, cognitive distortions were positively related to drug use within both groups. Giancola, P.R., Mezzich, A..C., Clark, D.B., and Tarter, R.E. Cognitive Distortions, Aggressive Behavior, and Drug Use in Adolescent Boys With and Without a Family History of a Substance Use Disorder. *Psychology of Addictive Behaviors*, 13(1), pp. 22-32, 1999.

Adolescent School Experiences and Dropout, Adolescent Pregnancy, and Young Adult Deviant Behavior

Predictive effects of school experiences were studied over a 7-year interval in a random community sample of 452 adolescents, 12 through 18 years of age. Outcomes examined included dropping out of school, adolescent pregnancy, engaging in criminal activities, criminal conviction, antisocial personality disorder, and alcohol abuse. Logistic regression showed academic achievement, academic aspirations, and learning-focused school settings to be related to a decline in deviant outcomes independent of the effects of disadvantaged socioeconomic background, low intelligence, childhood conduct problems, and having deviant friends during adolescence. Associations between school conflict and later deviancy were mediated by deviant peer relationships in adolescence and other school characteristics. Prior research reporting continuity of childhood conduct problems and the influence of adolescent affiliations with deviant peers on negative outcomes was supported. Implications for using the school context in risk factor research and the practical applications of such research for intervention are discussed. Kasen, S., Cohen, P., and Brook, J.S. *Journal of Adolescent Research*, 13 (1), pp. 49-72, 1998.

Resisting Temptations To Smoke: Results Using Within-Subjects Analyses

This study used within-subjects analyses to examine resisted temptations to smoke and lapses, providing a methodological advance over most previous studies of cigarette smoking relapse. One hundred thirty participants who lapsed within one month after a self initiated cessation attempt were questioned about both a resisted temptation to smoke and their first lapse. Participants were much more likely to report using coping strategies during the resisted temptation than during the lapse, and those who reported coping during both situations were more likely to report that they used multiple strategies and combined cognitive and behavioral strategies during the resisted temptation. Participants were more likely to report that the lapse was precipitated by others' smoking, but this difference was not significant when the sample was restricted to participants who reported a specific close call. Results support previously reported findings that the use or nonuse of coping strategies during a temptation to smoke is the variable most strongly associated with its outcome. Bliss, R.E., Garvey, A.J., and Ward, K.D. *Psychology of Addictive Behaviors*, 13 (2), pp. 143-151, 1999.

Parents Educational Attainment Influences Prevention Assessment Attrition

This study examined whether family risk factors predict attrition in a prevention intervention project that incorporated procedures to increase retention in assessment and intervention activities. Data from 667 rural families collected in four waves were analyzed. Data consisted of young adolescent and parent reports of internalizing and externalizing problems, observer rating of distress in parent-child interactions, and family socioeconomic status (SES). SES was a significant predictor of assessment attrition: follow-up analyses indicated that this relationship was due to lower educational attainment rather than income. None of the social-emotional or SES factors examined predicted intervention participation. Spoth, R., Goldberg, C., and Redmond, C. *Engaging Families in Longitudinal Preventive Intervention Research: Discrete-Time Survival Analysis of Socioeconomic and Social-Emotional Risk Factors*. *Journal of Clinical and Consulting Psychology*, 67(1), pp. 157-163, 1999.

Interpersonal Aggression in Urban Minority Youth

This study examined perceived social environmental and personal control variables as predictors of interpersonal aggression in urban minority youth. Perceived environmental factors including neighborhood risk, friends' delinquency, and parental monitoring practices, were examined as direct predictors of aggression and as indirect predictors mediated by anger control skills and risk-taking characteristics. The sample consisted of 452 primarily African-American sixth graders attending New York City public schools. Results of structural equation modeling indicated that perceived higher levels of parental monitoring were directly associated with less aggression and had an indirect effect mediated through better anger control skills. Perceived neighborhood risk and friends' delinquency were directly associated with more aggression and were indirectly effected through greater individual risk-taking. Griffin, K.W., Scheier, L.M., Botvin, G.J., Diaz, T. and Miller, N. *Interpersonal Aggression in Urban Minority Youth: Mediators of Perceived Neighborhood, Peer, and Parental Influences*. *Journal of Community Psychology* 27(3), pp. 281-296, 1999.

Drug Use Among Puerto Ricans: Ethnic Identity as a Protective Factor

This study assessed the relationship of multiple drug risks, Puerto Rican identity, and drug use. Structured interviews were conducted with 555 Puerto Rican males and females whose mean age was 19. Each risk factor and two ethnic variables were related to drug use. Regressions showed that cultural knowledge, being culturally active, group attachment, and identification with Puerto Ricans offset the impact of risk factors on drug use. Ethnic variables also enhanced the protective effect of other protective factors. In sum, the results substantiate expanding risk-buffering models to include ethnic identity and the protective role of ethnic identity for Puerto Rican youth. Brook, J. S., Whiteman, M., Balka, E. B., Win, P. T., and Gursen, M. D. *Journal of Hispanic Research*, 20(2), pp. 241-254, 1998.

Different Characteristics Associated with Reported Versus Unreported Cases of Childhood Rape; Few Cases of Childhood Rape Actually Reported to Authorities

This study was to examine whether there would be differences in reported versus unreported cases of childhood rape on incident characteristics including life threat, physical injury, identity of the perpetrator, frequency of assault(s),

and rates of posttraumatic stress disorder or major depression. Using a telephone interview, a national probability sample of 4,008 (weighted) adult women was screened for a history of completed rape in childhood. Respondents were also assessed for DSM-III-R diagnoses of major depressive episode and/or posttraumatic stress disorder (PTSD), and substance use. Three hundred forty-one (8.5%) of these women were victims of at least one rape prior to the age of 18, for a total of 437 completed rapes. Of these 437 rape incidents, 52 (11.9%) were reported to the police or other authorities. Significant differences were obtained between reported versus nonreported cases on incident characteristics, including life threat, physical injury, identity of the perpetrator. Reported cases were more likely to involve life threat and/or physical injury, and were more likely to have been committed by a stranger than nonreported cases. No significant differences between reported and nonreported cases were found concerning whether the rape involved a single incident versus series of events, or rates of PTSD or major depression. Findings suggest that different characteristics are associated with reported versus unreported cases of childhood rape. Hanson, R.F., Resnick, H.S., Saunders, B.E., Kilpatrick, D.G., and Best, C. Factors Related to the Reporting of Childhood Rape. *Child Abuse and Neglect* 23(6) pp. 559-569, 1999.

Vulnerability to Drug Use Among Latino Adolescents

In this study, risk and protective factor indices were developed to examine vulnerability to drug use among Latino high school students. Survey data were collected from 516 Latino 9th and 10th grade youth in the Los Angeles area. Frequency and quantity of use data were collected for cigarettes, alcohol, marijuana, inhalants, cocaine, and other illicit drugs. Few gender differences emerged in prevalence of drug use and about 25% were already involved in heavy drug use. Seventeen variables were examined for inclusion in a risk factor index (RFI) or protective factor index (PFI). Bivariate, multivariate, and structural equation models (SEM) were employed in the analysis of data. All of the variables except for one were more risk-inducing than protective for these Latino youth. However, as a group, the PFI predicted several types of drug use for boys and girls, and moderated the adverse effects of the RFI. At a high level of risk, a high level of protection was associated with reduced use for some types of drugs. In the SEM, vulnerability to drug use as indicated by the RFI and PFI was strongly associated with drug use for both boys and girls and more strongly related to drug use than the RFI or PFI alone. These results have exciting implications for intervention. Felix-Ortiz, M. and Newcomb, M.D. *Journal of Community Psychology*, 27(3), pp. 257-280, John Wiley & Sons, Inc., 1999.

Effect of Parent-Child Relations on Child Oppositional Behavior

This study is one of a series modeling sequences of intervention effects on parenting or family protective processes influencing various distal child outcomes. It was hypothesized that (1) positive parent-child affective quality would have a direct negative effect on child oppositional behavior both concurrently and across time, (2) that over time child oppositional behavior would have a negative effect on positive parent-child affective quality, and (3) that child's sense of mastery would have a negative effect on oppositional behavior. Data were obtained from family members participating in a family competency building intervention studies. The model was tested twice with independent samples. Sample one (n=171) participated in a pilot study of the Preparing for the Drug Free Years Intervention (PDFY); sample two (n=361) participating in a longitudinal evaluation of the PDFY. Attendance in the intervention was used as a control factor, with those in control groups being scored zero. Results of covariance structure modeling were generally consistent with the hypothesized model for both samples. Consistent with prior research, parent-child affective quality played a significant role in oppositional behavior. However, the opposite was not true in this general population study. That is, adolescent oppositional behavior did not have a strong negative effect on subsequent parent-child affective quality. There was also a weaker than expected relationship between sense of mastery and oppositional behavior. Spoth, R., Redmond, C., Shin, C., and Huck, S. A. Protective Process Model of Parent-Child Affective Quality and Child Mastery Effects on Oppositional Behaviors: A Test and Replication. *Journal of School Psychology*, 37(1), pp. 49-71, 1999.

Victimization--Socioeconomic Impact of Interpersonal Violence on Women

Prospective data from a nationally representative sample of women were used to examine 4 objective indexes of social adjustment following direct, interpersonal crime. Household income, marital status, employment, and education level were evaluated as risk factors for, and outcomes of victimization. Data were collected in 3 waves at 1-year intervals, and 2,863 women completed all 3 waves. Results indicate that women experience increased risk for victimization when income is below poverty level and when newly divorced. Further, victimization appears to increase women's risk for unemployment, reduced income, and divorce. The cyclical nature of victimization is discussed.

Byrne, C.A., Resnick, H.S., Kilpatrick, D.G., Best, C.L., and Saunders, B.E. The Socioeconomic Impact of Interpersonal Violence on Women. *Journal of Consulting and Clinical Psychology* 67(3), pp. 362-366, 1999.

Family and Peer Correlates of Behavioral Self-Regulation in Boys at Risk for Substance Abuse

A study at CEDAR focused on behavioral self-regulation (BSR), which was operationally defined as the degree to which one can control one's own activity and reactivity to environmental stimuli. BSR has been posited to be an important determinant of the onset of adolescent substance abuse. The goal of this study was to clarify particular family and peer correlates of BSR in at-risk sons. Subjects were 10-12-year-old sons of substance-abusing fathers (high-average risk [HAR]; n = 176) and normal controls (low-average risk [LAR]; n = 199). A BSR latent trait was developed using multiple measures and multiple informants. Analyses included separate hierarchical linear regressions for HAR and LAR groups. In the hierarchical linear model for HAR sons, family dysfunction and deviant peer affiliation were significantly associated with BSR, whereas for LAR sons, only peer affiliation was significantly associated with BSR. These findings suggest that empirical, theory-guided interventions to prevent worsening of BSR in HAR boys should address specific interpersonal family, and peer factors. Dawes, M., Clark, D., Moss, H. Kirisci, L., and Tarter, R. *American Journal of Drug and Alcohol Abuse*, 25(2), pp. 219-237, 1999.

The Validity of Drug Use Reporting Based on Hair Tests

Hair specimens were collected from 322 subjects and analyzed as part of an experimental study administering household surveys during 1997 to a high-risk community sample of adults from Chicago, Illinois. Toxicologic results were compared with survey responses about use of cocaine and heroin. About 35% of the sample tested positive for cocaine, and 4% tested positive for heroin. Sample prevalence estimates of cocaine use based on toxicological results were nearly five times the survey-based estimates of past month use and nearly four times the survey-based estimates of past year use. With the hair test results as the standard, cocaine and heroin use were considerably underreported in the survey. Underreporting was more of a problem for cocaine than for heroin. Among those who tested positive, survey disclosure of cocaine use was associated with higher levels of cocaine detected in hair. In general, when recent drug use was reported, it was usually detected in hair. When a drug was detected in hair, use was usually not reported in the survey. When heroin was detected in hair, cocaine was almost always detected as well. Fendrich, M., Johnson, T.P., Sudman, S., Wislar, J.S., and Spiehler, V. *Validity of Drug Use Reporting in a High-Risk Community Sample: A Comparison of Cocaine and Heroin Survey Reports with Hair Tests. American Journal of Epidemiology*, 149(10), pp. 955-962, 1999.

Social Influence and Psychological Determinants of Smoking Among Inner-City Adolescents

Adolescent economically disadvantaged households appear at high risk for smoking. This study focused on a sample of economically disadvantaged adolescents attending New York City schools (N=1875). Longitudinal predictors of smoking from four domains (socio-demographic background, social influences, social and personal competence, and individual differences) were tested. Social influences to smoke from mothers and friends both predicted smoking one year later. Poor decision-making skills and low psychological well-being also predicted subsequent smoking. Results suggest that training adolescents to resist social influences to smoke, problem solve, make sound decisions, and to cope with psychological distress are key components for effective smoking prevention approaches. Epstein, J.A., Botvin, G.J., and Diaz, T. *Social Influence and Psychological Determinants of Smoking Among Inner-City Adolescents. Journal of Child & Adolescent Substance Abuse*, 8(3), pp. 1-19, 1999.

Marijuana Use Among Minority Youths Living in Public Housing Developments

Youths residing in public housing developments are at heightened risk for drug use. The purpose of this study was to develop and test a model of marijuana etiology with adolescents (N=624) residing in public housing. African-American and Hispanic seventh graders completed questionnaires about their marijuana use, social influences to smoke marijuana, and sociodemographic and psychosocial characteristics. Results indicate that social influences, such as friends' marijuana use and perceived ease of availability of marijuana significantly predicted both occasional and future intentions to use marijuana. Individual characteristics such as anti-marijuana attitudes and drug refusal skills also predicted marijuana use. The findings imply that effective prevention approaches that target urban youths residing in public housing developments should provide them with an awareness of social influences to use marijuana, correct misperceptions about the prevalence of marijuana smoking, and train adolescents in relevant psychosocial

skills. Williams, C, Epstein, J., Botvin, G.J., and Ifill-Williams, M. Marijuana Use Among Minority Youths Living in Public Housing Developments. *Journal of Urban Health: Bulletin of the New York Academy of Medicine*, 76(1), pp. 85-101, 1999.

Comparison of Live and Video Prevention Messages

A Perception of Performance Scale was developed to compare delivery of a single drug prevention message which was modified into one of two modalities: live performance versus video performance. Scale development was undertaken in a pilot study with 334 undergraduate students at a large university in the southwestern U.S. Exploratory and Confirmatory Factor Analysis showed the scale had three dimensions; identification, interest, and realism with reliabilities of .86, .89 and .90, respectively. The main study consisted of 465 students (52% female, 75% European American, 12% Hispanic, and 13% other) in a single high school who were randomly assigned to either performance condition. Results indicate that live performance was significantly more interesting and realistic than video performance, suggesting that live performance may be a more effective medium for engaging high school aged youth. Miller, M., Hecht, M. & Stiff, J. An Exploratory Measurement of Engagement of Live and Film Media. *Journal of the Illinois Speech and Theatre Association*, 49, pp. 69-83, 1998.

The Role of Personal Relationships in Drug Resistance

The purpose of this study was to better understand the role of adolescents' personal relationships in drug offer scenarios. More than 2,000 junior high school students from 31 schools participated in a questionnaire study that asked them to describe a time when they were offered drugs. Results indicate that adolescents are most frequently offered drugs by close associates (same-sex friends, romantic partners, and brothers or male cousins), with offers from family members or romantic partners being particularly difficult to resist. Although simpler offers were the most frequent type of offer, nonverbal presentation of the drug was the most effective. Students typically resisted by saying no and leaving the situation, but these strategies were not as effective across all relational partners. Response complexity (more involved than simple answers of 'no') was a better predictor of resistance than offer complexity. Trost, M.R., Langan, E.J., & Kellar-Guenter, Y. Not Everyone Listens When You 'Just Say No': Drug Resistance in Relational Context. *Journal of Applied Communication Research*, 27, pp. 120-138, 1999.

Close Parent-Child Bond Mitigates Risks of Adolescent Drug Use and Delinquency

A study was conducted to identify general and differentiating risk and protective factors from domains of culture and ecology, peer, family, and personality, related to adolescent delinquency and marijuana use, and to examine the protective role of the parent-child mutual attachment in offsetting cultural and ecological risk factors, leading to less delinquency and marijuana use. The study design consisted of a cross-sectional analyses of interview data collected in Colombia. A total of 2837 Colombian adolescents, 12 to 17 years of age participated. Adolescents were interviewed in their homes. Independent variables included measures from 4 domains: culture and ecology, peer, family, and personality. The dependent variables were delinquency and marijuana use. Results show that several risk factors, such as tolerance of deviance and sensation seeking, were similarly related to both delinquency and marijuana use, suggesting that a common cause underlies the propensity to engage in different deviant behaviors. Some risk factors were more involved in delinquency and other risk factors were more highly related to the adolescent's marijuana use. Finally, when violence is endemic and illegal drugs are readily available, a close parent-child bond was capable of mitigating these risk factors, leading to less marijuana use and delinquency. The findings have implications for public health policy related to interventions in countries in which violence and drug use are prevalent. The results point to intervention procedures aimed at adolescents vulnerable to marijuana use and delinquency as well as efforts aimed at specific vulnerabilities in these areas. For example, reducing the risk factors and enhancing the protective factors for marijuana use and delinquency may result in less adolescent marijuana use and delinquency. Brook, J., Brook, D., De La Rosa, M., Whiteman, M., and Montoya, I. The Role of Parents in Protecting Colombian Adolescents from Delinquency and Marijuana Use. *Arch Pediatr Adolesc Med*, 153(5), pp. 457-64, 1999.

Substance Abuse as a Predictor of VA Medical Care Utilization among Vietnam Veterans

The primary objective of this research was to determine whether Vietnam veterans who had alcohol or drug use problems prior to, during, or immediately after the war, used Veteran's Administration (VA) health care services more intensively during the next two decades than Vietnam veterans without these behaviors. The secondary objective was

to identify predictors of VA health services utilization among data collected at service discharge. Logistic and ordinary least squares regression were used to model the effect of predisposing, enabling, and need factors on utilization of VA health services (N=571). Results show that Vietnam veterans who had substance use problems, whether before or immediately after Vietnam, used VA health care services more intensively during the next two decades than Vietnam veterans without these behaviors. Depression and psychiatric care seeking were also important predictors. These findings suggest that more research is needed to evaluate the impact of health system characteristics and private sector use on the predictive ability of the models. Virgo, K.S., Price, R.K., Spitznagel, E.L., and Ji, T.H. *The Journal of Behavioral Health Services & Research*. 26(2), pp. 126-139, 1999.

Adolescent Marijuana Use Found Incompatible with Assumption of Adult Roles

A longitudinal study examined the relationship between marijuana use and the assumption of adult roles, as well as the relationship between assuming adult roles and the likelihood of later marijuana use. Data were collected at 5 points in time from childhood through early adulthood (late 20s) by means of a structured questionnaire. Participants' marijuana use and the assumption of adult roles, including employment, marriage, parenthood, and living arrangements, were measured, and the data were analyzed with logistic regression analyses. A history of marijuana use was associated with an increased risk of adopting more unconventional adult roles, such as postponement of marriage, having a child out of wedlock, and unemployment. These results suggest that frequent prior marijuana use may adversely affect one's ability to successfully assume conventional adult roles. Furthermore, controlling for earlier marijuana use, marriage during early adulthood significantly decreased the risk of later marijuana use. Brook, J., Richter, L., Whiteman, M., and Cohen, P. *Consequences of Adolescent Marijuana Use: Incompatibility with the Assumption of Adult Roles*. *Genet Soc Gen Psychol Monogr*, 125(2), pp. 193-207, 1999.

Job Strain and Non-Medical Drug Use

In this study, the Karasek demand/control hypothesis of job strain, initially used in research on cardiovascular health, was extended to drug use. Full time nurses (n=2,375), all participants in a national anonymous mailed survey, were an estimated 1.5 times more likely to be a recent non-medical drug user if they had a high strain job as compared to nurses in low strain jobs. The psychosocial work environment might influence whether nurses become and remain non-medical drug users, over and above the risk modifying functions related to nurses' individual vulnerabilities and their greater access to controlled substances. Storr, C.L., Trinkoff, A.M., and Anthony, J.C. *Drug and Alcohol Dependence*, 55, pp. 45 -51, 1999.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse
September, 1999**

Research Findings

Intramural Research

Molecular Neuropsychiatry Section, Cellular Neurobiology Branch

Comparative Toxic Effects of Methamphetamine and Dopamine in Cell Culture Potentiation by Serum Withdrawal

Methamphetamine (METH)-and dopamine (DA)-have been shown to cause neurotoxic damage both in vitro and in vivo. The mechanisms of action are thought to involve the production of pathophysiologic concentration of free radicals. It is, however, not clear to what extent the effects of these two toxins mimic each other. The present study was undertaken to compare and contrast the toxic effects of METH and DA by using an immortalized neural cell line. Both METH and DA caused dose-dependent increased production of reactive oxygen species (ROS) and cell death. Cell death caused by these agents was characterized by cytoplasmic vacuolar formation, shrinkage of cytoplasm and nuclear dissolution. Flow cytometric evaluation also revealed that these toxins cause changes similar to those observed in cells undergoing apoptosis. Furthermore, DNA electrophoresis showed that both METH-and DA-induced DNA ladder formation. When taken together these observations suggest the METH and DA cause these cells in low (1%) serum or in the absence of serum markedly enhanced the apoptotic effects of both drugs. These data provide further support for the idea that both METH and DA can cause ROS mediated apoptosis. Cadet, J.L., Ordonez, S., and Burrell, S., Panel Presentation, 1999. Satellite Meeting of the International Society for Neurochemistry and European Society of Neurochemistry, Cellular and Molecular Mechanisms of Drugs of Abuse: Cocaine, Ibogaine and Substituted Amphetamines, Berlin, Germany, August 7-15, 1999.

Clinical Pharmacology Section/Clinical Pharmacology & Therapeutics Branch

Influence of Enforced Abstinence on Cocaine Use by Research Subjects

Clinical experience suggests that enforced abstinence, per se, without treatment intervention, has little influence on future drug use, nor does research exposure to abusable drugs. We addressed these issues in 14 chronic heavy cocaine users undergoing 90 days of abstinence (with 6 subjects getting an intranasal cocaine challenge at the end of the first and last weeks) on the closed NIDA IRP research ward. Subjects were followed for several weeks prior to admission to evaluate their baseline pattern of drug use by self-report and urine drug screening. There were no explicit treatment activities on the ward. Subjects returned for follow-up visits weekly for the first month after discharge; none were participating in treatment. At each visit they reported their daily drug use since the last visit and provided a sample for urine toxicology. Over the month prior to admission and after discharge, subjects used cocaine on 74+5% and 28+7% of the days, respectively ($p=0.003$), and spent \$41.60+10.10 and \$56.40+14.00 per day of use on cocaine ($p=0.26$). There were no significant changes in subjects' alcohol or marijuana use. Subjects

receiving a cocaine challenge did not differ from others in drug use after discharge. These findings suggest that a period of enforced abstinence without treatment during research participation can significantly decrease the frequency of cocaine use in the short-term, while not changing amount of cocaine used per day of use. Study limitations include small sample size (yielding low power to detect differences) and 22% missing data. Gorelick, D.A., Sacks, N., Nelson, R., Bencherif, B., and Frost, J.J. Influence of Enforced Abstinence on Cocaine Use by Research Subjects. Presented at American Society of Addiction Medicine, 30th Annual Medical-Scientific Conference, New York, NY, April, 1999. *Journal of Addictive Diseases* 18(2), p. 115, 1999.

Chemistry & Drug Metabolism Section/Clinical Pharmacology & Therapeutics Branch

Smoking Enhances Cognitive Performance and Decreases Tobacco Craving

This study investigated the effects of nicotine deprivation and smoking on cognitive abilities and tobacco craving. Twenty smokers with histories of drug abuse completed the Questionnaire on Smoking Urges (QSU) and two cognitive tests before and after smoking two cigarettes during two 90-min sessions. After two cigarettes were smoked at Session 1, subjects were tobacco abstinent for 18 hr until Session 2 the next morning. Response time on a logical reasoning test was unchanged by tobacco deprivation and was faster after smoking on Session 2. Deprivation slowed responding on a letter search test, which was reversed by smoking to predeprivation baseline. Tobacco deprivation increased scores on the QSU; smoking after deprivation reduced craving scores to smoking baseline levels. These results confirmed the utility of the QSU to measure changes in craving induced by tobacco deprivation and smoking. Further, the data suggest that deprivation-induced deficits and smoking-induced enhancements in performance may be specific to certain cognitive domains. Bell, S.L., Taylor, R.C., Singleton, E.G., Henningfield, J.E. and Heishman, S.J. *Nicotine and Tobacco Research*, 1, pp. 45-52, 1999.

Preclinical Pharmacology Section/Behavioral Neuroscience Branch

Noradrenergic Modulation of the Discriminative-Stimulus Effects of Methamphetamine

Although most behavioral effects of methamphetamine are mediated by the dopaminergic neurotransmitter system, neurochemical findings suggest that there is also strong involvement of noradrenergic neurotransmission. To analyze the involvement of norepinephrine in the subjective effects of methamphetamine, IRP scientists tested different noradrenergic compounds in Sprague-Dawley rats trained to discriminate methamphetamine from saline. Antidepressants such as desipramine and nisoxetine, and selective norepinephrine uptake inhibitors, that increase brain norepinephrine levels, potentiated the discriminative-stimulus effects of methamphetamine, whereas antagonists of alpha-2 (yohimbine) and partially also alpha-1 (prazosin) adrenergic receptors, attenuated methamphetamine's discriminative-stimulus effects. These findings suggest that the noradrenergic system plays a modulatory role in mediation of the subjective effects of methamphetamine. These effects appear to involve norepinephrine uptake sites and alpha-2 receptors, with limited involvement of alpha-1 receptors. Noradrenergic compounds might produce their effects either directly or, more likely, indirectly through the modulation of dopaminergic transmission. Munzar, P. and Goldberg, S.R. *Psychopharmacology*, 143, pp. 293-301, 1999.

Potent Local Anesthetic-like Effects of Cocaine on Cardiovascular Function

Cocaine use continues to be associated with a large number of hospital emergency room admissions, many of which are related to cardiovascular complications. To determine the potential role of cocaine's local anesthetic properties in these effects, the cardio-respiratory effects of cocaine were compared to various local anesthetic (sodium channel blocking) Class I antiarrhythmics. Anesthetized rabbits were treated with various doses of cocaine, quinidine, procainamide, lidocaine or flecainide. Cocaine produced larger increases in QRS duration, an effect typically related to sodium channel blockade, than were observed for the 4 sodium channel blockers. All 5 drugs produced comparable increases in respiratory rate. The large effect of cocaine on QRS duration suggests that cocaine may act at sodium channels in a manner different from the other drugs. This unique effect of cocaine may contribute to the sudden death associated with cocaine use in some individuals. Erzouki, H. K., Goldberg, S. R. and Schindler, C. W. *European Journal of Pharmacology*, 377, pp. 195-206, 1999.

Neuroimaging Research Branch

Accurate Determination of the Binding Constants for the High Affinity Nicotinic Agonist Epibatidine Requires Precise Experimental Conditions

Several compounds, such as epibatidine, A-85380, and their analogs, have been identified recently as high affinity nicotinic cholinergic receptor ligands whose affinities lie in the low picomolar range. Accurate measurement of such high affinities is fraught with certain technical difficulties, which may account for the inconsistency of previously reported affinities of epibatidine, ranging from 4 to 60 pM. Using newly developed conditions specifically for ligands with subnanomolar affinities, it was demonstrated that (\pm)-[³H]epibatidine (1--500 pM) binds to a single population of sites in rat brain with K_D of 8 ± 2 pM. This affinity was confirmed in both kinetic experiments and competition assays with (\pm)-[³H]epibatidine and (-)-[³H]cytisine using the same conditions. Variations from these conditions decreased the observed affinities. Gŷndisch, D., London, E.D., Terry, P., Hill, G.R. and Mukhin, A.G. *NeuroReport*, 10, pp. 1631-1636, 1999.

Dopaminergic Abnormalities in the Midbrain of Children Diagnosed With ADHD

Attention-Deficit/Hyperactivity Disorder (ADHD) is a highly prevalent childhood psychiatric disorder characterized by impaired attention, excessive motor activity, and impulsivity. Despite extensive investigation of the neuropathophysiology of ADHD by many methodologies, its neurobiochemical substrate is still unknown. Converging evidence, however, suggests a primary role of the dopaminergic system. This study examined the integrity of presynaptic dopaminergic function in ADHD children using positron emission tomography and the tracer [¹⁸F]-18F-fluoroDOPA (18F-DOPA). Accumulation of 18F-DOPA in synaptic terminals, a measure of DOPA decarboxylase activity, was quantified in regions rich in dopaminergic innervation, including caudate nucleus, putamen, frontal cortex, and midbrain (i.e., substantia nigra and ventral tegmentum). Accumulation of 18F-DOPA in the right midbrain, was higher by 48% in 10 ADHD children than in 10 normal children, and values of 18F-DOPA in this region were correlated with symptom severity. No other dopamine-rich regions significantly differed between groups. These findings suggest a dopaminergic dysfunction at the level of the dopaminergic nuclei in ADHD children. Abnormality in DOPA decarboxylase activity may be primary or secondary to deficits in other functional units of the dopamine pathway. Efforts toward defining the origin of this abnormality should help delineate mechanisms of midbrain control of attention and motor behavior important for the understanding of the causes and treatment of ADHD. Given the role of dopaminergic abnormalities in substance abuse, this finding could potentially explain the increased incidence of substance abuse in individuals with histories of ADHD. Ernst, E., Zametkin, A.J., Matochik, J.A., Pascualvaca, D., Jons, P.H. and Cohen, R.M. *Am J Psychiatry*, 156, pp. 1209-1215, 1999.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****September, 1999**

Program Activities

New PAs/RFAs

On May 25, 1999, NIDA issued a Program Announcement entitled **Behavioral Therapies Development Program (PA-99-107)**. The purpose of this program announcement is to reaffirm NIDA's continued and ongoing commitment to a major program of research on behavioral therapies for drug abuse and dependence.

On June 14, 1999, NIDA issued a Program Announcement entitled **Drug Use and Related Adverse Behavioral and Social Consequences (PA-99-113)**. The purpose of this PA is to stimulate research on behavioral and social adverse consequences of drug use and/or abuse. It is intended to elucidate the nature and extent of drug-related consequences and their development. An understanding of the full range of these consequences and the factors that contribute to or protect against these consequences is essential to the development of effective prevention programs. This announcement encourages local, national and international research on community/contextual and individual level risk and protective factors and processes that influence drug use and/or abuse and their consequences.

On August 5, 1999, NIDA, in conjunction with a number of other NIH institutes, issued a Program Announcement entitled **Career Development Awards: Child Abuse and Neglect Research (PA-99-133)**. This PA is designed to encourage qualified applicants who (1) are beginning their research careers and who have an interest in child abuse and neglect research, or (2) are already involved in research on child and adolescent abuse and neglect and who wish to increase the sophistication of their research through research career development or (3) conduct research in related disciplines, such as adult and child psychiatry, developmental neurology, neurobiology, developmental psychology, social work, and nursing and who wish to broaden their foci in order to be able to conduct research on child abuse and neglect.

On August 5, 1999, NIDA, in conjunction with a number of other NIH components and the National Science Foundation, issued a Program Announcement entitled **Curriculum Development Award in Neuroinformatics Research and Analysis (PAR-99-135)**. The purpose of this PA is to encourage and support applications from individuals with the requisite scientific expertise and leadership for the development of courses and curricula designed to train interdisciplinary Neuroinformatics scientists and U.S. educational institutions. The field of Neuroinformatics combines neuroscience research with informatics research developed from the computer sciences, mathematics, physics, engineering, or closely related sciences.

On August 5, 1999, NIDA, in collaboration with numerous other NIH institutes and other Federal agencies, issued a Program Announcement entitled **Neuroinformatics Institutional Mentored Research Scientist Development Award (PAR-99-136)**. The purpose of this Program Announcement is to encourage and support the development of applications from U.S. educational institutions for Institutional Mentored Research Scientist Development Awards

(K12). These awards are intended to foster the career development of individuals with interdisciplinary expertise bridging the fields of neuroscience and behavioral science research with that in informatics.

On August 5, 1999, NIDA, in collaboration with numerous other NIH institutes and other Federal agencies, issued a Program Announcement entitled **Short Courses in Informatics (PAR-99-137)**. The purpose of this Program Announcement is to encourage and support short-term Education Grants in Neuroinformatics Research. Support is provided for the development of short courses, seminars and workshops on interdisciplinary Neuroinformatics education. This short-term training will be provided to scientists seeking to combine knowledge about the various subdisciplines of neuroscience and behavioral science research with expertise in informatics research.

On August 5, 1999, NIDA, in collaboration with numerous other NIH components and other Federal agencies, issued a Program Announcement entitled **The Human Brain Project (Neuroinformatics): Phase I and Phase II (PAR-99-138)**. The purpose of this initiative is to encourage and support investigator-initiated, Neuroinformatics research that will lead to new digital and electronic tools for all domains of neuroscience research reflecting normal and diseased states across the life span. Neuroinformatics combines neuroscience and informatics research to develop and apply advanced tools and approaches essential for a major advancement in understanding the structure and function of the brain.

On May 26, 1999, NIDA in conjunction with a number of other NIH Institutes, issued an RFA entitled **Hepatitis C Cooperative Research Centers (AI-99-007)**. This RFA invites applications for the establishment of multi-project or single-project Hepatitis C Cooperative Research Centers (HC CRCs). The purpose of this RFA is to stimulate high quality, multidisciplinary, innovative yet systematic, collaborative research on hepatitis C virus (HCV). Such clinical and basic research is meant to provide further understanding of the stages and manifestations of hepatitis C infection, disease and recovery. The HC CRCs also will have a mandate to build on new findings to explore new vaccine and therapy strategies.

On June 18, NIDA, in conjunction with three other NIH institutes, issued an RFA entitled **HIV Prevention Trial Units (AI-99-010)**. This RFA solicits applications for HIV Prevention Trial Units (HPTUs) which will be integral parts of an HIV Prevention Trials Network (HPTN) designed to carry out a comprehensive scientific agenda on HIV prevention strategies. The HPTN will conduct domestic and international research on promising biomedical and behavioral strategies for the prevention of HIV transmission among adult, pediatric and adolescent populations.

On July 8, 1999, NIDA issued a Notice entitled **Supplements for the Study of Drug Abuse and HIV/AIDS**. With this Supplement Announcement, NIDA plans to continue to develop a strong, multidisciplinary basic, clinical, epidemiologic, behavioral, and ethics research program in response to the challenge of the interactions of drug abuse with the HIV/AIDS epidemic. The Supplement program is designed to encourage and enhance interactive, multidisciplinary collaborative projects involving researchers with primary foci both within and outside the area of drug abuse.

Other Program Activities

Buprenorphine/Naloxone NDA

On June 7, 1999 Reckitt & Colman Pharmaceuticals, Inc., filed an NDA for buprenorphine combined with naloxone for the treatment of opiate dependence. This NDA, as well as an NDA for buprenorphine filed previously were, in significant part, made possible by clinical trials undertaken by NIDA's Medications Development Division under a Cooperative Research and Development Agreement (CRADA), and by the work of numerous NIDA grantees who previously had published findings supporting the use of buprenorphine as a potential treatment for opiate dependence. Dr. Nora Chiang and Mr. Robert Walsh of MDD played major roles in coordinating and directing much of the research and data assembly that constituted the NIDA contribution under this CRADA. The FDA will review both NDAs simultaneously.

NIDA/VA Study #1018

On July 16, 1999 MDD and the Veterans Administration Cooperative Studies Program held an investigator's meeting in Los Angeles regarding the commencement of the NIDA/VA Study # 1018: A Multicenter Safety Trial of Buprenorphine/Naloxone for the Treatment of Opiate Dependence. Mr. Robert Walsh is the MDD Study Director, Dr. Ahmed Elkashef is the Medical Safety Officer, and Dr. Nora Chiang is the Buprenorphine/Naloxone Project Director. Drs. Paul Casadonte, Paul Fudala, and Walter Ling are the co-PIs of the study. The NIDA/VA Study # 1018: A Multicenter Safety Trial of Buprenorphine/Naloxone for the Treatment of Opiate Dependence started enrollment in New York on August 4, 1999. Six hundred subjects will be enrolled in this study. Enrollment is projected to be complete by January 2000 and the study will continue until January 2001. The study will primarily evaluate "best practices" of physicians in treating opiate dependent patients in a variety of clinical settings, ranging from single practitioners to community mental health clinics. Clinical sites in California, Florida, New York, Illinois, Texas, and Washington will participate.

Review of MDD's Preclinical Cardiovascular Toxicology Program

On July 29, 1999 a consultant meeting was held in Bethesda, MD to review MDD's preclinical cardiovascular toxicology program. The meeting was chaired by Dr. James Terrill (MDD, Pharmacology & Toxicology Branch). Participating consultants were Dr. Carrie Branch (Pharmacia & Upjohn), Dr. George Billman (Ohio State University), Dr. Mark Knuepfer (St. Louis University), and Dr. N. Bari Olivier (Michigan State University). Other meeting participants included staff from NIDA, the FDA and USUHS (a site where clinical cardiovascular safety assessments are conducted for MDD). Beyond the usual "medication alone" cardiovascular safety testing conducted by all pharmaceutical companies, NIDA is faced with the unique challenge of assessing the cardiovascular safety of medication/cocaine interactions. Preclinical data on the interaction of GBR 12909 and cocaine received a favorable review from the consultants; based on the data, no concerns were voiced regarding MDD's plan to proceed to clinical GBR 12909/cocaine interaction studies at USUHS. Although several types of in vitro cardiovascular studies were suggested by the consultants as important supplements to the current in vivo procedure, it was concluded that MDD's cardiovascular toxicology program is of comparable quality to programs found in leading pharmaceutical companies.

VA Medications Development Research Unit (MDRU) Updates

All MDRUs are currently running rapid screening protocols of various currently marketed medications looking for potential effect on cocaine dependence.

Methylphenidate Trials

MDD has received the methylphenidate ADHD study final database and first draft of the study report from the Cincinnati MDRU. Re-analysis of the primary measures is currently underway.

P-50 Medications Development Center Grants Update

All P-50 center grant principal investigators and study directors attended a reverse site visit where they briefed MDD staff on their progress to date and their future plans.

Strategic Program for Innovative Research on Cocaine Pharmacotherapy (SPIRCAP)

A third RFA for the SPIRCAP program (also includes research on other psychostimulants) has been issued with a receipt date of August 25, 1999. Currently there are 4 SPIRCAP grants funded from previous RFAs. Cantab Pharmaceuticals Research, Ltd., the successor to ImmuLogic Pharmaceuticals, Inc., has completed a Phase I trial of a cocaine vaccine and is now planning future clinical trials.

New Workgroup

The Emerging Technologies Workgroup, Chaired by Dr. Tom Aigner of the Division of Basic Research, will draw on the

talents and interests of NIDA staff to identify the leading scientists and their latest innovations in biology, biomedical engineering, computer science and neuroinformatics, and to evaluate their potential applications to drug abuse research.

Summer Research Program for Students

Since 1986, NIDA's IRP has had a summer research program for students. During the summer of 1999, a total of 47 students participated in the program through either the NIH Summer Internship Program or the Minority Research and Training Program. Each student participant was assigned to work with an IRP scientist on a research project. The students' training program is individually developed and includes directed readings, tutorials, attendance at seminars, and actual laboratory experience under the direction of the scientist. The culmination of the summer program was the students' presentation of their research at the NIH Student Poster Session held at the Bethesda campus on August 5, 1999. The NIH Summer Internship Program is coordinated by Dr. Stephen Heishman and the Minority Research and Training Program is coordinated by Dr. Jean Lud Cadet and Ms. Mary Affeldt.

NIDA's New and Competing Continuation Awards Since February 1999

Adler, Martin W. --- Temple University School of Medicine
Training Program: Drugs of Abuse Related Neuropeptides

Bayer, Barbara M. --- Georgetown University Medical Center
Prenatal Effects of Cocaine on Immunity

Bayer, Barbara M. --- Georgetown University Medical Center
Neurotoxicity of Drug Abuse

Bechara, Antoine --- University of Iowa
The Pharmacological Basis of Decision-Making

Bergman, Jack --- McLean Hospital
Boston '99: Behavioral Pharmacology Societies Meeting

Bergmeier, Stephen C. --- Ohio State University
Analogs of Methyllycaconitine: Selective Nicotinic Agents

Bevins, Rick A. --- University of Nebraska
Pavlovian Conditioning Processes Involving Nicotine

Bisaga, Adam --- Columbia University
Evaluation of NMDA Antagonist for Opiate Dependence

Blakely, Randy D. --- Vanderbilt University Medical Center
Regulation of Serotonin Transporters

Booth, Robert E. --- University of Colorado Department of Psychiatry
Antecedents to HIV Risk Behaviors Among Drug Users

Boyd, Carol J. --- University of Michigan
Substance Abuse Interdisciplinary Training Program

Brady, Kathleen T. --- Medical University of South Carolina
Clinical Investigation of Drug Abuse Disorders

Braithwaite, Ronald L. --- Emory University
HIV Interventions with Adult Male Inmates

Budney, Alan J. --- University of Vermont and State Agricultural College
Behavioral Treatment of Marijuana Dependence

Burstein, Sumner H. --- University of Massachusetts Medical School
Non Psychoactive Cannabinoids with Therapeutic Potential

Butler, Stephen F. --- Innovative Training Systems
Computerized ASI Consultation for Addictions Counselors

Cabral, Guy A. --- Virginia Commonwealth University
Effect of Marijuana on Macrophage Effector Molecules

Carroll, Frank I. --- Research Triangle Institute
Scientific Evaluation Chairman Grant

Carroll, Frank I. --- Research Triangle Institute
Selective Opioid Antagonist as Medication for Drug Abuse

Case, Patricia --- Harvard Medical School
HIV Risk and Club Drugs Among MSM: A Two City Comparison

Chang, Linda --- Harbor-UCLA Research and Education Institute
Monitoring Methamphetamine Abuse Treatment with 1h MRS

Chavkin, Charles --- University of Washington
Training in Molecular Pharmacology of Abused Drugs

Chesselet, Marie-Francoise S. --- University of California Department of Neurology
Gordon Conference on Catecholamines

Clatts, Michael C. --- National Development and Research Institute Inc.
HIV Transmission in Crack Injection Practices

Clayton, Richard R. --- University of Kentucky
Drug Use in Rural Kentucky: A Contextual Analysis

Cohen, Mark S. --- University of California
Real Time Imaging of Mental Activity

Coles, Claire D. --- Emory University
Maternal Substance Abuse: Outcome at School Age

Cottler, Linda --- Washington University
T32 in Drug Abuse Comorbidity and Biostatistics

Crabbe, John C., Jr. --- Portland VA Medical Center
Genetic Vulnerability to Drugs of Abuse

Crystal, Jonathon D. --- University of Georgia Research Foundation, Inc.
Cannabinergic Modulation of Time Estimation

Cunningham, Kathryn A. --- University of Texas Medical Branch
Neural and Pharmacological Mechanisms of Abused Drugs

Curran, Patrick J. --- University of North Carolina
Innovative Latent Curve Models of Adolescent Drug Use

Dani, John A. --- Baylor College of Medicine
Analysis of Nicotinic Cholinergic Systems in Mutant Mice

Darmani, Nissar A. --- Kirksville College of Osteoporosis Medicine
Mechanisms of Cannabinoid's Antiemetic Actions

Dennis, Michael L. --- Chestnut Health Systems
DOMS Early Re-Intervention (ERI) Experiment

Des Jarlais, Don C. --- Beth Israel Medical Center
Risk Factors for AIDS Among IV Drug Users

Desiderio, Dominic M. --- University of Tennessee Department of Neurology
Mass Spectrometry Analysis of the Human CSF Proteome

Desiderio, Dominic M. --- University of Tennessee
Mass Spectrometry of Opioid Neuropeptidergic Systems

Diaz, Rafael M. --- University of California San Francisco
Drug Use and Risky Sexual Behavior in Latino Gay Men

Dunlap, Eloise E. --- National Development and Research Institute
Males in Distressed Households: Drugs and Violence

Duvauchelle, Christine L. --- University of Texas
Dopamine Response to Predicted and Unpredicted Cocaine

Dworkin, Steven I. --- Federation of American Sociologists for Experimental Biology
FASEB Summer Research Conference: Drug Abuse

Dwoskin, Linda P. --- University of Kentucky
Development of Selective Nicotinic Receptor Antagonists

Eggert, Lona L. --- University of Washington
Preventing Drug Abuse - Parents and Youth in Schools

Elifson, Kirk W. --- Georgia State University
Emerging Drugs and Users: Social and Health Consequences

Elliot, Diane L. --- Oregon Health Sciences University
School-Based Drug Use Prevention for Girl Athletes

Fals-Stewart, William --- Old Dominion University
Behavioral Couples Therapy in Drug Abuse Treatment

Fisher, Dennis G. --- University of Alaska
Follow-Up for Needle Exchange Trial

Flay, Brian R. --- University of Illinois at Chicago
Postdoctoral Training Program in SAS Prevention

Fowler, Stephen C. --- University of Kansas Center for Research Inc.
Craving and Sensitization Models in Inbred Mice Strains

Fox, Howard S. --- Scripps Research Institute
Interactions of Methadone and SIV in the Central Nervous System of Monkeys

Frank, Deborah A. --- Boston Medical Center
Cocaine Exposure In-Utero: Elementary School Follow-Up

Friedman, David P. --- Bowman Gray School of Medicine
Addiction Studies Institute for Journalists

Fried, Peter A. --- Carleton University Department of Psychology
Prenatal Cannabis and Cigarettes-Outcomes in Adolescents

Frost, J. James --- Johns Hopkins University
Brain Opioid Receptors and Cognition in Cocaine Abuse

Gintzler, Alan R. --- State University of New York Health Sciences Center
Adenylyl Cyclase GBG Stimulation and Opioid Tolerance

Glowa, John R. --- Louisiana State University Medical Center
Determinants of Drug Effects on Drug-Maintained Behavior

Goeders, Nicholas E. --- Louisiana State University Medical Center School of Medicine
Stress and the Neurobiology of Drug and Alcohol Dependence

Goldberg, Linn --- Oregon Health Sciences University
Student Athlete Drug Surveillance Trial

Gonzalez, Jose, Jr. --- T.R.I. Center, Inc.

Virtual Reality: Application in the Field of Addiction

Grant, Igor --- University of California

NeuroAIDS: Effects of Methamphetamine

Griffin, Kenneth W. --- Weill Medical College of Cornell University

Self-Regulation Distress and Adolescent Drug Use

Grisel, Judith E. --- Furman University

OFG Modulation of Opiate Tolerance Dependence and Reward

Groves, Philip M. --- University of California, San Diego

Mechanism of Action of Drugs of Abuse--Amphetamine

Haidt, Jonathan --- University of Virginia

Reason vs. Intuition in Moral Judgment

Hammond, Donna L. --- University of Chicago

Opioid Mechanisms of Analgesia

Harrison, Lana D. --- University of Delaware

A Cross-National Study of the Youth Drug-Violence Nexus

Hawkins, J. David --- Social Development Research Group

Substance Use and Transitions to Adult Roles

Hen, Rene --- Columbia University

Drugs of Abuse in Serotonin Receptors Knock-Out Mice

Holmes, Philip V. --- University of Georgia

New Model of Drug Abuse with Depression Comorbidity

Howlett, Allyn C. --- Saint Louis University

Cannabinoid Receptors in Neuronal Cells and Brain

Ialongo, Nicholas --- Johns Hopkins University

Follow-Up of Two Universal Preventive Interventions

Irvine, A. Blair --- Oregon Center for Applied Sciences Inc.

Interactive Training for Parents of At-Risk Adolescents

Johnson, Bruce D. --- Medical and Health Research Association of New York City Inc.

Behavioral Sciences Training in Drug Abuse Research

Kalyuzhny, Alexander E. --- University of Minnesota

Opioid-GABA Interactions and Antinociception

Kaminski, Norbert E. --- Michigan State University

Repression of T-Cell Activation by Endocannabinoids

Kessler, Ronald C. --- Harvard Medical School

Mental Disorders as Risk Factors for Substance Disorders

Komiskey, Harold L. --- Xavier University of Louisiana

MIDARP at Xavier University of Louisiana

Konradi, Christine --- Massachusetts General Hospital

Psychostimulant Regulation of Neural Gene Expression

Koob, George F. --- Scripps Research Institute

Central Mechanisms of Opiate Reinforcement and Dependence

Lai, Shenghan --- University of Miami

Subclinical Atherosclerosis in HIV+ Black Cocaine Users

Law, Ping-Yee --- University of Minnesota
G Proteins and Opioid Receptor Functions

Liddle, Howard A. --- University of Miami
Research Training in Adolescent Drug Abuse Intervention

Loh, Horace H. --- University of Minnesota
Neurochemical Mechanism of Narcotic Action

Longshore, Douglas Y. --- UCLA Drug Abuse Research Center
Treatment Motivation in Drug Users

Lundahl, Leslie H. --- BPRL/East House III
Marijuana Cue-Induced Craving and Relapse in Adolescents

Lutfy, Kabirullah --- University of California Los Angeles
Orphanin FQ and Cocaine Sensitization

Mactutus, Charles F. --- University of Kentucky Medical Center
Developmental Neurotoxicity of Cocaine: An IV Rat Model

Madden, Pamela A. --- Washington University
The Genetics of Adolescent Tobacco Use and Dependence

Makriyannis, Alexandros --- University of Connecticut
Training in Medications Development for Drugs of Abuse

Malison, Robert T. --- Yale University School of Medicine
Spectrum Imaging of Dopamine Function in Daytop Subjects

Mannes, Andrew J. --- University of Pennsylvania
Viral Expression of Opioid Receptors for Severe Pain

Margolin, Arthur --- Yale University
HIV and Cocaine Use: Cardiovascular Effects and Therapy

Martin, Billy R. --- Temple University School of Medicine
College on Problems of Drug Dependence Meeting (1999)

Martin, Billy R. --- Medical College of Virginia
Center for Drug Abuse Research (supplement)

Mathier, Michael A. --- Allegheny University of the Health Sciences
Cardiovascular Effects of Cocaine in Cardiomyopathy

McGinty, Jacqueline F. --- Medical University of South Carolina
Regulation of Rat Brain Glutamate-Dopamine Interactions

McNamara, Cecelia L. --- University of Alabama at Birmingham
A Real-Time Assessment of Crack Cocaine Relapse Risk

Moerschbaecher, Joseph M. --- Louisiana State University Medical Center
Effects of Cannabinoid Abuse on Learning and Memory

Moore, Gregory J. --- Wayne State University
Neurochemistry and Treatment in Young Cocaine Users

Morgan, James P. --- Beth Israel Deaconess Medical Center
Mechanisms of Cocaine-induced Exacerbation of Viral MYO

Morgenstern, Jonathan --- Mount Sinai School of Medicine of Central
University of New York Restructuring Services for Drug Abusing TANF Women

Murphy, Laura L. --- Southern Illinois University School of Medicine
Cannabinoids and the Hypothalamic-Pituitary-Adrenal Axis

Murrelle, Edward L. --- Virginia Commonwealth University
Gene-Environment Interaction in Development of Drug Use

Nair, Madhavan P. --- Buffalo General Hospital
Cocaine and Immuno- and Neuropathogenesis of HIV-1 Infection

Negus, S. Stevens --- Alcohol and Drug Abuse Research Centers
Novel Delta Opioids: Analgesic Effects and Abuse Liability

Newton, Thomas F. --- UCLA Neuropsychiatric Institute
Brain Changes in Drug Dependence: Clinical Implications

Nichols, David E. --- Purdue University
Stereochemical Aspects of Hallucinogenesis

Owens, Michael S. --- University of Arkansas for Medical Sciences
Immunotherapy for Drug Abuse

Pasternak, Gavrill W. --- Sloan Kettering Institute for Cancer Research
Opiate Receptor Pharmacology

Peterson, Phillip K. --- Minneapolis Medical Research Foundation
Dynorphin and Glial Cell Immunomodulation

Piomelli, Daniele --- University of California, Irvine
Control of Endocannabinoid Release in Vivo

Porreca, Frank --- Arizona Health Sciences Center
Bifunctional Opioid/CCK Ligands for Pain

Potterat, John J. --- El Paso County Department of Health and Environment
Interviewer Factors in Solicitation of HIV Risk Networks

Pottieger, Anne E. --- University of Delaware
Drug Court Offenders in Outpatient Treatment

Price, Rumi K. --- Washington University
Psychopathology and Environments in Drug Abuse

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

Richardson, Gale A. --- Western Psychiatric Institute and Clinic
Effects of Prenatal Cocaine Use: 10-Year Follow-Up

Ridenour, Ty A. --- Washington University
Analyses to Improve Reduction in Crack Use

Roll, John M. --- Wayne State University
Motivational Properties of Drugs

Rosen, Jeffrey B. --- University of Delaware
Cocaine, Corticosterone and Emotional Behavior

Roy, Sabita --- VA Medical Center
Role of Mu-Opioid Receptor in Immune Function

Sadee, Wolfgang --- University of California San Francisco
Opioid Receptor Regulation

Schiller, Peter W. --- Clinical Research Institute of Montreal
Development of Receptor Specific Opioid Peptide Analogs

Sciarra, John J. --- Sciarra Laboratories, Inc.
Self-Administered Metered Dose Gel Medication Systems

Seroogy, Kim B. --- University of Kentucky - Anatomy and Neurobiology
1999 Summer Neuropeptide Conference: Addiction Symposium

Sharp, Burt M. --- University of Tennessee
Opiate Receptor Mediated Effects of Stress on Immunity

Shields, George C. --- Hamilton College
Computational Design of Haptens to Destroy Cocaine

Sholomskas, Diane E. --- Applied Behavioral Research
Evaluating Manual-Guided Training in Clinical Settings

Shor-Posner, Gail --- University of Miami
Neuroprotection with Selenium Therapy in HIV+ IDUs

Silverman, Kenneth --- Johns Hopkins Bayview Medical Center
A Therapeutic Workplace to Prevent HIV Transmission

Simon, Eric J. --- New York University Medical Center
Biochemical Research on Opioid Receptors

Singer, Merrill --- Hispanic Health Council
Syringe Access and HIV Risk

St. Pierre, Tena L. --- Pennsylvania State University
Teen-Led vs. Adult-Led Drug Prevention in Schools Via 4-H

Stefano, George B. --- State University of New York College at Old Westbury
The Old Westbury Neuroscience Research Institute

Stevens, Craig W. --- Oklahoma State University
Functional Evolution of Opioid Receptors

Stolerman, Ian P. --- Institute of Psychiatry
Comprehensive Database of Drug Discrimination Research

Sullivan, Maria A. --- Columbia University
Opiate and Nicotine Dependence: Medications and Therapy

Sulzer, David L. --- Columbia University
Amphetamine and D2 Regulation of Dopamine Quantal Size

Svikis, Dace S. --- Johns Hopkins Bayview Medical Center
Behavioral Therapies for Drug Dependent Pregnant Women

Tanner, T. Bradley --- Clinical Tools, Inc.
Education on Opiate Addiction and Methadone Treatment

Thayer, Stanley A. --- University of Minnesota
HIV Neurotoxicity: Mechanism and Modulation Y Cannabinoids

Thomas, Brian F. --- Research Triangle Institute
Unique Probes for Cannabinoid Receptors

Unterwald, Ellen M. --- Temple University
Cocaine-Induced Opioid, Dopamine and Behavioral Changes

Vaughan, Roxanne A. --- University of North Dakota
Phosphorylation and Regulation of Dopamine Transporters

Vega, William A. --- University of Texas
Patterns of Drug Use Among Mexican American Adults

Von Zastrow, Mark --- University of California San Francisco
Novel Proteins That Regulate Opioid Receptors

Vorhees, Charles V. --- Children's Hospital Research Foundation
Developmental Effects of Methamphetamine-Like Stimulants

Weinstein, Harel --- Mt. Sinai School of Medicine
Structure and Function of Neurotransmitter Transporters

Wentland, Mark P. --- Rensselaer Polytechnic Institute
Aminobenzomorphan: Potential Cocaine Abuse Medications

White, Francis J. --- Finch University of Health Sciences - Chicago Medical School
Prefrontal Cortex Neurophysiology after Chronic Cocaine

White, Francis J. --- Chicago Medical School Finch University of Health Sciences
Scientific Evaluation Chairman Grant

Yaksh, Tony L. --- University of California, San Diego
Spinal Action of Opiates

Yurgelun-Todd, Deborah A. --- McLean Hospital
Residual Cognitive Effects of Cannabis: An FMRI Study

Review Activities

Staff Development

NIDA's Office of Extramural Program Review (OEPR) completed a number of reviews this summer. In addition to the reviews in the chartered committees NIDA-E (Treatment Review Committee), NIDA-F (Health Services Review Committee), NIDA-L (Medications Development Committee), and NIDA-K (Training Committee), and mechanism based reviews such as those for centers, program projects, B-Start, and conference grants, a number of special committees were constituted for RFA reviews. Reviews for the following RFAs were conducted:

- DA-99-003 Genetics of Drug Addiction Vulnerability
- DA-99-004 National Drug Abuse Treatment Clinical Trials Network
- DA-99-006 Prevention Services Research Replicating a School-based Program
- DA-99-007 Bringing Drug Abuse Treatment from Research to Practice
- DA-99-008 Research on Drug Courts
- DA-99-009 Behavioral Therapy Development and Behavioral Science

In addition to the grant application reviews noted above, contract proposals received in response to the following RFPs were reviewed by the Contracts Review Branch:

- N44DA-9-5059 Guidelines/Strategies for Ethnic/Racial Minorities
- N01DA-9-7079 NIDA Center for Genetic Studies
- N44DA-9-5064 Developing Prevention Research Dissemination
- N01DA-9-CTDP - Compound Identification

8094

N01DA-9- Administrative Coordinating Center for the Clinical Trials Network
6507

N01DA-9- Clinical Trials - Regulatory Affairs and Data Management
8097

N01DA-9- Communications Support Contract
2067

N01DA-9- Medication Discovery Using Rat Models of Relapse to Cocaine Self-administration
8096

N01DA-9- NIDA INFO/FAX
2064

N01DA-9- Clinical Trials Operations Support and Management
8095

N01DA-9- INVEST
2068

N01DA-9- Development of Science Education Materials on Drug Abuse
2070

N01DA-9- Production, Analysis, and Distribution of Cannabis/Marijuana Cigarettes
7078

In addition, outside peer reviews of project concepts for four potential future contracts were completed.

Dr. Teresa Levitin, Director, OEPR spoke at the May 21st annual meeting of the Directors of NIDA Training Grants to provide an update on NIH extramural policies and procedures, particularly the policy on the inclusion of children and the policy on modular grants. She also spoke about the impact of the integration of some areas of NIDA's science into the Center for Scientific Review.

OEPR inaugurated its monthly OEPR Symposium Series on May 11, 1999 and held subsequent meetings on June 9, July 20, and August 17, 1999. The Symposium Series is designed to provide all NIDA staff with a forum for sharing ideas, brainstorming, developing creative solutions to concerns, and learning from one another. Case studies, discussion of day-to-day events, and information sharing are the main approaches used. Topics addressed to date have included the NIH policy on inclusion of children in research, review integration, and modular grants. Almost all NIDA Divisions and Offices have actively participated. Dr. William C. Grace, Deputy Director, OEPR, manages the symposium series.

Dr. Khursheed Asghar, Chief, Basic Science Review Branch, and Dr. Rita Liu, NIDA's Receipt and Referral Officer, made an invited presentation on the grant peer review process at the International Narcotics Research Conference (INRC) in Saratoga Springs, NY, in July. This was the first time that NIDA staff were invited to speak about the review process at INRC, and about 200 registrants attended. This presentation also gave Drs. Asghar and Liu the opportunity to get extramural researchers' perspectives on the integration of neuroscience reviews into the Center for Scientific Review.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****September, 1999**

Congressional Affairs

Hearings/Briefings of Interest

August 12, 1999 - **Medications Development** - Dr. Frank Vocci, Director, Medications Development Division, NIDA, briefed Marcia Lee, Senate Judiciary Committee staff to Senator Joseph Biden (D-DE), at her request. The briefing covered NIDA's medications development program, current research efforts, how NIDA works with the pharmaceutical industry, and information about various approaches to developing anti-addiction medications.

July 30, 1999 - **Drug Addiction Treatment Act** - Dr. Alan Leshner, Director, NIDA, and Dr. Frank Vocci, Director, Medications Development Division, NIDA, testified before the House Commerce Subcommittee on Health and Environment (Chairman Bilirakis, R-FL) at a hearing on medications for treating drug addiction, and on H.R. 2634, the Drug Addiction Treatment Act. (Dr. Leshner's statement is available at <http://www.nida.nih.gov/>)

July 15, 1999 - **Research Data Available Under Freedom of Information Act (FOIA)** - The Government Management, Information and Technology Subcommittee of the House Government Reform Committee held a hearing to discuss HR88, legislation concerning data availability under the FOIA. HR88 would amend the Treasury and General Government Appropriations Act, 1999, to repeal the requirement regarding data produced under Federal grants and agreements awarded to institutions of higher education, hospitals, and other nonprofit organizations. Members heard widely divergent opinions on the impact of legislation to mandate the release of data collected under federal grants through the FOIA. At issue was language inserted by Sen. Richard Shelby (R-AL) into last year's omnibus appropriation bill directing the OMB to revise its Circular A-110 to require the release to the public of research data from federally funded grants under FOIA. The subcommittee heard from 2 panels consisting of 6 witnesses each. Dr. Harold E. Varmus, Director, NIH, who was among the witnesses, testified that the "pitfalls of unrestrained openness" include "the chilling effect that inappropriate public scrutiny could have on the free exchange of ideas and the willingness to take risks to find answers." He said "... inappropriate sharing of preliminary data could lead to misinterpretation of results."

June 16, 1999 - **Legalization of Drugs** - The Subcommittee on Criminal Justice, Drug Policy and Human Resources held a hearing on legalization of drugs. Witnesses included Gen. Barry McCaffrey, Director, ONDCP; Dr. Alan I. Leshner, Director, NIDA; and Donnie Marshall, DEA, among others. (Dr. Leshner's statement is available at <http://www.nida.nih.gov/>)

June 7, 1999 - **Roundtable Discussion of Dopamine: Too Much, Too Little, and Addiction** - Dr. Alan Leshner, Director, NIDA, made a presentation to Members and staff of the House Commerce Subcommittee on Health and The Environment who attended an NIH-sponsored Roundtable Discussion of Dopamine: Too Much, Too Little, and Addiction. Dr. Leshner focused on the important role that dopamine plays in addiction. He discussed how a series of basic scientific discoveries demonstrate that independent of an addictive drug's initial site of action, every drug - be it nicotine, heroin, cocaine, marijuana or amphetamine - appears to increase levels of the neurotransmitter dopamine in the brain's reward pathway. It is this effect on the dopamine system, either directly or indirectly, that is thought to contribute to the addictive nature of these substances. Dr. Leshner stressed that by having a better understanding of

dopamine and the other neurochemical systems and neurocircuits that might be involved in the addiction process, scientists will be in a better position to develop more effective medications for addiction. As new medications are developed and tested for addiction including treatments for emerging drug problems like methamphetamine, NIDA will be in a position to test these promising medications in its National Drug Abuse Treatment Clinical Trials Network.

Bills of Interest

HR 2130 - Date-Rape Prevention Act. Sponsored by Fred Upton, R-MI, this bipartisan bill aimed at curbing the abuse of three sedatives that have emerged as so-called "date rape" drugs, was approved August 5, 1999 by the House Commerce Committee. The measure would add GHB (gamma hydroxybutyric acid, also known as Liquid Ecstasy) and GBL (gamma butyrolactone, a primary component of the GHB) to Schedule I, and ketamine to Schedule III of the Controlled Substances Act. The legislation also would require the Justice Department to assist with the development of forensic tests to detect the ingestion of GHB or related substances; direct the HHS Secretary to submit annual reports to Congress estimating the number of sexual assault cases involving date-rape drugs; and require the HHS Secretary to develop a national awareness campaign to educate people about the dangers of date-rape drugs and the strong CSA criminal penalties that could be imposed on those who abuse them.

HR 2260 - On June 17, 1999, Rep. Henry Hyde (R-IL) introduced **The Pain Relief Promotion Act of 1999**. The bill is designed to amend the Controlled Substances Act to promote pain management and palliative care without permitting assisted suicide and euthanasia. The bill, which has 152 co-sponsors, was approved for full committee action by the House Judiciary Committee, Subcommittee on the Constitution on July 20, 1999.

H.R. 2391- On June 30, 1999, Representative Jesse Jackson, Jr. (D-IL) introduced the **National Center for Research on Domestic Health Disparities Act**. The bill would create at NIH a National Center for Research on Domestic Health Disparities, responsible for coordinating its activities with the national research institutes; developing a comprehensive plan for minority health research at NIH; and ensuring the inclusion of members of minority groups in clinical research. H.R. 2391 also would provide an advisory committee for the Center and authorize \$100 million for FY 2000 and such sums as may be necessary for the four succeeding years, in addition to other authorizations of appropriations for the other agencies of the NIH. In addition, the bill would authorize the Center Director to carry out a program to facilitate minority health research by providing for research endowments at centers of excellence. H.R. 2391, which has 70 co-sponsors, was referred to the House Committee on Commerce.

H.R. 2634 - Drug Addiction Treatment Act of 1999 - On July 29, 1999, Representative Tom Bliley (R-VA) introduced H.R. 2634, the Drug Addiction Treatment Act of 1999, which would amend the Controlled Substances Act with respect to registration requirements for practitioners who dispense narcotic drugs in schedule IV or V for drug addiction treatment. The bill would allow qualified physicians, as determined by DHHS, to prescribe schedule IV and V anti-addiction medications in physicians' offices without an additional DEA registration if certain conditions are met. These include certification by participating physicians that: they are a physician licensed under state law; they are trained to treat opiate abuse; they have the capacity to refer patients for counseling and other appropriate ancillary services; the total number of patients shall not exceed a specified number unless the Secretary HHS adjusts the number. Other key provisions include the following: the drug involved must be approved by the FDA for use in maintenance or detoxification treatment and must not have been the subject of an "adverse determination;" if a physician dispenses a narcotic drug in Schedule IV or V in violation of this law, a practitioner may lose his registration with DEA; during the first 3 years either the Secretary or the Attorney General may make a determination that the law should not remain in effect; states can overrule the 3 year grace period with their own legislation if they deem this appropriate. On July 30, 1999, the House Commerce Subcommittee on Health and Environment (Chairman Bilirakis, R-FL) held a hearing on H.R. 2634. A similar measure (S. 324) was introduced in the Senate on January 28, 1999, by Senator Orrin Hatch (R-UT), and referred to the Senate Committee on the Judiciary.

S. 486 - Methamphetamine Anti-Proliferation Act of 1999 -- On August 5, 1999, S. 486 was reported to the Senate with an amendment in the nature of a substitute and without a written report by the Senate Committee on the Judiciary. The bill has been placed on the Senate Legislative Calendar. S. 486 was introduced on February 25, 1999, by Senator John Ashcroft (R-MO) and, as reported, includes several provisions of interest to NIH. S. 486 would require the head of each department, agency, and establishment of the Federal Government to place anti-drug messages on appropriate Internet websites; require the Secretary, HHS, to submit annually to Congress a report on the problems caused by methamphetamine consumption, and the incidence of and treatment available for methamphetamine abuse; authorize the Office for Substance Abuse Prevention to carry out school-based programs regarding the dangers of abuse and addiction; authorize the Director, NIDA, to expand current and on-going interdisciplinary research and clinical trials with treatment centers of the National Drug Abuse Treatment Clinical Trials Network relating to methamphetamine abuse and addiction; require the Secretary, HHS, in consultation with

the Institute of Medicine, to conduct a study on the development of medications for the treatment of addiction to methamphetamines; and waive the requirement for practitioners, who dispense narcotic drugs to individuals for maintenance or detoxification treatment, to annually obtain a separate registration for that purpose. The language of S. 324, The Drug Addiction Treatment Act, was swept into S. 486 during markup.

S. 883 - On April 27, 1999, Senator Joseph Biden (D-DE) introduced S. 883, the **New Drugs of the 1990's Act**, which would amend the Controlled Substances Act to authorize the Attorney General to schedule a substance in either Schedule I or II if she determines that the scheduling on a temporary basis is necessary to avoid "an imminent hazard to the public safety." The temporary scheduling would be in effect "until a final order becomes effective." The bill was referred to the Senate Committee on the Judiciary.

S. 885 - On April 27, 1999, Senator Joseph Biden (D-DE) introduced S. 885, the **New Medications to Treat Addiction Act of 1999**. The bill would amend Section 464P(e) of the PHS Act to reauthorize NIDA's Medications Development Program through the year 2002. It also includes provisions to encourage private sector development of drugs to treat cocaine and heroin addiction. The bill was referred to the Senate Committee on Health, Education, Labor, and Pensions.

S. 976 - On May 6, 1999, Sen. William Frist (R-TN) introduced **The Youth Drug and Mental Health Services Act**, which authorizes SAMHSA and introduces some new youth-related programs. On July 28, 1999 the bill was ordered reported by the full Senate Health, Education, Labor & Pensions Committee with an amendment in the nature of a substitute. Under the bill SAMHSA would end the practice of requiring states to expend a certain portion of federal funds on specified programs, but states would be required to file more comprehensive progress reports. The bill also would set up grant programs under SAMHSA to support: youth and adolescent substance abuse prevention and treatment initiatives; mental health initiatives designed to combat teen violence; mental health and substance abuse programs for the homeless; emergency funds for mental health and substance abuse needs; and treatment services for juvenile delinquents. The bill did not include a provision that would have permitted blending of substance abuse and mental health block grant funds without accountability for the purpose of servicing individuals diagnosed with co-occurring substance abuse and mental health disorders. Instead the bill restated current law. The Committee amended the bill by adopting a charitable choice provision that permits religious organizations to receive federal funds to provide alcohol and drug treatment and prevention services. The Senate is expected to vote on final passage of the bill before the end of the session.

S. 1447 - On July 28, 1999, Senator Paul Wellstone (D-MN) introduced the **Fairness in Treatment: The Drug and Alcohol Addiction Recovery Act of 1999**. The bill would require private insurance plans to cover alcohol and drug treatment on par with physical health services. The bill was referred to the Committee on Health, Education, Labor and Pensions. On August 5, 1999, Senator Paul Wellstone (D-MN) introduced S. Res. 177, a resolution to designate September, 1999, as **National Alcohol and Drug Addiction Recovery Month**. The resolution passed the Senate on the same day.

S. 1507 - On August 5, 1999, Senator Ben Nighthorse Campbell (R-CO) introduced S. 1507, the **Native American Alcohol and Substance Abuse Program Consolidation Act of 1999**. This bill would require the Secretary of the Interior, in cooperation with specified Federal agencies (including NIH), to authorize an Indian tribe to coordinate and consolidate Federally funded alcohol and substance abuse programs. According to Senator Campbell's introductory remarks, funds available through NIH and NIAAA include several different grant programs for minorities and the prevention of alcohol abuse that could be integrated with other programs into a single program. S. 1507 was referred to the Senate Committee on Indian Affairs.

S. 1561 - On August 5, 1999, Senator Spencer Abraham (R-MI) introduced S. 1561, the **Date Rape Control Act of 1999**, which would amend the Controlled Substances Act to require the Attorney General to add gamma hydroxybutyric acid to Schedule I and ketamine to Schedule III. It also would require the Secretary of HHS to submit to Congress reports on the number of incidents of the abuse of date-rape drugs that occurred in the most recent 1 year period, and to develop a plan, in consultation with the Attorney General, for carrying out a national campaign to educate the public on the dangers of date-rape drugs. Finally, the Secretary of HHS would be required to establish an advisory committee to make recommendations to the Secretary on issues related to date rape. S. 1561 was referred to the Senate Committee on the Judiciary.

Other Events

September 15-18, 1999 -- At the request of the American Psychological Association, Lula Beatty, Chief, Special Populations Office, NIDA, and Charlene Woodard, Office of Science Policy and Communications, NIDA, will participate as panel members for the Congressional Black Caucus Annual Conference. They have been asked to speak on the

relationship between depression and substance abuse in African Americans.

(Congress in recess August 7- September 7)

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International Activities

In late May 1999, the review committee for the NIDA INVEST Drug Abuse Research Fellowships met to select three Fellows for 1999-2000. Dr. Vaughan Rees, Australia, will conduct research with NIDA grantee Dr. Jeffrey Samet at Boston University School of Medicine; Dr. Abdel Assi, Egypt, will work with NIDA researchers Dr. Charles Chavkin at the University of Washington; and Dr. Elisa Mengual, Spain, will spend her Fellowship year with Dr. Virginia Pickel at Cornell University Medical University.

The U.S.-Russia Binational Workshop on Drug Abuse and Infectious Disease Prevention Strategies was organized May 24-27, 1999 by NIDA and Pavlov Medical University, St. Petersburg. The workshop featured multidisciplinary working groups of drug abuse researchers, treatment providers, community organizers, health care professionals, policymakers, law enforcement officials, educators, youth leaders, and media representatives who focused on drug abuse prevention, drug abuse treatment, and community prevention intervention strategies for drug-using populations. NIDA staff Drs. Peter Delany, DCSR, Elizabeth Robertson and Richard Needle, DEPR, and Patricia Needle, OSPC, joined 9 NIDA-funded researchers and Dr. Paul Gaist, Office of AIDS Research, NIH, as plenary session presenters.

On June 8, 1999 NIDA Humphrey Fellow alumna Dr. Berna Ulug, drug abuse treatment researcher at Hacettepe University, Ankara, Turkey, made a presentation to NIDA and NIAAA staff at the Neuroscience Center. Dr. Ulug shared findings on a two-year study of drug abuse conducted in 11 cities in Turkey.

NIDA hosted the fourth international satellite to the annual meeting of the College on Problems of Drug Dependence (CPDD) in Acapulco, Mexico, on June 11 and 12, 1999. The two-day meeting, "Building International Research on Drug Abuse: Continuing Focus on Children and Youth," brought together more than 60 scientists from 17 nations to explore the relationships among drug abuse research, practice and policy. NIDA Director Dr. Alan Leshner, Dr. Frank Vocci, Director, MDD, Moira O'Brien, DEPR, and Patricia Needle addressed the meeting participants.

Drs. Alan Leshner, Director, Timothy Condon, Associate Director, and Patricia Needle, Director, International Program, met in August 1999 with the Deputy Secretary of the Hungarian Ministry of Youth and Sport and Hungarian drug abuse researchers to plan the forthcoming East European regional meeting on methamphetamine abuse, which will be held in Budapest in early spring 2000. Following the Budapest meeting, Dr. Leshner gave the plenary address "The Nature of Addiction: Research Challenges and Opportunities" to the congress of the International Council on Alcohol and the Addictions (ICAA) in Vienna. NIDA also presented two workshops at the ICAA meeting: "New Directions in Drug Abuse Treatment: Behavioral Models and Pharmacotherapies, chaired by Dr. Betty Tai, MDD, and including presentations by Drs. Andrea Barthwell, Encounter Medical Group, Chicago, and Kenzie Preston, IRP; and "Transforming Drug Abuse Research into Practice for Prevention and Treatment," chaired by Timothy Condon, Associate Director, and with presentations by Drs. Claire Sterk, Emory University School of Public Health, Atlanta, and Richard Rawson, UCLA and Matrix, Los Angeles.

On July 12, 1999, NIDA hosted a group of German visitors, including representatives of the German Federal Ministry for Education, Science, Research and Technology and two drug abuse researchers, to discuss a joint workshop to encourage binational research collaboration in the areas of epidemiology, prevention and drug abuse treatment. The

visitors met with Moira O'Brien and Jacques Normand, DEPR; Peter Delany, DCSR; and M. Patricia Needle, Director, International Program, OSPC.

Dr. James Colliver of the Division of Epidemiology and Prevention Research represented NIDA at the 29th **Meeting of Experts in Epidemiology of Drug Problems** (Pompidou Group) in Strasbourg, France June 7 and 8, 1999. He presented a paper on drug abuse trends in the United States and NIDA activities.

Mr. Nicholas J. Kozel (DEPR) cochaired a joint meeting of the **East and South Asian Multi-City Epidemiology Work Group** held in Penang, Malaysia on May 10-13, 1999. Researchers from Malaysia, Japan, the Philippines, Thailand, Burma, China, Laos, Cambodia, Vietnam, Bangladesh, India, Pakistan, Sri Lanka and Papua New Guinea participated in the meeting and reported on patterns and trends of drug abuse in their countries and on emerging problems and related issues. Major drugs of abuse include: opium smoking and injection, heroin injection and "chasing the dragon", buprenorphine injection, cannabis smoking, inhalation of volatile substances, abuse of benzodiazepines and sharp increases in methamphetamine abuse. The emergence of MDMA and ketamine abuse in a number of countries in the region also has been noted.

Mr. Nicholas J. Kozel (DEPR) chaired a meeting of the **Border Epidemiology Work Group** (BEWG) held in San Diego, California on July 14-15, 1999. The BEWG is composed of researchers and program officials from the United States and Mexico and from the Pan American Health Organization. The major illicit drugs of abuse on the U.S. side of the Border are heroin cocaine, marijuana and methamphetamine. In Mexico, the major drug of abuse is marijuana; however, indicators of heroin, cocaine and methamphetamine abuse have been increasing sharply in recent years, especially in the Border cities of Tijuana, Juarez and Nogales.

Richard Needle, Ph.D., MPH, Dionne Jones, Ph.D., and Helen Cesari, M.Sc., CRB, DEPR, planned and led the second annual meeting of the **Global Research Network on HIV Prevention in Drug-Using Populations**, in Atlanta, Georgia, August 26-28, 1999. The meeting was sponsored by NIDA in collaboration with the Office of AIDS Research, NIH, the Centers for Disease Control and Prevention, Health Canada, the Joint United Nations Programme on HIV/AIDS, and the World Health Organization Substance Abuse Department. The meeting objectives included: 1) identifying emerging issues in the epidemic with implications for HIV, HBV, and HCV prevention; 2) discussing the nature, status, and effectiveness of HIV prevention efforts among injecting drug users in different countries; and 3) increasing research capacity through collaborative efforts nationally and internationally.

Richard Needle, Ph.D., Chief, Community Research Branch, DEPR, participated as an observer and resource person at the **Intercountry Technical Workshop on the Prevention of Drug Use and HIV/AIDS** in New Delhi, India on June 1-4, 1999. The workshop was held for senior personnel of drug control and public health agencies dealing with HIV/AIDS in countries of South Asia (Bangladesh, India, Nepal, Pakistan, and Sri Lanka) to update knowledge and skills on technologies for reducing the risk for transmission of HIV among IDUs; to exchange experiences and transfer technologies between drug control and public health agencies on addressing the joint problems of IDUs and HIV/AIDS; and to facilitate the establishment of working relations on issues related to IDUs and HIV/AIDS between drug control and public health agencies of countries in the region.

Drs. M. Patricia Needle and Elizabeth Robertson met with members of the United States Information Agency, International Visitors Program in Drug Education and Prevention on April 30, 1999 to exchange information on research and practice.

Drs. Robertson and Seitz from the Prevention Research Branch, DEPR met with Fiona Young of the United Kingdom's Home Office on July 22, 1999. Ms. Young is in the process of establishing a research group in the U.K. to integrate the prevention interests of a number of government departments in relation to the commissioning and use of research to guide policy and practice.

On July 9, 1999, Dr. Larry Seitz met with Augusto Perez-Gomez from Columbia, South America. Mr. Gomez is in charge of demand reduction for Colombia. The discussion involved the various aspects of prevention and what constitutes a good prevention program.

On July 12, 1999, Moira O'Brien, Division of Epidemiology and Prevention Research, met with Mr. Maurides De Melo Ribeiro, President of the State of Sao Paulo's Narcotics Council, Brazil, to discuss NIDA's role in assessing the nature and extent of drug abuse in the U.S.

Helen Cesari represented CRB, DEPR, at the **4th International Conference on the Biopsychosocial Aspects of HIV Infection**, "AIDS Impact 1999: Connecting a World of Resources", July 15-18, 1999, in Ottawa, Canada. The conference was hosted by the Canadian Psychological Association and supported by Health Canada through the Canadian Strategy on HIV/AIDS.

Dr. Bennett Fletcher, Chief of Services Research Branch, attended the **WHO/NIH Joint Project on Assessment and Classification of Disablements Steering Committee Meeting** in Geneva, March 1999.

Dr. Peter Delany served on the planning committee and represented the Division of Clinical and Services Research at the **U.S.-Russia Bilateral Workshop: Drug Abuse and Infectious Disease Strategies**, May 22-28, 1999 in St. Petersburg, Russia. Dr. Delany presented on The Nature of Drug Abuse, Science-Based Approaches to Drug Abuse Treatment, and co-lead a multi-disciplinary working group on the Principles of Drug Abuse Treatment with Dr. Ivgeny Krupitsky of the Pavlov Medical University.

Dr. Alexey Mukhin presented "Radiohalogenated Analogs of A-85380, Novel Ligands for Imaging the $\alpha 4\beta 2$ Subtype of Nicotinic Receptors" at the International Symposium "Neuronal Nicotinic Receptors - Their Functional Role In CNS Disorders with Focus on New Therapeutic Implications", Stockholm, Sweden, May 27-29, 1999.

Dr. Jean Lud Cadet, NIDA, IRP, was invited to speak at a special symposium on Ecstasy: Mechanisms of Action and Pathology. The symposium took place at the College de France in Paris on June 2-5, 1999.

Dr. Jean Lud Cadet, NIDA, IRP, moderated two sessions of the Satellite Meeting of the International Society for Neurochemistry and European Society of Neurochemistry held in Copenhagen, Denmark on August 4-6, 1999. This year's Satellite Meeting focused on Cellular and Molecular Mechanisms of Drugs of Abuse: Cocaine, Ibogaine, and Substituted Amphetamines. Dr. Cadet moderated the meeting's first session on Gene Expression/Molecular Mechanisms of Drug Addiction, as well as the meeting's final session, Panel Discussion and Open Forum: Summary and Recommendations.

Dr. Jean Lud Cadet, NIDA, IRP, presented a poster at the International Society for Neurochemistry and European Society of Neurochemistry Meeting held in Berlin, Germany on August 7-15, 1999. The poster was entitled "Comparative Toxic Effects of Methamphetamine and Dopamine in Cell Culture Potentiation by Serum Withdrawal."

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Meetings/Conferences

NIDA's Genetics Workgroup sponsored a workshop on **The Role of Behavior Genetics in NIDA's Vulnerability to Drug Addiction Initiative** at the Neuroscience Center on May 27, 1999. Chaired by Dr. Naimah Weinberg, DEPR, this meeting included six outside experts and several NIDA program staff members.

NIDA's Special Populations Office sponsored its annual workshop **Cannabinoid, Opiate, and Estrogen Vascular Neuroimmunology**, in Melville, New York on June 23-25, 1999. The workshop, which was co-sponsored by the State University at Old Westbury and the Nikon Corporation, offered minority and women investigators opportunities to learn cutting-edge research and methodology in this area, and techniques such as computer-assisted microscopic image analysis. The workshop was chaired by Pamela Goodlow, Special Populations Office, Dr. Joseph Frascella of the Division of Clinical and Services Research, and Dr. George Stefano from SUNY/Old Westbury.

The National Institute on Drug Abuse sponsored a satellite meeting to the AIDS Impact meeting in Ottawa Canada on July 15, 1999 entitled **Drug Abuse and AIDS: Intertwined Epidemics**. Ms. Helen Cesari, DEPR, Dr. Henry "Skip" Francis, CAMCODA, and Dr. David Shurtleff, DBR chaired the event which was supported by the Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA), the Division of Basic Research, the Division of Epidemiology and Prevention Research and by the Behavioral Sciences Workgroup. Drs. Linda Erinoff and David Shurtleff served as co-organizers of the event.

NIDA co-sponsored the Technical Assistance Workshop held July 16, 1999, for 112 applicants applying to RFA OD-99-006 Research on Child Neglect sponsored by the NIH Child Abuse and Neglect Working Group and Consortium. In addition to institutes within NIH, the Consortium includes the Children's Bureau, the National Institute of Justice, the Office of Juvenile Justice and Delinquency Prevention, and the Office of Special Education. Coryl Jones, ERB, DEPR, presented a paper on human subject concerns and methodological issues. Vince Smeriglio, CAMCODA, Kathie Etz, PRB, DEPR, and Jacques Normand, CRB, DEPR served as faculty. Applications under the RFA were due September 14, 1999.

The FASEB Summer conference entitled **Pulmonary Pathophysiologic and Immune Consequences of Smoked Substance Abuse**, partially supported by the National Institute on Drug Abuse, was convened in Copper Mountain, Colorado, July 18-23, 1999. The conference was co-chaired by Dr. Donald P. Tashkin and Dr. Michael Roth of the University of California at Los Angeles and Dr. Pushpa V. Thadani of NIDA's Division of Basic Research.

NIDA's MDD and CAMCODA organized NIDA's first Workshop on Drug-Drug Interactions where nation's leading pharmacologists/pharmacokineticists and clinicians discussed issues on **Interactions Between Pharmacotherapeutic Agents Used in the Treatment of AIDS and Drug Addiction**. The meeting was held September 9-10, 1999, in the Neuroscience Center. Contact: Jag Khalsa, Ph.D., CAMCODA.

NIDA staff members Arthur MacNeill Horton, Jr., Ed.D., ECNB, DCSR, Teri Levitin, Ph.D., OEPR, and Vincent Smeriglio, Ph.D., CAMCODA, recently organized a symposium at the April 1999 Meeting of the **Society for Research on Child Development** in Albuquerque, New Mexico--the premier gathering of child development researchers--as part of NIDA's "Early Career Pathways-Opportunities for Behavioral Researchers" series of events that were held at scientific meetings sponsored by the Behavioral Science Work Group. The SRCD events were also co-sponsored by

NIDA's Child and Adolescent Work Group. The first event was a symposium entitled How to Create Your Research Career: Mentoring, Networking and Grant Writing. The symposium brought together NIDA supported early career investigators to discuss their experiences. It provided an interesting look at the opportunities afforded by various NIDA funding mechanisms, as each young investigator was supported by a different mechanism. After Dr. Levitin described the importance of research on child development to NIDA, a senior researcher and three junior/young NIDA-funded investigators presented brief talks. Dr. Jeanne Brooks-Gunn discussed her mentoring activities. The young investigators described how NIDA has facilitated their research careers within the context of their research and current findings. The young investigators were Arnise Johnson of the University of Miami Medical School Department of Pediatrics (Pre-doctoral Minority Supplement), Mark Myers, Ph.D., of the Department of Psychiatry of the University of California at San Diego (FIRST Award) and Lauren Wakschlag, Ph.D., of the Department of Psychiatry of the University of Chicago (B/START). Dr. Lucinda Miner, SPB, OSPC gave an overview of the Institute and delivered a presentation on NIDA's mechanisms for research and career development support.

At the June, 1999 CPDD meeting, MDD held a workshop entitled A Evaluation of Selegiline as a Cocaine Treatment Medication: The Path to a Multi-Site Phase III Trial. The meeting was chaired by Dr. Frank Vocci (Director, MDD). Preclinical findings obtained under NIDA's Cocaine Treatment Discovery Program contracts were presented by Drs. David McCann and Jane B. Acri (MDD Pharmacology and Toxicology Branch) and clinical findings were presented by Dr. Deborah Leiderman (MDD Clinical Trials Branch). Most notably, it was found that selegiline, when administered to rhesus monkeys in a single dose with an appropriately long pretreatment time (24 hours) or by continuous i.v. infusion for several days, can antagonize the subjective and rewarding effects of cocaine (results of cocaine drug discrimination and self-administration experiments). Consonant with the preclinical findings, selegiline caused a significant blunting of cocaine's subjective effects in man. The effects of selegiline on cocaine use (Phase II study) appeared promising. The design of NIDA's Phase III studies were presented and discussed. Drs. Steve Negus, Nancy Mello, Mike Forster, Jack Bergman and Tom Newton participated as discussants.

The Etiology and Clinical Neurobiology Branch, DCSR sponsored an exhibit booth at the Cognitive Neuroscience Society meeting in Washington, D.C. April 11-13, 1999. NIDA was the first NIH institute to sponsor an exhibit booth at this meeting and has been the sole NIH institute with an exhibit booth for the last 3 years.

The Etiology and Clinical Neurobiology Branch, DCSR, sponsored a booth at the International Society for Magnetic Resonance in Medicine, May 22-28, 1999, in Philadelphia. Drs. Joseph Frascella and Steven Grant attended the meeting. NIDA was the first NIH institute to sponsor an exhibit booth at this meeting.

NIDA's Etiology and Clinical Neurobiology Branch was a co-sponsor with NIMH of the annual Summer Training Institute in Cognitive Neuroscience, held at Dartmouth University, Hanover, NH, June 21-July 8, 1999.

NIDA Director Dr. Alan I. Leshner and Dr. Timothy P. Condon, Associate Director, NIDA, Director, Office of Science Policy and Communications, participated in the launch of the Kmart Foundation-sponsored Kids Race Against Drugs on April 15, 1999 in Los Angeles, CA.

Richard A. Millstein, Deputy Director, NIDA, spoke on "The Future of Drug Courts" at the National Association of Drug Court Professions (NADCP) 5th Annual Conference, Miami Beach, Florida, on June 4, 1999.

Richard A. Millstein, Deputy Director, NIDA, spoke on "Confronting Drug Abuse and HIV/AIDS" at the 20th Anniversary Conference of the Hubert H. Humphrey Fellowship Program, Washington, D.C., June 18, 1999.

Richard A. Millstein, Deputy Director, NIDA, met with the Steering Committee of the National Hispanic Network on Drug Abuse to discuss program initiatives in Bethesda, Maryland, July 8 and 9, 1999.

Richard A. Millstein, Deputy Director, NIDA, met with the Board of Directors, presented a plenary address, and participated in a research workshop at the 10th Anniversary Conference of the National Asian/Pacific-American Families Against Substance Abuse (NAPAFASA), Los Angeles, CA, July 21-22, 1999.

Dr. Timothy Condon, participated in a meeting of the Inter-Federal Agency Methamphetamine Task Force, May 3-5, 1999 in San Diego, CA.

Dr. Timothy P. Condon made a keynote presentation, "Drugs and the Brain: Implications for Social Work Practitioners," at the annual Social Work and Addictions Conference of the National Association of Social Workers, May 8, 1999 in New York City.

Dr. Timothy P. Condon addressed the American Psychiatric Association's Council on Research and Council on Addictions, May 18 and 19, 1999, in Washington, D.C.

Drs. Timothy P. Condon, Andrea Baruchin, and Lucinda Miner addressed the NIDA Research Training Coordinators at

their annual meeting on May 21, 1999 in Bethesda, MD.

Dr. Timothy P. Condon presented a keynote address, "Recent Advances in Drug Addiction Research" at the annual meeting of the National Association of Alcoholism and Drug Abuse Counselors, May 27, 1999 in Philadelphia, PA.

Dr. Timothy P. Condon presented a keynote address, "Understanding the Science of Addiction" at the NIDA-sponsored Join Together Graduate Fellows Institute, June 26-29, 1999 in Falmouth, MA.

Dr. Timothy P. Condon presented a keynote address, "NIDA: Researching the Health Effects of Smoked Drugs of Abuse" at the annual meeting of the Federation of American Societies for Experimental Biology, July 19, 1999 in Copper Mountain, CO.

Dr. Timothy P. Condon presented a keynote address, "Scientific Based Research," at the Executive Drug Prevention and Demand Reduction Symposium of the National Interagency Civil-Military Institute, July 21, 1999 in San Luis Obispo, CA.

Dr. Timothy P. Condon participated on a Federal panel at a national meeting of the Child Welfare League of America, August 7, 1999 in Portland, ME.

Dr. Timothy P. Condon chaired a symposium on "Research to Practice," at the International Congress on Alcohol and Drugs, August 17, 1999 in Vienna, Austria.

Dr. Timothy P. Condon addressed staff and executives of MTV during a briefing on accurate depiction of drugs in the media, August 19, 1999 in New York City.

On June 27, Beverly Wyckoff Jackson, Chief, Public Information and Liaison Branch, participated in the 1999 National Media Education conference sponsored by the Partnership for Media Education. Ms. Jackson was part of the planning committee for this conference and also conducted a presentation about outreach to the entertainment industry. NIDA was a cosponsor of the conference.

Dr. Tom Aigner, DBR, represented NIDA at The Second Bioengineering Consortium (BECON) symposium "Visualizing the Future of Biology and Medicine", held June 25-26, 1999 on the NIH campus in Bethesda, Maryland. NIDA grantees invited to present their latest research findings at the symposium were Nora Volkow of the Brookhaven National Laboratory who spoke on "Functional Imaging in the Early Detection of Disease" and Thomas Meade of the California Institute of Technology who spoke on "Design Issues for Novel Contrast Agents and Biological Probes". Posters were presented by: NIDA grantee Leonard Howell of Emory University on "Positron Emission Tomography Imaging in Awake Nonhuman Primates During Cocaine Use"; NIDA grantee Eric Ahrens of the California Institute of Technology on "Magnetic Resonance Microscopy of the Mouse Nervous System at 12 Tesla"; Bruce Vaupel of the NIDA Intramural Research Program (IRP) on "In Vitro and in Vivo Evaluation of 5-[I-123]IODO-A-85380 as a Radiotracer for Single Photon Emission Computed Tomography Imaging of Nicotinic Acetylcholine Receptors"; Monique Ernst of the NIDA IRP on "Nicotine and Cerebral Blood Flow During a Working Memory Task"; and Patricia Janak of the NIDA IRP on "Spatiotemporal Maps of Brain Function: Using Ensemble Recording to Image Function in Behaving Animals".

On May 21, 1999, Mr. Joel Egertson, MDD hosted a meeting on Buprenorphine and Buprenorphine/Naloxone Products with representatives from 10 state governments and other medical and professional organizations. Presentations were made by Dr. Camille Barry of CSAT, Dr. Frank Vocci of MDD, Dr. Paul Fudala of the Philadelphia VAMC, and Dr. Paul Casadonte of the Manhattan VAMC regarding buprenorphine and buprenorphine /naloxone. Federal regulatory issues were discussed by Mr. Nick Reuter and Dr. Alan Trachtenberg of SAMHSA, and Ms. Denise Curry of DEA. Mr. Egertson spoke on current Federal legislative efforts. Following the morning presentations, Mr. Jack Gustafson of NASDAD moderated a discussion of the State's comments and concerns regarding implementation issues for this potential new opiate pharmacotherapy.

On July 14 -15, 1999, Dr. Lula Beatty, Chief, Special Populations Office, attended an HBCU Recruited Scientist Advisory Board meeting in Tallahassee, Florida.

On July 6-7, 1999, Dr. Lula Beatty, attended a technical assistance meeting sponsored by CSAP/SAMHSA for the project "Science Based Strategies for Alcohol Prevention at HBCUs" in Hilton Head, South Carolina.

On April 29-May 1, Dr. Lula Beatty was a keynote speaker for the Youth Science Fair at the Lonnie Mitchel HBCU conference. She also received a Lonnie Mitchel HBCU Award.

On May 20, 1999, Dr. Lula Beatty attended a Grantsmanship Workshop for faculty at Morgan State University in Baltimore, Maryland.

On July 27, 1999, as a representative of the Section on the Psychology of Black Women, APA, Dr. Lula Beatty was a reviewer for a small grant program for HIV/AIDS Interventions with Black Women.

On July 8-9, 1999, as a representative of the Special Populations Office, Arnold Mills, chaired a technical assistance workshop for faculty and staff of Historically Black Colleges and Universities (HBCUs) in Bethesda, Maryland. At the workshop, sponsored by the Special Populations Office, participants learned about the NIH research grants application and review processes, various funding mechanisms available through NIDA and NIH, and consulted with NIDA supported investigators about the research plans.

On July 8-9, 1999, Ana Anders, Senior Advisor on Special Populations, Special Populations Office, chaired a meeting of the National Hispanic Science Network (NHSN), formerly the Hispano/Latino Researchers and Scholars Work Group (HLRSWG). The mission of the NHSN is "to foster science on drug use among Hispanics and its application to practice and public health."

In July 1999, as a representative of NIDA, Ana Anders lectured to group of nine scholars who are faculty at Hispanic Serving Institutions (Institutions of higher learning that have over 25% Hispanic student enrollment).

Through the Hispanic Association of Colleges and Universities (HACU), the Special Populations Office sponsored Dr. Elba Herrero, a Hispanic Serving Institution faculty member for two weeks in July 1999. Under the guidance of Ana Anders, she learned of NIDA's operation.

In July 1999, Ana Anders held a meeting with NIDA staff to inform them of NIDA's plans to develop an Asian and Pacific Islander (API) initiative. At the meeting Ana Anders updated staff on NIDA's activities with respect to the API population and received advice from the group.

On July 30, 1999, as a representative of NIDA, Ana Anders made a presentation to a group of professional faculty of the Universities of Bolivia, Ecuador and Peru in Washington, D.C. The group was a part of the "Project to Assist Nursing Schools" program, conducted by the Organization of American States (OAS) and its component, the "Comision Interamericana para el Control del Abuso de Drogas" (CICAD).

On June 23-25, 1999, as a representative of NIDA, Ana Anders attended the Annual U.S./Mexico Demand Reduction Conference in Tijuana, Mexico.

On July 21-24, 1999, Ana Anders attended the National Asian and Pacific American Families Against Substance Abuse (NAPAFASA) conference in Los Angeles, California. At the conference, which was co-sponsored by NIDA, she met with NAPAFASA board members to identify research issues of concern to Asian and Pacific Islanders.

Jag H. Khalsa, Ph.D. of CAMCODA presented a review of the "Medical and Health Consequences of Marijuana and Its Uses for Medical Purposes" at the NIDA-supported FASEB Summer Conference in Copper Mountain, Colorado, July 18-23, 1999. He also co-chaired with Dr. Alex Makriyannis, a Workshop on "Therapeutic Potential of Cannabinoids," where the speakers presented on the therapeutic potential of novel cannabinoids, pharmacological mechanisms, animal studies (Billy Martin), clinical trials (Don Abrams), and potential formulations and routes of administration (M. ElSohly).

Mr. Richard Harrison, Chief, Contracts Review Branch, presented a welcome and participated in an August meeting entitled "American Indian Research Training Needs" sponsored by NIH and the Indian Health Service.

OEPR and MDD hosted a training symposium, "From Bench to Pharmacy: Discovering and Developing Medications," on June 30. This session was attended by staff from NIDA, NIMH, and NINDS and focused on the regulatory, scientific, and administrative aspects of medications development. Organized by Drs. Betty Tai (MDD) and William C. Grace (OEPR), the symposium included talks on FDA procedures (Dr. Celia Winchell, FDA), Clinical Development (Dr. Betty Tai, MDD), Preclinical Development (Dr. James Terrill, MDD), Pharmacokinetic and Pharmacodynamic issues (Dr. Nora Chiang, MDD), Tools for Collaboration with Drug Companies (Mr. Lee Cummings, MDD), and Review of Applications (Dr. Khursheed Asghar, OEPR).

Dr. Mark Swieter gave two talks at the annual meeting of the College on Problems of Drug Dependence (CPDD). One was for the workshop titled "Women, Gender and Behavioral Research: Focus on Early Career," which was organized by Drs. Cora Lee Wetherington (DBR) and Lynda Erinoff (DEPR). Dr. Swieter's presentation was "NIDA Training Opportunities for Junior Investigators." The second talk, "Demystifying the Review Process, or Inside the Black Box Called Review," was given as part of a grant writing workshop organized by Dr. Cindy Miner (OSPC).

Also at CPDD, Dr. Teri Levitin organized and chaired a workshop entitled "Update on the Grant Review Process, New Review Groups and Changes in Review Procedures at NIH".

On May 28, 1999, Dr. Frank Vocci, Director, MDD delivered a plenary lecture on the Neurobiology of Drug Dependence at the International Society for Magnetic Resonance in Medicine meeting in Philadelphia, PA.

On June 5, 1999, Dr. Frank Vocci spoke on medications development issues pertaining to buprenorphine and buprenorphine/naloxone at the NASADAD meeting in St. Petersburg, FL.

On June 11, 1999, Dr. Frank Vocci spoke on the Neurobiology of Drug Addiction at the NIDA International satellite meeting, " Building International Research on Drug Abuse: Continuing Focus on Children and Youth" in Acapulco, Mexico.

On July 14, 1999, Dr. Frank Vocci discussed the NIDA medications program history and current status at an NHLBI symposium on Medications Development for Rare Blood Disorders at the Lister Hill Center.

On August 6, 1999, Dr. Frank Vocci presented an Overview of the NIDA Medications Development Program at the FASEB Conference: Biological Vulnerability to Alcoholism and Drug Addiction held in Copper Mountain, Colorado.

Dr. Steven Grant, DCSR, presented a talk entitled "Activation of the Ventromedial Prefrontal Cortex Correlates with Gambling Task Performance: An FDG-PET Study" at the annual meeting of the College on Problems of Drug Dependence, June 11-17, 1999, in Acapulco, Mexico.

Dr. Harold Gordon attended the 40th Annual Short Course in Medical and Experimental Mammalian Genetics in Bar Harbor, ME, July 1999.

Dr. Harold Gordon organized, together with members of the Developmental Workgroup, a Workshop held on September 9, 1999 entitled, "Early Environmental Stress and Biological Vulnerability to Drug Abuse" held in Bethesda, Maryland.

Arthur MacNeill Horton, Jr., Ed.D. co-chaired with Minda Lynch, Ph.D. the symposium "Motives for Behavior: From Neurobiology to Cognitive Perspectives" which was presented at the American Psychological Society meeting in Denver, Colorado, on June 5, 1999.

Drs. Steven Grant and Joseph Frascella attended the Society of Biological Psychiatry annual meeting in Washington, DC, May 13-14, 1999.

Dr. Joseph Frascella made presentations on NIDA's neuroscience programs and on the NIH grant process at the NIDA Special Populations Research Development Seminar "Cannabinoids, Opiate Immunology and Estrogen Vascular Neuroimmunology" in Melville, Long Island, New York, June 22-25, 1999.

On May 19, 1999, Dr. Jack Blaine was a discussant for the symposium on Science-Based Behavioral Therapies for Drug Addiction at the American Psychiatric Association annual convention in Washington, D.C.

On March 17, 1999, Dr. Lisa Onken gave a presentation on NIDA treatment research and suicidal behavior at an NIMH-sponsored workshop, "Assessment and Treatment of Suicidal Behavior in Clinical Trials," in Washington, D.C.

On April 28, 1999, Dr. Lisa Onken gave a presentation on the behavioral therapy component in cocaine addiction medications development research at the CPDD/NIDA/FDA/NIAAA/SNRT Meeting on Clinical Outcomes in Washington, D.C.

On May 19, 1999, Dr. Lisa Onken chaired a symposium on Science-Based Behavioral Therapies for Drug Addiction at the American Psychiatric Association annual convention in Washington, D.C.

On May 27, 1999, Dr. Lisa Onken gave a presentation on the translation of basic behavioral and cognitive science into novel behavioral therapies to the NIMH Council Behavioral Science Workgroup, in Tysons Corner, Virginia.

On June 8, 1999, Dr. Elizabeth Rahdert participated in the Workshop on the Role of Co-occurring Substance Abuse and Mental Illness in Violence. The workshop, held in Washington, DC, was co-sponsored by the Board on Neuroscience and Behavioral Health, IOM, and the MacArthur Foundation.

On June 22, 1999, Dr. Elizabeth Rahdert conducted a POSIT (Problem Oriented Screening Instrument for Teenagers) Training Workshop for the 7th Annual Montgomery County Public Schools Safe & Drug-Free Schools Summer Institute, held in Rockville, Maryland.

On August 11-12, 1999, Dr. Elizabeth Rahdert participated in a meeting, sponsored by The Robert Wood Johnson Foundation, and held in Princeton, New Jersey, on the topic of "Restorative Justice Responses to Adolescent Substance Abuse." Meeting participants included professionals from the areas of juvenile justice and adolescent

treatment.

On August 20, 1999, Dr. Elizabeth Rahdert chaired the symposium, "Promising Approaches to Treating Substance Abuse in High Risk Adolescents" at the 107th Annual Convention, American Psychological Association, Boston, MA. Symposium participants included NIDA grantees Dr. Peter Monti, "Reaching Adolescents Through Brief Motivational Interviewing for Smoking," Dr. Neil McGillicuddy, "Coping-Skills Training for Parents of Adolescent Drug Abusers," Dr. Robert Malow, "Cognitive-Behavioral Therapy to Reduce HIV Risk Among Drug Abusing Adolescents," and Dr. Arthur M. Horton, DCSR, NIDA, as discussant.

On August 31, 1999, Dr. Elizabeth Rahdert presented a poster presentation, "Development of an Adolescent HIV/STD Risk-of-Exposure Mini-Questionnaire," at the 1999 National HIV Prevention Conference held in Atlanta, Georgia.

On May 26-27, 1999, Debra Grossman, DCSR, participated in a Youth Tobacco Cessation Collaborative Workshop. Meeting participants represented a variety of organizations that fund activities related to youth tobacco-use cessation.

Dr. Bennett Fletcher, Chief, Services Research Branch, DCSR, made a presentation on "Research and Practice: Stimulating Interdependence" at the NASADAD Annual Meeting in Tampa, Florida on June 5, 1999.

Dr. Bennett Fletcher chaired a symposium on "Research on Linkages Between Drug Treatment and Other Systems of Care" at the Annual Meeting of the Association for Health Services Research (AHSR) held in Chicago on June 26, 1999.

Dr. Bennett Fletcher made a presentation on research funding opportunities in health services research at the Annual Meeting of the AHSR held in Chicago on June 27, 1999.

Dr. Bennett Fletcher chaired a panel on "Bridging the Gap: Bringing Drug Abuse Treatment From Research to Practice" at the Annual Meeting of the AHSR held in Chicago on June 28, 1999.

Dr. Peter Delany co-chaired the NIDA-NDRI meeting on "HIV/AIDS in Drug Abuse Treatment Settings: Expanding Research & Practice", held March 25-26, 1999 in Bethesda, Maryland.

Dr. Peter Delany made a presentation on research funding opportunities to the Alcohol, Tobacco, and Other Drugs Section of the National Association of Social Workers, May 8, 1999 in New York City.

Dr. William S. Cartwright, SRB, DCSR presented a paper "The Economics of Public Health: Financing Drug Abuse Treatment Services." (with Dr. Paul Solano, University of Delaware) at the Western Economics Association International meeting held in San Diego, July 9, 1999.

Dr. Jerry Flanzer, SRB, DCSR spoke about NIDA's interest, current funding and related findings concerning co-occurring mental health and substance abuse disorders at the Multiple Disorders, Multiple Perspective Conference held by MCP Hahnemann University, Philadelphia, April 28-30, 1999.

Dr. Jerry Flanzer, SRB, DCSR moderated a panel/workshop on "Solutions Based Addiction Treatment", and assisted new investigators and doctoral candidates address applying to NIH for support at the Annual Addictions Institute, Addictions Through the Life Cycle Conference of the Alcohol, Tobacco and other Drugs Section of the National Association of Social Workers, at Fordham University, New York, May, 7-8, 1999.

Dr. Jerry Flanzer, SRB, DCSR co-led two workshops on "Substance Abuse Treatment within ASFA (Adoption and Safe Families Act) Timelines" at the Administration for Children and Families-Region V conference "Honoring the Promise of Permanency," Chicago, Ill. May 11-12, 1999.

Dr. Jerry Flanzer, SRB, DCSR presented a talk entitled "Working With Clients With Substance Abuse Issues-New Research Findings in the Field of Drug Abuse Research that Effects Decisions for Child Protection Workers" at the child abuse and neglect discretionary grant meeting of the Children's Bureau, Administration for Children, Youth and Families, June 3, 1999.

Dr. Jerry Flanzer, SRB, DCSR participated as an advisor/teacher in the Institute for the Advancement of Social Work Research's Ph.D. Dissertation Research Technical Assistance Workshop at IASWR's headquarters on June 4, 1999.

Dr. Jerry Flanzer represented SRB, DCSR at the Institute of Medicine's Meeting of Co-Occurring Disorders, Washington, D.C., June 8, 1999.

Dr. Jerry Flanzer and Dr. Tom Hilton represented SRB, DCSR at the 16th Annual Meeting of the Association of Health Services Research, Chicago IL on June 25-29, 1999.

Dr. Meyer Glantz (DEPR) was a panel participant and copresenter at the Center for Mental Health Services Resilience Conference, June 17 & 18, 1999 in Chantilly, Virginia.

Dr. William J. Bukoski, DEPR, served as the program conference chair for the 1999 Annual Meeting of the Society for Prevention Research (SPR) which was held June 24-26, 1999, New Orleans, LA.

Dr. Bukoski, DEPR, with Dr. Minda Lynch, DBR, co-chaired a scientific symposium on the topic of "The Integration of Basic Research and Prevention Science" at the 1999 Annual Meeting of the Society for Prevention Research. The session was titled: "Pre-clinical, Clinical, and Preventive Perspectives on Protection and Liability to Drug Abuse and Mental Disorders." Dr. Bukoski, also helped plan and co-chair two additional symposia at SPR. The titles of these symposia were: "Innovations in Training at Mental Health, AIDS, Drug Prevention Research, and Alcohol Prevention Research Centers," and "Just Say 'huh'? Integrating Indicated Prevention with Primary and Selective Substance Abuse Prevention Programming."

Drs. Kathy Etz and Elizabeth Robertson represented NIDA at the Society for Prevention Research in June, 1999. As part of the behavioral sciences work group tour, they led a session highlighting the research of early career investigators, mentoring advice from a senior investigator, and mechanisms to support early career investigators. Drs. Tony Biglan and Phil Fisher presented as part of the session.

Susan David, Jacques Normand, and Elizabeth Robertson hosted an agenda setting meeting titled Drugs and the Workplace on May 3 and 4, 1999. Researchers and representatives from multiple government agencies discussed new directions for research. A document summarizing the outcomes of the meeting is in preparation.

Arnold Mills, M.S.W., organized and chaired the Technical Assistance Workshop for Faculty and Staff from Historically Black Colleges and Universities, in Bethesda, MD, July 8-9, 1999. The purpose of the workshop was to provide an overview of funding mechanisms at NIH and information on proposal plan development, to review elements of a well-written proposal, and to discuss the proposal assessment process.

Richard Needle, Ph.D., Chief, Community Research Branch, DEPR, moderated two panels at the Centers for Disease Control and Prevention's National HIV Prevention Conference in Atlanta, Georgia, August 29-September 1, 1999. The first panel was on "HIV Prevention Interventions with Demonstrated Evidence of Effectiveness in Injecting Drug Users" and the second was a panel of international researchers on the topic of "Global Perspectives on Epidemiology and HIV Prevention in Drug-Using Populations."

Jacques Normand, Ph.D., CRB, DEPR presented a poster on research agendas and funding opportunities at the annual meeting of the American Sociological Association held in Chicago, IL, August 6-10, 1999.

Dr. Kathy Etz presented a poster co-authored with Drs. Robertson, Colliver and Glantz at the Society for Research on Child Development. The poster was entitled: The Gateway Theory of Adolescent Drug Use. The meeting was held in Albuquerque, New Mexico.

Dr. Elizabeth Robertson is representing NIDA on the Alcohol Coordination Team of the United States Public Health Services Guide to Community Preventive Service. The lead agencies for the coordination team are SAMHSA and CDC.

Dr. Jean Lud Cadet, Molecular Neuropsychiatry Section, NIDA IRP, presented a talk entitled "The Role of Free Radicals in METH-induced Neurotoxicity: Implications for Parkinsonism" at NIH, in June 1999.

Dr. Jean Lud Cadet, Molecular Neuropsychiatry Section, NIDA IRP, presented a talk entitled "The Role of Free Radicals and Death-Related Genes in METH-induced Apoptosis" at NIDA Headquarters, in July 1999.

Dr. Jonathan Katz presented a paper entitled: "The Dopamine Transporter Hypothesis of Cocaine Effects" at the FASEB Summer Conference on Biological Vulnerability to Alcoholism and Drug Addiction.

Dr. David Gorelick presented an invited lecture on "Interrelationships among Tobacco, Marijuana, and Cocaine Smoking" at the 1999 FASEB Summer Research Conference on Pulmonary Pathophysiology and Immune Consequences of Smoked Substance Abuse, Copper Mountain, CO, July 18-23, 1999.

Dr. D. Bruce Vaupel presented "In Vitro and In Vivo Evaluation of 5-[I-123]iodo-A-85380 as a Radiotracer for Single Photon Emission Computed Tomography Imaging of Nicotinic Acetylcholine Receptors" at the Biomedical Imaging Symposium "Visualizing the Future of Biology and Medicine", Bethesda, MD, June 25-26, 1999.

Dr. Monique Ernst presented "High-Resolution Noninvasive Vascular Imaging Using Real-Time Magnetic Resonance Imaging Techniques" at the Biomedical Imaging Symposium "Visualizing the Future of Biology and Medicine",

Bethesda, MD, June 25-26, 1999.

Dr. Monique Ernst presented "Nicotine and Cerebral Blood Flow During a Working Memory Task" at the Biomedical Imaging Symposium "Visualizing the Future of Biology and Medicine", Bethesda, MD, June 25-26, 1999.

"Pharmacokinetics of Liquid Vs Tablet Buprenorphine" K. Ajir, N. Chiang, and W. Ling, Presented at the 61st Annual Scientific Meeting of the College on Problems of Drug Dependence, 13 June 1999, Acapulco, Mexico.

"How to Use Quantitative Benzoyllecgonine Levels for the Interpretation of Cocaine Usage in Clinical Trials" C.N. Chiang, S.H. Li, B. Tai, C. Marschke, K.L. Preston, R.L. Hawks, and F. Vocci, Presented at the 61st Annual Scientific Meeting of the College on Problems of Drug Dependence, 13 June 1999, Acapulco, Mexico.

"The Effect of Chronic Cocaine Use on MAO and COMT Activities in the Human Brain: A Postmortem Study". A. Elkashef, D. Mash, G. Eisenhofer, S. Izenwasser, J. Pablo, T. Bridge, and F. Vocci, Presented at the 61st Annual Scientific Meeting of the College on Problems of Drug Dependence, 13 June 1999, Acapulco, Mexico.

"Inpatient Evaluation for the Tolerability of High Dose Dextromethorphan in Methadone-Maintained Subjects" B.H. Herman, J.W. Cornish, R.N. Ehrman, A.R. Rose, V. Bead, C. Hackett, K. Martz, F.S. Caruso, F. Vocci, and C.P. O'Brien, Presented at the 61st Annual Scientific Meeting of the College on Problems of Drug Dependence, 13 June 1999, Acapulco, Mexico.

"Inpatient Safety Evaluation of Lofexidine, An Alpha-2 Adrenergic Agonist As A Medication for Opiate Withdrawal" E. Yu, B.H. Herman, K. Miotto, A. Montgomery, P.J. Fudala, C. Fisher, C.N. Chiang, W. McFadden, K. Kampman, V. Dhopes, J. Cornish, B. Walsh, K. Davies, F. Vocci, W. Ling, C.P. O'Brien, Presented at the 61st Annual Scientific Meeting of the College on Problems of Drug Dependence, 13 June 1999, Acapulco, Mexico.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****May, 1999**

Media and Education Activities

Awards

The "NIDA Goes to School" program continues to receive awards. In recognition of the development, promotion and dissemination of the program, NIDA received an NIH Director's Award. The program also received an APEX '99 Award of Excellence, which is sponsored by Communications Concepts, Inc.

NIDA's video, "Treatment Solutions," received a bronze award for video communications from Questar Awards 99. This award is from MerComm, Inc., which is affiliated with the International Academy of Communication Arts and Sciences.

Media Activities

June 11, 1999, Los Angeles Times - Commentary by Alan I. Leshner, Ph.D. - Why Shouldn't Society Treat Substance Abusers? Drugs: Let's get past the moral outrage and use available solutions to help addicts and, in turn, to help everyone. The piece was also carried by the LA Times Syndicate and appeared in the St. Louis Post Dispatch.

Three by-lined columns have been distributed nationwide in the last three years through a news service. Topics include, The Essence of Addiction, Nicotine Addiction, and Why Do Sally and Johnny Use Drugs? To date, the columns have generated more than 3,400 newspaper articles around the country.

Press Releases

June 14, 1999 - Combined Drug Counseling Approach Works In Treating Cocaine Addiction. Drug addiction treatment combining individual and group drug counseling reduced cocaine use more effectively than group drug counseling alone or in combination with cognitive or supportive-expressive psychotherapy, according to a study reported in the June 1999 issue of *The Archives of General Psychiatry*. The findings are from the multi-center NIDA Collaborative Cocaine Treatment Study. This study sites included: University of Pennsylvania; Brookside Hospital (Nashua, New Hampshire); Western Psychiatric Hospital and Clinic, University of Pittsburgh; and McLean Hospital and Massachusetts General Hospital, Harvard Medical School. Extramural scientists from NIDA also collaborated on the study. The University of Pennsylvania provided overall coordination for the project. As a result of this news release, the articles appeared in *Reuters Health*.

June 14, 1999 - Severity of Problems is Key to Best Type of Treatment for Cocaine Addiction. Cocaine addicts with problems such as unemployment, poor support from family and friends, current alcohol or multidrug use, depression or anxiety require more intensive and lengthier treatment to overcome their drug abuse than those without such problems according to a new study in the June 1999 issue of *Archives of General Psychiatry*. The study investigated 1,605 cocaine patients admitted during 1991-1993 to 55 community based treatment programs in

NIDA's nationwide Drug Abuse Treatment Outcome Study (DATOS). As a result of this news release, articles appeared in *The Wall Street Journal*, *CNN* and *Reuters Health*.

June 14, 1999 - Long-Term Brain Injury From Use of "Ecstasy." The designer drug "Ecstasy," or MDMA, causes long-lasting damage to brain areas that are critical for thought and memory, according to new research findings in the June 15 issue of *The Journal of Neuroscience*. In an experiment with red squirrel monkeys, researchers at the Johns Hopkins University demonstrated that 4 days of exposure to the drug caused damage that persisted 6 to 7 years later. As a result of this news release, articles appeared in *The Los Angeles Times*, *The Toronto Star*, *The Boston Globe*, *The Wall Street Journal*, *Reuters Health*, *The Journal of Neuroscience*, *The Chicago Tribune*, *The Orlando Sentinel*, *The New York Post*, *The Mirror*, and on *MSNBC* and *CNN*.

June 14, 1999 - NIH Institute Opens Treatment Research Center in Baltimore to Help Teens Quit Smoking. NIDA announces the opening on June 23rd of its Teen Tobacco Addiction Treatment Research Clinic (TTATRC), at the new Adolescent Clinic in the IRP's laboratories on the Johns Hopkins Bayview Campus in East Baltimore. This Center will assess which smoking cessation methods, including the use of nicotine patches and gum, with supportive counseling, are effective with teenagers. As a result of this news release, the article appeared in *The Washington Post* and as a *Substance Abuse Report*.

August 1, 1999 - Chronic, Heavy Cocaine Use Associated with Long-Lasting Impaired Function. The detrimental effects of heavy cocaine use on an individual's manual dexterity, problem solving, and other critical skills can last for up to a month after the drug was taken, according to a study reported in the Summer issue of *The Journal of Neuropsychiatry and Clinical Neurosciences*. The study, which was conducted by researchers at NIDA's Intramural Research Program and the Johns Hopkins University School of Medicine, found that heavy cocaine users were outperformed by moderate users and non-users on most tests measuring verbal memory, manual dexterity, and other cognitive skills. Heavy cocaine use was defined as two or more grams a week. As a result of this news release, articles appeared in *The Washington Times*, *Washington Dateline* and *The Journal of Neuropsychiatry*.

August 2, 1999 - Boys Treated With Ritalin, Other Stimulants Significantly Less Likely to Abuse Drugs Later. Boys with attention deficit hyperactivity disorder (ADHD) who are treated with stimulants such as Ritalin are significantly less likely to abuse drugs and alcohol when they get older, according to a new study funded by NIMH. The study, which appeared in the August 2, issue of *Pediatrics*, compared three groups of boys - those with ADHD who had been treated with stimulants, those with ADHD who had not been treated with stimulants, and those without ADHD -- and their susceptibility to substance use disorder.

On June 21, 1999, Dr. Jean Lud Cadet was interviewed by Maryland Public Television on the Teen Tobacco Addiction Treatment Research Center.

On June 23, 1999, Dr. Jean Lud Cadet was interviewed by Fox 45 on the Teen Tobacco Addiction Treatment Research Center.

Media Advisories

January 13, 1999 - **NIDA Launches a Major Effort to Establish National Drug Abuse Treatment Clinical Trials Network.** NIDA has taken major steps forward in establishing a critically needed research infrastructure that will test and disseminate science-based addiction treatments in real life settings throughout the country by establishing the National Drug Abuse Treatment Clinical Trials Network. As a result, articles appeared in the AAAP Newsletter, the American Psychological Society Observer, and CADCA's Coalitions.

March 9, 1999 - **Miramax, NBC, CBS, & ABC Among Winners of PRISM Awards Which Champion Accurate Depiction of Drug Use In Movies & On TV.** The Third Annual PRISM Awards, which spotlight outstanding efforts of the entertainment industry to accurately depict drug use and addiction in entertainment products, were presented at the Beverly Hills Hotel, Beverly Hills, CA. As a result, stories appeared on all TV Channels in LA, plus in *USA Today*, *The Los Angeles Times*, *Daily Variety*, *The Hollywood Reporter*, *Substance Abuse Report*, *Alcoholism and Drug Abuse Weekly*, and *TV Guide On-Line's Daily Dish*, and an Associated Press story ran in over 100 newspapers nationwide.

NIDA Exhibits Program

The following are meetings where NIDA exhibited its publications and program announcements over the past several months:

June 3-5, 1999 -- National Association of Drug Court Professionals

June 3-6, 1999 -- American Psychological Society

June 5-9, 1999 -- National Association of State Alcohol and Drug Abuse Directors and National Prevention Network

June 26-29, 1999 -- 103rd Annual National Congress of Parents and Teachers Association

July 14-17, 1999 -- Association on Higher Education and Disability

July 15-18, 1999 -- AIDS Impact 1999

August 15-20, 1999 -- International Congress on Alcohol and Drug Dependence

August 20-24, 1999 -- American Psychological Association

Planned Meetings

On September 22, 1999, the MDD will sponsor a symposium on HPA dysfunction in psychiatric disorders. The aim of this symposium is to discuss similarities and differences, and biological significance of HPA hypo and hyperactivity in mental illness, including drug dependence.

CAMCODA is organizing a workshop on the **Role of Neuroendocrines and Micronutrients in Neuropsychiatric Complications in HIV Infection and Drug Abuse**. The workshop is scheduled for September 29-30, 1999, Conference Room D, Natcher Building, NIH Campus. Contact: Dr. Walter Royal or Jag Khalsa, Ph.D., CAMCODA, 301-443-1801

The Behavioral Science Workgroup is sponsoring a satellite symposium on **"Career Pathways in Behavioral Neuroscience"** at the Society for Neuroscience's annual meeting in October of 1999 in Miami, Florida. The symposium is one in a series of events on "Early Career Pathways: Opportunities for Behavioral Researchers" hosted by the workgroup throughout 1999. The events showcase particularly promising early career investigators whose behavioral science research programs in drug abuse are supported through a variety of different funding mechanisms. NIDA grantees Dr. Robert L. Balster and Dr. Lisa Gold will deliver oral presentations on "mentoring and being mentored" with NIDA support. Dr. Lucinda Miner from NIDA's Office on Science Policy and Communications will discuss sources of support that are appropriate for research and career development at the predoctoral, postdoctoral and junior investigator level. Twenty poster presenters will represent the diversity of behavioral research in neuroscience sponsored by the institute and were selected from among present training center fellows, individuals supported by minority supplements, B/START or FIRST/* awardees and career development (K mechanisms) grantees.

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National Institute on Drug Abuse
Director's Report to the National Advisory Council on Drug Abuse
September, 1999

Publications

Dr. Naimah Weinberg and Dr. Meyer Glantz, of the Division of Epidemiology and Prevention Research, served as guest editors for a Special Section on Child Psychopathology Risk Factors for Drug Abuse, for the September 1999 issue of the *Journal of Clinical Child Psychology*. This section includes six original papers by participants in NIDA's July 1997 Workshop on Child Psychopathology Risk Factors for Drug Abuse, and a discussion piece by Dante Cicchetti. Many of the contributors are NIDA grantees. The three population-based studies move the field beyond cross-sectional comorbidity surveys, by studying children and risk factors longitudinally. The three family-based studies apply novel methodologic approaches to understanding familial risk and comorbidity. In addition to serving as guest editors, Drs. Weinberg and Glantz contributed an overview paper which reviews the current literature and introduces the special section. Weinberg, N.Z., and Glantz, M.D. "Child Psychopathology Risk Factors for Drug Abuse: Overview." *Journal of Clinical Child Psychology*, 28, pp. 290-297, 1999.

A new research volume, supported in part by NIDA, the American Anthropological Association, and the Wenner Gren Foundation for Anthropological Research, reviews the past contributions of research that has combined ethnography with epidemiology to understand risks for HIV in drug using populations. Chapters in this new volume cover such issues as the application of ethnographic and other qualitative methods in epidemiological research on drug use and HIV/AIDS in diverse community settings; the significance of historical, political, economic, and sociocultural factors for understanding drug use behavior and risks for HIV/AIDS; the integration of methodological approaches in collaborative studies involving ethnography and virology; the challenges that often arise in ethnographic and epidemiological research on drug abuse and HIV transmission, such as studies of social and sexual risk networks, needle exchange programs, gender-based/sensitive issues, and violence; the role of multidisciplinary and qualitative research in developing treatment and prevention strategies and evaluating interventions; and the nature and resolution of ethical dilemmas in anthropological and epidemiological research on drug abuse and HIV/AIDS. Marshall, P., Singer, M., Clatts, M. (Eds.) with Guest Editors, R. Needle and E. Lambert. *Integrating Anthropological Approaches in Epidemiological and Prevention Research on Drug Abuse and HIV/AIDS*. NIDA Research Volume, September 1999.

Weinberg, N.Z. "Cognitive and Behavioral Deficits associated with Parental Alcohol Use." In: M.E. Hertzog and E.A. Farber (Eds.), *Annual Progress in Child Psychiatry and Child Development 1998*, Philadelphia: Brunner/Mazel, pp. 315-329, 1999. Reprinted from *Journal of the American Academy of Child and Adolescent Psychiatry*.

Weinberg, N.Z. "Commentary: Behavioral Inhibition and Developmental Risk." *Journal of the American Academy of Child and Adolescent Psychiatry*, 38, pp. 417-420, 1999.

Simpson, D.D., Joe, G.W., Fletcher, B.W., Hubbard, R.L., and Anglin, M.D., *A National Evaluation of Treatment Outcomes for Cocaine Dependence*. *Archives of General Psychiatry* 56(6), pp. 507-514, 1999.

Hilton, T. "Enrolling Management Support for Dealing with Poor Performers", *Government Executive Magazine Online*, June 8, 1999.

Avants, S.K., Margolin, A., Sindelar, J.L., Rounsaville, B.J., Schottenfeld, R., Stine, S., Cooney, N.L., Rosenheck, R.A., Li, Shou-Hua, and Kosten, T.R. "Day Treatment versus Enhanced Standard Methadone Services for Opioid-Dependent

Patients: A Comparison of Clinical Efficacy and Cost." Am J Psychiatry, 156, pp. 27-33, 1999.

Bolla, K.I., Rothman, R., and Cadet, J.L. "Dose-Related Neurobehavioral Effects of Chronic Cocaine Use." J Neuropsychiatry Clin Neurosci 11(3), pp. 361-369, 1999.

Jayanthi, S., Ladenheim, B., Andrews, A.M., and Cadet, J.L. "Overexpression of Human Copper/Zinc Superoxide Dismutase in Transgenic Mice Attenuates Oxidative Stress Caused by Methylenedioxymethamphetamine (Ecstasy)." Neuroscience 91(4), pp. 1379-1387, 1999.

Herning, R.I., King, D.E., Better, W.E., and Cadet, J.L. "Neurovascular Deficits in Cocaine Abusers." Neuropsychopharmacology 21(1), pp. 110-118, 1999.

Bell, S.L., Taylor, R.C., Singleton, E.G., Henningfield, J.E., and Heishman, S.J. "Smoking after Nicotine Deprivation Enhances Cognitive Performance and Decreases Tobacco Craving in Drug Abusers." Nicotine and Tobacco Research 1, pp. 45-52, 1999.

Heishman, S.J. and Henningfield, J.E. "Is Caffeine a Drug of Dependence? Criteria and Comparisons." In B.S. Gupta and U. Gupta (Eds.), Caffeine and Behavior: Current Views and Research Trends, pp. 137-150. Boca Raton, FL: CRC Press, 1999.

Shurtleff, D. "Comment: Applying Behavioral Economics to the Challenge of Reducing Cocaine Abuse." In: Chaloupka, F.S., Grossman, M., Bickel, W.K., and Saffer, H. (Eds.). The Economic Analysis of Substance Use and Abuse. Chicago, IL.: University of Chicago Press, pp. 180-184, 1999.

Epidemiologic Trends in Drug Abuse: Community Work Group, Volume II, December 1998: Proceedings

NIH Pub. No. 99-4527

This publication provides an in-depth analysis of the epidemiologic trends in drug use reported by NIDA researchers located in selected cities and states throughout the United States.

Pending Publications

Approaches to Substance Abuse Counseling

NIH Pub. No. 99-4151

This publication will detail descriptions of 12 counseling approaches currently being used in the United States. Contributions from the University of Pennsylvania, the Hazelden Foundation, and the Betty Ford Center, among others, are included.

Integrating Cultural, Observational, and Epidemiological Approaches in the Prevention of Drug Abuse and HIV/AIDS: Current Status and Future Prospects

NIH Pub. No. 99-4565

This publication, developed in conjunction with the American Anthropological Association, will report on a variety of topical areas including the application of ethnographic methods to epidemiological research on drug use and HIV/AIDS prevention and the role of multidisciplinary and qualitative research in developing treatment and prevention strategies.

Measuring and Improving Cost, Cost-Effectiveness, and Cost-Benefit for Substance Abuse

NIH Pub. No. 99-4518

This "how to" manual will provide managers of substance abuse programs with a step-by-step approach to conducting cost-effectiveness and cost-benefit analyses of their programs.

Mind Over Matter-The Brain's Response to Methamphetamine

NIH Pub. No. 99-4394

This addition to NIDA's award-winning "Mind Over Matter" series targeting middle school age youth will address scientific information about how methamphetamine acts in the brain and body.

National Survey Results on Drug Use from the Monitoring the Future Study, 1975-1998: Volume I: Secondary School Students

NIH Pub. No. 99-4660

Volume II: College Students and Young Adults

NIH Pub. No. 99-4661 These two publications will report on the cumulative findings of the NIDA-supported Monitoring the Future study which examines the prevalence of drug use among American secondary students (i.e., 8th, 10th,

and 12th grades), college-age, and young adults.

Principles of Drug Addiction Treatment-A Research-Based Guide

NIH Pub. No. 99-4180

The publication will provide over-arching principles related to effective drug addiction treatment based on 25 years of NIDA research. Also included will be answers to commonly asked questions about drug treatment, descriptions of major kinds of treatment, examples of effective therapies, and a resource section.

NIDA NOTES

NIDA NOTES, Vol. 14, Issue No. 2

The association between drug abuse and infectious diseases is highlighted in this issue in an article about heroin snorters and their risk of contracting several infectious diseases and transitioning to injecting drug use. The Director discusses the ways in which NIDA's drug abuse research helps curb the spread of HIV/AIDS, tuberculosis, and hepatitis B and C. New medication compounds that attach cocaine in the bloodstream before it affects the brain are discussed, as well as the role of two neurotransmitters in affecting cocaine's action in the brain. Other articles feature the new members of NIDA's Advisory Council and how NIDA has tracked drug abuse patterns over the years.

NIDA NOTES, Vol. 14, Issue No. 3

This issue's lead article and Director's Column deal with the subtle but significant effects of prenatal cocaine exposure. NIDA's most recent Town Meeting in Atlanta is covered. Another article looks at how a NIDA-supported science education project in a California high school is sparking student interest in science in general and drug abuse research. The Tearoff offers information in brief on cocaine abuse and treatment.

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National Institute on Drug Abuse

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Staff Highlights

Honors and Awards

NIH Director's Award

Donna M. Jones, OPRM

Frank Vocci, Ph.D., MDD, (as part of a group entitled "Conference Planning Committee: Biomarkers and Surrogate Endpoints")

Jonathan D. Pollock, Ph.D., DBR, (as part of a group entitled "Trans-NIH Zebrafish Coordinating Committee")

Beverly Jackson, Jan Lipkin, Joan Nolan, Catherine Sasek, Ph.D., Jack Stein, LCSW, and Keith Van Wagner, OSPC, (as part of the NIDA Goes to School Working Group)

Other Honors and Awards

Dr. William J. Bukoski, DEPR, was the recipient of the Society for Prevention Research Public Service Award presented at the 1999 Annual Meeting of the Society held in New Orleans, June 24-26, 1999. The award was given in recognition of Dr. Bukoski's "leadership in supporting drug abuse prevention research in the Federal government."

Arthur MacNeill Horton, Jr., Ed.D., DCSR, has been elected to the office of Secretary in the newly formed Coalition of Clinical Neuropsychology Practitioners (CCNP).

Roy Pickens, Ph.D., IRP, was awarded the J. Michael Morrison Award at the 1999 Annual Meeting of the College on Problems of Drug Dependence in Acapulco, Mexico in recognition of his outstanding contributions in the area of scientific administration related to drug abuse. This award is given in memory of J. Michael Morrison, who was a well-liked and respected administrator at NIDA.

Staff Changes

Ann Anderson, M.D., M.P.H., formerly of the Centers for Disease Control and Prevention, joined the Clinical Trials Branch of the Medications Development Division as a Medical Officer, July 1999. Dr. Anderson received her M.D. degree from the University of Illinois and was in the private practice of family medicine for 12 years before obtaining an M.P.H. from the University of Washington. Dr. Anderson then joined the Centers for Disease Control, where she worked in the Epidemiology Intelligence Service and Fetal Alcohol Prevention Branch.

Janice Collins joined CAMCODA as a secretary on May 9, 1999.

Michel Desbois joined NIDA as Chief of OPRM's Information Resource Management Branch on July 4, 1999. Mr. Desbois has a degree in engineering and a masters in information systems. In addition to working as an engineer, he has experience in running a LAN, managing a helpdesk, and, most recently, developing and running large oracle-based data systems for the Department of Defense.

Juanita Johnson joined OSPC's Science Policy Branch as a Program Assistant on June 6, 1999. Ms. Johnson was formerly with the Department of Defense.

David Lisle, previously a Management Intern with NIH, joined OPRM's Contracts Management Branch on August 1, 1999 as a Contract Specialist.

Marilyn Thomas joined OEPR on May 23, 1999 as a Grants Technical Assistant in the Clinical, Epidemiological, and Applied Sciences Review Branch. Ms. Thomas comes to NIDA from the National Institute of Nursing Research.

Dr. Peter Delany, Deputy Chief, Services Research Branch, has accepted a detail as Acting Deputy Director of NIDA's Division of Clinical and Services Research.

Dr. Stephen Heishman, IRP, has been appointed Associate Director for Education and Training.

Dr. Alane S. Kimes, IRP, has been appointed Acting Chief, Neuroimaging Branch and Acting Director, Brain Imaging Center.

Dr. Robert Battjes retired July 31, 1999, after a long and distinguished career in the Public Health Service. He began his career in 1969 as a clinician and ward administrator at the Lexington, KY treatment facility and held a number of important positions during his 30 years in the Service, including Director of the Alcohol, Drug Abuse and Mental Health Division in the Kansas City Field Office. Dr. Battjes came to NIDA in 1977 and held senior positions in the Division of Prevention and Treatment Development, as Chief of the Prevention Research Branch, and as Associate Director for Planning of the Division of Clinical Research. He also held a detail to the Office of the Assistant Secretary of Defense where he coordinated and edited the congressionally mandated report of the blue ribbon panel on health promotion. Most recently, Dr. Battjes held the position of Deputy Director of NIDA's Division of Clinical and Services Research.

Grantee Honors

Dr. E. Jane Costello of Duke University has been named to receive the Rema Lapouse Award at the 1999 meeting of the American Public Health Association. This award, from the sections on Mental Health, Epidemiology, and Biostatistics, recognizes outstanding contributions to the field of mental health epidemiology. Dr. Costello will be honored at the annual meeting of the APHA in November, in Chicago, where she will give a talk entitled "Public Health And Child Mental Health: Past, Present, And Future".

Dr. Dennis McCarty of Brandeis University was selected to join the editorial board for the Journal of Behavioral Services & Research.

Dr. Lester Luborsky, Professor Emeritus at the University of Pennsylvania, was awarded the Gold Medal Award for Lifetime Achievement in the applications of psychology, by the American Psychological Foundation. Dr. Luborsky is recognized as a pioneer and leading senior scientist in the field of psychodynamic psychotherapy for general mental disorders and for drug abusers.

Dr. Richard N. Zare of Stanford University was honored in 1998 by the Royal Society of Chemistry in the United Kingdom and also by the American Chemical Society. He was the 1999 recipient of the prestigious Welch Award in Chemistry for his lifetime achievements.

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