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

September, 1995

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

Basic Research

Cloning and Functional Characterization of a k3-Related Opioid Receptor:

Dr. Gavril W. Pasternak of Memorial Sloan-Kettering Cancer Center and of Cornell University Medical College and his research team have identified a putative opioid receptor from mouse brain (KOR-3), belonging to the G protein-coupled receptor family, that is distinct from the previously cloned μ, d, and k receptors.

Assignment of the clone to the opioid receptor family derives from both structural and functional studies. Its predicted amino acid sequence is highly homologous to that of the other opioid receptors, particularly in many of the transmembrane regions, where long stretches are identical to μ, d, and k1 receptors. Both cyclazocine and nalorphine inhibit cAMP accumulation on COS-7 cells stably expressing the clone. Northern analysis shows that the mRNA is present in brain but not in a number of other organs. Southern analysis suggests a single gene encoding the receptor. A highly selective monoclonal antibody directed against the native k3 receptor recognizes, in Western analysis, the clone expressed in COS-7 cells. The in vitro translation product is also labeled by the antibody. Additional clones reveal the presence of several introns, including one in the second extracellular loop and another in the first transmembrane region.

Antisense studies with an oligodeoxynucleotide directed against a region of the second extracellular loop reveal a selective blockade of k3 analgesia in vivo that is not observed with a mismatch oligodeoxynucleotide based upon the antisense sequence. The μ, d, and k1 analgesia is unaffected by this antisense treatment. Antisense mapping of the clone downstream from the splice site in the first transmembrane region reveals that six different antisense oligodeoxynucleotides all block k3 analgesia. In contrast, only one of an additional six different antisense oligodeoxynucleotides directed at regions upstream from this splice site is effective. This strong demarcation between the two regions raises the possibility of splice variants of the receptor. An additional clone reveals an insert in the 3' untranslated region. It is concluded that the antibody and antisense studies strongly associate KOR-3 with the k3-opioid receptor, although it is not clear whether it is the k3 receptor itself or a splice variant. (Yin-Xian Pan, Jie Cheng, Jin Xu, Grace Rossi, Elissa Jacobson, Jennifer Ryan-Moro, Andrew I. Brooks, Gary E. Dean, Kelly M. Standifer, and Gavril W. Pasternak. Cloning and Functional Characterization Through Antisense Mapping of a k3-Related Opioid Receptor. Mol. Pharmacol. 47:1180-1188 (1995))

PCP Induced Permanent Brain Damage:

Dr. John Olney (Washington University) is examining the neurotoxicity in the rat brain produced by antagonists of the NMDA (*N*-methyl-d-aspartate) subtype of glutamate receptor, such as phencyclidine (PCP), ketamine, or MK-801 (dizocilpine). The vacuolar injury (low dose) or death (high dose) of neurons in several corticolimbic regions of the adult rat brain is hypothesized by Dr. Olney to model schizophrenia, and NMDA receptor hypofunction has been proposed (by Dr. Olney and others) as a possible mechanism in schizophrenia.

Two studies focused on factors that influence vulnerability of rats to the NMDA antagonist neurotoxicity. In the first study (Farber, Wozniak, Price, Labruyere, Huss, St. Peter & Olney, Biological Psychiatry, in press), they found that

this neurotoxic syndrome (now called the "Olney lesion" by most other workers in this field) has an age dependency resembling schizophrenia, with age of onset of full susceptibility being early adulthood. In the second study (Farber & Olney, 1994, Society for Neuroscience Abstracts), they confirmed their previous data showing that adult female rats are more sensitive than males to NMDA antagonist neurotoxicity, but extended this finding by demonstrating that during pregnancy they become hyposensitive.

The ability of a high dose of PCP to kill neurons in rat brain was described for the first time (Corso, Wozniak, Sesma & Olney, 1994, Society for Neuroscience Abstracts). A single 50 mg/kg IP dose in adult female rats killed many neurons in the posterior cingulate and retrosplenial cortices; occasionally it killed neurons in other neocortical and limbic regions. They also found that a high dose of MK-801 in adult male mice causes a permanent memory acquisition deficit (Brosnan-Watters, Wozniak, Nardi, Olney & Fix, 1994, Society for Neuroscience Abstracts). Scopolamine provides partial protection, and pentobarbital complete protection, against MK-801 induced neuronal necrosis (Wozniak, Nardi, Corso & Olney, 1995, Society for Neuroscience Abstracts). The necrotic action of NMDA antagonists does not appear to involve apoptotic cell death processes (Ishimaru, Der, Tenkova, Sesma, Thurston & Olney, 1995, Society for Neuroscience Abstracts).

Stress and Sensitization in Animals:

Current research being conducted by Dr. Sydney Antelman at the University of Pittsburgh is directed to studying the hypothesis that sensitization is a time-dependent phenomenon. He and his collaborators have shown that cocaine administration to animals sensitized to the limits of their systems results in an "on-off" oscillatory pattern of physiological, neurochemical and behavioral responses. These results suggest that a host of systems - both neuronal and hormonal - when maximally sensitized, respond to further stimulation by "toggling" back and forth. This has implications for improving our understanding of cycling illnesses such as recurrent depression, manic disorders, and drug addictions.

Ibogaine: Preclinical Studies:

Dr. Stanley Glick (Albany Medical College) is studying the effects of ibogaine and ibogaine congeners on cocaine and morphine self-administration in the rat. He has shown that ibogaine blocks the rewarding effects of cocaine and morphine in the animals for several days after the motoric effects had dissipated, and that these effects last for up to 27 days, depending upon the dose. Marked decreases in dopamine levels were seen in brain levels using microdialysis methodology, indicating that the effects appear to be correlated. Dr. Glick has developed a sensitive (20 ng/ml) and highly specific GCMS analytical method for measuring ibogaine in biological samples. Using this technique, he has reported that ibogaine disappears rapidly from rat brain (40 mg/kg IP injection resulted in 3.3 ug/g in brain at 1 hour but only 190 ng/g at 19 hours). He is currently developing a method to measure noribogaine levels.

Finally, Dr. Glick reported that ibogaine (100 mg/kg/day IN x 3) resulted in bilaterally symmetrical, parasaggital strips of Purkinje cell degeneration in the rats. The degeneration was similar, but more severe, than Molliver and O'Hearn reported. A lower dose (40 mg/kg/day IP x 3) did not produce these effects.

Dopamine Receptors and Reinforcement:

Dr. James Belluzzi (University of California, Irvine) has been investigating the involvement of different dopamine receptor subtypes in the mediation of reinforcement (primary vs. conditioned vs. classical). Using a series of D1 (SKF 82958, SCH 23390) D2 (N-0923, [+]-PHNO, pergolide) and D3 compounds (7-OH-DPAT, PD-128,907), Dr. Belluzzi has concluded that cocaine-like self-administration is most closely mimicked by D1 agonists and that D1 receptors have a primary role in cocaine place preference and classical conditioning phenomena.

Prenatal Cocaine: Effects on the Offspring:

Dr. Larry Middaugh (Medical University of South Carolina) has been investigating the effects of prenatal cocaine in rats on the developing fetus and through the lifespan of the offspring. Dr. Middaugh has found that prenatal cocaine produces long-term alterations in the offspring's neural systems which utilize dopamine as the transmitter. This was seen by studies which showed a greater response to D2 agonists in the cocaine-treated offspring as compared to placebo-treated control offspring. Neither D1- nor D2-binding was altered in these cocaine-treated offspring, further

suggesting an alteration in their neural systems rather than a change in their receptor binding.

Prenatal Cocaine: Effects on the Offspring:

Dr. Charles Mactutus (University of Kentucky) used a novel vascular port model to inject IV cocaine daily to pregnant rats and measure arterial sampled plasma levels of cocaine and metabolites in the dams. Studies in the offspring indicated an attentional disorder in the weanlings that apparently dissipated by 6 months of age. However, when these animals were given a challenge dose of cocaine at that time, they produced a markedly exaggerated behavioral response to the cocaine (sensitization).

Phospholipase A2 Modulation of the Dopamine Transporter:

In recent years arachidonic acid has been found to inhibit sodium dependent substrate transport including the dopamine transporter. Since dopamine stimulation has recently been reported to induce arachidonic acid release as a signal transduction pathway, it is conceivable that cocaine induced arachidonic acid release could indirectly inhibit dopamine uptake, in addition to the direct inhibition of dopamine uptake by cocaine. NIDA grantee Dr. Paul S. Berger of the University of California, San Francisco and his coworkers have observed that activation of phospholipase A2, the major enzyme which releases arachidonic acid, by local injections of the drug melittin into the VTA leads to a persistent sensitization of cocaine possibly by activating a dopaminergic signal transduction pathway.

Consistent with this hypothesis they have found that co-administration of quinacrine (a phospholipase A2 inhibitor) with cocaine prevents the development of sensitization to cocaine. These results are described in a manuscript in press in the journal Psychopharmacology and may be potentially useful in developing novel cocaine pharmacotherapies.

Opiates and Neonatal Respiratory Function:

Morphine-6-beta-D-glucuronide (M6G), an active metabolite of morphine, causes respiratory depression similar to the parent compound. However, in neonatal animals, the potency of M6G with respect to respiratory depression increases with aging. As there are no developmental changes in the distribution of M6G in the brain, an alteration in opioid receptors may explain these differences. Drs. Laine Murphey and George D. Olsen, in a recent short communication, report developmental changes of *mu* receptors in the brain stem of neonatal guinea pigs and the significance of increased *mu* receptors in the augmented potency of M6G respiratory effects during the first week after birth. (L.J. Murphey & G.D. Olsen, Developmental Brain Research 85:146-148,1995.)

Marijuana and Pregnancy:

NIDA supported researchers, Dr. S.K. Dey and his associates from the University of Kansas Medical Center, Kansas City, recently reported that both brain- and spleen-type cannabinoid receptor mRNAs are expressed in the preimplantation mouse embryo; whereas in the mouse uterus, only the brain-type cannabinoid receptor mRNA is expressed. They also observed that both oviduct and uterus had the capacity to synthesize the putative endogenous cannabinoid ligand, anandamide, suggesting the preimplantation mouse embryo and the uterus as targets for cannabinoid ligand-receptor signaling. Although the significance of these findings especially in the preimplantation mouse embryo with the cannabinoid binding sites several fold higher than those in the brain needs to be determined, these findings are still important from the public health view/concern. From these results, the P.I. suggests that the reported adverse effects of cannabinoid use or abuse seen during pregnancy and in uterine disorders could be due to an aberrant expression of the endogenous ligand in the reproductive tract and of the receptors in the embryo and uterus. (S.K. Das, B.C. Paria, I. Chakraborty and S.K. Dey, Proc. Natl. Acad. Sci. 92: 4332-4336, 1995; B.C. Paria, S.K. Das and S.K. Dey, Proc. Natl. Acad. Sci., in press.)

Excitotoxic Insult Due to Ibogaine Leads to Delayed Induction of NADPH-diaphorase and Neuronal NOS in Purkinje Cells.

The cover of NeuroReport, vol. 6, #12, August, 1995, featured plates of immunohistochemical data from an accompanying journal article by Elizabeth O'Hearn, M.D., Peisu Zhang, and Mark Molliver, M.D. of Johns Hopkins

University School of Medicine. Mature cerebellar Purkinje cells do not normally express neuronal nitric oxide synthase (nNOS) or NADPH-diaphorase activity, but this study demonstrates the induction of these enzymes in response to ibogaine treatment. Ibogaine treatment leads to the rapid, dose-dependent degeneration of Purkinje cells due to excitotoxic injury; however, the induction of nNOS in surviving Purkinje cells follows a delayed time course. The functional significance of nNOS induction following neuronal injury is unknown. It also remains to be determined whether nNOS expressing Purkinje cells go on to degenerate or whether nNOS is associated with recovery from sub-lethal neuronal injury.

Morphine Stimulates Growth of HIV in Brain Cell Cultures:

In early studies, Peterson and colleagues observed an increase in the production of HIV in co-cultures of humanymphocytes with the addition of either cocaine or morphine. More recently, they have also shown this relationship extends to co-cultures of human microglia with a HIV-growth-culture-clone U1. That is, morphine stimulates HIV growth in this co-culture in the presence of a cytokine-stimulant LPS; this upregulation is naloxone sensitive. In a second study, two new antiviral agents were tested as inhibitors of HIV growth in these cultures and were observed to be more potent than AZT. Morphine amplifies HIV-1 expression in chronically infected promonocytes co-cultured with human brain cells. (J Neuroimmunology 50:167-75, 1994, Peterson, P; Gekker, G; Hu, S.; Anderson, W.R.; Kravitz, F.; Portughese, P.S.; Balfour, Jr., H.H.; Chao, C.C.)

Previous studies have shown that morphine promotes the replication of human immunodeficiency virus (HIV)-1 in peripheral blood mononuclear cell co-cultures. In one recent study the hypothesis that morphine would amplify HIV-1 expression in the chronically infected promonocytic clone U1 when co-cultured with lipopolysaccharide-stimulated human fetal brain cells was tested. Marked upregulation of HIV-1 expression was observed in these co-cultures (quantified by measurement of HIV-1 p24 antigen levels in supernatants) and treatment of brain cells with morphine resulted in a bell-shaped dose-dependent enhancement of viral expression. The mechanism of morphine's amplifying effect appears to be opioid receptor-mediated and to involve enhanced production of tumor necrosis factor by microglial cells.

Antiviral activities of the reverse transcriptase inhibitors U-90152 and 3'-azido-2',3' dideoxythymidine and the protease inhibitor U-75875 were compared in two culture models of human immunodeficiency virus type 1 brain infection. In a model involving acutely infected microglial cells, U-90152 was the most active, whereas in a model using chronically infected promonocytes, U-75875 was the most active. (Anti-Human Immunodeficiency Virus Type 1 Activities of U-90152 and U-75875 in Human Brain Cell Cultures, P.K. Peterson, G. Gekker, S. Hu, and C.C. Chao. Antimicrobial Agents Chemotherapy 38:2465-8;1994.)

Gender Differences in Responses to Acute Cocaine:

Gender differences after acute cocaine administration have received little attention despite the fact that males and females respond differently to many other drugs. Dr. Scott Lukas and colleagues of McLean Hospital and Harvard Medical School have recently reported (in press) the results of a study examining seven male and seven female occasional cocaine users who received either an intranasal dose of cocaine hydrochloride (0.9 mg/kg) or placebo powder. Women studied during the follicular and luteal phase of their menstrual cycle had peak plasma cocaine levels of 77.5±13.6 ng/ml and 61.3±17.5 ng/ml, respectively. Male subjects achieved the highest peak plasma cocaine levels (144.4± 17.5 ng/ml), detected cocaine effects significantly faster than females and also experienced a greater number of episodes of intense good effects or "euphoria." Cocaine-induced tachycardia paralleled the subjective effects and plasma levels. Peak increases in heart rate occurred more rapidly in males. These data suggest that there are significant gender differences in the responses to acute intranasal cocaine.

Alcohol Pretreatment Increases Preference for Cocaine over Monetary Reinforcement:

Dr. Steven Higgins and colleagues at the University of Vermont previously have reported a laboratory procedure in which subjects can choose between either cocaine or a monetary reinforcer. They find that choice of cocaine over the monetary alternative reinforcer decreases as an orderly function of increases in the amount of the monetary reinforcer. This laboratory arrangement was developed as an analog of a current behavioral treatment for cocaine dependence that increases cocaine abstinence by systematically increasing the availability of alternative nondrug reinforcers. Dr. Higgins and his colleagues (in press) have now reported that when subjects were given alcohol prior to experimental sessions, choice for cocaine over the monetary reinforcer was significantly increased. The researchers

note that these data are consistent with prior reports that alcohol abuse is associated with poorer treatment outcomes in cocaine abusers. Given that the blood alcohol levels were equivalent to those obtained under conditions of social drinking, Dr. Higgins and colleagues recommend alcohol abstinence for individuals seeking to reduce or eliminate their cocaine use.

Effects of Prenatal Exposure to Cocaine on Infant Cognition and Emotional Regulation:

Dr. Linda Mayes and her colleagues at the Yale Child Center assessed the effects of prenatal cocaine exposure on cognitive and psychomotor performance beyond the newborn period. In a recent study, at 3-months of age, 61 cocaine-exposed infants and 47 non-cocaine-exposed infants participated in an infant-control habituation and novelty responsiveness procedure. The task assessed the organization of looking behavior and attention to determine infants early stages of cognitive processing. The Bayley Scales of Infant Development (BSID) was also administered to assess cognitive and psychomotor development. Based on their results, the authors concluded that a substantial proportion of cocaine-exposed infants were more reactive, or aroused by novel stimuli, than non-cocaine-exposed infants. A marked increase in reactivity, or negative affective state can prevent an infant from attending to stimuli. Increased reactivity may reflect differences in temperament, which may have an impact on parental responsiveness. Starting at 5 months of age, parental responsiveness to an infant can influence later cognitive development. Cocaine-using mothers may already be less responsive to their infants which may further place highly reactive cocaine-exposed infants at risk. The potential of reduced parental responsiveness of cocaine-using mothers and increased reactivity in cocaine-exposed infants can have a profound influence on an infant's cognitive performance. Importantly, these conditions could negatively affect later development of attention regulation and learning ability. (Mayes, et al., Pediatrics, **95**(4):539-545, 1995).

Motivational Effects of Marijuana:

At the July 19-20, National Conference on Marijuana Use: Prevention, Treatment, and Research, Dr. Don R. Cherek reported on studies conducted at the University of Texas-Houston which demonstrated that marijuana smoking can produce diminished motivation. This controlled laboratory study measured the acute effects of marijuana smoking among 18-22 year old male subjects who had histories of occasional marijuana use and had 10-12 years of education. Marijuana smoking produced diminished motivation to perform a work task which required increasing effort over one hour sessions. This reduced motivation could only be partially reversed by large increases in the monetary value of the incentives. These effects of marijuana on motivation were directly related to the potency of the marijuana smoked. Future research will examine characteristics of the smoker which may contribute to these effects.

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Research Findings

Clinical and Services Research

Physiological and Subjective Responses to Food Cues as a Function of Smoking Abstinence and Dietary Restraint

Tobacco smokers gain weight after quitting smoking with women usually gaining more weight than men. This weight gain after quitting smoking appears to be from increased eating, especially of sweet-tasting between-meal snacks. The investigators examined the influence of smoking abstinence on physiological (salivary habituation) and subjective (cigarette desire, hunger, taste liking, emotional arousal) responses to food cues in women smokers, 10 each in high or low dietary restraint groups, respectively. Dietary restraint is associated with chronic concerns about weight and dieting to attempt to maintain an unreasonably low body weight and is measured by the Revised Restraint Scale of Herman and Polivy. The subjects were divided into two groups: those who scored >15 (high restraint) and low restrainers who scored <15 on the scale. The salivary responses to taste increased significantly more in high vs. low restraint women smokers during the first trial of taste, especially on the smoking day. However, the salivary habituation to strawberry yogurt was significantly disrupted by smoking abstinence in high restraint women. High restraint women also reported increasing desire for cigarettes and emotional arousal across food taste trials on both days, while the low restraint women reported no changes over trials. Results indicate that brief smoking abstinence attenuates salivary habituation to taste in high restraint women, suggesting a marker for processes responsible for increased food intake after quitting smoking. Repeated exposure to food stimuli may also increase emotional distress in high restraint women smokers, enhancing desire to smoke (Perkins KA, Mitchell SL, Epstein LH, Physiol Behav 58(3):000-000, 1995).

Individual Variability in Responses to Nicotine:

Individual variability in acute responses to nicotine is generally attributed to stable characteristics of tobacco users such as genetic/constitutional factors (e.g., gender) and chronic environmental experience (behavioral factors). Perkins et al. show that the situational factors such as acute stress or physical activity may also play an important role in variability to nicotine effects. The situational influences may determine why smokers are more likely to smoke under certain conditions, such as high stress. Females may be more responsive than males to non-nicotine stimuli associated with smoking (e.g., sight and taste of smoke). The effects of many psychoactive drugs (including nicotine) on behavior may be strongly determined by the situational context surrounding drug intake (e.g., accompanying environmental and social stimuli, temporal factors), and not simply the pharmacology of the drug. The pre-drug subjective state, ongoing level of physical activity vs. rest, and concurrent drug intake, all are situational factors that may result in individual variability in nicotine's subjective, behavioral, and physiological responses (Perkins, Behavior Genetics, 25(2): 119-132, 1995).

Cannabis Psychotic Disorder: Does it Exist?

Although "cannabis psychotic disorder"with delusions or with hallucinations is recognized in DSM-IV, relatively little information is available on the entity. Pope and his colleagues reviewed 395 eligible charts of the 9,432 admissions at

two psychiatric centers between 4/91 and 10/92, and 10/89 and 11/92, respectively, seeking cases of cannabis-induced disorders. There were no convincing cases of a cannabis-induced psychotic syndrome. The authors also reviewed published studies on the subject. There were 10 series of 10 or more cases, all describing primarily cannabis-induced psychotic syndromes. None of the ten studies was performed in the US; only two were published in the last 10 years and neither supported the existence of a distinct cannabis-induced psychosis. Further, most studies were retrospective and uncontrolled. The overall evidence from both reviews was inadequate to be certain that cannabis alone can produce a psychotic syndrome in previously asymptomatic individuals. The authors suggest that further research is needed to validate the diagnosis of cannabis psychosis (Gruber AJ and Pope, HG, American Journal on Addictions, 1(1):72-83, 1994).

Attributes of Heavy vs. Occasional Marijuana Smokers in a College Population:

Forty-five long-term heavy marijuana smokers were compared with 44 occasional smoker students who were drawn from two Boston colleges. The heavy smokers smoked marijuana daily for at least two years (an average of approx. 27d in the last month) and the "occasional" smokers never smoked more than ten times in a month at any time in their lives (average 2.7d in the last month). The drug use was assessed by urine toxicology screen. Heavy smokers reported higher rates of use of other substances, especially hallucinogens and cocaine, and described greater subjective impairment of memory and motivation than occasional smokers. However, on a wide range of demographic, family-background, and mental health measures, the heavy smokers proved almost indistinguishable from occasional smokers. The authors conclude that even the heaviest college marijuana smokers exhibit few demographic or psychiatric features which distinguish them from students who smoke only occasionally (Kouri E, Pope HG, Yurgelun-Todd D, and Gruber S, Biological Psychiatry, in press).

Substance Use Reduction in the Context of Outpatient Psychiatric Treatment: A Collaborative, Motivational, Harm Reduction Approach:

Carey's conceptual model incorporates four themes familiar to addiction treatment researchers and demonstrates how these can work within ongoing mental health treatment. The themes are: treatment intensity, stages of change, motivational interventions, and harm reduction. The five steps of the model include:

1. establishing a working alliance,
2. evaluating the cost-benefit ratio of continued substance use,
3. individualizing goals for change,
4. building an environment and lifestyle supportive of abstinence, and
5. anticipating and coping with crises.

This model integrates clinical realities of mental health treatment with empirically-grounded strategies applicable to substance abuse problems (Carey, Community Mental Health Journal, in press).

Gender Differences in Cerebral Perfusion in Cocaine Abuse: Technitium-99m-HMPAO SPECT Study of Drug-Abusing Women:

Mendelson and his colleagues measured cerebral perfusion of 13 cocaine-dependent men (average age of 32.4+6.7 years) and 13 women (average age of 34.6+4.6 years), and an equal number of controls. The investigators found that cocainedependent women had much less abnormal findings of cerebral perfusion (both in terms of number of defects/patient and the proportion of patients affected) than cocaine-dependent men and were indistinguishable from normal women. These gender differences could not be explained by age, race, body mass index, alcohol use, amount of cocaine use, amount of heroin use, the route of drug administration, or any other structural abnormality. The underlying mechanism of these gender differences remains to be established.

The concurrent use of heroin and cocaine was associated with more perfusion abnormalities in both sexes, that has been reported also in animals (Levin JM, Holman LB, Mendelson JH, Teoh SK, Garda B, Johnson KA, Springer S, Journal of Nuclear Medicine, 35(12):1902-1909, 1994).

Increased Mu-opioid Receptors in Cocaine Abuse Demonstrated by PET: Association with Craving:

Frost and his colleagues examined mu-opioid receptor binding in ten cocaine dependent men and seven non-addicted controls using positron emission tomography and 11C-carfentanil. Mu-opioid binding was increased (range 25-50%) in several brain regions (caudate, thalamus, and neocortical regions) of the cocaine addicts studied 1-4 days after their last use of cocaine. Craving was significantly correlated with mu-opioid binding in amygdala, anterior cingulate gyrus, frontal and temporal cortex and negatively correlated with the urinary levels of the cocaine metabolite benzoylecgonine prior to scanning. The upregulatory changes observed persisted after 4 weeks of monitored cocaine abstinence in the majority of subjects. These findings demonstrate for the first time the involvement of the endogenous opioid system in cocaine dependence and cocaine craving in living human subjects (Zubieta JK, Gorelick D, Stauffer R, Dannals RF, Ravert HT, and Frost J, presented at the 42nd Annual Meeting of the Society of Nuclear Medicine, June-12-15, 1995, Minneapolis, MN).

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Research Findings

Treatment and Services Research

Treatment Research

Depression in Substance Dependent Adolescents:

Although depression is common among youths diagnosed with a Substance Use Disorder (SUD), the relationship among these two disorders is still unclear. To address this question, 99 delinquent boys, ages 13-19 years, admitted to a residential drug treatment program, were administered the adolescent form of the Comprehensive Addiction Severity Index, the Diagnostic Interview Schedule for Children, and Children's Depression Rating Scale-Revised. Results indicated that depressed boys received more Substance Dependence diagnoses than did the non-depressed boys (4.2 versus 3.0; $p<.008$), with differences most significant for amphetamines and opioids. However, depressed boys did not report initiating or regularly using drugs at an earlier age. Depression preceded regular drug use in 43% of the cases while regular drug use preceded or was concurrent with depression in 48% of the cases (9% did not report). The findings lend modest support to clinical reports that in those cases where signs of depression precede substance abuse, the boys may have used psychoactive substances to relieve their dysphoric feelings or more severe depressive symptomatology. (Riggs, P.D., Baker, S., Young, S.E., and Crowley, T.J. J Am Acad Child Adolesc Psychiatry, in press).

Methadone Treatment: Behavioral/Pharmacological Variables:

This study examined sexual and drug use behavior in 247 methadone maintenance patients, to explore the association of cocaine use with HIV risk behavior. In univariate analysis, cocaine use was positively associated with any drug injection, number of injections, and sexual intercourse without condoms. These relationships remained significant after controlling for other drug use and demographic factors. Heroin use also contributed to injection-related risk. It is concluded that cocaine use represents a continued source of risk for exposure to HIV in this population, and that more aggressive efforts are warranted to reduce illicit drug use, particularly of heroin and cocaine, in methadone patients. (Bux, D.A., Lamb, R.J., and Iguchi, M.Y. Cocaine Use and HIV Risk Behavior in Methadone Maintenance Patients. Drug and Alcohol Dependence, 1995, 37, 29-35).

Behavioral-Pharmacological Treatments to Reduce Drug Abuse and HIV Spread:

Intensive HIV counseling and testing programs were established at the outset of this research to examine the interrelation between abused drugs, treatment factors, medications, and consequent HIV risk behaviors. Data on HIV risk behaviors, and HIV rates were accumulated. These data indicated that lower behavioral risk was found in HIV negative cocaine users with higher levels of depressive symptomatology, and further, that the HIV negative users were more anxious than the HIV positive matched controls. The data also indicate that women report more HIV risk behaviors than men, regardless of HIV status or primary drug of dependence (heroin or cocaine). Overall, drug use, as measured by twice weekly drug screens, was not found to differ as a direct function of HIV status or primary drug

of abuse. (Presented at the 57th Annual Meeting of the College on Problems of Drug Dependence, June 10-15, 1995 in Scottsdale, Arizona).

Behavior Therapy for Antisocial Opioid Abusers:

Antisocial personality is commonly detected in drug abusers, where the diagnosis is associated with a poor prognosis and increased risk of HIV transmission. In a controlled clinical trial to improve treatment outcome of antisocial opioid abusers in methadone substitution therapy, subjects were randomly assigned to either an experimental group, which incorporates a 9-step contingency management approach for reducing drug use, or a control group. Each step, in the experimental group, rapidly conveys greater or less control to patients over major aspects of treatment (e.g., number of counseling sessions, methadone dose levels) based on urine results from the prior 2-weeks. Significant outcome differences were found favoring the experimental treatment. This group had a lower rate of urine specimens positive for any substance, including opioids and cocaine. The control group also selfreported an increased severity of drug use over time. Preliminary results support the viability of reducing drug use in antisocial opioid abusers with a structured behavioral intervention using positive and negative contingencies delivered in a timely manner. (Presented at the 57th Annual Meeting of the College on Problems of Drug Dependence, June 10-15, 1995 in Scottsdale, Arizona).

Pharmacological Treatment of Intravenous Drug Abuse

This project is looking at the most effective parameters for methadone treatment delivery, which is known to be an important HIV risk-reduction intervention. In this study the dose-related efficacy of methadone treatment was clearly demonstrated, with the highest dose tested producing the best results on all outcome measures. HIV risk behavior (i.v. drug use in particular) was shown to be inversely related to methadone dose with higher doses producing more risk reduction. In addition to conducting important controlled research that should result in improving HIV risk reduction outcomes for methadone treatment, the project has offered HIV testing, counseling and risk reduction education to over 400 opioid-dependent patients since its inception. (Strain, E.C., Stitzer, M.L., Leibson, I.A., and Bigelow, G.E. Outcome After Methadone Treatment: Influence of Prior Treatment Factors and Current Treatment Status. Drug and Alcohol Dependence, 1994, (35), 223-30).

Services Research

Treatment Services in Two National Studies of Community-Based Drug Abuse Treatment Programs.

Recently published findings suggest that drug abuse treatment programs have eroded over the past decade in terms of their ability to meet the service needs of their clients, at a time when these needs are increasing due to such factors as increasing prevalence of cocaine use, psychological problems, AIDS and other infectious diseases, and unemployment among clients.

Two national studies conducted a decade apart document a striking decline over time in the kinds of services received during treatment: the Treatment Outcome Prospective Study (TOPS) based on clients admitted to treatment during 1979-81, and the Drug Abuse Treatment Outcome Study (DATOS), based on treatment admissions 1991-93. The TOPS sample was drawn from 41 programs, and the DATOS from 99 programs. Clients in the TOPS and DATOS samples were interviewed 3 months after treatment entry and asked whether they had received services in specific problem areas similar to those (other than substance abuse) in the Addiction Severity Index (ASI): medical, psychological, family, legal, educational, vocational and financial services. A comparison of the studies indicates statistically significant declines in many of the services received by clients in the later study. The percentage having received no services (other than substance abuse counseling) in the 3 month period were:

- in DATOS, 65% of methadone clients (vs. 49% in TOPS);
- 23% of long-term residential clients (vs. 7% in TOPS);
- 60% of drug-free outpatient clients (vs. 18% in TOPS).

Most commonly reported services were medical, psychological, and family. TOPS vs. DATOS comparisons of medical

services showed statistically significant declines in methadone clients (33% vs. 27%) and long-term residential clients (78% vs. 55%), while drug-free outpatient clients' reports of such services were not significantly different (25% vs. 23%). Similar comparisons for psychological services showed more pronounced declines in methadone clients (16% vs. 3%), long-term residential (58% vs. 13%) and outpatient drug-free (67% vs. 9%). For family services, declines among methadone clients (9% vs. 2%), drug-free residential (33% vs. 20%), and outpatient drug-free (43% vs. 8%) were noted. With the exception of medical services for outpatient drug-free clients, all differences reported were significant beyond the .01 level.

Assessment of unmet needs was accomplished by identifying percentages of clients across programs in each modality who reported that they needed but did not receive a service during the first 3 months of treatment. Within and across modalities, the percentage reporting unmet service needs increased considerably, and by statisticaly significant amounts, over the period from TOPS to DATOS. The percentages with unmet needs increased for:

- medical services from 18% to 40% among methadone clients, 6% to 25% in drug-free residential, and 9% to 32% in drug-free outpatient programs and
- psychological services increased from 19% to 54% in methadone programs,10% to 57% in drug free residential, and 7% to 57% in outpatient drug free programs.

The general pattern of services provided and unmet needs suggest that programs have access to fewer services and resources with which to meet needs than was the case a decade earlier. The apparent trend that emerges from the data is cause for concern about the drug abuse treatment system nationwide. Additional data on programs is being collected to further clarify and elaborate on the observations reported here. Published in R. M. Etheridge, S.G. Craddock, G.H. Dunteman, and R.L. Hubbard (1995) "Treatment Services in Two National Studies of Community-Based Drug Abuse Treatment Programs," Journal of Substance Abuse 7, 9-26

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Director's Report to the National Advisory Council on Drug Abuse
September, 1995

Research Findings

AIDS Research

Comparison of Education Versus Behavioral Skills Training Interventions in Lowering Sexual HIV-Risk Behavior of Substance-Dependent Adolescents:

The training based on cognitive-behavioral principles may be effective in lowering high-risk adolescents' vulnerability to HIV infection. Substance-dependent adolescents (n=34) in a residential drug treatment facility received either a 6-session behavior skills training HIV-risk reduction intervention or standard HIV education. After the intervention, adolescents who received behavior skills training exhibited increased knowledge about HIV-AIDS, more favorable attitudes toward prevention and condom use, more internal locus of control, increased self-efficacy, increased recognition of HIV risk, and decreases in high-risk sexual activity. Self-report data were corroborated by records for the treatment of sexually transmitted diseases (St.Lawrence JS, Jefferson KW, Alleyne E, Brasfield TL, Journal of Consulting and Clinical Psychology 63(1):154-157, 1995).

Not-in-treatment Male and Female IDUs and Crack Smokers:

Sherry Deren and colleagues examined data from a national sample of not-in-treatment male and female IDUs and crack smokers to determine relative risks of HIV positive serostatus by sexual orientation. Data were collected on sexual orientation from 11,956 respondents in 16 cities participating in NIDA's Cooperative Agreement for AIDS Outreach/Intervention Research Program from 1990 to 1993. There were 8,423 men (70%), 47% of whom were IDUs, 31% crack smokers, and 21% both IDUs and crack smokers, and 3,533 women (30%), 37% of whom were IDUs, 44% crack smokers, and 18% both. Significant differences were found in drug use by sexual orientation for both males and females. Gay and bisexual males were more likely to be crack smokers and heterosexual males were more likely to be IDUs; gay and bisexual females were more likely to be both injectors and crack smokers. HIV positive serostatus among males was highest among gay men, followed by bisexuals; there was no significant difference in seropositivity within risk category by sexual orientation among females. The paper discusses the implications of relative HIV risks among not-in-treatment drug users by sexual orientation for improving targeted outreach and prevention interventions. Sexual Orientation and HIV Risk Behaviors in a National Sample of Injection Drug Users and Crack Smokers. Drugs and Society (in press).

Behavior Change Among a Cohort of Men

Sally M. Blower and colleagues examined the process of risk behavior change among a cohort of men who have sex with other men in Amsterdam through the use of time series data. Their analyses demonstrate how risk behavior change in this cohort may be viewed as a homogeneous one-step Markovian process. The authors discuss the implications of their findings for long-term prediction of HIV seroconversion rates, for design and evaluation of HIV behavioral intervention studies and vaccine trials, and for understanding and interpreting relapse behavior. An Analysis of the Process of Human Immunodeficiency Virus Sexual Risk Behavior Change. Epidemiology. 1995;6;238-242.

Drug Use and AIDS Risk Behavior Among Homeless Women:

A causal model consisting of personal and social resources, threat appraisal processes, coping styles, and barriers to risk reduction as predictors of general AIDS risk and specific drug use behaviors was investigated among homeless African American (N=714) and Latina (N=691) women aged 18 to 69 years (mean age 32). The model, which was based on a stress and coping framework, supported many of the hypothesized relationships. Active coping was associated with fewer general AIDS risk behaviors for both groups and less specific drug use behavior among African American women. Specific drug use behavior was predicted by high threat appraisal and more avoidant coping for both groups. Behavioral differences between the two ethnic groups were found, especially on the risky AIDS and drug use behavioral measures. Furthermore, less self-esteem predicted more barriers to condom use among the African American women whereas more social resources predicted more barriers among the Latinas. Thus, culture-specific strategies may be necessary to increase condom use among such high risk populations. Nyamathi A, Stein JA & Brecht M. Psychosocial Predictors of AIDS Risk Behavior and Drug Use Behavior in Homeless and Drug Addicted Women of Color. Health Psychology, 14:1995:265-273.

Barriers to Condom Use and Needle Cleaning Among Impoverished Minority Female IDUs and Their IDU Partners:

Based on a study of women recruited primarily from homeless shelters and drug recovery programs, the most commonly cited barriers to condom use were belief that partners did not have acquired immunodeficiency syndrome (AIDS), lack of knowledge about where to get and how to use condoms, and discomfort discussing condom use with partners. African-American women were more likely to report having multiple partners and unprotected sex, and more likely to report barriers in using, discussing and obtaining condoms. Latina women were more likely to report partners' dislike of condoms. African- American and highly acculturated Latina women were more likely to be IDUs than less acculturated Latina women. The more pervasive barriers for needle cleaning were not having personal needles, being high and not interested in needle cleaning, and not having disinfectant available. In a multiple logistic regression analysis for engaging in unprotected sex and cleaning needles, no ethnic or acculturation differences were found after controlling for selected demographic characteristics and risk factors. The data indicate a need to increase the supply of free or low cost condoms, to provide easily accessible sites for obtaining condoms, and to focus counseling for women on negotiating condom use with partners and the skillful and correct placement of the condoms. Nyamathi, A., Lewis, C., Leake, B., Flaskerud, J., Bennett, C. Barriers to Condom Use and Needle Cleaning Among Impoverished Minority Female Injection Drug Users and Partners of Injection Drug Users. Public Health Reports, 110:1995:166-172.

Knowledge, Beliefs, and Attitudes About AIDS, Drug Use, and Sexual Behavior Among Young Children:

AIDS education for children and adolescents is the ultimate goal of the Children's Health Awareness Project conducted by Drs. Elizabeth Wells and her colleagues at the University of Washington, Seattle. This longitudinal study which began in 1991-92 involves annual surveys of children then in grades 3, 4, 5 and 6 (N=1,173; 51% female; 47% white, 24% African American, 20% Asian American, 9% other ethnic groups). Analysis at time one demonstrated a high level of recognition of the three primary routes of HIV transmission (sex, drug use, and in utero exposure). However, children who knew about these routes also had misconceptions about the mechanisms involved in acquiring HIV through these routes and about behaviors through which HIV in not transmitted. Older children had fewer misconceptions than younger children, and children of higher socioeconomic status (SES) had fewer misconceptions than those of lower SES. Ethnic differences in knowledge about the primary routes of HIV transmission were not evident. Hoope, M.J., Wells, E.A., Morrison, D.M., Gillmore, M.R. & Wilsdon, A. Misconceptions About AIDS Among Children Who Can Identify the Major Routes of HIV Transmission. Journal of Pediatric Psychology, 20(50):1995:671-686.

IDU Networks in Three Cities

Mark L. Williams and colleagues investigated the structures of IDU networks in three cities with varying HIV infection rates among IDUs (Rio Piedras, Puerto Rico, with an HIV positive rate among IDUs of 60% or higher; Houston, Texas, with an HIV positive rate among IDUs of 6%; and Dayton/Columbus, Ohio, with an HIV positive rate among IDUs of 1%). They found that network size did not vary among the sites, ranging from as small as two IDUs to as large as six

or more IDUs, nor did the length of time respondents reported using drugs with their network counterparts. However, there were significant differences in the frequencies of drug use within a network, with the majority of networks in Rio Piedras reporting drug use together two or more times daily and the majority of networks in Houston and Dayton/Columbus reporting drug use together weekly or less than weekly. The networks in Puerto Rico were significantly more homogeneous than those in Houston and Dayton, being predominately single gender injectors only. Houston and Dayton/Columbus networks were mixed gender and mixed IDUs and crack smokers. An Investigation of the HIV Risk Behaviors of Drug Use Networks. Connections. Vol 18; 1; April 1995; pp. 58-72.

Paradigm Shift:

Robert Trotter and collaborators Richard B. Rothenberg and Susan Coyle have written a recent article about a paradigm shift in social research on HIV transmission, drug abuse, and risk reduction. They provide an environmental-epidemiological rationale for the use of social network analysis to explore facilitating factors or barriers to the transmission of HIV infection in drug using populations. The authors present an overview of the theoretical, empirical, and practical conditions that have led to the paradigm shift in social research, including a discussion of research trends and support for social network analysis in the HIV and drug risk field. Drug Abuse and HIV Prevention Research: Expanding Paradigms and Network Contributions to Risk Reduction. Connections. Vol 18; 1; April 1995; pp. 29-45.

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Research Findings

Etiology, Prevention, and Epidemiology Research

Increased Smoking Among Adolescents and Link to Marijuana Use:

Reporting on their 20th national survey of American high school seniors and their fourth national survey of eighth and tenth grade students (both conducted in 1994), Drs. Lloyd Johnston, Patrick O'Malley, and Jerald Bachman, all at the University of Michigan, reported that cigarette smoking is on the increase among students at all three grade levels. The national smoking results were released separately for the first time this year because smoking data usually get lost in the larger story about illicit drug use. After more than a decade of level cigarette usage rates, twelfth graders showed an increase which began in 1992, with 30-day prevalence rising from 27.8% in 1992 to 31.2% in 1994. The increases among the younger students started earlier and were greater in proportional terms: among eighth graders, 30-day prevalence increased from 14.3% to 18.6% between 1991 and 1994, and among tenth graders it increased from 20.8% to 25.4% over the same interval. Increases in the daily smoking rates were of the same order of magnitude. Increases appear to be very broad and are found in virtually all demographic subgroups. The investigators note that peer norms against smoking have been receding in the past few years, advertising and promotion have been increasing, and that portrayals of cigarette smoking in entertainment programming may be on the rise. They find that youngsters seriously underestimate the dangers of smoking, with only about half of the eighth graders saying that a person runs a "great risk of harming themselves (physically or in other ways)" if they smoke a pack-or-more of cigarettes per day. They also report from their panel studies that many smokers have not been able to quit smoking five years after high school even though they said they would in twelfth grade. The study's latest findings on marijuana use, presented at the NIDA-sponsored National Marijuana Conference in July, noted the very high degree of association between cigarette smoking and all forms of drug use, but particularly between cigarette smoking and marijuana use. For example, among eighth graders fewer than 3% of those who never smoked cigarettes had ever tried marijuana versus 73% of those who were current pack-a-day smokers. In the great majority of cases cigarette use began prior to the use of the illicit drugs. The increase in cigarette smoking in recent years may be one factor contributing to the increase in marijuana use.

Community Epidemiology Work Group Reports:

The biannual meeting of the Community Epidemiology Work Group (CEWG) was held in Chicago, Illinois on June 13-16, 1995. The CEWG is composed of researchers from 20 selected metropolitan areas of the United States who meet semiannually to report on patterns and trends of drug abuse in their respective areas; emerging drugs of abuse; vulnerable populations and factors that may place people at risk of drug use and abuse; and, negative health and social consequences. Reports are based on drug abuse indicator data, such as morbidity and mortality information, treatment data and local and State law enforcement data. Additional sources of information include criminal justice, correctional, medical and community health data, local and State survey information and research findings from ethnographic studies. Highlights from findings from the most recent CEWG meeting include:

- Cocaine remains the most serious drug problem in the country in terms of prevalence and consequences, but data suggest an aging effect and level or declining trends in many areas. Reports also suggest an increasingly negative image of cocaine among youth.

- Indicators of heroin use, including morbidity, mortality and treatment data, continue to show an increasing trend. Treatment admission for primary heroin use has surpassed cocaine admissions in Newark, New York, Boston, San Francisco and Los Angeles. Three populations of abusers are appearing: an aging cohort of addicts who are switching to intranasal use; crack users who combine heroin with crack; and in some areas a cohort of new younger users among which heroin has become part of the club scene.
- As reported previously, a variety of opiates other than heroin are abused in various CEWG sites: propoxyphene in Seattle, New Orleans, Dallas and Phoenix; codeine in Detroit, San Francisco, Minneapolis/St. Paul, Chicago, New York and Phoenix; hydrocodone in Detroit, Phoenix, Dallas, New Orleans and San Francisco; oxycodone in Boston, Philadelphia and New York; hydromorphone in Atlanta, New Orleans, New York, Phoenix and St. Louis and fentanyl in Boston.
- Quantitative data and qualitative reports continue to indicate increasing marijuana use, especially among adolescents, across the country. The use of blunts (gutted cigars refilled with marijuana is prevalent throughout the country both in urban areas and in the suburbs. In many areas blunts are combined with other drugs, such as crack and PCP.
- Methamphetamine abuse is the most frequently reported primary drug of abuse among treatment admissions in San Diego and Honolulu and indicators of abuse have are increasing in Denver, Los Angeles, Minneapolis/St. Paul, San Francisco, Seattle and areas of Texas. Trafficking appears to be shifting from outlaw bikers to large-scale operations run by Mexican nationals. Among other stimulants, methylphenidate is commonly abused in Chicago, MDMA is reported in Atlanta, Denver, Detroit, Miami, New Orleans, St. Louis, San Francisco and in various areas of New Jersey and Texas; and methcathinone indicators suggest availability and abuse in Michigan's Upper Peninsula, Wisconsin and Minnesota.
- Flunitrazepam abuse has been spreading rapidly across Florida and Texas among a variety of populations, including gang members, cocaine addicts and high school students. Indicator data and other reports confirm its availability and abuse throughout the country, but largely concentrated in Florida, Louisiana, Texas and Arizona.
- A resurgence of PCP abuse appears to be occurring, especially in the Washington, D.C. area and in Chicago, Miami and in Texas. LSD also appears to be resurging in San Francisco and in Atlanta, Denver, Minneapolis/St. Paul, Miami and New York. Club drugs that are appearing include ketamine in Miami and St. Louis and "nexus" in Atlanta.

Natural History of Drug Use:

The natural history of involvement in various classes of drugs, and in particular, patterns of initiation, persistence and cessation, was investigated from adolescence to the mid-thirties by Dr. Denise Kandel and her colleagues. The period of risk for initiation into alcohol, cigarettes and marijuana largely terminates by the early twenties, while for cocaine it lasts until the late twenties. The largest proportion of new use after age 29 is observed for prescribed psychoactives. There appears to be a maturational trend in the use of marijuana and alcohol but not for cigarettes. The late teens and early twenties are the periods of highest use for alcohol, marijuana and cocaine, with sharp declines thereafter. This is in contrast to cigarettes, for which periods of highest use are distributed almost evenly from the early twenties through the end of the observational period at age 34-35. Not only does the prevalence of high frequency use decline in adulthood, but for most substances, except cigarettes, the quantities consumed during periods of heavy use decline as well. Furthermore, persistent use of the less commonly used illicit drugs preserves the use of more commonly used illicit and licit drugs. Cigarettes smoking, manifested in regular and persistent usage throughout adulthood, constitutes one of the most serious drug-related health problems in the population. Most drug-related intervention programs, whether focused on prevention or on treatment, must target adolescents and young adults in their early to mid-twenties. By the mid-twenties, most drug use is discontinued. Chen, K. & Kandel, D.B. The Natural History of Drug Use from Adolescence to the Mid-Thirties in a General Population Sample. American Journal of Public Health 85 (1):41-47, 1995.)

Research Center for Education and Drug Abuse Research (CEDAR), University of Pittsburgh:

Research studies on vulnerability to drug use at the University of Pittsburgh (Ralph Tarter, PI) demonstrate that childhood conduct disturbances (Moss, Vanyukov, Majumder, et al., 1995), heightened aggression (Moss, Mezzich, Yao, et al., 1995), and temperament deviations (B1ackson, 1995) are over-represented in children from substance abuse families. Such children also have significantly lower IQ scores, poorer school performance and impairments of

the executive functions of the brain, which are generally accepted to be localized to the prefrontal cortex. CEDAR studies show that these conduct disturbances are transmissible within families. These findings have been integrated into an epigenetic model of substance abuse liability describing the developmental trajectory that unfolds concomitant to quality of person-environment interactions (Tarter, Moss, and Vanyukov, 1995). CEDAR research on biological components of substance abuse liability provides electrophysiological evidence of altered neurocognitive functioning among high risk children (Brigham, Herning, Moss, et al, 1995), and preliminary evidence of an association between a polymorphic gene and early-onset substance abuse (Vanyukov, Moss, Yao, et al., 1995). CEDAR research projects are based on prospective, longitudinal data from high and low risk 10-12 year old subjects (250 male and 200 female) drawn from substance abuse and control families tracked biannually. The studies employ a comprehensive biopsychosocial protocol including methods from molecular and quantitative genetics, neuro- and reproductive endocrinology, neurochemistry, electro- and psychophysiology, diagnostic psychiatric evaluation, neuropsychological tests of brain function, self-report and laboratory tests of psychological functioning, in vivo family interaction study, home and neighborhood visits to assess child's ecology and peer as well as teacher informant reporting. CEDAR's overarching mission is to disaggregate the multifactorial liability to substance abuse. These findings are based on a few of over 40 papers published and accepted for publication by CEDAR researchers between January and July 1995:

Blackson, T., Temperament and IQ Mediate the Effects of Family History of Substance Abuse and Family Dysfunction on Academic Achievement. Journal of Clinical Psychology, 51:1955:113-122.
Brigham J., Herning, R.I., Moss, H.B., Murrelle E.L. & Tarter, R.E. Event-Related Potentials and Alpha Synchronization in Preadolescent Boys at Risk for Substance Abuse. Biological Psychiatry, 37:1995:834-846.
Moss, H.B., Vanyukov, M.M., Majumder, P.P., Kirisci, L. & Tarter, R.E. Prepubertal Sons of Substance Abusers: Influences of Parental and Familial Substance Abuse on Behavioral Disposition, IQ, and School Achievement. Addictive Behaviors, 20:1995:1-4.
Moss, H.B., Mezzich, A, Yao, J.K., Gavaler, J. & Martin, C. Aggressivity Among Sons of Substance Abusing Father: Association with Psychiatric Disorder in the Father and Son, Paternal Personality, Pubertal Development and Socioeconomic Status. American Journal of Drug and Alcohol Abuse, 21(2):1995:195-208.
Tarter, R.E., Moss, H.B. & Vanyukov, M. Behavior Genetic Perspective of Alcoholism Etiology. In H Begleiter & B Kissin (Eds.), Alcohol and Alcoholism (Vol 1): Genetic Factors and Alcoholism. New York: Oxford University Press, 1995.
Vanyukov, M.M., Moss, H.B., Yu, L.M., Tarter, R.E. & Deka R. Preliminary Evidence for an Association of a Dinucleotide Repeat Polymorphism at the MAO-A Gene with Early Onset Alcoholism/Substance Abuse. American Journal of Medical Genetics (Neuropsychiatric Genetics), 60:1995:122-126.

Drug Use and Deviant Behavior:

Stacy and Newcomb explored the extent to which drug use, as one form of deviance, may influence another form of deviance (crime and violence) over time. The effects of adolescent drug use on criminal deviance and social conformity, an attempt to see if theories of associations between different forms of deviance showed merit, were examined over an 8 year period (N=536; 72% women). The predictive effects of several constructs relevant to traditional theoretical perspectives (strain, control, and differential association theories) were also investigated. Results showed that a general factor of drug use in adolescence (rather than use of only certain, specific drugs) significantly predicted criminal deviance in adulthood. This finding is consistent with several theories suggesting that different forms of deviance may influence each other over time. In particular, the results were consistent with theories that suggest that effects of drug use on crime operate through a general factor of polydrug use on deviance, unmediated by differential association or by specific drug effects. Theories that rely on disinhibiting, addictive, and/or illegal properties of a specific drug were not supported by these results. Finally, social support was found to negatively predict one specific type of criminal deviance (violent confrontations) over time, consistent with control theory. That is, individuals with greater social support in adolescence exhibited less violence as adults. Stacy AW & Newcomb MD. LongTerm Social Psychological Influences on Deviant Attitudes and Behavior. In H.B. Kaplan (Ed.), Drugs, Crime and Other Deviant Adaptations. New York: Plenum: 1995.

Gene-Environment Interaction in Genesis of Aggressivity and Conduct Disorder:

This study examined the effect of an adverse adoptive home environment upon adoptee conduct disorder, adult antisocial behavior, and two measures of aggressivity - behaviors which contribute to adult antisocial personality and which also are associated with increased vulnerability to drug abuse/dependency. Remi J. Cadoret, M.D. and his colleagues used an adoption paradigm in which adopted away (at birth) offspring of biologic parents with documented (by prison and hospital records) antisocial personality and/or alcohol abuse/dependency were followed up as adults. Multiple regression analysis was used to measure separately genetic and environmental effects. Conclusions indicated that environmental effects and gene-environment interaction account for significant variability in adoptee

aggressivity, conduct disorder and adult antisocial behavior. Cadoret, R.J., Yates, W.R., Troughton, E, Woodworth, G. & Stewart, M.A. Gene-Environment Interaction in Genesis of Aggressivity and Conduct Disorders. Archives of General Psychiatry, 10, 1995.

Drug Use, Delinquency and Dropping Out of School:

This study based on data from the Rochester Youth Development Study, examines the effect of drug use and delinquency on the probability that adolescents will drop out of school and the effect that dropping out of school has on subsequent drug use and delinquency. Dr. Terence P. Thornberry and his colleagues found that prior drug use increased the probability of dropping out of school by 18%, while serious delinquency did not significantly increase the likelihood of dropping out. Dropping out of school predicts subsequent drug use but not serious delinquency when other school related variables are not included in the equation. However, when school related variables are included in the equation the relationship between dropping out and subsequent drug use is not significant. This suggests that dropping out of school may be a proxy for other sources of dissatisfaction with school. To respond to problems of both drug use and school drop outs, the reasons for dissatisfaction with and failure in school must be addressed. Krohn MD, Thornberry T.P., Collins-Hall L & Lizotte, A.J. School Dropout, Delinquent Behavior, and Drug Use: An Examination of Causes and Correlates of Dropping Out of School. In Howard B. Kaplan (Ed.), Drugs, Crime, and Other Deviant Adaptations: Longitudinal Studies. New York: Plenum Press, 1995, 163-183.

Cumulative Effect of Protective Factors

The Rochester Youth Development Study is an ongoing panel study of urban adolescents. Terence P. Thornberry, Ph.D. first selected youth at high risk for drug use and then identified protective factors associated with resilient outcomes. A number of variables in the areas of school (e.g., high achievement), family (e.g., supervision), and peer relations (e.g., having conventional friends) were found to protect against the risk of drug use. The most important finding concerns the cumulative effect of protective factors; only 14% of the high-risk youth who had at least six protective factors actually used drugs, an effect that persisted but at diminished levels over the next three years. Smith C, Lizotte, A.J., Thornberry, T.P. & Krohn, M.D. Resilient Youth: Identifying Factors that Prevent High-Risk Youth from Engaging in Delinquency and Drug Use. In John Hagan (Ed.), Delinquency and Disrepute in the Life Course. Greenwich, C.T.: JAI Press, 1995, 217-247.

Fatal Injuries After Cocaine Use

P The neurobehavioral effects of cocaine use may increase the likelihood that users will receive fatal injuries. In a toxicologic study of 14,843 New York City residents who died of fatal injuries from 1990 to 1992, cocaine use, as detected by benzoylcgonine in the urine or blood, was found in 26.7 percent of decedents, and free cocaine was detected in 18.3 percent. Among fatal injury victims 15 to 44 years of age, cocaine was as likely to be detected as alcohol. Approximately one-third of deaths after cocaine use were the direct result of drug intoxication, but two-thirds involved traumatic injuries resulting from homicides, suicides, traffic accidents, and falls. If considered as a separate cause of death, fatal injury after cocaine use ranked among the five leading causes of death of persons 15 to 44 years old in New York City. In some age groups, the number of these fatal injuries exceeded deaths from AIDS, other fatal injuries not known to involve cocaine, cancer, and heart disease. This study suggests that despite reported declines in the overall rate of cocaine use in the 1990s, certain segments of the population, particularly members of minority groups, may be continuing their heavy drug use and are at high risk of fatal consequences. Marzum, PM; Tardiff, K; Leon, A.C., Hirsch, C.S., Stajic, M., Portera, L., Hartwell, N., Iqbal, MI. Fatal Injuries After Cocaine Use as a Leading Cause of Death Among Young Adults in New York City. New England Journal of Medicine, 332:1995:17531757.

Antecedents and Consequences of Drug Abuse:

Predictors and outcomes of various types of drug use are examined in prospective data spanning four years in the lives of young adult men and women (N=547, 156 women). It was hypothesized that the causes and consequences of drug use are different for this stage of life (compared to childhood and adolescence) and would involve gender-role expectations that women are most directed toward communality issues, whereas men are concerned with agenetic tasks. It was also hypothesized that failure in these gender-specific tasks would lead to more future drug use and that earlier drug use would hinder the development of these skills for men and women. Analyses were conducted with

structural equation models incorporating repeatedly-measured constructs of polydrug use, communality, and agency. Results generally supported these expectations when both specific and general effects were considered. In addition, women's drug use also interfered with their agenetic goals and men's drug use damaged their communal relationships. Newcomb, M.D., & Jack, L.E. Drug Use, Agency, and Communality: Causes and Consequences Among Adults. Psychology of Addictive Behaviors, 9:1995:67-82.

Female Gangs and Involvement of Women in Drug Distribution:

Joan Moore and John Hagedorn who previously studied male gangs, conducted an ethnographic study of female gangs. As with the males, not all gang members are the same: *Legits* have left the gang and "hood" behind; *Dope fiends* are addicted to cocaine and need drug treatment; *New jacks* have given up on the legal economy and see no wrong in selling cocaine to anyone; *Homeboys/Homegirls*, the majority, work regular jobs but when they can't make enough money, sell cocaine which bothers them because they want to settle down and have a decent life. Gangs fall apart over selling drugs which is typically done by individuals who compete with one another. Among African American and Hispanic gangs, sales are more to Whites, outsiders, and middle class customers; markets are closed to rival gangs and as profits increase, gangs tend to become more organized. Latinos tend to stay involved with their gang as adults while adult African Americans tend to be less involved with their gang. Moore, J. & Hagedorn, J. Gangs in America, R. Huff, (ed.), 1995.

Prevention Interventions for Tobacco Use

The development of interventions for the prevention of tobacco use is an ongoing concern, particularly in minority communities. Examination was made of the prevalence and sociodemographic predictors of having a cigarette brand preference in African-American, Mexican-American, and White primary and secondary school students. Cross-sectional data were used from a school based survey of drug use sequencing conducted in 1992 which included students from 47 schools. The prevalence of having a preferred brand of cigarette increased with grade level, with over 20% of 11th graders reporting a preference. White females and males, and Mexican-American males were more likely to have a preferred brand of cigarette than African-American females and males, and MexicanAmerican females. Brand preference was related to cigarette use in a dose response fashion for all subgroups, with African-American "regular" smokers most likely to report a preferred brand of cigarette. Cigarette brand preference was a strong risk factor for daily cigarette use. Volk, R.J., Edwards, D.W., Lewis, R., Schulenberg, J. Paper presented at Research Society on Alcoholism, June 1995.

The Role of Sexual Assault in Adolescent Pregnancy and Drug Use:

In a longitudinal natural history of drug use among young women who become pregnant before reaching age 18 (N=241) 32% reported a history of early forced sexual intercourse (rape or incest) according to Dr. Lewayne Gilchrist and her colleagues at the University of Washington, Seattle. These adolescents compared with non-victims used more crack, cocaine, and other drugs (excepting marijuana), had lower self-esteem, and engaged in a higher number of delinquent activities. A discriminant function analysis incorporating a model of negative consequences of early forced intercourse (which included drug use variables) distinguished reported victims from non-victims 67% of the time. Roughly half the sample is non-white (28% African-American; 8% American Indian, 5% Latinas, 4% Asian; 4% mixed ethnicity). All are low-income. They represent the population of young urban women who received at least minimal services from health and social service providers serving pregnant women and were not recruited on the basis of known drug use. Being pregnant, unmarried, under 18, and planning to parent their child were the inclusion criteria. Subjects average age was 16 (range=12 to 17). Self report and urine toxicology analyses were used to assess drug use. Less than 0.5% of self-report drug use had to be adjusted based on lab results. The principle question eliciting the intercourse data was "Have you ever been forced to have sex when you had no choice and had to do it?" Findings indicate that drug use among the teen pregnancy population may be part of a syndrome of effects associated with sexual abuse among girls. Rates for sexual abuse as well as for drug use before and after pregnancy in this school-age sample were high. Forced sex may be one of many aspects of a context of risk that affect drug initiation and maintenance of drug use among young women of child-bearing age. The effects of early forced intercourse are detectable in their women's psychological, behavioral, and social functioning several years after the original incident. (Lanz, J.B. Psychological, Behavioral, and Social Characteristics Associated with Early Forced Sexual Intercourse Among Pregnant Adolescents. Journal of Interpersonal Violence, 10(2):1995:188-200.)

Undernutrition Significantly Associated With More Drug Use:

Factors associated with undernutrition in a broad community-based sample of 457 homeless adults (M=344, F=113; 16 to 78 years, mean age 34 years) were examined. Latent variables representing drug use, alcohol use, a stereotyped homeless appearance, mental illness, poor physical health status and measured variables of age, gender, income, and number of free food sources were used as predictors of undernutrition. Undernutrition was indicated with three anthropometric measures (weight, triceps skinfold, and upper arm muscle area in the lowest 15th percentile) and one observational measure. Of this sample, 33% was undernourished as defined by at least one of the anthropometric measures. Undernutrition was significantly associated with more drug use, fewer free food sources, less income, and male gender. Gelberg L, Stein J.A. & Neumann C.G. Determinants of Nutritional Status Among Homeless Adults. Public Health Reports, 110:1995:448-454.

Drug Use and the Severity of Homelessness:

Latent variable multiple-group confirmatory factor analyses assessed gender differences in relations among drug and alcohol use, measures indicating severity of homelessness, criminal history, prior institutionalization, and mental illness (N=531 homeless persons, [145 women]; age 16-78; mean age 34 years). Severity was indicated by time homeless, housing quality, and victimization. Men reported more substance use, a longer time homeless, poorer housing quality, greater criminal involvement, and less likelihood of living with a child. Constrained multiple-group models surfaced five significantly different relationships between latent constructs. Men had stronger relationships between mental illness and prior institutionalization, drug use and mental illness, and drug use and victimization, whereas women had stronger relationships between drug use and alcohol use, and criminal involvement and drug use. Stein, J.A., & Gelberg L. Homeless Men and Women: Differential Associations Among Substance Abuse, Psychosocial Factors, and Severity of Homelessness. Experimental and Clinical Psychopharmacology, 3:1995:75-86.

Long-term Efficacy of Intervention Efforts to Reduce Anger:

Oetting et al. have conducted a fifteen month follow up (n=140) comparing three different intervention approaches to general anger reduction in college students. The three compared approaches were inductive social skills training, assembly social skills training, and cognitive-relaxing coping skills. Findings for anger reduction at the 15 month follow-up showed consistent, long term maintenance of intervention effects including less trait and general anger, less anger in response to various situations, and lower anger related physiological arousal than did members of the control group. Intervention groups did not differ significantly from one another. However, there was a lack of change on nontargeted measures. This argues that the effects obtained were specific to the planned intervention and there was no generalizability to other situations. It appears that generalization of principles and strategies to other concerns (e.g., drug abuse prevention intervention efforts) would need to be systematically built into the anger reduction drug abuse prevention programs. Deffenbacher, J.L., Oetting, E.R., Huff, M.E., Thwaites, G.A., Fifteen-Month Follow-Up of Social Skills and Cognitive-Relaxation Approaches to General Anger Reduction, Journal of Counseling Psychology, 42(3) 400-405, 1995.

Factors Mediate Relationship Between Temperament and Substance Abuse

Recent research has shown that the temperament characteristic of high activity level among early adolescents is a risk factor for substance use, whereas positive mood protects against substance use. The effect of temperament is not direct, but is mediated through self-regulation and coping variables. In this model derived by Thomas Wills and his colleagues from their data, the mediating variables of behavioral coping and self-control are related to constructs of maladaptive coping (anger and helplessness) and novelty seeking (sensation seeking and risk taking), which in turn are related to affiliation with substance-using peers, the proximal factor for becoming involved in substance use. These findings are based on cross-sectional data from a sample of 1,826 7thgrade public school students (mean age 12.3 years) who were 27% African-American ethnicity, 24% Hispanic ethnicity, and 36% Caucasian ethnicity. Self-report questionnaires were administered to students in classrooms by project staff using a standardized protocol. The questionnaire included five scales from the Revised Dimensions of Temperament Survey (Windle & Lerner, 1986) and items on tobacco, alcohol, and marijuana use. The study findings emphasize the importance of self-regulation ability as a construct that is antecedent to deviant peer affiliations. (Wills, T.A., DuHamel, K. & Vaccaro, D. Activity and Mood Temperament as Predictors of Adolescent Substance Use: Test of a Self-Regulation Mediational Model. Journal of Personality and Social Psychology, 68:1955:901-916.)

African American 8th, 10th, and 12th Grade Students:

J.M. Wallace and colleagues at the Institute for Social Research analyzed self-reported drug use data from a nationally representative sample of African American 8th, 10th, and 12th grade students, collected as part of the Monitoring the Future project. In a chapter of Multi-Ethnic Drug Abuse Prevention (edited by G. Botvin, S. Schinke, and M. Orlandi; Sage Publications, in press, 1995), the authors report their findings, including: African American high school students initiated illicit drug use later than their white counterparts; if they used cocaine, they tended to use more of the drug more frequently than white students; prevalence rates of illicit drug use among African American students appear to be increasing over time; and predominately low income, African American communities had a disproportionate share of retail liquor outlets relative to geographic and population densities, indicating that community residents are at an increased risk of alcohol consumption and alcoholrelated morbidity and mortality.

Sensation Seeking and Drug Use Among High Risk Latino and Anglo Adolescents:

Sussman and associates examined the relationship between sensation seeking and drug use in a sample of white and Latino southern California adolescents enrolled in continuation high schools. The 11 item sensation seeking portion of the Zuckerman Kuhlman Personality Questionnaire was found to have adequate reliability and to be positively associated with use of each of the drugs examined. Sensation seeking was examined as a correlate of self reports of tobacco, alcohol, marijuana, cocaine, stimulants, and LSD use. The relationship between sensation seeking and drug use was found to vary across ethnic backgrounds. Among white students sensation seeking was positively associated with drug use only among those with low to moderate scores on sensation seeking. Among the Latino students increased sensation seeking levels were consistently associated with increased drug use. Differences were found in the pattern of drug use across ethnicity. White students reported significantly higher use levels of tobacco, stimulants, and LSD than did the Latino students. Latino students reported trying fewer drugs than white students. The ranking of drugs by level of use also differed across ethnicity. Among white students tobacco was the most commonly used drug and cocaine the least used. Among the Latino students alcohol was the most commonly used drug and LSD showed the lowest use levels. These findings suggest that different norms may be operating across ethnic groups. Adolescents who are high in sensation seeking needs may benefit from programs designed to direct those needs in healthy directions. Simon, T., Stacy, A., Sussman, S., Dent, C. Sensation Seeking and Drug Use Among High Risk Latino and Anglo Adolescents. Personal Individual Differences, 17, 665, 1994.

Integrating Theories of Adolescent Substance Use

Over the decades, scientists have advanced a number of theories in the attempt to understand why some adolescents experiment with substance use while others do not. To make sense of these theories, researchers at the University of Illinois at Chicago have developed a model of adolescent experimental substance use that integrates aspects of theories based on substance-specific cognitions, social learning processes, commitment to conventional values and attachment to families, and intrapersonal processes. Commitment and attachment theories and intrapersonal theories show how adolescents become involved with deviant peers; social learning theories show how this involvement affects an adolescent's beliefs about substance use; and cognitive-affective theories show how substancespecific beliefs affect initial use. A rapprochement among these theories is possible because they are largely complementary. The integrated theory proposes a matrix reflecting the crossing of three types of influence (social, attitudinal, and intrapsychic) and three levels of influence (proximal, distal, and ultimate); definitions and constructs associated with each matrix cell are provided. The cell representing the ultimate level of intrapersonal influences, for example, focuses on personality traits and inherited dispositions that are difficult to modify, such as genetic susceptibility, lack of impulse control, external locus of control, aggressiveness, extraversion, risktaking, sensation seeking, sociability, and chronic emotionality. By contrast, other intrapersonal features appear as distal (i.e., intermediate) causes of experimental substance use because they appear somewhat more controllable by adolescents; these include changeable affective states (e.g., low self-esteem, anxiety, and depressed affect) and general behavioral skills (e.g., poor social and academic skills) that might contribute to experimentation with substance use. Flay B.R., Petratis, J., & Miller T.Q. Reviewing Theories of Adolescent Substance Use: Organizing Pieces of the Puzzle. Psychological Bulletin, 117: 1995:67-86.

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

Etiology, Prevention, and Epidemiology Research

Continued

The Effects of a Multicomponent Prevention Intervention Program:

The Adolescent Transitions Program (ATP) is a multicomponent intervention program for prevention of substance use and other behaviors. It consists of two coordinated prevention intervention packages aimed at parents (Parent Focus) and youths (Teen Focus). Dishion and colleagues evaluated the basic prevention program components with 158 families. Information collected to help judge program effectiveness included program engagement, skill acquisition, improvement in family interaction, and reductions in problem behavior. The study found that these basic components were effective in engaging students and their parents, teaching them skills and improving parent-child relations. In addition, the Parent Focus curriculum had a short term effect on the incidence of aggressive and delinquent behaviors of young teens. The Teen Focus curriculum, while enhancing parent-child relations, did not influence problem behavior in short term evaluations. Teens participating in the Teen Focus curriculum seem to escalate in their problem behavior after experiencing the intervention. Andrews, D.W., Soberman, L.H. & Dishion, T.J. The Adolescent Transitions Program for High-Risk Teens and Their Parents: Toward a School-Based Intervention. Education and Treatment of Children., in press.

Effects of Parent and Peer Factors on Refusal Skills to Prevent Early Adolescent Alcohol Use

Peer refusal techniques have been used with some success in drug abuse prevention intervention efforts. Spoth and colleagues have tested a model of protective parent and peer factors in peer refusal skills. Data from a sample of 209 families who were Caucasian and recruited from economically stressed rural midwestern school districts were used. Two versions of the model were tested, one version addressing attachment and skills training attendance specific to mothers and one specific to fathers. Strong fits with the data were achieved for both mother and father versions of the model; hypothesized protective factor effects and skill training effects were significant. The degree to which findings would generalize to a more diverse sample is unknown. Spoth, R., Yoo, S., Kahn, J., Redmond, C. A Model of the Effects of Protective Parent and Peer Factors on Early Adolescent Alcohol Refusal Skills, Journal of Primary Prevention, in press.

Evaluation of a Prevention Intervention Program in an Economically Stressed Rural Area:

Spoth and colleagues have completed the evaluation of a prevention intervention program, Preparing for the Drug (Free) Years, with a sample of 209 families residing in an economically stressed rural area. The study was an experimental test of intervention versus control differences on directly targeted protective parenting behavior and more general child management skills. The study showed significant intervention effects on both measures for both mothers and fathers. Results also indicated that both mothers' and fathers' level of intervention attendance and expressed readiness for parenting change were significant predictors of the targeted parenting outcome which in turn significantly affected the general child management outcome for both mothers and fathers. Spoth, R., Redmond, C.,

Haggerty, K., Ward, T. A Controlled Parenting Skills Outcome Study Examining Individual Difference and Attendance Effects, Journal of Marriage and the Family, 57:449, 1995,

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Drug Use in the Workplace:

Etiological theories regarding drug use and intoxication on the job tend to emphasize either personal characteristics or job conditions. Using prospective data from a community sample (N=545) assessed in young adulthood (20-25 years) and again four years later (25-29 years), both cross-sectional and longitudinal analyses evaluated associations among multiple measures of intoxication in the workplace, job instability and satisfaction, and social conformity. Being high on the job was more prevalent, frequent, and stable over time for men than women, although rates decreased for both genders with age. Measures of social conformity were most related to drug use on the job within time, but had few unique effects over time. After controlling for prior intoxication on the job, only a few earlier work characteristics (but no personal traits) affected later intoxication on the job, providing little support for either etiological position. However, several significant interactions were found between personal and job variables that predicted increased intoxication in the workplace. On the other hand, earlier intoxication on the job increased later measures of job instability.

Newcomb, M.D. Prospective Dynamics of Drug Use in the Workplace: Personal and JobRelated Predictors and Consequences. Experimental and Clinical Psychopharmacology, 3:1995:56-74.

Community Readiness for Drug Abuse Prevention:

Eugene Oetting and colleagues have published an article which for the first time has defined stages in community readiness for drug abuse prevention and other intervention efforts. One cannot simply impose a prevention program. The community has to grow through a series of stages prior to initiating a prevention program. In addition, there are stages that mark the quality of a community's readiness. The article also provides a set of anchored rating scales for assessing community readiness. The article has become the basis for many workshops and programs for minority communities. Oetting, E.R., Donnermeyer, J.J., Plested, B.A., Edwards, R.W., Kelly, K., and Beauvais, F. Assessing Community Readiness for Prevention, The International Journal of the Addictions, 30(6), 659, 1995.

Adaptive Behaviors Among Psychiatrically Hospitalized Children: The Role of Intelligence and Related Attributes:

Intelligence has previously been found to serve protective functions for the maintenance of socially competent behaviors. As a part of a larger study of children of substance abusers, this study of 126 psychiatrically hospitalized children studied intelligence and two constructs possibly associated with the protective effects of intelligence: level of academic achievement and the distinction between internalizing and externalizing symptomatology. Of the variables examined, achievement showed the strongest associations with different types of adaptive behaviors. Further, achievement levels appeared to mediate even the modest associations that were found for intelligence. Type of symptomatology had significant associations with adaptive behaviors chiefly in the socialization domain, and these effects seemed largely independent of both IQ and achievement. Luthar, S.S., Woolston, J.W., Sparrow, S.S., Zimmerman, L.D., & Riddle, M.A. Adaptive Behaviors Among Psychiatrically Hospitalized Children: The Role of Intelligence and Related Attributes. Journal of Clinical Child Psychology, 24:1995:98-108.

"Unselling" Drugs: The Marketing of Prevention

Kathleen Kelly has published an article that provides a valuable foundation for understanding the use of media in prevention intervention efforts. It reviews the literature on "social marketing" and relates social marketing to traditional marketing, pointing out crucial differences. For example, traditional marketing urges immediate gratification of immediate wants and needs through purchase or use of a product. Drug prevention requires delay of gratification of immediate needs in exchange for long term gain. Nevertheless, basic principles of marketing are often ignored by drug prevention programs. The paper gives practical advice noting that marketing methods can be used to improve our ability to convince the public to support drug prevention efforts and to improve the efficacy of our prevention programs. Kelly, K. "Unselling" Drugs: The Marketing of Prevention, The International Journal of the Addictions, 30(8), 1043, 1995.

Immediate Impact of Social Influence-Oriented Substance Abuse Prevention Curricula in High Schools:

A study examining the immediate impact of social influence-oriented activities on drug related knowledge and beliefs for students at traditional versus continuation high schools has been completed by Sussman and colleagues. The relative effectiveness of two intervention program delivery methods (active versus passive) was also examined. Continuation high school students reported much higher levels of overall drug use. Across school type, the activities showed the most impact on knowledge change. Overall, the comparison evaluation study of the social influence lessons suggests that most of the components of a social influence curriculum can have an immediate effect on knowledge regardless of school type or delivery method. Taken together, the immediate impact findings suggest that (1) it is more difficult to achieve an immediate impact on beliefs than knowledge, (2) students in continuation high schools are less likely to experience immediate changes in beliefs from single social influences lessons, and (3) actively participating in a curriculum is more likely to lead to a significant change in beliefs than is passive participation. Sussman, S., Dent, C., Simon, T., Stacy, A., Galaif, E., Moss, M., Craig, S., Johnson, C. Immediate Impact of Social Influence-Oriented Substance Abuse Prevention Curricula in Traditional and Continuation High Schools. Co-published simultaneously in Drugs & Society, 8, 65, 1994. and Drug Prevention Research and Practice, Leukefeld, C., (ed.), The Haworth Press, Inc., 1994,

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Parental Influences on Early Adolescent Deviant Behavior:

Having fewer than two supportive parents generally increases the risk of deviant behavior, but more so for boys than for girls. This is the conclusion of a longitudinal study of 601 families examining the separate and combined effects of parental psychiatric disorders, supportive parent-child communications, and household income on the development of deviant behavior in boys and girls 11 to 14 years of age. Deviance in this study was defined on the basis of 15 specific behavior patterns, including three related to substance use (began drinking or using drugs, smoked cigarettes during the past 30 days, and drank alcohol in the past 30 days). The relationships between having fewer than two supportive parents and deviant behavior was more pronounced when one or more parents had a chronic mental disorder (principally depression and substance abuse), but the combination of fewer than two supportive parents and one psychiatrically impaired parent had a particularly marked effect on girls. Moreover, older children's behavior is affected more dramatically by parental mental disorders, especially among girls; 13-to-14-year-old girls with both parental risk factors were virtually as deviant as male agemates with both risks. Each of these effects is present regardless of family income level, but without these risks, household income is negatively related to deviant behavior. Johnson, R.A., Su, S.S., Gerstein, D.R., Shin, H.C. & Hoffmann, J.P. Parental Influences on Deviant Behavior in Early Adolescence: A Logistic Response Analysis of Age- and Gender-Differentiated Effects. Journal of Quantitative Criminology, 11:1995:167-193.

Natural History of Crack Cocaine Users:

Bruce Johnson and colleagues reported recent findings from their analysis of data from an eight year (1989-1997) natural history cohort study of crack cocaine dealers and users in New York City. They found that crack cocaine use has been on a steady decline since peaking in the mid to late 1980s and that crack dealing has shifted from conspicuous sales in open, outdoor drug markets to clandestine sales in private settings in apartments buildings. The decline in use of crack cocaine appears to reflect both changing attitudes and norms among youth as well as general shifts among drug users to powdered cocaine and smokable heroin. The authors report there has been a notable increase in the number of female crack cocaine sellers; they speculate that this may be because of the high incarceration rates of male crack cocaine dealers as well as the declining profitability from selling the drug. Golub, A., Johnson, B., and Fagan, J. Careers in Crack Use, Drug Distribution, and Nondrug Criminality. Crime and Delinquency; 41; 3; 1995; 275-295.

Biological Mechanisms Related to Prevention of Drug Abuse:

Bardo et al. have published a review article that examines biological mechanisms that have potential implications for prevention intervention of drug abuse. In this article, scientific evidence is provided to support the contention that drug seeking behavior is rewarding because it activates a brain system similar to that normally activated by novelty seeking (i.e., the mesolimbic dopamine system). The hypothesis is that individual differences in the need for novelty make individuals differentially susceptible to drug use. There are a number of indications that novelty or sensation

seeking in humans in biologically based as well as evidence of high heritability of the trait. Despite the role of genetics, however, evidence from animals indicates that early developmental experiences alter many both novelty- and drug-seeking behaviors. Within the context of this biological formation, implications for the prevention of drug abuse are discussed. Bardo, M.T., Donohew, R.L, and Harrington, N.G., Psychobiology of Novelty-Seeking and Drug-Seeking Behavior. Behavioral Brain Research, In press, 1995.

Group Self-Identification and Adolescent Cigarette Smoking: A One Year Prospective Study:

As an extension of previous work on prevention interventions, this study by Sussman, et al. analyzed the longitudinal relations and predictive precedence of group self-identification and adolescent cigarette smoking. Results indicated that 7th-grade group self-identification predicted 8th-grade cigarette smoking, whereas 7th-grade cigarette smoking did not predict 8th-grade group self-identification. Group self-identification was also compared with 7 other psychosocial variables as predictors of smoking 1 year later. The pattern of results suggests that group selfidentification is about as good a predictor of smoking as other psychosocial variables, and that group self-identification is more than a mere proxy of other psychosocial variables. Sussman, S., et al. Group Self-Identification and Adolescent Cigarette Smoking: A 1-Year Prospective Study. Journal of Abnormal Psychology, 103, 1994.

Five Methods of Assessing Use of Cigarettes and Alcohol at High Schools to Better Target Prevention Intervention Efforts:

Sussman and Stacy explored five methods of estimating school-level daily use of cigarettes and alcohol by adolescents at 20 continuation high schools in southern California. Campbell and Fiske's criteria were used to estimate convergent and discriminant validity of a correlation matrix consisting of two "traits" (daily use of cigarettes or alcohol) and five "methods" (aggregated student self-report, school personnel prevalence estimate, student prevalence estimate, naturalistic observation of use, and school refuse evidence). The different methods varied dramatically in convergent and discriminant validity. The findings, as well as assessment cost considerations, suggest that refuse analysis is the most economic proxy measure for estimating school-level daily student cigarette smoking and other drug use.

Sussman, S., Stacy, A. Five Methods of Assessing School-Level Daily Use of Cigarettes and Alcohol by Adolescents at Continuation High Schools. Evaluation Review, 18, 741, 1994.

Components of an Anabolic Steroid Prevention Intervention Program

Anabolic androgenic steroids (AAS) prevention efforts have involved alternatives to athletic enhancing drugs, including strength training instruction; however, this component of an AAS intervention has never been studied among a group of adolescent athletes. Forty-eight high school varsity football players completed an 8 week AAS education program which was composed of 8 didactic sessions and 8 weekly strength training periods. The overall satisfaction with the program was 95%. Students reported positive benefits concerning physical changes after the intervention. Those who participated in the intervention were less willing to try ASS after the intervention. Results suggest that as part of an AAS prevention program, 8 sessions of strength training can enhance adolescent self-efficacy in the weight room and enhance a successful school-based anabolic steroid drug prevention program. Green, C.P., Goldberg, L., Elliot D., Moe, E. Adolescent Attitudes Toward a Strength Training Program: A Component of an Anabolic Steroid Program Intervention. Medicine and Science in Sports and Exercise, (Supplement), 1995, 27:S173.

Defining Steroid Users' Characteristics to Allow Rational Structuring of Prevention Intervention Programs

Goldberg et al. studied the characteristics of the users of anabolic steroids (AS) comparing high intent athletes to players having less predisposition toward AS use. High intent athletes had more access to AS, reported greater belief in AS's beneficial effects, felt greater influence to use AS by teammates' and friends' AS use, experienced less parental influence not to use, had less comfort refusing AS, and were more impulsive and stronger believers in "winning at all costs." Understanding of specific AS risks and benefits did not differ between groups. Elliot, D., Goldberg, L., Clarke, G., Zoref, L., Moe, E., MacKinnon, D., Green, C., Wolf, S., Miller, D., Greffrath, E. Characterization of Adolescent Athletes with High Behavioral Intent to Use Anabolic Steroids. Paper presented at the

Third IOC World Congress on Sports Sciences, Atlanta, Georgia, September, 1995.

Examination of Development Risk Factors Leading to Steroid Use:

To determine the need for differential prevention interventions for anabolic steroid (AS) use, Goldberg et al. conducted a study to determine the developmental sequence of factors relating to AS. High school football players age 14, 15, 16, 17 and 18 from 31 schools in the Portland, Oregon metropolitan area were given a 168 item confidential questionnaire. Significant differences were present among the ages. Older students were more likely to use protein and carbohydrate supplements and less curious to try AS. Older athletes had less belief that parents would disapprove of drug use, believed more in "winning at all costs" and reported more understanding of alternatives to AS (e.g., strength training and nutrition to gain muscle). Factors which did not differ by age included peer influences, perceived coach disapproval and concern about drug side effects. Younger high school athletes' knowledge gaps in nutrition and strength training suggest intervention programs correcting these gaps may enhance athletic development and deter future AS use. Interventions for older athletes may be enhanced more by impacting on attitudes about winning and peer/non-peer influences. Goldberg, L., Elliott, D., Clarke, G., Zoref, L. Moe, E. MacKinnon, D., Green, C., Wolf, S., Miller, E., Greffrath, E. Does Age Affect Factors that Relate to Ergogenic Drug Use? Differences Among Athletes Aged 14 to 18. Paper presented at the Third IOC World Congress on Sports Sciences, Atlanta, Georgia, September, 1995.

The ATLAS Prevention Program

Researchers at the Oregon Health Sciences University have developed and are testing a school-based intervention to prevent anabolic steroid (AAS) use among high risk adolescent athletes. Eight weekly, one hour classroom sessions delivered by the coach and adolescent team leaders and eight weightroom sessions delivered by research staff were part of the intervention. Other components were sports nutrition and strength training as alternatives to AAS use, drug refusal role play and anti-AAS media campaigns. Comparison of the experimental group with controls indicates that the intervention was successful based on a variety of indices. Significant beneficial effects were found despite a small sample size, suggesting that the effect of the intervention was large. Goldberg, L., Elliot, D., Clarke, G., Zoref, L., MacKinnon, D., Moe, E., Green, C., Wolf, S., Schoenherr, D. The Adolescent Training and Learning to Avoid Steroids (A.T.L.A.S.) Prevention Program: Background and Results of a Model Intervention. Archives of Pediatrics & Adolescent Medicine, in press; and Adolescents Training and Learning to Avoid Steroids (ATLAS): Initial Results of a Prevention Program. Medicine and Science in Sports and Exercise, (Supplement), 1995, 27:S173.

Strategies to Prevent Drug Abuse in Ethnic Minorities

Dr. Trimble has written a book chapter which reviews and comments on research on the prevention of drug problems in America's ethnic minority populations. The chapter examines the inaccurate stereotype of drug use as a minority problem and examines the gaps that exist in knowledge about drug use and risk factors for drug use among ethnic minorities. Trimble, J.E. (1995) Ethnic Minorities. in R.H. Coombs & D. Ziedonis (Eds.), Handbook on Drug Abuse Prevention: A Comprehensive Strategy to Prevent the Abuse of Alcohol and Other Drugs. (pp. 379-409). Boston: Allyn & Bacon.

Reaching Parents of At-Risk Populations for Prevention Intervention Program Participation

To understand the motivation behind parents' decisions to involve themselves in prevention intervention programs, Spoth and Redmond studied a heuristic model of health belief and family context factors associated with parent inclination to enroll in parenting skills programs. They collected data from 1,192 rural midwestern parents of 5th graders. Perceived program benefits, program barriers, and past parenting resource use showed the strongest influence on the parents' inclination to enroll. Parents' predisposition toward parenting skills enhancement efforts in general and parenting skills programs in particular may be operative in addition to rational choice factors such as costs and benefits. Spoth, R., Redmond C., Parent Motivation to Enroll in Parenting Skills Programs: A Model of Family Context and Health Belief Predictors, Journal of Family Psychology, 9(3), in press.

Likelihood Ratio Test for the Correlation Coefficient:

Many studies of drug abuse causes and consequences by necessity must rely on correlational designs. One of the most commonly used analytic tools in drug abuse research is the correlation coefficient. Therefore, improving methods of estimation and model based hypothesis testing using correlations is of considerable importance. To replace the approximate methods, the exact likelihood ratio test for the correlation coefficient was developed, along with other technical features such as its power curve. The new procedure is available to researchers in the form of a personal computer program. Liu, W.C., Woodward, J.A. & Bonett, D.G. The Generalized Likelihood Ratio Test for the Pearson Correlation. Communications in Statistics, 1995.

Parameter Estimation in Structural Equation Modeling

A general review of parameter estimation in structural modeling, and procedures for evaluating model fit under nominal conditions and under conditions of nonnormal distributions such as are typically found in drug abuse research was undertaken. It was found that researchers cannot simply use a program default to analyze their data under nonstandard conditions, because the standard methods could lead to very misleading results. While normal theory maximum likelihood estimates were good even under violation of normality, the associated standard errors and test statistics could not be trusted. The Satorra-Bentler scaled chi-square statistic, and the robust standard errors, were found to work better under various conditions than any alternative (these methods are available in EQS). A new empirical computer study was undertaken to provide a solid foundation for these recommendations. (Chou, C.P. & Bentler, P.M. Estimates and Tests in Structural Equation Modeling. In R.H. Hoyle, (ed.), Structural Equation Modeling: Concepts, Issues and Applications, Thousand Oaks, CA: Sage, 1995, 37-55.

Evaluation of Chi-Square Tests:

When the sample size is large, or when nonstandard conditions exist, the chi-square test for model evaluation often leads to misleading results. For example, even trivial discrepancies between model and data may yield a test statistic that implies an unacceptable model with large samples. As a result, a wide variety of fit indices have been developed to supplement the chi-square test. A new classification of these fit indices in terms of the amount of information they utilize is provided. The various pitfalls associated with chi-square tests and fit indices, and reports on a new computer sampling study that evaluated the various indices was reviewed. In general, it was found that indices that incorporate more correct information, such as the expected values of the chi-square under the correct model, and especially the expected values of the chi-square under misspecification (noncentral chi-square), work best. (Hu, L.T. & Bentler, P. M. Evaluating model fit. In RH Hoyle (Ed), Structural Equation Modeling: Concepts, Issues and Applications Thousand Oaks, CA: Sage, 1995, 76-99).

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Research Findings

Intramural Research

Molecular Pharmacology Section, Neuroscience Branch

A desirable feature of cocaine-like agonist-substitute medications is that they have a long duration of action, reducing cost and simplifying dosing schedule. In collaboration with the Brookhaven National Lab PET scanning group, Dr. Kuhar has shown that a potential cocaine analog medication termed RTI-55 has such a long duration of action. Using PET scanning with a babboon, it was possible to show that this compound occupies dopamine transporters (a cocaine receptor) with a half life of clearance of 2-3 days. This supports findings with rodents suggesting that a large number of medication candidates identified by Dr. Kuhar and collaborators are long lasting. Interest in these compounds continue and many of them are being considered for industrial development. Key collaborators in this work include Dr. Ivy Carroll and Dr. Nora Volkow.

Neuroimaging and Drug Action Section, Neuroscience Branch

This paper describes findings from positron emission tomographic studies on effects of exposure to cocaine-related stimuli on brain metabolism. Exposure to the stimuli (videotape related to cocaine and paraphernalia) and anticipation of cocaine self-administration produce a widespread activation of glucose metabolism in the cerebral cortex, most prominently in occipital and frontal regions. Metabolism in subcortical regions is not affected. The findings support the view that environmental cues can trigger drug craving and measurable changes in brain activity. The distribution of the cerebral effects suggests that non-dopaminergic systems may be important therapeutic targets for antagonizing drug craving and relapse. ED London, S Grant, and D Newlin (1995): Identifying the Substrates in Brain that Underlie Cocaine Craving. NIH Catalyst: Jun/Jul.

Studies which measure regional cerebral glucose metabolism in rats using the 2-deoxy-D-[114C]glucose autoradiographic method and those in human volunteers using PET and 2-deoxy-[218F]fluoro-D-glucose are reviewed. Acute nicotine increases cerebral glucose metabolism in brain regions containing high densities of nicotinic acetylcholine receptors in rats; the drug has similar effects after chronic administration. In contrast, acute nicotine administration to human volunteers produces a generalized reduction in cerebral metabolic activity. ED London (1995): Mapping the Cerebral Metabolic Responses to Nicotine. In: Brain Imaging of Nicotine and Tobacco Smoking, pp 153-166, EF Domino, ed., NPP Books Inc., Ann Arbor, MI.

To assess the neuroprotective effects of sigma (s) receptor ligands in transient focal ischemia, 4phenyl-1-(4-phenylbutyl)piperidine (PPBP), a potent s receptor ligand, was evaluated in the cat. Intravenous administration of PPBP beginning at 75 min after the infusion of a 90 min focal ischemia insult and continuing for 240 min of reperfusion substantially reduced the volume of acute brain injury in the cerebral hemisphere and caudate nucleus. Recovery of somatosensory evoked potentials was greater in cats treated with PPBP as compared to controls. It is concluded that s receptors have an important role in the mechanism of acute ischemic injury within the brain, and the protective effect of PPBP suggests s receptors may contribute to the progression of injury in ischemic border regions. H Takahahsi, JR Kirsch, K Hashimoto, ED London, RC Koehler, and RJ Traystman: PPBP[4-Phenyl-l-(4-phenylbutyl) piperidine], A Potent Sigma-Receptor Ligand, Decreases Brain Injury Following Transient Focal Ischemia in Cats.

Stroke, in press.

A modulatory role for nitric oxide (NO) in the mediation opioid withdrawal is supported by the ability of four inhibitors of nitric oxide synthase (NOS) to partially attenuate signs of the naloxone precipitated morphine abstinence syndrome. Effects of the NOS inhibitors were similar to clonidine, a drug used clinically to treat opioid withdrawal. Additional evidence has linked NOS with the development of opioid tolerance. Thus, two lines of pharmacologic evidence demonstrate a role for NO in phenomena associated with chronic opiate use and suggest that future studies care warranted to explore the potential clinical application of NOS inhibitors to treat opioid dependence. DB Vaupel, AS Kimes, and ED London: Nitric Oxide Synthase Inhibitors: Preclinical Studies of Potential Use for Treatment of Opiate Addiction. Neuropsychopharmacol., in press.

Molecular Neuropsychiatry Section, Neuroscience Branch

p53-knockout transgenic mice provide a useful toxicity model because p53 has been shown to be involved in the development of apoptosis in a number of cell lines. In order to assess if p53 is involved in the neurotoxicity caused by methamphetamine (METH) on the dopaminergic systems, scientists have evaluated the effects of this drug in male wild-type as well as heterozygous and homozygous p53-knockout mice. The status of dopaminergic terminals was determined after the administration of 3 different doses of METH (2.5, 5.0, and 10mg/kg were given 2 hours apart for a total of 4 injections in one day). In wild-type mice, METH caused dose-dependent decreases in DA uptake sites in both the striatum and nucleus accumbens. The percentage of decrease was greater in the striatum. In p53-knockout mice, the depletion caused by METH was attenuated in a strain-dependent fashion, with the homozygous mice showing the greatest protection. These results provide evidence for a role of p53 in the neurotoxic effects of METH on the dopaminergic system. They also suggest a role for p53 in the development of neurodegenerative disorders such as Parkinson's disease.

Molecular Neurobiology Branch

During the latter part of Fiscal Year 1995 the Branch completed a CRADA with Guilford/Gel Pharmaceuticals and has begun exciting collaborative work with novel approaches to cocaine antagonist development. Investigators have licensed dopamine transporter cDNAs and expressing cells, and mu receptor cDNAs and expressing cells.

The Branch has now identified more than 200 candidate drug-related genes using techniques developed and refined at the NIDA/DIR. They have reported detailed structures of human and mouse dopamine transporter gene loci and identified details of the dopamine transporter and mu receptor distributions in brain identified at light and ultrastructural levels. In addition, investigators have described behavioral effects of morphine and cocaine to be altered by manipulations of single genes in transgenic mouse models.

Psychobiology Section, Behavioral Pharmacology Laboratory

Studies of benztropine analogs continue to provide interesting leads for a better understanding of how actions at the dopamine transporter may or may not be translated into physiological effects that lead to drug abuse. Several benztropine analogs, most notably the 4',4"-dihalogenated compounds, demonstrate high affinity binding (Ki<30 nM) to the dopamine transporter that is selective (>100-fold) over the other monoamine transporters. These compounds block dopamine uptake in vitro but do not produce behavioral effects like those produced by cocaine. For example, the drugs are not effective locomotor stimulants nor do they produce subjective effects like cocaine. A recently synthesized analog within this series is distinctive from the others in that it has cocaine-like behavioral activity. As a result, we now have a lead for the development of structure-activity relations that may reveal the pharmacophore for cocaine-like behavioral effects. Further, studies of the interaction of these drugs with the dopamine transporter will provide models of specific sites on the transporter that are responsible for cocaine-like behavioral effects. Further, radiolabelled ligands are being prepared that may be suitable for imaging the dopamine transporter in mammalian brain using SPECT and PET. These compounds represent an unprecedented class of dopamine uptake inhibitors that may have potential as cocaine-abuse therapeutics.

Cocaine binding curves have two components (high and low affinity) and the inhibition of dopamine uptake can exhibit two components. One of these components, comprising approximately 25% of the total dopamine uptake, exhibits a high sensitivity to cocaine and is inhibited by low concentrations of the drug. The other component is much less sensitive to inhibition. We have recently shown that meperidine, an atypical opioid agonist that shares some structural features with the phenyltropane (WIN) analogs of cocaine, selectively inhibits only the high affinity

component of dopamine uptake. This effect is mediated by the dopamine transporter and is not produced by opioid mechanisms. Further, meperidine, in the presence of naltrexone to block its prepotent opioid actions, produces subjective effects like those of cocaine in primates trained to discriminate cocaine from saline. These data suggest that the actions of meperidine that are atypical of opioids are due at least in part to activity at the dopamine transporter. In addition, meperidine appears to interact predominantly with the high-affinity component of the dopamine transporter, and this high-affinity component may be the site of importance for the production of cocaine's behavioral effects.

Recent preclinical findings and anectodal clinical reports have suggested the potential for ibogaine to treat drug dependence, however, its mechanism of action has remained elusive. In conjunction with collaborators in the Laboratory of Neuroscience, NIDDK, NIH, we have demonstrated, a plausible mechanism of action of ibogaine. Electrophysiological, neurochemical, and behavioral data indicate that ibogaine functions as a low affinity blocker of the NMDA-associated ion channel. Current efforts are focused on the discovery of other compounds in this class that do not have the ancillary side-effect profile of ibogaine (tremor, ataxia, and phencyclidine-like effects). Studies of strychnine-insensitive glycine site antagonists have shown that low-efficacy partial agonists, block the development and expression of behavioral and toxicological sequalae of abused drugs and produce subjective effects that are driven by agonist binding to that site.

These effects are distinct from the sedative and psychotomimetic effects produced by other drugs which produce functional blockade of NMDA-associated neurotransmission.

Chemistry and Drug Metabolism Section, Clinical Pharmacology Branch

Despite the current popularity of smoking as a route of drug self-administration, there have been no human studies characterizing the pharmacokinetics and pharmacodynamics of smoked heroin. Researchers administered heroin by the smoking route to human subjects and found that this route of administration produced effects similar to those produced by the intravenous route. The rapid onset of pharmacologic effects together with the early appearance of heroin and metabolites in blood following smoked heroin demonstrated the effectiveness of this route of drug administration. Heroin abuse by this route could increase as the price of illicit heroin decreases and its purity increases.

Researchers have demonstrated that adults exposed to cocaine smoke under naturalistic or artificial conditions absorbed small amounts of cocaine that were insufficient to produce positive urine specimens at standard DHHS cutoffs. However, passive exposure conditions could be produced that would result in absorption of cocaine in amounts exceeding one milligram. This could result in the production of cocaine positive urine specimens and would be especially important if passive exposure of small children was involved.

A dramatic shift has occurred over the last decade in the route of cocaine administration by drug abusers in the United States. The favored route has changed from intranasal and intravenous use to administration of cocaine ("crack") by the smoking route. Researchers have demonstrated that cocaine administration by the smoked route produced substantially higher behavioral responses than an equivalent dose of cocaine administered by the intravenous route. This finding suggests that smoked cocaine ("crack") has a higher abuse liability and greater dependence-producing properties than equivalent doses of cocaine administered by the intravenous or intranasal route.

Assays have been developed to evaluate in vitro binding of drugs to hair. Preliminary studies have shown significant differences in cocaine binding between Caucasoid and Africoid hair, between male and female Africoid hair, and between dark colored and light colored hair. These studies also provided evidence that supported the use of in vitro studies to evaluate the binding of drugs to hair.

Clinical Psychopharmacology Section

1. Novel binding sites for cocaine in mammalian brain.
[125I]RTI-55 is a cocaine analog with high affinity for the DA and 5-HT transporters. Its high specific activity (2200 Ci/mmol) and low nonspecific binding (typically less than 100 dpm) makes it an extremely useful ligand for detecting and characterizing multiple binding sites for biogenic amine transporter ligands. Quantitative binding studies in rat, guinea pig, monkey and human brain have identified two additional [125I]RTI-55 binding sites which are not associated with the classic DA, 5-HT and NE transporters. These sites, termed DATsite2 and SERTsite2 are associated with the DAergic and 5-HTergic nerves, respectively. Each site has a unique anatomical distribution and structure-

activity profile. Cocaine, the prototypical addictive DA uptake inhibitor, has Ki values at these sites ranging from 500 to 1000 nM. The functional role of these sites remains to be determined. Efforts to clone DATsite2 and SERTsite2 will soon be underway.

2. Modulation of μ-opiate receptor density by the anti-opioid peptide, NPFF.
A variety of data support the hypothesis that endogenous neuropeptides act as part of a homeostatic mechanism to attenuate the effects of morphine. Previous studies from this laboratory indicated that whereas chronic i.c.v. infusion of NPFF down-regulated, chronic i.c.v. infusion of polyclonal anti-NPFF IgG up-regulated mu opioid receptors. The aim of this study was 1) to determine the effect of chronic i.c.v. infusion of the purified mouse monoclonal anti-NPFF IgG on the mu receptors using whole brain homogenate binding technique and 2) to characterize the anatomical distribution of [125I]DAMGO binding sites in discrete brain nuclei of rats treated chronically with anti-NPFF IgG. The data indicate that chronic i.c.v. infusion of mouse monoclonal anti-NPFF IgG up-regulated mu receptors labeled with [3H]DAMGO to 102%, 128%, and 172% of control at the 0.001, 0.01, and 0.1 μg/μl doses, respectively. At the level of the caudate, a significant increase in the number of [125I]DAMGO binding sites was observed in specific anatomical regions for the anti-NPFF IgG treated animals, while brain regions caudal to the striatum showed no changes from control. These data suggest that the density of mu opioid receptors in rat brain is tonically controlled by NPFF. Viewed collectively with other information, the pharmacological manipulation of μ-opiate receptor density by the anti-opioid system may provide a novel clinical approach in treatment of nociception, opiate addiction, and psychiatric disorders.

3. Attenuation of cocaine-seeking behavior in the rhesus monkey by administration of phentermine, a clinically available DA releasers.
The combination of the dopamine (DA) releaser, phentermine, and the serotonin releaser (5-HT), fenfluramine, have been reported in case series to decrease craving for alcohol and cocaine and to facilitate abstinence in self-referred patients motivated to stop using cocaine and alcohol. The present study reports the effects of these medications alone and together (0.3 - 3.0 mg/kg, i.v. slow infusion) on cocaine-maintained responding in 8-9 kg male rhesus monkeys. Lever-pressing was maintained under multiple FR 30-response schedules of food and intravenous cocaine delivery. Intermediate unit doses of cocaine (10-30 μg/kg/inj) maintained high levels of responding in the drug delivery components, comparable to those maintained by food presentation. Cumulative doses of fenfluramine produced slight, dose-related decreases in both behaviors that were nonselective. Cumulative doses of phentermine produced selective decreases in cocaine-maintained responding. When assessed as a single bolus dose (i.v., given over 15 min, 15 min before the testing session), the effect of both agents in combination (1 mg/kg fenfluramine + 0.3 to 3.0 mg/kg phentermine) was similar to that of phentermine alone. The effect of phentermine determined as a single dose confirmed the selective decreases on cocaine self-administration produced by cumulative dosing with phentermine, and these effects could be sustained with repeated daily administration. These results demonstrate that clinically available DA releasers with low abuse liability such as phentermine can suppress cocaine self-administration in an animal model of cocaine-seeking behavior. These findings are consistent with case series (J. Subst. Abuse Treatment 11:273-275, 1994) reporting therapeutic effects of phentermine combined with fenfluramine in the treatment of cocaine addiction. The apparent inactivity of fenfluramine in the self-administration paradigm may reflect the fact that this paradigm does not mimic some aspects of the compulsive drug use often seen in humans. Viewed collectively, these results provide a preclinical rationale for clinical trials of non-addicting DA releasers as substitution-type medications for cocaine addiction.

4. GBR12909 Attenuates Cocaine-Induced Activation Of Mesolimbic Dopamine Neurons In The Rat.
Previous studies have shown that the dopamine (DA) reuptake inhibitor GBR12909 (1-{2-[bis(4fluorophenyl)-[methoxy]ethyl}-4-(3-phenylpropyl)piperazine) antagonizes the increase in extracellular DA evoked by local perfusion of cocaine into the striatum. In the present work, in vivo microdialysis methods were used to examine the effects of i.v. cocaine, GBR12909, and combinations of the 2 drugs on DA overflow in the nucleus accumbens of awake rats. Both cocaine and GBR12909 (0.3-3.0 mg/kg) caused dose-related elevations in extracellular DA when given alone. However, the temporal profile of DA overflow was different with each drug: cocaine caused a rapid and short-lived increase in DA whereas GBR12909 caused a slow and sustained elevation of transmitter. In drug combination studies, the rise in extracellular DA after a modest dose of cocaine (1.0 mg/kg) was significantly reduced from 250% to 175% of baseline by pretreatment with a subthreshold dose of GBR12909 (0.3 mg/kg). A high dose of cocaine (3.0 mg/kg) increased dialysate DA by 600%; this massive surge in DA was decreased to 450% and 325% of baseline by pretreatment with 0.3 and 1.0 mg/kg GBR12909, respectively. The neurochemical effect of the combination of GBR12909 plus cocaine was clearly not additive. GBR12909 also dramatically blocked the DA-releasing action of amphetamine (1.0 mg/kg). Our findings show that GBR12909 antagonizes the rise in extracellular DA produced by systemic cocaine, and these results provide further evidence that DA reuptake inhibitors may be useful pharmacological adjuncts in the treatment of cocaine addiction and withdrawal in human patients.

5. Effects Of Phentermine And Fenfluramine On Extracellular Dopamine And Serotonin In Rat Nucleus Accumbens.

Preliminary evidence suggests that combined administration of the amphetamine derivatives, phentermine (PHEN) and fenfluramine (FEN), may be useful for treating cocaine and alcohol addiction. In open-label studies, some addicts report marked decreases in drug craving within hours of taking this medication. While these medicines are thought to modulate monoamine neurotransmission, the precise mechanism of action has not been characterized. In the present work, we used in vivo microdialysis methods to assess the neurochemical effects of PHEN, FEN, and PHEN/FEN combinations in rat nucleus accumbens. Microdialysis experiments were performed in awake rats, and dialysate samples were analyzed for dopamine (DA) and serotonin (5-HT) using high pressure liquid chromatography followed by electrochemical detection. All drugs were dissolved in Ringers' perfusion fluid (148 mM NaCl, 4 mM KCl and 2 mM CaCl2) and infused locally via the probe (0-100 µM). PHEN selectively increased DA at 1 µM, but at higher doses, both DA and 5-HT levels were elevated. FEN selectively increased 5-HT at all doses, and even at 100 µM, effects on DA were minimal. Infusion of the PHEN/FEN combination elevated extracellular DA and 5-HT to a similar degree at all doses. Our data support the notion that PHEN/FEN treatment causes dual stimulation of DA and 5-HT neurotransmission. Moreover, this action may underlie the ability of PHEN/FEN to reduce drug craving and alleviate withdrawal symptoms in abstinent addicts.

6. Identification of a Novel d Opioid Receptor Binding Site in Rat Brain Membranes
Our laboratory was among the first to propose the existence of d receptor subtypes: a d site thought to be associated with a µ-d opioid receptor complex termed the dcx binding site and d site not associated with the µ-d opioid receptor complex, termed the dncx site. In previous studies we assayed the dcx site with [3H][D-Ala2,D-Leu5]enkephalin using rat brain membranes depleted of dncx sites by pretreatment with the site-directed acylating agent, (+)-trans-SUPERFIT. In the present study we investigated, using (+)-trans-SUPERFIT-pretreated membranes, the possibility of heterogeneity of the dcx binding site. Two sites were resolved: the dcx-1 site at which µ-ligands are potent non-competitive inhibitors and d-ligands are weak competitive inhibitors and the dcx-2 site where d-ligands are potent and µ-ligands are weak, mixed competitive-noncompetitive inhibitors. Although the dcx-2 site has a d-like ligand-selectivity profile, several experiments distinguished it from the dncx site. Two lines of evidence suggest that the dncx site corresponds to the cloned d receptor. One, the d receptor was cloned from the NG108-15 cell line, and this receptor, like the dncx binding site, irreversibly binds SUPERFIT and (+)-trans-SUPERFIT. Secondly, administration of d-antisense DNA selectively decreases dncx binding. Viewed collectively, the major finding of this study is the discovery of a novel SUPERFIT-insensitive and d-antisense-insensitive dcx-2 binding site. Efforts to clone this receptor will soon be underway.

7. Discovery Of A Novel Chiral Benzazepine Derivative, RTI-4793-41, Whose Enantiomers Bind Potently And With Moderate Enantioselectivity To PCP Site 2 And Cloned DA Transporters.
Recently, we reported that RTI-14, a novel pyrrole compound, showed high affinity (IC50 = 38 nM) and selectivity for the MK801-insensitive [3H]TCP binding site (PCP site 2) and moderate affinity for the biogenic amine transporters (BAT). These findings provided further evidence that PCP site 2 may be associated with the BAT system. In the present study, we determined the IC50 values of RTI-14, the novel benzazepine derivative RTI-41 and their enantiomers at PCP site 1 & 2 and the cloned human and rat DA transporters. Using guinea pig membranes, PCP site 1 was labeled with [3H](+)-MK801, while [3H]TCP in the presence of 500 nM (+)-MK801 was used to label PCP site 2. The DA transporter was labeled with [125I]RTI-55. RTI-41 bound potently and selectively to PCP site 2 (IC50 = 15 nM). The enantiomers of both RTI-14 and RTI-41 demonstrated moderate enantioselectivity at PCP site 2. The enantiomers of RTI-41 showed opposite enantioselectivity at PCP site 2 and the DA transporter, supporting the hypothesis that PCP site 2 and the cocaine recognition site on the DA transporter may be different.

The behavioral effects of these novel drugs are just now being explored. In one study an in vivo model was used which detects antidepressant activity by monitoring the effects of drugs on brain beta-adrenergic receptors. According to this well accepted model, drugs with antidepressant properties down-regulate beta receptors. Employing the technique of quantitative receptor autoradiography we showed that continuous i.c.v. infusion of RTI-4793-14 down-regulated beta receptors by about 50% in several nuclei measured at the striatal level.

Other behavioral studies performed in this laboratory attempted to investigate the ability of RTI4793-41 and its enantiomers to alter the conditioned psychomotor stimulant properties of cocaine. Dose response curves showed (+)-RTI-4793-41 increased locomotor activity while the (-)-isomer was devoid of any activity. Preliminary experiments showed that (-) RTI-4793-41 had cocaine antagonist activity - it blocked the conditioned locomotor effect of cocaine. Viewed collectively, these studies suggest that PCP site 2 ligands are promising candidates for the design and synthesis of potential treatment medications for cocaine addiction and depression.

Treatment Branch

P Buprenorphine is an opiate agonist/antagonist with demonstrated efficacy as short-term maintenance treatment for

opiate dependence. It has been suggested that it also reduces the cocaine use common in opiate addicts. Scientists in the Treatment Branch have recently completed one of the first controlled clinical trials evaluating buprenorphine's efficacy and safety in outpatients dually dependent on both opiates and cocaine. Preliminary results indicate that buprenorphine is effective in reducing both opiate and cocaine use in such patients, with the highest buprenorphine dose (16 mg daily) more effective than lower doses in reducing cocaine use.

HIV infection is a frequent medical co-morbidity among injection drug users, but relatively little is known about the influence of such infection on pharmacotherapy for drug abuse. In the course of evaluating buprenorphine as a detoxification or short-term maintenance treatment for opiate dependence, scientists in the Treatment Branch have treated some patients with asymptomatic HIV infection. Such patients had a similar treatment response and similar frequency of medication side-effects as did non-infected patients, suggesting that buprenorphine can be safely and effectively used in HIV-infected opiate addicts.

The use of combinations of medications has been suggested as an approach to pharmacotherapy of drug abuse that might enhance medication efficacy while minimizing side-effects. Scientists in the Treatment Branch recently completed an open-label pilot study of outpatient treatment for cocaine dependence, using bromocriptine + bupropion, two medications which increase dopamine activity by different mechanisms. Results suggest that this medication combination is safe in cocaine addicts, and can reduce cocaine use.

Plasma butyrylcholinesterase (BChE) is the main cocaine-metabolizing enzyme in humans. In theory, changes in BChE activity might alter an individual's response to cocaine, but there is little information available on BChE activity in cocaine addicts. Scientists in the Treatment Branch recently completed an evaluation of endogenous plasma BChE activity in a convenience sample of cocaine addicts, abusers of other substances (alcohol, tobacco, heroin, marijuana), and normal controls. Preliminary results suggest that cocaine addicts do not differ from others in their level of BChE activity, and that such activity remains stable over time (up to one year).

Heroin dependence remains a serious and costly public health problem, even in patients receiving methadone maintenance treatment. A within-subject reversal design was used to assess the effectiveness of a voucher-based abstinence reinforcement contingency in reducing opiate use in methadone patients of the Archway Clinic, National Institute on Drug Abuse Intramural Research Program. Throughout the study subjects received standard methadone maintenance treatment involving methadone, counseling, and urine monitoring (three times per week). Thirteen patients who continued to use opiates regularly during a 5-week baseline period were exposed to a 12-week program in which they received a voucher for each opiate-free urine sample provided; the vouchers had monetary values that increased as the number of consecutive opiate-free urines increased. Subjects continued receiving standard methadone maintenance for 8 weeks after discontinuation of the voucher program (return-to-baseline). The percentage of urine specimens positive for opiates decreased significantly when the voucher program was instituted and then increased significantly when the voucher program was discontinued during the return-to-baseline condition. Voucherbased reinforcement contingencies can decrease opiate use in heroin dependent patients receiving methadone maintenance treatment.

A schedule of voucher-based reinforcement involving escalating pay for sustained abstinence has been effective in treating cocaine abuse. Under this schedule, patients receive a voucher for each cocaine-free urine; vouchers have monetary values that increase with the number of consecutive cocaine-free urines. While this schedule has been effective for many patients, some patients have failed to achieve sustained abstinence. A modification of this schedule was tested in an effort to improve abstinence outcomes. Cocaine abusing methadone patients were randomly assigned to receive vouchers for 12 weeks under 1) an escalating pay schedule, 2) an escalating pay schedule with start-up bonuses, or 3) a noncontingent schedule. The start-up bonuses were designed to provide substantial immediate reinforcement for initiating abstinence. The contingent voucher interventions significantly increased subjects' longest duration of sustained cocaine abstinence and the percent of subjects who were cocaine abstinent across the 12 weeks of the voucher intervention, and significantly decreased craving for cocaine. In addition, a significantly larger percent of subjects receiving the voucher intervention were opiate abstinent. Unexpectedly, adding start-up bonuses significantly decreased the percent of subjects who were cocaine abstinent, relative to abstinence rates under the escalating pay schedule alone. These results replicate the efficacy of voucher-based reinforcement of cocaine abstinence, show that it can have broad beneficial effects as evidenced by its effects on opiate use, and demonstrate that the schedule of reinforcement can be an important determinant of efficacy.

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Director's Report to the National Advisory Council on Drug Abuse
September, 1995

Program Activities

NIDA Research Center Grant Program Guidelines

As a followup to discussions at the May 1995 Council meeting, NIDA's center grant guidelines will be available on September 22. A notice stating their availability will be published in the *NIH Guide for Grants and Contracts*, on that date. These Guidelines will apply to new and competing continuation center grant applicants. NIDA's policies for its center grant program are delineated in the guidelines. Major changes include the following:

- NIDA will support all NIH center grant mechanisms (P20, P30, P50, P60).
- Center grant applications will be accepted on an ongoing basis in any of scientific areas of NIDA. (This eliminates the former requirement to have a program announcement or RFA that specifically solicits center grant applications.)
- Center grant applicants must be able to demonstrate "centerness" and the concept that the "whole is greater than the sum of the parts."
- Receipt dates for center grant applications are October 1 and June 1 only. (Applications submitted for February 1 will be held for the June 1 receipt date.)
- NIDA center grants must be or demonstrate the potential to be significant regional or national resources.
- Funds can be requested for pilot projects.
- Center grant directors will generally be expected to spend a minimum of 25 percent time on research and administration related to the center.
- Pre-application consultation will be strongly encouraged and provided by NIDA staff.
- Center grant review criteria have been enhanced.
- A separate center grant review committee will be established.
- Meetings with center grant directors will be convened on an as-needed basis.

NIDA Initial Review Group Restructure

NIDA's restructure plan has been approved by the Office of the Director, NIH and is being implemented for the October/November initial review round (February 1996 Council). The National Institute on Drug Abuse Initial Review Group is chartered, with 10 subcommittees designated. The sub committees are also listed in table form.

Neuropharmacology Research Subcommittee - NIDA -A

Administrator- Syed Husain, Ph.D., Basic Sciences Review Br. Rm. 10-42, #301/443-2620
Replaced- DABR/1

Research Areas: Neurobiological mechanisms underlying various behaviors including physical dependence,

tolerance, developmental and reproductive functions, as well as neuroendocrinology

Molecular, Cellular & Chemical Neurobiology Research Subcommittee - NIDA -B

Administrator- Rita Liu, Ph.D., Basic Sciences Review Br., Rm. 10-42, #301/443-2620
Replaced- DABR/2

Research Areas: Molecular and cellular biology, receptor biochemistry, as well as synthetic, organic, analytical and biophysical chemistry

Neurophysiology and Neuroanatomy Research Subcommittee - NIDA - C

Administrator- Gamil Debbas, Ph.D., Basic Sciences Review Br., Rm. 10-42, #301/443-2620
Replaced- DABR/3

Research Areas: Neuroanatomy, neurophysiology, cardiovascular pharmacology, and neuroscience mechanisms of non-behavioral manifestation of developmental, toxicological, and teratological effects. This subcommittee will also review proposals dealing with pharmacokinetics and metabolism

Basic Behavioral Science Research Subcommittee - NIDA - D

Administrator- William C. Grace, Ph.D., Clinical Epidemiological/Applied Sciences Rev. Br., Rm. 10-22, #301/443-9042
Replaced- DACB

Research Areas: Basic/clinical interface of basic animal models and human laboratory biobehavioral studies including the areas of pharmacology, neuropsychology, cognition, perception and motivation

Treatment Research Subcommittee - NIDA - E

Administrator- Kesinee Nimit, M.D., Clinical Epidemiological/Applied Sciences Rev. Br., Rm. 10-22, #301/443-9042
Replaced- DACB

Research Areas: Behavioral and/or pharmacologic treatment, medication application, and marketed medications clinical trials

Health Service Research Subcommittee - NIDA - F

Administrator- William C. Grace, Ph.D., Clinical Epidemiological/Applied Sciences Rev. Br., Rm. 10-42, #301/443-2620
Replaced- DACB

Research Areas: Health services research including the organization, management, financing, delivery, effectiveness, and impact of the drug abuse health services delivery system

Epidemiology and Prevention Research Subcommittee - NIDA - G

Administrator- Raquel Crider, Ph.D., Clinical Epidemiological/Applied Sciences Rev. Br., Rm. 10-22, #301/443-9042
Replaced- DAPA

Research Areas: Epidemiology, prevention, and studies of risk and protective factors

Human Development Research Subcommittee - NIDA - H

Administrator- Kesinee Nimit, M.D., Clinical Epidemiological/Applied Sciences Rev. Br., Rm. 10-22, #301/443-9042
Replaced- SRCD-G

Research Areas: Pre/postnatal exposure to drugs of abuse in humans. This subcommittee will also review research concerning the maternal/infant dyad, early childhood and adolescent development, and interventions for women and their offspring

AIDS Biomedical and Clinical Research Subcommittee - NIDA - I

Administrator- Mary C. Custer, Ph.D., Basic Sciences Review Br., Rm. 10-42, #301/443-2620
Replaced- DAAR-I

Research Areas: Biochemistry, immunology, virology, and associated areas of neuroscience

AIDS Behavioral Research Subcommittee - NIDA - J

Administrator- Raquel Crider, Ph.D., Clinical Epidemiological/Applied Sciences Rev. Br., Rm. 10-22, #301/443-9042
Replaced- DAAR-2

Research Areas: Epidemiology, prevention, counseling, behavior change, and health services research

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HHS Drug and Alcohol Prevention Strategy

The Department has initiated a Drug and Alcohol Prevention Strategy involving all relevant HHS components. A senior-level steering committee, co-chaired by Peter Edelman, Counselor to Secretary Shalala and Nelba Chavez, Administrator, SAMHSA are providing overall guidance to this effort. Dr. Leshner is a member of this steering committee. In addition, two working groups have been established: a Public Affairs Working Group of which Robin Kawazoe and Susan David are members and a Policy/Managed Care Working Group of which Tom Vischi and Robin Kawazoe are members. On the public affairs side, new and expanded collaborative activities among HHS components are being identified and implemented, communications opportunities for the Secretary and other senior HHS officials are being identified, and all planned activities are being closely coordinated. Significant events include release of the latest data from the National Household Survey on Drug Abuse. This press conference will showcase NIDA's booklets on marijuana for parents and teenagers, NIDA's video for parents on the importance of talking to children about marijuana use, and a poster about marijuana and its effects which was produced through a collaborative effort between NIDA and the Weekly Reader. In addition, the Secretary will be speaking about drug abuse and other public health issues at a number of meetings and events which tentatively include: Partners for Change; a meeting involving State alcohol and drug and mental health directors and State Medicaid Directors, the Entertainment Industries Council, and the American Public Health Association. On the policy/managed care side, efforts are underway to identify, develop, and disseminate information about the costs of drug and alcohol abuse and the cost-benefits of treatment as well as meetings and collaborative activities related to managed care.

Basic Behavioral Sciences at NIDA

Staff in the new Behavioral Sciences Research Branch (Division of Basic Research) have been traveling to a large number of conferences and workshops this spring. They are both spreading the word about NIDA's expansion of research in behavioral sciences (see *NIDA NOTES* March/April 1995, Volume 10, Number 2) and are also learning about newly emerging areas of basic behavioral research. Drs. Turkkan, Erinoff, Shurtleff and Wetherington have attended scientific meetings of the American Academy of Child and Adolescent Psychiatry, the Behavioral Pharmacology Society, the Association for Behavior Analysis, the College on Problems of Drug Dependence, the American Psychological Society, and the American Psychological Association. BSRB staff also attended a workshop on Neural Modeling Techniques at the University of Maryland College Park in June. Particularly notable was the College of Problems of Drug Dependence meeting in Scottsdale Arizona at which a standing-room-only audience attended a productive question and answer session about the new branch. Also, Dr. Turkkan, Chief of the BSRB, addressed the Executive Board of the American Psychological Society in June in New York City about new directions in the basic behavioral sciences at NIDA (see *APS Observer* articles in the May/June and July/August issues).

NIDA Resource Center on Health Services Research

NIDA recently awarded a contract to Behavior and Health Research, Inc., to establish and operate a resource center

on health services research. The center will compile, summarize, and analyze key data bases and selected literatures, and will convene small meetings of experts to consider key topics in health services research. In the first year of the contract, while it is building its data bases and literature collections, the contractor will make its products available only to NIDA staff. In the second and third years of this three-year contract, the contractor may make some of its resources available to other researchers and practitioners as well. The center will not, however, be a national clearinghouse. Rather, it will help sharpen the focus on key research questions, relevant data bases, and relevant literatures, and it will support meetings and develop materials that can advance research and the utilization of research in this field.

NIDA/Department of Veterans Affairs IAAs

The Medications Development Division and the Department of Veterans Affairs are in the final stages of establishing interagency agreements to select a network of 4-6 NIDA/VA Substance Abuse Medication Development Centers. The objective of this VA network is to implement single and multi-center clinical trials to evaluate the efficacy and safety of novel pharmacotherapeutic compounds (i.e., marketed or investigational) for the treatment of substance abuse and addiction. The primary focus will be on cocaine treatment trials.

The site visit team, consisting of NIDA, DVA and ad hoc committee members, has completed its site inspections. The team visited seven candidate Veterans Affairs Medical Centers (VAMCs). The purpose of the site visits was to evaluate the programmatic capabilities (i.e., due diligence) as reported in the application proposal and ascertain preliminary budget estimates. In addition, the team was assessing each of the proposed centers specialized services which could act as a center of excellence within the network. The purpose of these centers of excellence would be to provide specialized services to support medication clinical trials throughout the network.

NIDA/CSAT Study on Alternative Pharmacotherapies for Opioid Addiction

NIDA and the Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration, will co-sponsor a study of the cost of alternative pharmacotherapies used in the treatment of opioid addiction. The goal of the study is to provide State level program officials, substance abuse treatment providers, researchers, and others with data and information on the cost of various medications in a narcotic treatment setting. NIDA and CSAT will jointly plan and participate in the study. The study will be conducted utilizing an existing CSAT contract and is expected to commence this fall.

NIDA/CSAT Policy Symposia

NIDA and CSAT are co-sponsoring a series of policy symposia on various subjects involving pharmacotherapy for opioid addiction. The goals of the symposia are to provide State level policy and regulatory officials and substance abuse treatment providers with information on state-of-the art research and clinical applications of methadone, LAAM, and investigatory opioid treatment therapies. Symposia have been held for the Northeast Region (Boston, April 28) and the MidAtlantic Region (Princeton, June 15). A third symposium will be held November 16-17 in Tampa, Florida.

Program Announcements/RFAs

Basic Behavioral Sciences RFA

The Behavioral Sciences Research Branch (Division of Basic Research) has issued a Request for Applications that aims to encourage research in diverse areas of the basic behavioral sciences. The RFA is titled **"Broadening Basic Behavioral Science Research In Drug Abuse"** (RFA: DA-96-001), and appeared in the *NIH Guide* on August 11, 1995 (Volume 24, Number 29).

The purpose of the RFA is to broaden basic behavioral science research in drug abuse. A key feature of basic behavioral research is the use of laboratory and other comparably controlled procedures to elucidate underlying behavioral mechanisms or processes. As a primary goal, basic behavioral research establishes a scientific foundation for later application in treatment and prevention research. Several important research areas in behavioral sciences

such as cognitive, motivational, and social processes as well as health behavior research have the potential to address questions of underlying behavioral mechanisms, determinants and correlates of drug abuse, as well as to better characterize the harmful sequelae of drug use and abuse. These and other basic behavioral science areas currently are underrepresented at the National Institute on Drug Abuse (NIDA). The RFA Letter of Intent receipt date is October 13, 1995, and the deadline for applications is November 14, 1995. The full text of the RFA can be viewed and downloaded from the internet at gopher://gopher.nih.gov:70/00/res/nih-guide/rfa-files/RFA-DA-96-0 01.

A new Program Announcement, **"Local Population/Area Epidemiologic Research on Drug Abuse,"** (PA 95-059) was issued in April 1995. The purpose of this PA is to stimulate research on local area epidemiology of drug abuse and its correlates and consequences, with emphasis on methodological research and studies of factors which influence local area patterns of drug abuse.

On May 5, 1995, NIDA released a program announcement (PA 95-057) on **"HIV Risk Behaviors, Determinants and Consequences."** The propose of this announcement is to stimulate research on the social and other environmental factors that influence the drug injecting and sexual HIV risk behaviors of drug users and their sexual partners.

A new Program Announcement, **"HIV Risk Behaviors, Determinants, and Consequences,"** (PA 95-057) was issued in May 1995. The purpose of this PA is to support a program of research on the social and socio-cultural/environmental factors that influence drug injecting and sexual risk behaviors among drug users and their sexual partners.

A new Program Announcement, **"Drug and Alcohol Use and Abuse in Rural America,"** (PA 95-060) was issued in May 1995 by NIDA as the lead agency, in collaboration with NIAAA and the U.S. Department of Agriculture. The purpose of this PA is to encourage research on drug and alcohol use and abuse behaviors, on the consequences of such behaviors, and on the delivery of prevention and treatment services in rural America.

A new Program Announcement, **"International Research on the Epidemiology of Drug Abuse,"** (PA 95-072) was issued in June 1995. The purpose of this PA is to stimulate international research on similarities and variations in drug using behaviors, factors influencing the initiation, progression, and cessation of drug abuse, and social and health consequences of drug abuse including HIV transmission.

A new Program Announcement, **"Women's HIV Risk and Protective Factors,"** was issued in August 1995. The purpose of this PA is to support research on the HIV risk and protective behaviors of women and on community-level intervention strategies for women who use drugs and practice sexual risk behaviors which increase the opportunity of exposure to HIV. This includes women who are not-in-treatment IDUs, who use crack cocaine, who are sexual partners of IDUs, and/or who exchange sex for drugs or money.

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Congressional Affairs

H.R. 2127 - The FY 1996 Labor, HHS, Education Appropriations Act

On August 4, the House passed H.R. 2127 (the FY 1996 Labor, HHS & Education Appropriations Act) by vote of 219 yeas to 208 nays.

Overall, H.R. 2127 upholds the House Appropriations Committee's July 24 approval of an $11.9 billion FY 1996 budget for NIH. This represents a 5.7%, or $642 million increase over FY 1995, and $166 million more than President Clinton's request. NIDA's funding level would rise to approximately $458 million, a 4.8% increase ($20.9 million) from FY 1995.

With the exception of an amendment offered by Rep. James Moran (D-VA) to earmark $7.5 million in the Office of the Director account for the Office of Alternative Medicine, no floor amendments were adopted which would directly affect NIH. [OAM's increase ($1.9 million over the amount proposed by the Appropriations Committee) would not change NIH's total budget since, as a component of the OD, the funds would simply be reallocated.]

Stated below are selected provisions included in the House Committee Report (H.Rpt. 104-209, Committee Print).

National Institutes of Health

The bill removes the separate appropriation for the NIH Office of AIDS Research, and its funding "would be appropriated to the individual Institutes without an earmark for AIDS." The Committee Report states that:

> "... the Committee believes the Director of NIH should decide how much of the total NIH appropriation should be allocated to AIDS research. The Committee expects the Director of NIH to identify the total allocated for AIDS and his intended distribution by institute under the House funding level prior to the conference on the [FY] 96 bill...The Committee wants to make clear that it continues to support the Office of AIDS Research... The Committee assumes that the NIH Director's decisions on allocating AIDS funding will be fully consistent with the plan developed by the OAR..." [pages 57-58]

Chairman John Porter (R-IL), stated that the AIDS earmark was removed in an effort to give scientists more authority to set the biomedical research agenda. He offered assurances that he is not trying to reduce funding for AIDS research; that with increased funding for NIH overall, he expects NIH spending on AIDS to increase.

Other Selected Report Language Pertaining to NIH:

The Committee:

> "...directs that research management and support costs at NIH will be reduced 7.5 percent below 1995 levels, and that costs associated with congressional and public affairs functions will be reduced a total of 10 percent below 1995 levels. ..." [page 58].
>
> "...believes ... [indirect costs] is a key area in which savings could be generated." [page 58]

> "...believes that the concept of a central planning authority, such as that vested in the OAR, could have broader applicability to other research areas in NIH with trans-Institute scope. ... would like the NIH Director's assessment of the utility of establishing a broader central policy office... that would handle crosscutting issues." [page 59]
>
> "... believes it is critical for NIH to use all the media at its command to publicize the benefits and results of NIH research ... [page 59]

The Committee Report does not include comments about NIDA, other than the following description of its mission:

> "...NIDA supports much of the world's biomedical research in the area of drug abuse and addiction. NIDA's basic research furthers knowledge about the ways in which drugs act on the brain to produce drug dependence and about how the brain works. In addition, NIDA research identifies pharmacological and behavioral drug abuse treatments. NIDA conducts research on the nature and extent of drug abuse in the U.S. and monitors drug abuse trends nationwide to provide information for planning both prevention and treatment services. NIDA's mission is also to study the outcomes effectiveness, and cost benefits of drug abuse services delivered in a variety of settings." [page 74]

For NIAAA the Committee said it is

> "...pleased that research supported by NIAAA has led to the approval of naltrexone by FDA for alcoholism treatment. The Committee encourages NIAAA to support further research to determine the effects of naltrexone's longer-term use, side effects, and how it reduces alcohol craving." [page 74]

For NCI the Committee said it is

> "...disturbed to learn that NCI has funded a research grant studying tobacco industry campaign contributions to State legislators and voting records by those individuals on tobacco control initiatives...does not provide any further funding for this research grant." [page 61]

Substance Abuse and Mental Health Administration

The bill also includes major cuts for mental health and substance abuse programs. It provides $1.8 Billion for FY 96, which is $392 million below the 95 level. The Committee consolidated 26 programs into 6. Selected Committee Report language follows:

> " ... the Committee is concerned about the administrative inefficiency inherent in operating three agencies to provide substance abuse and mental health services [referring to CMHS, CSAP and CSAT]. It is particularly concerned about the maintenance of two agencies to administer substance abuse prevention and substance abuse treatment services ... directs the Administrator to begin consolidating substance abuse treatment and prevention activities in a single administrative authority ..." [page 84]
>
> "The Committee is aware of a substantial body of anecdotal evidence which purports to demonstrate the effectiveness and economic efficiency of substance abuse treatment. However, as the 1996 budget hearings revealed, SAMHSA has developed few if any comprehensive evaluation tools, and the Committee has little basis on which to evaluate the effectiveness of the overall federal investment in substance abuse prevention and treatment....directs SAMHSA to submit reliable and comprehensive information regarding the effectiveness of federal substance abuse programs in support of future request for funding." [page 89-90]

Although funding for the block grants does not change, funding for other programs drops dramatically. The mental health programs cut include clinical and AIDS training, community support demonstrations, grants to states for the homeless, and homeless services demonstrations. Substance abuse programs cut include treatment grants to crisis areas, training, AIDS demonstration and training, community partnership grants, public education and dissemination, and comprehensive community treatment programs. Finally, the Committee:

> "...directs SAMHSA to re-examine its administrative structure and to streamline management of the agency to improve efficiency, reduce duplication of effort, and contain costs." [page 98-99]

Rescissions Bill Signed Into Law

A new FY 1995 rescissions/emergency supplemental appropriations bill [H.R. 1944] passed both Houses of Congress

and was signed by the President on July 27 (P.L. 104-19). It includes a $70 million cut for the NIH -- $60 million to come from intramural construction [according to NIH sources some of these funds had been allocated for the new primate center in Frederick, Maryland and the second phase for the Natcher building], and $10 million from the extramural construction program administered by the National Center for Research Resources.

Senate Approves Funds for ONDCP

On August 5, the Senate voted to restore approximately $8 million for ONDCP, averting a move to close it down for at least a year. An amendment to restore the money [offered by Senator Richard Shelby (R-AL) for Senators Orrin Hatch (R-UT) and Joseph Biden, Jr. (D-DE)] passed on a voice vote. Senator Hatch said "I, along with many of my colleagues, think that the drug czar's office needs to be reorganized." He added that the Senate Judiciary Committee, which he chairs, will look at changes in staffing and mission. [On July 27, the Senate Appropriations Committee had approved an appropriations bill (H.R 2020) which would have removed all funding for the Office.]

Other Bills of Interest

Congressionally-Mandated Reports

S. 790, the Federal Reports Elimination and Sunset Act, passed the Senate on July 17. Immediately upon enactment, it would extend the due date of the jointly prepared NIDA, NIAAA and NIMH health services research report. It also would terminate the statutory requirement for all annual and other periodic congressionally-mandated reports 4 years after the bill is signed into law -- two exceptions are reports required under the Inspector Generals' Act and the Chief Financial Officers Act. Congress would have to specifically reauthorize those reports it wants to continue receiving.

Hearings/Briefings

Tobacco

On August 10th, President Clinton outlined the Administration's strategy to regulate tobacco sales and advertising to help reduce smoking among youth and keep nonsmoking children from starting. The nation has responded to the problem of illegal drug use among teens and drunken driving, Clinton noted at a White House news conference. "It is time to take a third step to free our teenagers from addiction and dependency," he said.

That same day, the Food and Drug Administration issued proposed rules to regulate the sale and distribution of tobacco products to youth. The FDA hopes to reduce access to cigarettes and decrease the "positive" images that make smoking attractive.

President Clinton invited Congress to pass legislation to achieve similar goals and thus prevent FDA intervention. However, as soon as the proposed rules were issued some members of Congress warned of a potential legislative battle on the issue. Also, industry groups filed suit to stop the FDA from instituting its tobacco regulations and from regulating cigarettes.

But some members, even those who support the tobacco industry, indicated a willingness to work on legislation. Senator Wendell Ford (D-KY), whose home state is the nations's Number 2 producer of tobacco, said he would introduce legislation after the August recess that would achieve the president's goals without hurting producers.

Dr. Leshner Testifies at SAMHSA Reauthorization Hearing

The Senate Labor & Human Resources Committee [chaired by Nancy Kassebaum (R-KS)] invited Dr. Alan I. Leshner, Director, NIDA, to testify at its July 27 hearing on the "SAMHSA Reauthorization, Flexibility Enhancement, and Consolidation Act." Other witnesses included Dr. Philip Lee, Assistant Secretary for Health; Nelba Chavez, Administrator, SAMHSA; Mathea Falco, Drug Strategies; John Walters, formerly with ONDCP; and Ellen Weber, Legal

Action Center, NY.

Dr. Leshner emphasized that 20 years of research has shown us the true nature of addictive disorders -- we now know that addiction is a brain disease that is expressed in behavioral ways and in a social context. He stated that drug abuse treatment can and does work and we know that the benefits to society far outweigh the costs. He went on to discuss the importance of pharmacological and behavioral treatment research. Senator Kassebaum asked Dr. Leshner several questions about methadone therapy and LAAM; discussed the Institute's activities in information dissemination; and asked about the effectiveness of coercive treatment.

Congressional Requests

The GAO has been asked by the House Labor/HHS appropriations subcommittee chairman John Porter (R-IL) to undertake an assessment of the costs of NIH-supported intramural and extramural research to determine how much Federal funding is spent on actual research. GAO has been directed to determine: (l) a breakdown of the categorical costs that "constitute the major expenditures for Federal research, i.e., research costs, costs for complying with Federal and State regulations, costs associated with animal research, etc."; (2) a percentage breakdown of these associated costs with the hopes of determining how much of the Federal dollar is in fact spent on actual research; and (3) a list of the primary regulations and their accompanying costs.

Other Items of Interest

Budget Resolution

The Congressional budget blueprint for fiscal years 1996 through 2002 [H.Con.Res. 67], approved by the House and Senate on June 29, 1995, contains the following provisions related to research which have not been widely publicized.

Sec. 304. Sense of the Congress Assumptions

> "It is the sense of the Congress that the aggregates and functional levels included in this budget resolution assume that ... (6) science and technology development are critical to sustainable long-term economic growth and priority should be given to Federal funding for science and basic and applied research."

Sec. 309. Sense of the Senate on the Assumptions

> "It is the sense of the Senate that the aggregates and functional levels included in this budget resolution assume that ... (3) in furtherance of the goals of the Decade of the Brain, full funding should be provided for research on brain diseases and disorders."

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International Activities

Led by Alan Leshner, a 13-member delegation traveled to Beijing during August for the **First U.S.-China Symposium on Drug Abuse and HIV/AIDS Research**

Delegation members included NIDA researchers Martin Adler, Judith Brook, Richard Clayton, Louis Harris, Don Des Jarlais, Mary Jeanne Kreek, Walter Ling, Clyde McCoy, Thomas McLellan, Steven Specter, and Lei Yu, and Patricia Needle, Acting Director, NIDA International Program. Supported through a Memorandum of Agreement with the Department of State, this collaborative scientific meeting brought together U.S. and Chinese scientists to explore the potential for establishing research cooperation on research issues relative to drug abuse and HIV/AIDS. Workgroups in the areas of basic research, epidemiology and prevention, and treatment produced a series of joint recommendations for collaborative research projects - focusing both on urgent issues and longerterm cooperation. Further, as a result of the enthusiastic participation and success of the symposium, the Chinese Ministry of Health has proposed the establishment of a formal collaboration with NIDA.

Jack Blaine, DCSR, participated in an August meeting at Washington University in St. Louis on the data analysis of the reliability and validity study of the substance use disorders sections of the Composite International Diagnostic Interview (CIDI) and Schedules for Clinical Assessment in Neuropsychiatry (SCAN). These instruments were developed under a World Health Organization (WHO)/NIH Cooperative Agreement titled **"WHO/NIH Joint Project on Diagnosis and Classification of Mental Disorders and Alcohol- and Drug-Related Problems."** Also participating in the meeting were collaborators from WHO, NIAAA and NIH as well as investigators from research sites in Nigeria, The Netherlands, India, Farmington, Connecticut, Turkey, Greece, Australia, Luxembourg, Romania, San Juan, Puerto Rico, and St. Louis, Missouri.

Dr. Blaine also cochaired a symposium in Jerusalem, Israel in September at the Second International Conference on New Directions in Affective Disorders. Titled **"Affective Disorders and Substance Abuse and Dependence,"** the symposium included presentations by several NIDA grantees and an NIAAA researcher.

Zili Sloboda, Nicholas Kozel, and Moira O'Brien, DEPR, participated in the **First International Epidemiology Network Conference**, Vienna, Austria, May 23-25, hosted by the United Nations Drug Control Program (UNDCP) and jointly planned by NIDA and UNDCP. This was the first meeting to link national/regional networks and regional/international organizations in order to exchange information on drug abuse trends, to explore the effect of international drug trafficking patterns on drug using behaviors, and to identify emerging priority research issues and areas for research cooperation. The meeting has resulted in the establishment of an electronic International Drug Abuse Epidemiology Network to facilitate information exchange and monitor drug trends internationally.

Zili Sloboda represented NIDA at the **22nd meeting of the Pompidou Group** in Strasbourg, France, May 4-5, 1995. The Pompidou Group is an international consortium of drug abuse epidemiology experts.

Nicholas Kozel cochaired the **South Asian Multi-City Epidemiology Work Group meeting** held in Colombo, Sri Lanka on April 18-20 and participated in an introductory training program in drug abuse epidemiology on April 21. The South Asian Work Group is composed of researchers from Bangladesh, India, Nepal, Pakistan, Sri Lanka and Turkey and is one of a series of regional programs being developed to provide assessment and surveillance of drug abuse with the objective of integrating these data on a global perspective. This meeting was funded by the U.S. Department of State.

Peter Hartsock, represented NIDA on July 5-7 at a meeting sponsored by the European Community and held at the Netherlands Institute of Public Health and Environmental Protection in Bilthoven, on **"European Community Concerted Action: Multinational Scenario Analysis Concerning Epidemiological, Social, and Economic Impacts on HIV/AIDS."** The purpose of the meeting was to plan and coordinate ongoing and future EC-wide research efforts in HIV/AIDS epidemiology and prevention. Dr. Hartsock provided information about NIDA-sponsored research on AIDS modeling and NIDA's Community Epidemiology Work Group (CEWG), emphasizing the potential role of CEWG for HIV/AIDS epidemiology in light of its unique capabilities for rapid epidemiologic assessment of newly emerging public health problems and as a guide and resource for research.

Dr. Frank Vocci, Deputy Director, MDD attended the **International Narcotics Research Conference**, St. Andrews, Scotland, where he presented a poster on the Medications Development Division's opiate treatment discovery program.

Dr. Dorota Majewska, MDD was an invited speaker at the congress of **"International Society of Psychoendocrinology"**, Munich, Germany, September 1995.

The National Institute on Drug Abuse played a major role in the **37th International Congress on Alcohol and Drug Dependence** which took place at the University of California at San Diego (UCSD) August 20-25, cosponsored by UCSD and the International Council on Alcohol and the Addictions. This year's Congress was attended by more than 1000 delegates from around the world. Alan Leshner, NIDA Director, delivered a plenary address on Science, Policy and Practice in the Addictions. Other NIDA staff speaking at the Congress included Donald Vereen, OD,; Frank Tims and Bennett Fletcher, DCSR; and Jack Henningfield, IRP. Drs. Tims and Henningfield served on the organizing committee for the Congress. Thirty NIDA grantees made presentations in the areas of Epidemiology, Prevention, HIV/AIDS, Treatment and Health Services Research.

On August 8, 1995 Arthur Hughes participated in a live broadcast to Latin America titled: **"Dialogue."** The program focus was on research methods used in drug abuse surveys. Issues discussed included techniques used in the U.S. to assess the validity of self-report and procedures used to analyze data across various surveys. This program was conducted via satellite transmission with a group of researchers in Quito, Ecuador, La Paz, Bolivia, and Santiago, Chile. Other panelists in the Washington studio were Joseph Gfroerer from SAMHSA and James Dandridge from the Department of State.

NIDA's International Program is pleased to announce the award of four **INVEST Research Fellowships** for the forthcoming year. Successful applicants and their NIDA research mentors are Irena Martin-Kleiner (Croatia) with Jean Bidlack (University of Rochester); Bashir Ahmad (Pakistan) with Nissar Darmani (Kirksville College of Osteopathic Medicine); Steven McGaraughty (Canada) with Mary Heinricher (Oregon Health Sciences University); and Zhengxiong Xi (China) with Elliot Stein (Medical College of Wisconsin).

NIDA Hubert H. Humphrey Drug Abuse Research Fellowships have been awarded for the 1995-96 academic year at Johns Hopkins University to Gyaw Htet Doe (Myanmar), Mohamed Adib Essali (Syria), Haydee Rosovsky (Mexico) and Berna Diclenur Ulug (Turkey). Following a period of academic coursework, the NIDA International Program office will be assisting these fellows in arranging professional research affiliations with NIDA-funded scientists around the U.S.

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Meetings/Conferences

On June 9-10, 1995, NIDA sponsored the **1995 Conference on AIDS and Drug Abuse**, in conjunction with the annual meeting of the College on Problems of Drug Dependence. From NIDA's perspective, it was a stimulating and productive conference with 18 plenary speakers, 38 oral presentations, 55 posters, and 196 paid registrants.

As part of the annual meeting of the College on Problems of Drug Dependence held in June, scientists at NIDA's Division of Intramural Research (DIR) organized a highly successful scientific symposium and a dinner in celebration of the **Addiction Research Center's 60th Anniversary**.

A 1995 FASEB Summer Research Conference entitled **"Drugs of Abuse - Psychostimulants: Issues Related to Craving, Dependence, and Treatment"** was held at Copper Mountain, Colorado on July 23-28, 1995. Partly funded by NIDA, Bowman-Gray School of Medicine, and the Texas College of Osteopathic Medicine, the meeting consisted of discussions by basic researchers as well as clinicians and their state-of-the-art research was presented. The clinicians discussed their frustrations with the less-than-expected positive outcomes of their trials and called for more animal models. The basic research community countered with a need to know more about the treatment failures. Dr. Roger Brown, Chief of the Behavioral Neurobiology Research Branch of the Division of Basic Research, chaired a session on status and future directions (**"Where Are We and Where Do We Need To Go?"**). Overall, the meeting was very productive and a great deal of enthusiasm was generated by the discussants. A major conclusion was that routes/sources of communication between the clinical community and the basic research community must be improved.

On August 3 & 4, 1995, a NIDA sponsored a workshop entitled **"Crack Cocaine-Associated Pulmonary and Cardiovascular Complications and Underlying Physiological Mechanisms"** was held at the NIH campus with Dr. Pushpa V. Thadani serving as Science Chair. The purpose of this workshop was to review and discuss the current findings, to foster cross-fertilization of ideas, develop collaborations and identify needs and opportunities for future research. There were fourteen invited participants/speakers and about 20 outside attendees.

Craving Round Table - On June 22, 1995 NIDA's Behavioral Science and Treatment Working Groups co-sponsored a roundtable discussion on the topic of craving. Prominent researchers and clinicians discussed the etiology and phenomenological aspects of craving, as well as relationships among drug, alcohol and food cravings. Other topics included the utility of craving measures in treatment of drug abusers, and new advances in craving instrument development.

Speaker Series - Dr. Arthur Stone, a behavioral medicine researcher at the State University of New York at Stony Brook kicked off the behavioral science speakers series with a presentation entitled **"Advantages of Daily and Momentary Study Designs; Examples from Behavioral Medicine Research"**.

Dr. Paul Rozin, a social psychologist at the University of Pennsylvania, spent two days at NIDA advising staff about issues relating to craving and ingestive behavior. He also presented a lecture entitled **"Food Abuse: Thinking About Food Risk and Health"**.

Speaker Series - Dr. David C. S. Roberts, Professor of Psychology at Carleton University in Ottawa, Canada, spoke to NIDA personnel in the Parklawn building in May on **"Pharmacologic Manipulations of Cocaine Self-Administration in the Rat"**. The following day, he visited the Addiction Research Center in Baltimore and spoke on **"Animal Models of Cocaine SelfAdministration"**. Dr. Roberts is funded by NIDA under a contract to explore

mechanisms of cocaine self-administration in rats.

The Resiliency and Risk Workgroup sponsored a scientific meeting entitled **"The Application of Resiliency and Risk Research to the Development of Preventive Interventions."** This day long roundtable discussion explored how the further application of available research based data can advance prevention effectiveness beyond current levels. The meeting took place on September 11, 1995 in Bethesda and was chaired by NIDA Director, Dr. Alan Leshner.

>Conference on Managed Care - NIDA, in collaboration with NIAAA and CSAT, cosponsored a national conference entitled **"Looking to the Future: Research on Managed Care for Alcohol and Drug Abuse Treatment,"** that was held August 17-18 in Bethesda, Maryland. Attending the conference were researchers, State officials, providers, and representatives from the managed care industry. The purpose of the conference was to develop a preliminary research agenda on managed care for alcohol and drug abuse treatment. A report summarizing the results is being produced. Mr. Tom Vischi of the Services Research Branch chaired the planning committee for the meeting.

DEPR, DCSR and DBR collaborated to present a symposium at the 1995 American Psychological Association Convention in New York. The symposium, entitled **"Research Perspectives and New Funding Priorities at NIDA"** presented background and program information about three of NIDA's newest research programs exploring the nature and origin of drug abuse. The three presentations by NIDA staff were: **Resiliency and Risk for Drug Abuse: Implications of a Developmental Systemic Approach** (Meyer Glantz), **Neurobiological Etiology of Drug Abuse** (Harold Gordon), and, **Basic Behavioral Sciences Research at NIDA: New Directions** (Jay Turkkan).

On May 5, the Community Research Branch, DEPR sponsored a seven-part series of workshops in Tysons Corner, VA. The workshops focused on methodologies to measure and analyze behavioral change in HIV and drug abuse prevention research, including such topics as network and path analysis, power analysis, ethnography, dimensional scaling, and the reliability and validity of self-reported data.

On June 19, the Community Research Branch, DEPR sponsored a seminar by Philippe Bourgois, Ph.D., Associate Professor of Anthropology at San Francisco State University and Charles Pearson, Ph.D., an ethnographer with the San Francisco Urban Institute, on **"An Anthropological Contribution to Understanding HIV Risk Behaviors in a Network of Homeless Heroin Injectors."** The seminar presented recent findings from a study of drug use practices among a group of homeless IDUs living under freeways in San Francisco in 1995.

In collaboration with the NIH Office of AIDS Research and Northern Arizona University, the Community Research Branch, DEPR sponsored the third science symposium: **"Current Status and Future Prospects of HIV Prevention Research,"** August 16-18 in Flagstaff, Arizona. The symposium addressed the efficacy of HIV prevention: What works? For whom? Under what circumstances? At what cost? The symposium featured the HIV prevention research portfolios of co-sponsoring NIH institutes and agencies (e.g., NIMH, NIAID, NICHD, NIAAA, and CDC) in a number of plenary sessions as well as funded researchers who presented findings from their HIV prevention research.

37th International Congress on Alcohol and Drug Dependence - NIDA staff participated in the 37th International Congress on Alcohol and Drug Dependence (August 20-25), at the University of California San Diego. Drs. Bennett Fletcher and Frank Tims conducted a workshop on preliminary findings (overview, intake sample characteristics, co-morbidity and dependence patterns, and service delivery) from the DATOS, NIDA's national program of treatment outcome research. Drs. Bennett Fletcher and Frank Tims co-chaired a symposium on **"Systematic Innovation in Drug Abuse Treatment"** (August 18-19). The symposium reviewed findings from SRB's portfolio of 15 research demonstration projects to improve service delivery in treatment. Papers from this meeting are to published in a special edition of the Journal of Drug Issues.

June 4-6 NIDA staff participated in the Annual Meeting of the Association for Health Services Research. Dr. Frank Tims and Mr. Tom Vischi, Services Research Branch, DCSR, conducted a session on **NIDA's Health Services Research Priorities**. Dr. Robert Battjes, Deputy Director, DCSR, chaired a panel entitled **"The Impact of Public Policy and Market Forces on the Drug Abuse Services System,"** with presentations by four NIDA-supported researchers, Drs. Thomas D'Aunno, Deborah Garnick, James Sorensen, and Constance Weisner.

Dr. Peter Delany participated in the Association of State Correctional Administrators meeting June 1, on research initiatives and incentives in prisons systems.

Dr. Peter Delany helped to develop and participated in the first **Institute for the Advancement of Social Work Research Technical Assistance Workshop** supported by NIDA (July 13-14). Other NIDA participants included Drs. Khursheed Asghar, Rebecca Ashery, Susan Coyle, Mario De La Rosa, and Jag Khalsa.

Dr. Bennett Fletcher participated in the annual meeting of the College on Problems of Drug Dependence, and the following posters:
Flynn, P.M., B.W. Fletcher, J.W. Luckey, and S.G. Craddock. (June, 1995). **Cocaine Treatment Outcomes from a National Multisite Study: Multivariate Explanatory Models of Outcomes.** Poster presented at the annual meeting of the College on Problems of Drug Dependence, June 11-15, 1995, Scottsdale, AZ.

Luckey, J.W., G.H. Dunteman, B.W. Fletcher, S.G. Craddock, and P.M. Flynn. (June, 1995). **Assessing the Accuracy of Self-Reported Cocaine Use: Methodological Issues with Underreporting of Use.** Poster presented at the annual meeting of the College on Problems of Drug Dependence, June 11-15, 1995, Scottsdale, AZ.

Wechsberg, W.M., S.G. Craddock, B.W. Fletcher, R.M. Etheridge, and R.L. Hubbard. (June, 1995). **AIDS-Risk Behaviors of Clients Enrolled in Drug Abuse Treatment: Findings from the NIDA Drug Abuse Treatment Outcome Study (DATOS).** Poster presented at the annual meeting of the College on Problems of Drug Dependence, June 11-15, 1995, Scottsdale, AZ.

Dr. Bennett Fletcher participated in the annual meeting of the American Psychological Association (August 14-17), and presented an **"Overview of NIDA's Role in Drug Abuse Treatment Outcome Research from 1974 to Present".**

Dr. Bennett Fletcher represented NIDA at the annual meeting of the National Treatment Consortium meeting in St. Louis, and presented a paper on the linkage between drug abuse treatment research and practice.

Dr. Frank Tims and Mr. Tom Vischi were speakers in the NIDA Research Agenda session at the Association for Health Services Research annual meeting in Chicago June 4-7.

Dr. Peter Delany coordinated a NIDA/NIJ Drug Court Initiative planning session.

Dr. Peter Delany participated in NIJ's Addiction Medicine planning session.

Dr. David Johnson, DBR, presented a paper entitled **"Olanzepine Decreases, while Clozapine Increases, the Reinforcing Effects of Self-Administered Cocaine in Rats"** at the College on Problems of Drug Dependence Meeting in Scottsdale, AZ on June 11, 1995.

On June 8 Drs. Robert Battjes and Bennett Fletcher, DCSR, participated in a planning meeting, sponsored by the Center for Substance Abuse Treatment, focused on developing their demonstration program priorities.

On July 19 Dr. Robert Battjes, Deputy Director, DCSR, served on the **Panel on Effectiveness and Outcomes**, one of four panels developing a health services research plan for the National Institute on Alcohol Abuse and Alcoholism.

On June 27 Ms. Robin Kawazoe and Drs. Robert Battjes and Frank Tims met with the Center for Substance Abuse Treatment's National Advisory Council to discuss NIDA-CSAT joint health services research initiatives and to obtain input regarding formulation of NIDA's health services research priorities.

At the Annual Meeting of the American Psychiatric Association in May 1995, NIDA staff (Drs. Condon, Czechowicz and Frascella) held a poster session on **Research Funding and Research Training Opportunities at NIDA** at the new Young investigator's session.
Coryl Jones ERB/DEPR participated in the **Abandoned Infants Conference** sponsored by the Children Bureau of the DHHS Administration for Children, Youth, and Families held May 31 through June 3.

On July 25th, Ro Nemeth-Coslett, PRB/DEPR represented NIDA at the **Speech Communication Association's Summer Conference on Communication and Health**. She and Dr. R. Lewis Donohew, PI, University of Kentucky, participated in a Dialogue Session with NIH Grantees and Program Officials.

Nicholas Kozel organized and participated in the **Kentucky State Epidemiology Work Group meeting** in Lexington on March 22 and, with Peter Hartsock, organized and participated in the **Alaskan State Epidemiology Work Group meeting** in Anchorage on July 13-14. The major purpose of the State Work Group is to develop and implement a community-based research network within States which provides ongoing surveillance of drug abuse patterns and trends and related activities and consequences. These meetings were co-funded by NIDA and the Department of Agriculture.

Dr. Dorota Majewska, MDD chaired the CPDD symposium, **"Neurotoxicity and Neuropathology Associated with Cocaine/Psychostimulant Abuse".** Publication in NIDA Monographs will follow.

Dr. Dorota Majewska, MDD was an invited speaker at a June meeting of the New York Academy of Sciences

conference **"Dehydroepiandrosterone and Aging"**, held in Washington, D.C. Dr. Majewska presented on the **"Neuronal Actions of Dehydroepiandrosterone"**; a following publication is in press.

Dr. Nancy Pilotte, MDD, Pharmacology and Toxicology Branch gave a presentation on how **"Cocaine Withdrawal Affects Dopaminergic Neurons"** on August 21 at Rockefeller University. Dr. Pilotte presented at the invitation of Dr. Mary Jeanne Kreek.

Dr. Frank Vocci, Deputy Director, MDD attended the **Department of Veterans Affairs' Opioid Substitution Therapy Conference** where he delivered a presentation on the development of LAAM and buprenorphine.

In June, Dr. Timothy P. Condon, Acting Deputy Director, OSPC addressed the Research Training Directors at the **57th Annual College on Problems of Drug Dependence Scientific Meeting**, in Scottsdale, Arizona. He discussed the status of NIDA's 42 training programs; and announced the creation of a research training newsletter to enhance information exchange.

Dr. Timothy P. Condon was a NIDA representative for the Federal Funding Poster Session held at the **American Psychiatric Association's 148th Annual Meeting** in Miami, Florida, May 1995. Dr. Condon discussed research and research training opportunities at NIDA for psychiatrists.

Dr. Timothy P. Condon gave a presentation highlighting NIDA's neuroscience research program and training opportunities in neuroscience to the **Association of Neuroscience Departments and Programs** on April 24, 1995 in Washington, D.C.

Dr. Cathrine Sasek participated in a national science and mathematics education forum sponsored by the White House Office of Science and Technology Policy entitled **"Making It Happen: First in the World in Science and Mathematics Education."** The purpose of the forum was to advise President Clinton on ways to improve our Nation's science and mathematics education efforts.

Richard H. Needle presented a paper entitled **"Ethnographic Observational Study of MultiPerson Use of Drug Injection Equipment in Injection Drug Use Networks"** at the International Social Network Conference in London, England, July 6-19, 1995.

Susan Coyle presented a paper entitled **"An HIV Intervention for Street Youth: Increasing Knowledge about Risky Behaviors"** at the Symposium on HIV Prevention Research at Flagstaff, Arizona.

Elizabeth Lambert, presented a poster entitled **"Prevalence Estimation and Hard-to-Reach Populations: Implications for Prevention Programs"** at the Symposium on HIV Prevention Research at Flagstaff, Arizona.

Mona Brown, NIDA Press Officer organized a session and made a presentation at the annual meeting of the CPDD on **"Working with the Media."** The session was well received by participants who were very interested in having positive relations with the media.

Dr. George Uhl and Dr. David Gorelick presented Grand Rounds at the NIH Clinical Center on **"Cocaine Addiction: Pathophysiology and Treatment"** (July 5, 1995)

Dr. Xiang Liu presented **"Regional Cerebral Volume and Asymmetries in Polydrug Abusers: A Volumetric Magnetic Resonance Imaging Study"** at the 57th Annual Committee on Problems of Drug Dependence scientific meeting, Jun. 10 - 15, 1995, Scottsdale, AZ.

Dr. Steven J. Grant presented **"Stimulation of Regional Cerebral Glucose Metabolism by Cocaine Related Cues"** at the 57th Annual Committee on Problems of Drug Dependence scientific meeting, Jun. 10-15, 1995, Scottsdale, AZ.

Dr. Robert L. Phillips presented **"Modeling the Concentration of Fluoro-deoxyglucose in Plasma to Calculate Cerebral Metabolic Rates for Glucose by the Positron Emission Tomography Method"** at the 42nd Society of Nuclear Medicine meeting, Jun. 11 -15, 1995, Minneapolis, MN.

Dr. Victor Villemagne presented **"Cocaine Craving: A PET FDG Study"** at the 42nd Society of Nuclear Medicine meeting, Jun. 11 -15, 1995, Minneapolis, MN.

Dr. Robert L. Phillips presented **"Modeling the Concentration of FDG in Arterial Plasma to Calculate Cerebral Glucose Metabolism by Single- and Multi-Scan Methods"** at XVIIth International Symposium on Cerebral Blood Flow and Metabolism, BRAIN 95, Jul. 2 - 6, 1995, Cologne, GE.

Dr. Edythe D. London presented a lecture entitled **"Brain Imaging: Acute Responses to Stimulants and Persistent Differences in Drug Abusers Compared with Controls"** at the First Federation of American Societies for Experimental Biology Summer Conference on Drug Abuse, Jul. 23 - 28, 1995, Copper Mountain, CO.

Dr. Edythe D. London presented a lecture entitled **"New Approaches to Understanding Drug Abuse"** at the International Workshop on Drug Abuse Treatment Technology, Sponsored by: The Counterdrug Technology Assessment Center, Office of National Drug Control Policy, Aug. 15 -16, 1995, Baltimore, MD.

Jonathan L. Katz presented an invited address entitled: **"Pharmacological Mechanisms Involved in Some Behavioral Effects of Cocaine"** at the First Federation of American Societies for Experimental Biology Summer Conference on Drug Abuse: Psychostimulants: Issues Related to Craving, Dependence and Treatment. Copper Mountain, Colorado.

Sari Izenwasser received a travel award from the International Narcotics Conference to attend the annual meeting held in St. Andrews, Scotland.

Sari Izenwasser was invited to present a seminar entitled: **"Neurochemical Mechanisms of Tolerance and Sensitization to Cocaine"** at the George Washington University School of Medicine's Department of Pharmacology.

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Media and Education Activities

Secretary's Marijuana Prevention Initiative Support

As the lead agency in the development of the Secretary's Marijuana Prevention Initiative, NIDA, in collaboration with CSAP, hosted a **National Conference on Marijuana Use: Prevention, Treatment, and Research**, July 19-20, 1995, in Arlington, Virginia. The Secretary has called for "a campaign designed to educate parents and their children about the consequences of marijuana and how to address the problem in their homes, their schools, and their communities." Her concern follows the significant upward trend in marijuana use among 8th, 10th, and 12th graders.

The conference was attended by a capacity crowd of more than 500 and received a significant amount of media coverage. Secretary Shalala, Dr. Lee Brown, and Mr. Ron Shafer (a parent with a meaningful story) joined Dr. Leshner as keynote speakers at the opening address. Overall, the conference was very successful in bringing new research findings to the public eye, especially related to dependence, developmental effects from maternal use; health and behavior consequences; etc.

In addition to the conference, the following activities are underway at NIDA as key elements of the Secretary's Initiative:

- Two companion booklets for parents and children on **Facts About Marijuana**
- A video for parents on the science-based facts about marijuana, how it fits in their children's lives, and what parents can do
- Television PSAs developed by the Partnership for a Drug Free America
- Expanded Marijuana Research Program

Public Information Materials for Racial and Ethnic Minority Audiences

Drug abuse is a major health problem for minority populations in the U.S., with consequences often more severe than for non-minorities. To address this high priority, NIDA will develop, prepare and disseminate culturally appropriate print and electronic media public information materials, designed to educate racial and ethnic minority audiences about the consequences, prevention, and treatment of drug abuse and addiction. NIDA has met with advisory groups from the Hispanic and African-American communities to develop the material and mechanisms for dissemination. This community-based approach represents an improvement over the previous practice of repackaging existing material for minority audiences.

Drug Abuse and AIDS National Media Campaign

The final phase of the **"Get High, Get Stupid, Get AIDS"** campaign will be launched in October 1995, with new television, radio and print public service announcements for young teens (12-16) and young adults (18-25). The young adult ads will continue to use the highly successful animation approach, and some of the same characters,

currently being used.

The teen materials represent a completely new approach to reaching this audience stop-action animation by the Brothers Quay, of MTV fame. The approach is well known and attractive to the audience, and will certainly stand out among public service announcements.

Public Information Campaign on the Scientific Basis for Understanding Drug Abuse and Addiction

An important communications goal for NIDA is to educate the general public and policy makers about the science-based knowledge assembled over the years about drug abuse and the brain and about understanding drug addiction as a disease. It is necessary to do this in order to bridge the disconnect between what people think about drug abuse and addiction and what scientific research has taught us.

This program is bringing information about these concepts to the attention of the general public through popular press and electronic media, including articles in magazines, op-ed articles in newspapers, spokesperson appearances on talk shows, community-based educational meetings, etc.

Public Information Materials for General Audiences

This program will develop useful print and electronic media material about the subjects of drug abuse and addiction for these audiences, emphasizing the public health nature of the problem and the science base of the knowledge.

An important way to reach the general public with this kind of information is through their contact with health care providers. Therefore, materials will be developed for primary care physicians and nurses to help them educate their patients about drug abuse and addiction, as well as for members of the general public who happen to be in a doctor's office.

The program will also produce materials for drug abuse clients/patients and members of their families about the nature of addiction and the treatment approaches available.

Press Activity

April 25 - **NIDA Presents Opportunities in Addiction Research for Young People** - NIDA sponsored a "Youth Science Fair" at Coppin State College on April 28. Scientists from the Division of Intramural Research provided talks and interactive demonstrations to about 300 4-12 grade students from Baltimore schools.

April 25 - Dr. Jack Henningfield participated in a press conference sponsored by the Tobacco Control Journal and the AMA to announce publication of several articles about smokeless tobacco. Dr. Henningfield's article focused on pH levels of smokeless tobacco and how that changes among different brands of the product.

May 24 - **NIDA Conference on Marijuana Research: Science to Aid Prevention and Treatment** - This media advisory was released to announce the marijuana conference

June 1- **NIDA Conference Agenda Focuses the Direction of Future Research on AIDS and Drug Abuse** - Media announcement of NIDA's AIDS and Drug Abuse conference held in conjunction with the annual meeting of the CPDD.

July 19, 1995 - **Secretary Shalala Cites Evidence of Marijuana Dependency and Effects on Children Exposed Before Birth** - An HHS news release of findings to be released at the Marijuana Conference.

The NIDA Press Office prepared and distributed press kits on drug abuse and AIDS to the Scottsdale/Phoenix media just prior to the conference.

During the Month of July, the NIDA Press Office handled a number of inquires regarding marijuana use and research. Press kits containing information on marijuana were prepared and distributed at the Marijuana Conference. Press officers assisted over 60 media representatives/reporters who attended the marijuana conference with interviews and information requests.

Exhibits

In recent months NIDA has exhibited at the following:

Coppin State College Eleventh Annual Substance Abuse Conference, April 27-28, 1995, Baltimore, MD

Prevention 2000: HIV, Violence, and ATOD Use - A Community Responsibility, May 5-9, 1995, Orlando, FL

American Cities Against Drugs, May 14-16, 1995, Atlanta, GA

American Psychiatric Association, May 20-25, 1995, Miami, FL

12th Annual Association for Health Services Research (AHSR) and the Foundation for Health Services Research (FHSR), June 4-6, 1995, Chicago, IL

National Association of State Alcohol and Drug Abuse Directors (NASADAD) and National Prevention Network (NPN), June 4-7, 1995, Chicago, IL

AIDS and Drug Abuse (CPDD Satellite Conference), June 9-10, 1995, Scottsdale, AZ

National Association of Alcoholism and Drug Abuse Counselors (NAADAC) Annual Meeting, July 5-7, 1995, Orlando, FL

American Psychological Society, June 29-July 2, 1995, New York, NY

NIDA National Conference on Marijuana Use: Prevention, Treatment and Research, July 19-20, Arlington, VA

Planned Meetings

NIDA is supporting the development and implementation of a day long Institute, entitled **"Comorbidity and Treatment Issues in Adolescent Substance Abusers"** which will be presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry on October 18, 1995 in New Orleans Louisiana. Dr. Alan Leshner, Director, NIDA will present and Chair this session. Dr. Dorynne Czechowicz has planned this Institute in collaboration with the AACAP Office of research and NIDA's Child and Adolescent Research Workgroup, chaired by Dr. Vincent Smeriglio.

NIDA has collaborated with the American Society of Addiction Medicine (ASAM), the College for Problems of Drug Dependence NIAAA, and the Research Society on Alcoholism in the planning of the ASAM State of the Art Conference entitled **"Expanding Role of Neurobiology in Addiction Medicine"**. This is an advanced level Program presenting a neuroscientific understanding of addiction and implications for treatment. The Conference will be held October 19-21 at the Marriott Metro Center in Washington, D.C. Dr. Dorynne Czechowicz, Treatment Branch, DCSR represented NIDA on the Conference Planning Committee.

The Medications Development Division (MDD) is planning with the Medications Development Committee of The American Society of Addiction Medicine (ASAM) for a joint presentation at an ASAM Sponsored State of the Art Conference on **"The Expanding Role of Neurobiology in Addiction Medicine"** on October 20 in Washington DC. A NIDA/ASAM panel moderated by Dr. Charles Grudzinskas, Director, MDD, will discuss "life-saving medications for drug addiction, and mainstreaming therapies into medical practice".

MDD is also planning with ASAM to sponsor a series of focus groups of physicians on issues of the unmet medical needs of drug abusers, and the role of pharmacotherapy in meeting those needs.

On October 23-24, 1995, NIDA will sponsor a meeting entitled, **"Drug Use, Gay Men, and HIV Infection."** The NIDA Office on AIDS is in the early planning stages for this meeting which was suggested by Representative Nancy Pelosi (California) following concern over reports of a resurgence of HIV infection among gay and bisexual men and its association with drug use. The meeting may be co-sponsored with the Centers for Disease Control & Prevention.

A satellite meeting of the Society for Neuroscience annual meeting is planned for November 11, 1995 and is entitled **"Advances in Drug Abuse Research on Nicotine."** Dr. David Johnson, DBR, is heading a NIDA committee arranging this meeting. Speakers will include Drs. Murray Jarvik, Allan Collins, James Patrick, John Rosecrans, William Corrigall, Kenneth Perkins, Neal Benowitz, Jack Henningfield, Dorothy Hatsukami, and Ovide Pomerleau.

An ancillary event at the Society for Neuroscience 25th Annual Meeting, **"NIDA: The Next Generation"**, will highlight new directions in neuroscience research on drug abuse. Dr. Floyd Bloom of The Scripps Research Institute will be the featured speaker. There will also be a poster session highlighting research by NIDA scientists supported through the Scientist Development Award and Scientist development Award for Clinicians. This event will take place from 6-8 p.m. on Tuesday, November 14, 1995 in Room 6F of the San Diego Convention Center.

NIDA is sponsoring a prevention intervention research symposium entitled **"Building Upon Diversity -- Striving for Scientific Excellence".** This meeting, to be held at the National Press Club in December of 1995 will present the state of the art in drug abuse prevention intervention research and its effectiveness.

In December 1995, NIDA will convene a workshop of NIDA-funded and other researchers to review the current status of needle exchange research. The primary purpose of the workshop would be to provide the opportunity for investigators to share information about their protocols, timelines, data collection instruments, and results and interpretations permitted by their methodologies.

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Publications

Clinical Report Series: Mental Health Assessment and Diagnosis of Substance Abusers

NCADI #BKD148
Provides detailed descriptions of psychiatric disorders which can occur among substance abusing clients. Presents the key components and processes involved in a comprehensive mental health assessment and describes a specific approach to achieving this. Detailed summaries of various assessment and interview tools are also provided.

Clinical Report Series:Assessing Drug Abuse Among Adults and Adolescents: Standardized Instruments

NCADI #146
Discusses the uses of standardized instruments as part of clinical assessment and treatment planning for adult and adolescent substance abusers. Provides detailed information on several standardized instruments including the different life problems they assess, recommended staff training for appropriate use, types of client populations, resources needs, and how to obtain the instruments.

Clinical Report Series: Relapse Prevention

NCADI BKD147
Discusses several major issues related to relapse prevention. Provides an overview of factors and experiences that can lead to relapse. Review general strategies for preventing relapses and describes four specific approaches in detail. Outlines administrative issues related to implementing a relapse prevention program.

Diagnosis and Severity of Drug Abuse and Dependence

NCADI BKD166
Provides clinicians and researchers summaries of the latest information, techniques and procedures regarding the diagnosis and severity of drug abuse and dependence.

Marijuana: Facts for Teens--Booklet

(Will be available in October 1995)
Designed specifically for teens, this booklet explains the current knowledge about marijuana, what it is, who uses it, how it affects a person physically and mentally through short-term and long-term usage, and where to seek help.

Marijuana: What Parents Need to Know--Booklet

(Will be available in October 1995)
Answers the most important questions that parents need to know to talk to their children about marijuana. Parents receive answers to questions such as: How is marijuana used?; What are the long-term effects of marijuana?; How

does it affect driving?; Are their treatments to help marijuana users?; How can I tell if my child has been using marijuana?; and more.

Research Monographs

Discovery of Novel Opioid Medications--Research Monograph 147

NCADI M147
Reviews the pharmacology, neuropharmacology, and molecular biology of potential pharmacotherapies for opioids, novel opioids, and non-opioids.

Epidemiology of Inhalant Abuse: An International Perspective--Research Monograph 148

NCADI M148
Describes the epidemiology of inhalant use and abuse in the United States and in selected countries around the world. Discusses unique problems associated with investigations of inhalant abuse and suggests methodologies that might be utilized to investigate the high risk, difficult-to-reach groups who abuse inhalants in various countries.

Medications Development for the Treatment of Pregnant Women, Infants, and Children Born to Drug Abusing Mothers--Research Monograph 149

NCADI M149
Reviews the current treatment strategies and approaches for the development of pharmacotherapeutic agents for the treatment of pregnant addicts and their children/infants.

Integrating Behavioral Therapies with Medications in the Treatment of Drug Abuse--Research Monograph 150

NCADI M150
Latest research findings including state-of-the-art techniques and procedures regarding the integration of psychosocial and pharmacological treatments.

Research Monograph 151: Social Networks, Drug Abuse and HIV Infection (1995)

NCADI M151
Brings together research in the areas of drug treatment and prevention. Offers a theoretical and methodological alternative to traditional behavioral epidemiology based on individual drug users by applying network analysis to the problems of drug abuse and HIV infection.

Problems of Drug Dependence, 1994: Proceedings from the 56th Annual Scientific Meeting--Volume I: Plenary Symposia and Annual Reports; and, II: Abstracts--Research Monograph 152 & 153

NCADI M152/NCADI M153
These two monographs contain the presentations from the 56th Annual Scientific meeting of the College on Problems of Drug Dependence, Inc. which includes the comprehensive, up-to-date reviews of research in progress from many disciplines in drug abuse and dependence.

NIDA NOTES Issues

Volume 10, No. 2 (March/April 1995)

Reports NIDA's refocusing of its research on drug-related violence and the broadening of its basic research on

behavior. Also discusses results of a study that shows 31% of New York murder victims had cocaine in their bodies; reports on NIDA's behavioral therapies development program launched in 1994; and presents results form NIDA's Monitoring the Future Study; and more.

Volume 10, No. 3 (May/ June 1995)

Discusses NIDA's role in studying links between AIDS and Drug Abuse; Treatment and outreach research on AIDS; Institute of Medicine's AIDS research recommendations; and more.

Videos

Drug Abuse Treatment in Prison

NCADI VHS72
Portrays two comprehensive drug abuse treatment approaches that have been effective with men and women in State and Federal prisons.

LAAM: Another Option for Maintenance Treatment of Opiate Addiction

NCADI VHS73
Shows how LAAM can be used to meet the opiate treatment needs of individual clients from the provider and patient perspective. Compares and contrasts LAAM with methadone.

Drug Abuse and HIV: Reaching Those at Risk

NCADI VHS74
Shows how three intervention models educate out-of-treatment injection drug users about AIDS, about the behaviors that transmit the disease, and about strategies that reduce the risk of contracting AIDS. Focuses primarily on indigenous leader community outreach.

Other Publications

Measuring Program Performance in Methadone Treatment Using In-Treatment Outcomes: An Illustration by Phillips, Hubbard, Dunteman, Fountain, Czechowicz and Cooper, published in the Journal of Mental Health Administration, Summer 1995, 22(3), 214-225. Quality measurement and quality assurance in drug abuse treatment has become a major issue. In addition, there is interest in the degree to which client outcomes can play a role in measuring treatment program performance. This paper discusses outcome-based performance measurement in narcotic addiction treatment and the importance of case-mix adjusted outcomes.

Colton, T., Johnson, T., and Machin, D. (eds). Proceedings of the Conference on Quantitative Methods for Studying AIDS, held in Blaubeuren, Germany, June 14-18, 1993. **Statistics in Medicine**; October 1994; 13 (19/20): 1899-2188. This conference was supported in part by a NIDA grant (#R01 DA04722, Donald Thomsen, Ph.D., Principal Investigator) to the Societal Institute of the Mathematical Sciences. Peter Hartsock, Ph.D., served as the NIDA Program Official.

Battjes, R.J., Pickens, R.W., and Brown, L.J. **HIV Infection and AIDS Risk Behaviors Among Injecting Drug Users Entering Methadone Treatment: An Update**. JAIDS:10, 1995.

Cooper, J.R. **Including Narcotic Addiction Treatment in an Office-Based Practice.** JAMA:273, 1619-1620, 1995.

Lambert, Elizabeth and Caces, Fe. **Correlates of Drug Abuse Among Homeless and Transient People in the Washington, D.C. Metropolitan Area in 1991. Public Health Reports**. Vol. 110; 4; July/Aug 1995; pp 455-461.

Kuhar, MJ, Boja, JW, Patel, A, Pilotte, N, Cerruti, C & Lever, J., (1995) **Cocaine and Dopamine Transporters**. In: Hammer, RP (Ed), The Neurobiology of Cocaine: Cellular and Molecular Mechanisms. CRC Press, Boca Raton, FL, pp.

201-213.

Drs. Barbara Herman and Frank Vocci have co-authored a manuscript, **Understanding Drug Addiction and the Brain** in The Medical Prescription of Narcotics, sponsored by the Swiss Office of Public Health, Fribourg: Huber Verlag, 1995, in press. Based on a talk delivered by Dr. Herman in Thun, Switzerland, November 9, 1993, it will be published in English, French, and German.

Vocci, F.J. **Development of Medications for Addictive Disorders**. In: Handbook of Experimental Pharmacology, Schuster, C.R., Gust, S.W., and Kuhar, M.J. (eds), Springer-Verlag, Heidelberg, in press.

Alim, T.N., Rosse, R.B., Vocci, F.J., Jr., Lindquist,T., and Deutsch, S.I. **Diethylproprion Pharmacotherapeutic Adjuvant Therapy for Inpatient Treatment of Cocaine Dependence: A Test of the Cocaine Agonist Hypothesis**. Clinical Neuropharmacology 18 (2): 183-195.

Vocci, F.J., Chiang, C.N., Cummings, L.B., and Hawks, R. **Overview: Medications Development for the Treatment of Drug Abuse**. In: Medications Development for the Treatment of Pregnant Addicts and their Infants, Chiang, C.N. and Finnegan, L.P., (Eds.), NIDA Monograph 149, pp.4-15, 1995.

McCann, D.J. and Vocci, F.J. **NIDA Opioid Discovery Program**. Anesthesia (in press).

Meyer Glantz, and Zili Sloboda published **"The Prevention of Drug Abuse Among the Elderly"** in R. Coombs and D. Ziedonis, (Eds.), Handbook on Drug Abuse Prevention: A Comprehensive Strategy to Prevent the Abuse of Alcohol and Other Drugs, New York: Allyn & Bacon, 1995.

Rebecca Ashery published **"Injection Drug Users, Crack Smokers, and the Use of Human Services"** by R. S. Falck, R. S. Ashery, R. G. Carlson, J. Wang, and H. A. Siegal, Social Work Research 19(3), 164-173, September, 1995.

Dr. Harry Haverkos, co-published an article in **Genetica** [95:157-164, 1995] on **"Measuring Inhalant Nitrite Exposure in Gay Men: Implications for Elucidating the Etiology of AIDSRelated Kaposi's Sarcoma."**

Dr. Harry Haverkos co-published an article in **International Journal of STD and AIDS**, Vol 6, #4, July/August 1995, pages 227-232, on **"The Third Wave: HIV Infection Among Heterosexuals in the United States and Europe."**

Dr. Harry Haverkos co-wrote a Letter to the Editor of **JAMA** (Vol. 274, 8/16/95, pages 535-536) updating readers on trends of reported cases of AIDS in the U.S.

Qualitative Methods in Drug Abuse and HIV Research, NIDA Research Monograph (in press, available October 1995). Elizabeth Y. Lambert, Rebecca Ashery, and Richard H. Needle, eds. Qualitative methods serve as central organizing research tools for accessing hidden populations, identifying drug use behaviors and practices that transmit HIV, developing culturally appropriate HIV risk prevention interventions, and evaluating and interpreting program results. This monograph is a comprehensive review of recent innovative research on drug abuse, HIV prevention, and program evaluation using qualitative methods.

Falck, R., Carlson, R., and Siegal, H. **HIV Risk Reduction for Injection Drug Users and Their Sexual Partners: Intervention Manual** (in press, available in October 1995). This manual describes the HIV/AIDS risk reduction intervention developed by the Dayton/Columbus, Ohio, National AIDS Demonstration Research (NADR) Project for IDUs who are not in treatment and their sexual partners. This is the fourth in a series of HIV intervention manuals produced under the sponsorship of the Community Research Branch, DEPR. It is intended to provide program administrators, clinical staff, counselors, and others involved in AIDS education and prevention efforts with a complete set of procedures for providing intervention sessions on HIV disease, health-promoting behaviors, and building skills and developing personal commitment to HIV risk reduction.

Eight peer reviewed articles will be published in the ACNP journal Neuropsychopharmacology, on or about December, 1995. The articles are based on the NIDA Technical Review entitled **"The Role of Glutamatergic Systems in the Development of Opiate Addiction"** held October 1718, 1994. The series is dedicated in tribute to the late Dr. Roland Ciaranello, Co-Editor-in-Chief. The series will contain a review article on **"The Effects of NMDA Receptor Antagonists and Nitric Oxide Synthase Inhibitors on Opioid Tolerance and Withdrawal: Medication Development Issues for Opiate Addiction"**, co-authored by Drs. Barbara Herman, Frank Vocci, and Peter Bridge of the Medications Development Division.

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Staff Highlights

Jaylan Turkkan, Ph.D., Chief of the Behavioral Sciences Research Branch, was elected to the Academy of Behavioral Medicine Research in June.

The College on Problems of Drug Dependence presented the J. Michael Morrison Award to **Dr. Jack D. Blaine**, Chief, Treatment Research Branch, Division of Clinical and Services Research, for outstanding contribution in the area of scientific administration, June 11, 1995.

Dr. Richard Needle, Chief, Community Research Branch, DEPR was a recipient of the 1995 Public Health Service Special Recognition Award. The award was given "for outstanding leadership and resourcefulness in advancing research on HIV/AIDS prevention and intervention among injecting drug users."

Nicholas Kozel, Associate Director, DEPR, was a recipient of the 1995 Public Health Service Recognition Award. The award was given for utilizing epidemiologic methods for community assessment of drug problems and in forming local, national, and international epidemiology networks.

Dr. Peter Hartsock was awarded a commendation by the National Science Foundation for his service, representing HHS, to the federal Interagency Arctic Research Policy Committee.

Dr. Mario De La Rosa, received an award for outstanding contributions and dedication toward health concerns of the Latino community from the State of Ohio Commission on Minority Health.

Dr. Nora Chiang, MDD, Chemistry and Pharmaceutics Branch received the PHS Special Recognition Award for her work on the development of buprenorphine and buprenorphine combined with naloxone.

Dr. George Uhl, Acting Scientific Director has served on the National Neurologic Research Brain Bank Advisory Board and has been asked to serve on the Scientific Advisory Board for the American Parkinsons Disease Association.

Dr. Edythe D. London was promoted to the rank of Adjunct Professor, Department of Pharmacology and Experimental Therapeutics, School of Medicine, University of Maryland.

Jane B. Acri, Ph.D., NIDA DIR PPL/Psychobiology Section, was selected by the Division of Psychopharmacology and Substance Abuse of the American Psychological Association to receive the Young Psychopharmacologist Award for 1995.

Mohammed Shoaib, Ph.D., NIDA DIR PPL/Behavioral Pharmacology and Genetics Section, won the Young Pharmacologist Prize presented by the British Association for Psychopharmacology, United Kingdom.
David A. Gorelick, M.D., Ph.D. was elected as an at-large member of the Executive Committee, Association for Medical Education and Research in Substance Abuse (term begins Nov., 1995) and has been appointed as member of the Committee on Practice Guidelines, American Society of Addiction Medicine.

Richard Nelson, M.D. is the first NIDA recipient of an NIH AIDS loan repayment award and has been elected co-chair of the NIH Fellows Committee (June, 1995).

Lawrence Cheskin, M.D. has been re-elected to a 3-year term on the Board of Directors, American Cancer Society, Maryland Division.

Jeffrey M. Witkin was elected to the Editorial Advisory Board of the Journal of Pharmacology and Experimental Therapeutics.

Ms. Jacqueline Porter, Special Assistant to the Director, OEPR, received the PHS Special Recognition Award for Productivity.

Ms. Jennifer Nakamoto, MDD received the PHS Special Recognition award for outstanding administrative support efforts.

Cora Lee Wetherington, Ph.D., has been appointed NIDA's Women's Health Coordinator. She continues part time her responsibilities as Program Officer in the Behavioral Sciences Research Branch, Division of Basic Research. Dr. Wetherington is aided by Adele Roman, M.S.N.

Karen Skinner, Ph.D., has been named Deputy Director, Division of Basic Research. Dr. Skinner previously served as the Chief of the Biomedical Branch, DBR.

Kathleen Creedon, Ph.D. joined the Medications Development Division, Chemistry and Pharmaceutics Branch, in August. Prior to joining MDD, Dr. Creedon was employed by the FDA where she had 10 years of medication review experience.

Deborah Liederman, M.D. joined the Medications Development Division, Clinical Trials Branch, in August. Dr. Liederman is a board certified neurologist. Prior to coming to MDD, Dr. Liederman worked in CNS research at Parke-Davis. Prior to her experience at Parke-Davis, Dr. Liederman was employed by the National Institute on Neurological Diseases and Stroke, Epilepsy Branch, where she was actively involved in research and development of anti-convulsant medications.

Nancy Pilotte, Ph.D. joined the Medications Development Division, Pharmacology and Toxicology Branch, in August. Dr. Pilotte came to MDD from the NIDA Intramural Research Program where she was a staff fellow in the Neuroscience Research Branch.

Carolyn Mosher, M.P.A., joins the Science Policy Branch, OSPC as a program analyst. She recently complete a two-year Presidential Management Internship with the Office of the Director, NIH.

William C. Grace, Ph. D., joined the staff of OEPR as Scientific Review Administrator, Basic Behavioral Sciences Research Review Branch, in September. Prior to service in the Health Resources and Services Administration, Dr. Grace was a program official in NIDA.

Theresa Levitin, Ph.D., has been appointed Deputy Director, OEPR. She served as Scientific Review Administrator and NIDA's Referral Officer, Division of Research Grants, NIH. Dr. Levitin will join NIDA on or about October 1.

Dr. Alan Trachtenberg returns to the Science Policy Branch, OSPC, after completing his tenure as Acting Director of the Office of Alternative Medicine, NIH.

Ms. Jacqueline Downing, Office of Science Policy and Communication (OSPC), retired from Federal service on June 30.

Mary Catherine (Kate) McGuire, Chief, Clinical, Epidemiological and Applied Sciences Review Branch, retired from Federal service, June 30.

Capt. Daniel L. Mintz, Scientific Review Administrator of the Clinical and Behavioral Research Review Committee, retired from the USPHS Commissioned Corp, August 31. Mr. Mintz received the Public Health Service Commendation Medal at his retirement ceremony.

Ms. Katherine E. Lenehan, Chief of NIDA's Executive Secretariat within the Office of the Director retired from Federal Service on June 30.

Ms. Vivianne Baskins of NIDA's Executive Secretariat retired from Federal service on June 30.

Ms. Carolyn Fisher, Grants Technical Assistant, Clinical and Behavioral Research Review Committee, retired from Federal service June 30.

Ms. Penny Paxton of the Planning and Financial Management Branch, OPRM, retired from Federal service on June 30.

Grantee Honors

Peter Bentler was named recipient of the first Distinguished Scientific Contributions Award from the Division of Evaluation, Measurement, and Statistics of the American Psychological Association. Description of the award in The Score Newsletter (July 1995) cites Dr. Bentler's research on methodology and structural equation modeling.

Suniya Luthar of the Department of Psychiatry, Yale University School of Medicine, received the American Mensa Education and Research Foundation Award for excellence in research on intelligence and intellectural giftedness. Dr. Luthar holds a career development award from NIDA and is co-investigator on several research studies focusing on the genetic epidemiology and the developmental etiology and consequences of drug abuse.

Thomas Wills was elected to Fellow status in Division 8 (Social Psychology) of the American Psychological Association, effective August 1995.

Terence P. Thornberry was elected a Fellow of the American Society of Criminology.

Linn Goldberg of Oregon Health Sciences University has developed and tested anabolic steroid education methods that have been cited and recommended in the 1995 publication "Athletic Drug Reference" approved by the NCAA and USOC.

Harvey Siegal, Principal Investigator for the Dayton/Columbus, Ohio site of the Cooperative Agreement for AIDS Community-Based Outreach/Intervention Research Program, was selected for the award of University Professor of Medicine at Wright State University, for the period July 1, 1995 through June 30, 2000.

Robert T. Trotter, Principal Investigator for the Flagstaff, Arizona site of the Cooperative Agreement for AIDS Outreach/Intervention Research Program, was selected in July for the permanent award of Regents Professor of Anthropology at Northern Arizona University.

The Student Award for Research Training Program (START) in the Department of Psychology at UCLA (**Dr. Peter Bentler, PI**) places outstanding minority students into research laboratories to introduce them to real-life research activities. For the school year that ended in June, 1995, 16 students received partial stipends. A START student, **David Garcia**, investigated gender differences in attitudes about condom use among Anglo and Hispanic students and was invited to present his results at the Psychology Undergraduate Research Conference held at UCLA in May, 1995.

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