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

February, 1995

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

Basic Research

Development of Novel, Highly Selective, Non-Peptide Opioid Delta Agonists and Antagonists.

The development of highly selective, systemically active and efficacious opioid delta agonists is a promising pathway for the identification of compounds of potential clinical importance. Such substances would provide effective medications for pain with decreased or no abuse liability. In an effort led by NIDA Grantee, Dr. Frank Porreca at the University of Arizona, a group of chemists and pharmacologists from the University of Arizona, University of Michigan, University of Texas and NIH has been actively exploring the development of systemically available analgesics acting through opioid delta receptors. Based on a large amount of information gained with highly receptor-selective peptides, this group has now succeeded in identifying families of molecules which show a high degree of selectivity for delta receptors and which are systemically active in producing analgesic actions in a variety of animal models. This group (Drs. Kenner Rice and Silvia Calderon at NIH, Dr. Victor J. Hruby, University of Arizona) has succeeded in synthesizing several compounds with significant selectivity at opioid delta receptors. One of the lead compounds, SNC80 shows more than 2000 fold delta (compared to mu or kappa) opioid receptor selectivity and has recently been reported (Journal of Medicinal Chemistry, 37:2125-2128, 1994). Furthermore, the analgesic actions of this compound have been characterized and shown to be mediated via both supraspinal and spinal opioid delta receptors (findings which will soon appear in the Journal of Pharmacology and Experimental Therapeutics). This compound, and others in this series and other chemical series are being further characterized by Dr. James Woods at the University of Michigan and by Dr. Thomas Burks at the University of Texas. They have shown that SNC80 produces minimal disturbance of gastrointestinal functions as would be predicted by previous studies with highly selective peptidic delta agonists. Further characterization of the consequences of systemic activation of opioid delta receptors is underway in the laboratory of Dr. Porreca who is investigating the possibility of development of physical dependence, whether selective agonists at these receptors will produce a positive reward, and whether such compounds can be useful in the treatment of morphine resistant pain states such as those observed in neuropathies.

Two Novel Cannabinoid Receptor Antagonists.

In 1994, two successful efforts were made towards the discovery of reversible cannabinoid antagonists. One of these (SR 141716A) was discovered by the French pharmaceutical company, Sanofi, through the screening of large numbers of analogs (high throughput screening). The other (AM630) was developed by Dr. Makriyannis, a NIDA grantee (University of Connecticut) and this was developed by rational design. The pharmacological properties of AM630 were studied by Dr.R. Pertwee in Aberdeen, Scotland. Although the two antagonists have very different structures they showed similar potencies when tested **in vitro**. However the two analogs showed different degrees of selectivity towards the two cannabinoid receptors (central and peripheral). These receptor antagonists are very valuable as they will be: 1) New, experimental tools for studying the biochemical and physiological properties of the cannabinoid receptors; 2) new templates for ligand design; and 3) may give rise to new therapies.

A High Affinity Electrophilic Probe for the Cannabinoid Receptor with Long-Acting Analgesic Properties.

A number of analogs have been designed to elucidate the structural features of the active site of the receptor site. A family of photoaffinity probes have been designed by Dr. Markiyannis and his colleagues (University of Connecticut.) These probes were found to be very useful for **in vitro** experiments but could not be used for in vivo experiments. More recently, potentially useful analogs were obtained through the development of affinity probes. The most useful of these ligands, (-)-7'-isothiocyanato-11-hydroxy-delta-8-tetrahydrocannabinol, was shown to fully occupy the cannabinoid receptor at concentrations as low as 2 nM. This molecule was found to act as antagonist when tested for its effects on the calcium current in neuroblastoma cells. However, when tested **in vivo** in rats this molecule behaves as an irreversible agonist demonstrating analgesic properties over a long period of time thus being potentially useful as a potent, non-opioid, long acting analgesic.

Rewarding Properties of Cocaine Linked to D3 Receptor.

Dr. George Koob and his colleagues from the Scripps Research Institute have been using a variety of behavioral methods in laboratory animals that simulate the human drug-seeking and drug-taking behaviors. These researchers have documented the withdrawal phase of cocaine addiction in the rat. This is similar to that reported for human addicts, and is characterized by a lowering of mood, hypersomnia, hyperphagia, psychomotor retardation, anhedonia and an intense craving for the drug. In the rat, elevations in reward thresholds and psychomotor retardation have been demonstrated during withdrawal from a cocaine binge. Markou, A. and Koob, G. Postcocaine anhedonia: An animal model of cocaine withdrawal. Neuropsychopharmacology 4: 17-26, 1991.

Dr. Koob and his colleagues have hypothesized that activation of dopamine transmission within specific structures of the basal forebrain is a major determinant for cocaine self-administration in laboratory animals, while decreased dopamine function may be responsible for some of the aspects of the withdrawal phase.

In a number of recent articles, Dr. Koob classifies potential treatment drugs for cocaine addiction in man. While there have been many clinical trials looking at the dopamine D2 agonists and antagonists, none have been very successful. However, increasing knowledge of a role for D1 and D3 receptors in cocaine dependence points to new targets for pharmacotherapeutics. Perhaps even more interesting, as Dr. Koob relates, the concept of partial dopamine agonists is gaining favor. These experimental compounds are not stimulatory or self-administered by naive animals, as cocaine is, yet they appear to attenuate the cocaine self-administration behaviors in the animals. The author concludes that "there is enough evidence to indicate that compounds with partial agonist activity at dopamine receptors may in the future represent novel psychoactive agents with important advantages compared to previously used antipsychotic drugs". Pulvirenti, L. and Koob, G. Dopamine Receptor Agonists, Partial Agonists and Psychostimulant Addiction. Trends in Pharmacological Sciences 15 (10): 374-379, 1994; Caine, B. and Koob. G. Modulation of Cocaine Self-Administration in the rat through D-3 Dopamine Receptors. Science 260: 1814-1816, 1993.

Cocaine During Pregnancy Disrupts Structure of the Cerebral Cortex.

Dr. Michael Lidow (Yale University) is studying the effects of orally administered cocaine to pregnant rhesus monkeys on the development of the cerebral cortex in the offspring. In his research presented at the Society for Neuroscience Meeting in November, Dr. Lidow discussed findings that cocaine virtually destroys the laminations of the cortex of the developing fetus so completely that no individual cortical layers could be discerned. Furthermore, there was an almost complete absence of glial fibers which are normally present in the upper layers of the cerebral cortex. In these studies, monkeys received 20 mg/kg/day from Day 40 to Da 102 of pregnancy, and were allowed to deliver at term (approximately Day 165). The offspring were allowed to develop normally for two months, at which time the observations were made. This study demonstrates that cocaine, administered daily during pregnancy, may significantly affect the development of the primate cerebral cortex, and that the rhesus monkey is a valuable and potentially predictive model for studies on the effects and mechanisms of action of cocaine during development of the cerebral cortex in embryos of human mothers addicted to this drug.

Potential Analgesic for Use in AIDS Patients.

Dr. Charles France (Louisiana State University, New Orleans) has been studying the properties of fentanyl derivatives. As part of his progress, he has examined a novel fentanyl derivative OHM3295 and found that it enhances natural killer cell (NK) activity in mice; all other mu opioids have been reported to decrease significantly NK activity. That OHM 3295 enhances NK activity while also producing opioid receptor-mediated antinociceptive effects suggests this compound might provide an important lead in the discovery of better treatments for pain in patients with compromised immune function.

Therapy of Memory Deficit Due to Drug Abuse and Other Causes.

Acquisition of eyeblink conditioning in rabbits is greatly delayed by PCP or MK-801 (dizocilpine) given daily, probably due to their blockade of NMDA receptors in the hippocampus. This is the primary model employed by Dr. John Disterhoft and his group at Northwestern University Medical School. Human PCP abusers show similar cognitive deficit. They had previously demonstrated that daily D-cycloserine, an agonist at the glycine site on the NMDA receptor (a site which can facilitate NMDA neurotransmission), enhances acquisition of trace eyeblink conditioning in *young* rabbits. They recently demonstrated the same effect, but more robust, in *aged* rabbits. They further showed that the most effective doses of cycloserine did not increase sensory sensitivity of the rabbits to the tone (conditioned stimulus) or airpuff (unconditioned stimulus). These studies have important implications for treatment of the cognitive consequences of drug abuse. It is possible that cycloserine, or other compounds acting as agonists at the glycine site on the NMDA receptor, can compensate for dysfunction in NMDA-mediated neural transmission as a result of a history of PCP abuse, and possibly other causes such as Alzheimer's disease.

Drug Discovery and Chemical Libraries.

High throughput screening of natural products and fermentation broths has resulted in the discovery of several new drugs. At present, generation and screening of chemical diversity is being utilized extensively as a major technique for the discovery of lead compounds, and this is certainly a major fundamental advance in the area of drug discovery. Peptide libraries present potential for producing millions of new peptide compounds for screening at a reasonable cost thus eliminating the time consuming, laborious and expensive procedures involved in the isolation, characterization, and synthesis of peptides obtained from natural sources (fermentation products) or conventional synthetic methods. It is not unusual to generate and screen tens of millions of peptides from a "peptide library". One of the approaches was earlier reported by a NIDA grantee, Dr. Richard Houghten. This approach consists of synthesis of non-support bound or soluble peptides (SPCLs= synthetic peptide combinatorial libraries) and these peptides can be used in all types of bioassays and screening methods. This method permits incorporation of D-amino acid or unnatural amino acid residues as well as specific secondary structures. Recently, an all-D-amino acid SPCL was successfully utilized to identify an all D-amino acid peptide ligand. Dooley et al. (in press), reported the identification of Ac-D-Arg-D-Phe-D-Trp-D-Ile-D-Asn-D-Lys-NH2 (Ac-rfwink-NH2), a potent mu agonist. This peptide bears no resemblance to any known opioid peptide and still, it produced an analgesic effect in mice. This effect, in comparison with morphine, was more potent and longer lasting. The fact that this highly stable peptide also induced analgesia after systemic administration demonstrates its ability to cross the blood-brain-barrier. Molecular dynamics calculations revealed similarity in the conformational characteristics of this peptide with PL 107, another potent opioid peptide. This result is of great fundamental importance because for the first time screening of an SPCL produced an agonist rather than an antagonist. These results also confirm the power of the SPLC approach for the discovery of novel analgesic drugs.

Cardiovascular Effects of Voltalized Cocaine Free Base.

The illicit use of cocaine is associated with a large array of mild stimulatory to deleterious effects to the cardiovascular system including cardiac arrhythmia, depressed contractility, myocardial infarction and sudden death. In particular, the increased popularity of smoking cocaine free base is associated with concomitant increase in its cardiotoxicity. The effects of cocaine are dependent, in part, upon prior and present history, dose, and route of administration. Dr. Billy Martin and his colleagues compared the cardiovascular effects elicited by voltalized cocaine to i.v. administration (in rats) and their findings indicate that inhalation of cocaine free base can produce cardiotoxic events with rapid onset that differ from i.v. drug administration. Acute exposure to voltalized cocaine produced a dramatic increase in blood pressure, a severe bradycardia, and heart blocks. In contrast, an i.v. injection of 1.5 mg/kg cocaine, a dose which has been estimated to be achieved after 5 min of inhalation exposure **failed** to elicit the profound bradycardia or heart blocks, but did increase mean arterial blood pressure (MAP). In addition, the cardiovascular effects that occurred during cocaine exposure underwent a rapid tolerance.

Diet and Taste Preferences May Predict Drug Use.

Dr. Blake Gosnell at the University of Wisconsin (Madison) has shown that preferences for fat and sweet tastes in rats predict a high preference for alcohol and/or morphine. Diet and taste preferences may be vulnerability factors for drug abuse, and raise the possibility that alteration of such preferences can be used in prevention and treatment efforts.

Other evidence that points to a role for diet and taste factors in the development of drug use is: (a) a high comorbidity between alcohol and drug abuse and eating disorders, (b) sweet cravings and high sweet intake in opiate addicts; and, (c) self-administration of a wide variety of drugs enhanced by food deprivation. Further research into the relationship between feeding motivation and drug motivation could lead to the development of important drug abuse prevention and treatment interventions.

Morphologic and Electrophysiologic Effects of Cocaine.

Dr. David Anderson at the Minneapolis Medical Research Foundation has shown that chronic cocaine abuse has definite morphologic and electrophysiologic effects on the brain. The studies are testing whether the long-term abuse of cocaine induces cerebral atrophy resulting in cognitive abnormalities, and whether these adverse consequences are partially reversible with abstinence from cocaine. Evidence for an ischemic mechanism for irreversible brain damage may suggest important approaches to treatment and prevention efforts.

NIDA-supported research at Columbia University is investigating whether children exposed to cocaine *in utero* are at increased risk of neurodevelopmental and behavioral impairments at 6-7 years of age. Dr. Margaret Heagarty has described the spectrum of neurodevelopmental and behavioral disabilities associated with maternal cocaine use during pregnancy. Importantly, she is distinguishing between neurodevelopmental effects directly attributable to intrauterine cocaine exposure and those caused by postnatal factors associated with maternal drug use, maternal education and IQ, and family environment.

Chimeras of Dopamine (DA) and Norepinephrine (NE) Transporters.

The dopamine (DA) and norepinephrine (NE) transporters share similar primary sequences and predicted topology, yet demonstrate important differences in their selectivity for ligands. To delineate discrete structural domains contributing to pharmacologic and kinetic differences between these transporters, a series of recombinant chimeras was generated by Susan Amara and her coworkers at Vollum Institute using a novel restriction site-independent method, and expressed in mammalian cells. Functional analyses of the chimeras delineate two discrete regions spanning the first through the third transmembrane domains (TM1-3) and TM10-11 that contribute to differences in their apparent affinities for DA, NE or MPP+(1-methyl-4-phenylpyridinium). These results also suggest that TM2-3 of the DA transporter have a role in selectively increasing the rate of DA uptake as compared to NE. TM4-8 of the DA transporter may influence the relative rate with which MPP+ is taken up into cells and could contribute to its selective toxicity in neurons expressing the DA transporter. These studies provide a framework for identifying the specific structural or regulatory determinants contributing to substrate recognition and translocation by the DA and NE transporters.

New Inhibitor of the Prohormone Convertase PC2.

Recently Dr. Iris Lindberg and her coworkers at Louisiana State University Medical Center discovered for the first time the properties of an endogenous inhibitor of PC2, the enzyme responsible for the synthesis of bioactive enkephalins and endorphins in brain and neural tissue. Deficiencies in the biosynthetic capacity for opioid peptides may be responsible for the addictive properties of opiate drugs in certain individuals. This discovery should greatly enhance our understanding of regulatory mechanisms in endorphin biosynthesis. A thorough understanding of regulatory mechanisms in opioid peptide synthesis might one day lead to enzyme-based drugs serving as therapeutic agents in opiate addiction.

Marijuana and Genetic Mutations.

Researchers at the University of Texas Medical Branch, Galveston, demonstrated a more than three-fold and more than two-fold increase over non-smoking pregnant women in mutations of the hypoxanthine phosphoribosyl transferase (hprt) gene among pregnant women who smoked marijuana and cigarettes, respectively, prior to and early in their pregnancies. Expansion of these preliminary studies should further establish the ability of marijuana to cause genetic mutations in women and the developing fetus (Ammenheuser, MM, Batinson, AB, Babiak, AE, et al. Elevated frequencies of hprt mutant lymphocytes in pregnant women who smoked marijuana, Environmental & Molecular Mutagenesis, 1995, in press).

In a twin study of drug abuse, 4,000 pairs of twins, monozygotic [MZ] and dizygotic [DZ], have been assessed for drug abuse and dependence. Research shows that there is a strong tendency that to a great extent, the abuse of

some drugs (cocaine and marijuana) is affected by genetic factors. For marijuana, the common or family environment also made a significant contribution. Initiation of marijuana and cocaine use was influenced by characteristics of the environment (drug availability, peer groups) and the characteristics of the individual (personality). Data suggest that for the continuation of drug use, other individual characteristics, such as physiological and subjective reactions to the drugs, may also be important. Further, among the marijuana users, suspiciousness and agitation appeared to be genetically related, while the pleasant psychological effects appeared to be mediated by the environment shared by twins, and not by genes. Using this twin model, additional studies are underway to examine medical and health, including psychiatric, consequences of drug abuse, and genetic influences on drug use/abuse and associated conduct disorders and antisocial behaviors in childhood and adults. (Tsuang, MT., Llyons, M., Isen, S., Goldberg, J., & True, W. Heritability of initiation and continuation of drug use. Psychiatric Genetics, 1993, 3(3):141; Tsuang, MT., Llyons, M., Goldberg, J., True, W., Meyer J., & Eaves, L. Genetic influences on abuse of illicit drugs: A study of 3,297 twin pairs, submitted to JAMA; Llyons, M., Tooney, R., Green, A., Isen, S., Goldberg, J., True, W., Meyer J., & Tsuang, MT. How do genes influence marijuana use? The role of subjective effects. Submitted to Am. J. Psychiatry.)

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Research Findings

Behavioral Research

Comprehensive Operant Behavioral Therapy for Treating Cocaine Addicts.

Cocaine abusers are hard to retain in treatment and difficult to treat successfully. However, Stephen Higgins and colleagues from the University of Vermont have developed a behavioral intervention that appears promising. The treatment program has four components: (1) quick detection of drug use based on frequent urine testing; (2) incentives (e.g., vouchers for pro-social items, positive reactions of counselors and significant others) or loss of incentives contingent upon urine testing results; (3) structured counseling sessions and (4) Disulfiram treatment for patients with substantial alcohol use. Drs. Higgins, Budney, and colleagues have reported on two trials comparing their behavioral treatment with "standard" drug treatment based on the 12-step disease model. The preliminary (non-random assignment) trial lasted for 12 weeks, and indicated that the behavioral treatment substantially and significantly retained patients in treatment better and engendered longer cocaine abstinence. The second trial randomly assigned 38 patients to the two groups and followed the patients for 24 weeks of treatment. As in the first trial, the behavioral treatment retained patients significantly longer than the standard 12-step treatment and resulted in greater abstinence. From both trials the behavioral treatment package appeared to be an effective intervention for retaining cocaine abusers in treatment and for establishing clinically significant abstinence.

Higgins and colleagues have also begun to investigate the therapy components. Forty cocaine addicts were randomly assigned to behavioral treatment with or without the voucher system. During weeks 1-12 one group received vouchers for cocaine-free urines while the other group received no vouchers. During weeks 13-24 the two groups were treated the same. The results showed that the vouchers contributed substantially to the outcome. Seventy-five percent of patients in the voucher group completed 24 weeks of treatment versus 40% in the no-voucher group. Continuous cocaine abstinence averaged 11.7 weeks in the voucher group versus 6.0 weeks in the no-voucher group. This study was a third replication demonstrating that the full behavioral treatment effectively retains cocaine-dependent patients in treatment and establishes significant periods of abstinence.

Most recently, Higgins and Budney have submitted a manuscript for publication describing a 12-month followup (i.e., after 6 months without treatment) of the patients in the two randomized trials. In comparing the full behavioral package with the 12-step disease model, Higgins and Budney found significantly greater cocaine abstinence at 12 months for the behavioral treatment-although both groups showed similar improvements on the Addiction Severity Index (ASI). In comparing the behavioral treatment with and without vouchers, they found that the voucher group showed more abstinence and used cocaine fewer days (nonsignificantly) and scored better on the ASI Drug Scale (significantly). Although the long-term followup suffered the usual complexities of patient dropout and attenuation of effects, the data continued to indicate greater efficacy of the behavioral treatment than for the comparison treatments.

The Economy of Drug Choices.

Studies being conducted by Dr. Stephen Higgins and Dr. Samuel Snodgrass at the University of Vermont are using models derived from economics to explore factors leading subjects to select alternative rewards to drug taking. For example, findings have shown that experienced cocaine users will prefer monetary rewards over intranasal cocaine for payments that are surprisingly small.

Animal studies at the University of Arkansas provide basic science support for these findings. Rats will prefer to ingest saccharine over cocaine if they are required to work substantially harder for a dose of cocaine. Alternative rewards to drug taking are of fundamental importance to the understanding and treatment of drug use and abuse.

Marijuana and Cognition.

Data from a recently completed NIDA-supported study show that long-term use of marijuana was associated with attentional deficit (selective attention, sustained attention, and/or divided attention) and difficulty with short-term memory tasks. The study was conducted in Costa Rican men of approximately 45 years of age who smoked marijuana for an average period of 8 years (4.9 marijuana cigarettes 2-7 times/week). There were two cohorts in the study: older cohort (42-45 years old) consisted of 23 users and 30 non-users of marijuana, and the younger cohort (27-30 years old) consisted of 61 users and 49 non-users of marijuana. These were assessed by Wechsler Adult Intelligence Scale, and various other sophisticated instruments to test for attentional and memory deficits. Results showed that chronic marijuana smoking was associated with attentional deficit (selective attention, sustained attention, and/or divided attention) and difficulty with short-term memory tasks in Costa Rican men (Fletcher, J., Adverse cognitive effects of chronic cannabis use, paper in preparation).

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Research Findings

Clinical and Services Research

Nosology, Diagnosis and Clinical Assessment.

A validation study in diagnosis and classification of drug and alcohol dependence (James Langenbucher, Jon Morgenstern, and Erich Labouvie, Rutgers University, in collaboration with Peter Nathan, University of Iowa) demonstrated diagnostic concordance of substance use disorders when diagnoses were made according to rules presented in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R), DSM-IV, and the World Health Organization's International Classification of Diseases, Tenth Edition (ICD-10). Results from the study will be published in the journal Drug and Alcohol Dependence. Another paper based upon this work that focuses on the generalizability of the dependence syndrome and the lifetime DSM-IV diagnosis of cannabis, cocaine and opiate dependence will appear in Addiction.

Smoking Cessation for Depressed Patients.

Smokers with a history of major depressive disorder constitute a significant proportion of smokers who present for cessation treatment. These smokers experience more frequent and intense depressive symptoms upon initial cessation and relapse at higher rates than other smokers. New and innovative interventions are needed to address the needs of these more recalcitrant smokers who may be unable to quit with standard interventions that are not matched or tailored to their particular needs.

Dr. Richard Brown, a NIDA investigator in Providence, Rhode Island, examined whether adding cognitive-behavioral treatment for depression to a standard smoking cessation protocol would enhance the achievement and maintenance of smoking cessation in smokers with a history of major depressive disorder. Preliminary results suggest that the addition of cognitive-behavioral treatment for depression (to standard smoking cessation treatment) results in superior rates of abstinence for smokers with a history of major depressive disorder, relative to standard smoking cessation treatment alone.

Dr. Arthur Garvey of the Harvard School of Dental Medicine found depressed smokers given nicotine gum were more likely to remain abstinent compared to depressed smokers receiving placebo gum. Although nicotine replacement appears to aid depressed smokers in their attempts to quit, this population may require a combination of nicotine replacement with other methods (anti-depressants, mood management therapy) to elevate abstinence rates.

Effects of Maternal Drug Use on Infant Birth Weight and ZOther Indices of Development and Health.

Preliminary analyses of early infant outcomes following prenatal exposure to cocaine and other drugs have been reported from a number of ongoing NIDA studies**1,2,3,4**. In one project, full-term infants exposed in-utero to cocaine were smaller in average birth weight, birth length, and head size than infants who were either drug-free or alcohol/non-cocaine-exposed, a finding consistent with several reports in the literature. There were no significant differences among the groups with regard to significant brain lesions (detected by cranial ultrasonography**1**), a finding also reported in another ongoing study**2**.

In one sample of 3-year-old children, prenatal exposure to marijuana is associated with impaired development of cognition in both African-American and white children**3**. For white children, there was a significant negative effect on performance on the Stanford-Binet Intelligence Scale which was offset by preschool/day-care attendance, while for the African-American children, significant effects were found on the composite score, short-term memory, and verbal reasoning subscales and the effects were not moderated by preschool/day-care attendance. Similar negative effects of prenatal marijuana exposure on the development of cognition (verbal reasoning and memory) have been reported in a different sample of 4-year old white children. At 5 and 6 years of age, prenatal marijuana exposure was not associated with performance on global tests of cognition and language, but at approximately these ages and slightly older, tests that examined more specific aspects of behavior (i.e., sustained attention) did appear to suggest a relationship between prenatal exposure and performance**4**. (1. Bandstra, ES; Montalvo, BM; Frank, JL et al. Cranial ultrasonography in term infants exposed in-utero to cocaine, Ped Res. 33:201, 1993; 2. Eyler, FD; Behnke, M; Woods, NS et al. Birth outcome from a longitudinal study of prenatally matched cocaine-using and non-using women, Ped Res 35:268a, 1994; 3. Day, NL; Richardson, GA; Goldschmidt, N; et al. Neurotoxicol Teratol, 16(2): 169-175, 1994; 4. Fried, P et al. Behavioral outcomes in preschool and school-age children prenatally exposed to marijuana: A review and speculative interpretation, NIDA Monograph Behaviors of Drug Exposed Offspring: Research Update, in press:, also Arch Toxicol, in press).

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Research Findings

AIDS Research

Efficacy of Vaccines and Behavior Change in Eradicating HIV.

Dr. Sally M. Blower of the University of California at San Francisco, presented results from her research at NIH on December 6, 1994. Dr. Blower and her colleague, Dr. A.R. McLean from Oxford University, employed mathematical modeling to assess the probability of eradicating HIV in San Francisco through the use of prophylactic vaccines (*Science*, September 2, 1994; 265: 1451-1454). Drs. Blower and McLean quantified necessary vaccine efficacy levels and population coverage levels for HIV eradication and assessed the likely impact of risk behavior changes on HIV vaccination campaigns. They determined that it is unlikely that vaccines will be able to eradicate HIV in San Francisco unless they are combined with considerable reductions in risk behaviors.

New Haven Needle Exchange Program: Decline in HIV-infected Needles Returned.

NIDA grantee Dr. Edward Kaplan and colleagues at the Yale University School of Medicine, published an article in December's American Journal of Public Health (1994;84: 1991-1994) entitled "A Decline in HIV-Infected Needles Returned to New Haven's Needle Exchange Program: Client Shift or Needle Exchange?" He and colleagues analyzed client demographic and behavioral data to determine possible reasons for a decline in the fraction of syringes returned to the New Haven needle exchange program that are contaminated with HIV-1. Only one variable, the race of participating clients, was found to have changed significantly over time, although there was a nonsignificant difference between HIV-1 prevalences in needles given to whites and to non-whites. The authors conclude that client shift does not appear responsible for the decline in the observed HIV prevalence in needles. Rather, they identified needle circulation time as a significant predictor of HIV prevalence.

Single-Use, Non-Retractable Syringe.

In an ongoing project, investigators have developed and have begun production of a single-use, non-reusable retractable syringe. This group also has begun the development of plans for clinical studies of this plastic syringe and has applied for approval from the Food and Drug Administration. The development of this invention could lead to the marketing of a product that -- depending on the extent of its deployment resulting from health care market forces and/or legislation -- could eliminate or significantly lessen the frequency of needle sharing among injection drug users (IDUs). Such would serve to significantly reduce the presently high rates of transmission of the human immunodeficiency virus (HIV) among members of this risk group and, consequently, to the general population. (NIDA-funded study "Single-use Non-reusable Retractable Syringe PI: Shaw).

Risk Factors for Bacterial Pneumonia Among HIV-Infected IDUs.

A study to identify factors that contribute to the excess risk of bacterial pneumonia observed among HIV-infected IDUs was recently completed. This study investigated risk factors for the first episode of bacterial pneumonia among HIV seropositives, using matched HIV seropositives without a first episode. Overall, the incidence of bacterial pneumonia among seropositives was 1.93 per 100 person years (PYS) and 0.45 per 100 PYS among HIV

seronegatives. On multivariate analysis, absolute CD4 <200 cells per mm3 and smoking of illicit drugs were significantly associated with bacterial pneumonia (OR=6.75 and OR=2.24, respectively). Cigarette smoking was associated with increased odds (OR=2.08) of bacterial pneumonia, but was not statistically significant because of nearly universal use in the cohort. Smoking illicit drugs had the strongest effect on risk of bacterial pneumonia among HIV positives with a prior history of Pneumocystis carinii pneumonia (OR=22.9). (Caiffa WT, Vlahov D, Graham NMH et al. Am J Respir Crit Care Med 1994; 150:1493-8).

Markers of Disease Progression Among HIV Seroconverters

A study of markers of disease progression among HIV seroconverters has compared longitudinal trends in CD4% and CD8% between cohorts of active IDUs and homosexual men. Prior to seroconversion, the two cohorts were similar in CD4% and CD8% levels. Greater changes in both markers overall were observed in the homosexual cohort compared with the IDUs ($p \leq 0.001$) in the first two years following seroconversion. Homosexual men had a higher median CD4% as compared to IDUs in the first 6 months post seroconversion, but subsequent trajectories of CD4% over two more years of follow-up coverged and then declined at similar rates in both cohorts. By four years post seroconversion, CD4% levels were 27% among homosexual men and 28% among IDUs. CD8% trajectories showed larger but not statistically significant increases among homosexual men as compared with IDUs in the third and fourth years post seroconversion. While these data suggest that the effect of injection drug use on rate of progression is limited, further follow-up is necessary to determine whether these trends persist. (Galai N, Vlahov D, Margolick JB et al. AIDS 1994; 8:66-74).

Alteration of Immune Function By Opioids.

Dr. Linda Dykstra and her colleagues have been examining conditioned immune suppression caused by prior exposure to morphine. These investigators have found that nadolol (a beta-blocker) may attenuate conditioned morphine-induced changes in immune status. Other studies administering naloxone showed that opioid receptor activity is necessary for the establishment and expression of this conditioned immunosuppression. These important studies describe mechanisms by which opioids can alter immune function, and possibly relate to disease progression in HIV-infected opioid users.

Drug Abuse Treatment for AIDS-Risk Reduction (DATAR).

In a research demonstration study of opioid addicts admitted to 3 methadone treatment programs, Dr. Dwayne Simpson of Texas Christian University found that illicit drug use decreased significantly during and after treatment. In a 12-month follow-up, self-reported weekly use of heroin decreased from 92 percent to 41 percent. Treatment process variables such as cognitive-based (vs. standard) counseling, client engagement in treatment, and therapeutic alliance with counselors were found to be more important than many pre-treatment client attributes in determining outcomes.

Drs. Dwayne Simpson and Don Dansereau of Texas Christian University have developed an innovative counseling tool using a visual representation strategy (called "node-link mapping"). Node-link mapping was found to improve client-counselor communication and the client's understanding of how to deal with problem situations. The strategy has been shown to strengthen the therapeutic relationship and decrease relapse to drug use.

Inhibition of Human T Cell Activation.

Researchers at UCLA have demonstrated that cocaine, alcohol, and cocaine/alcohol mixtures inhibit the in vitro activation of and ability to migrate of CD4+ but not CD4-T lymphocytes. Further studies will determine the extent and significance of the specific inhibition of the CD4+lymphocyte, the primary effector cell of cell-mediated immunity and the primary "target" of HIV, by these abused substances (Chiappelli, F., Frost, P., Kung, M., et al. Cocaine blunts human T cell activation. Immunopharmacol, 1995, in press).

Platelet Destruction in HIV Infected Individuals.

Researchers at the New York University School of Medicine found that the proportion of CD5+ to CD5-B lymphocytes is four-fold higher in HIV-1-infected individuals with thrombocytopenia than in controls (HIV-1-infected individuals without thrombocytopenia) and are attempting to establish the role of IgM and IgG and/or the complex of the two

antibodies in an autoimmune mechanism of platelet destruction in such patients. The results of this study, when completed, may definitively establish the mechanism involved in platelet destruction in HIV-infected individuals. (Karpatkin, S., Nardi, M.A., and Hymes, KB. Sequestration of antiplatelet GP3a and rheumatoid factor-immune complexes of HIV-1 and ITP patients, 1995, Proc Natl Acad Sci., in press; Kouri, YH., Basch, RS., and Karpatkin, S. B Cell subset and platelet counts in HIV-1 seropositive subjects, Lancet, 339:1445-1446, 1992).

Elucidating the Mechanism and Consequences of HIV Infection of the Brain.

Researchers at the University of Miami School of Medicine have developed methods for the isolation--from human brain tissue--of cells of the macrophage/monocyte series, which serve as primary reservoirs of HIV-I; detected macrophage infection in proximity to markers of inflammation in both brain and spinal cord neurons; and observed the apparent end-stage of HIV-1 infection in the form of the death of neurons and associated monocytes. Additionally, they have detected several specific HIV-1 genetic sequences and those for other biochemical mediators of inflammation in brain tissue from members of various HIV-1 risk groups. These studies, by elucidating the mechanism of HIV infection of the brain and its consequences, hopefully will suggest ways of intervening in this set of events in drug abusing populations. (Singer, EJ., Syndulko, K., Fay-Chandon, BN., Shapshak, P. et al. Cerebrospinal fluid p24 antigen levels and intrathecal immunoglobulin G synthesis are associated with cognitive disease severity in HIV-1, AIDS 8(2):197-204, 1994; Yoshioka M., Shapshak P., Srivastava AK., et al. Expression of HIV-1 and intraleukin-6 in lumbosacral dorsal root ganglia of patients with AIDS, Neurology, 44(6):1120-1130, 1994).

Mother-to-Child Transmission of HIV infection.

In a longitudinal project, risk of HIV infection was examined relative to a child's birth order following a mother's known HIV infection. Analyses to date suggest that in this sample a significantly higher HIV infection risk was found for children born subsequent to the birth of an older HIV-infected sibling than for those children born subsequent to the birth of an older, uninfected seroreverter. While additional information (e.g., stage of maternal disease progression) is critical for a conclusive interpretation of these results, the findings stimulate hypotheses with implications for research on mother-to-child transmission of HIV infection (Simpson, BJ; Andiman, WA; Shapiro, ED. The risk of HIV-1 infection in children born to HIV-infected women with serial pregnancies, Ped AIDS and HIV Inf 4:304, 1993).

HIV, Prenatal Care, and Disease Progression in the Children of HIV-Infected Mothers.

In a study attempting to identify health care delivery and clinical factors related to risk of infection and rate of disease progression in the child of an HIV-infected mother (e.g., methadone treatment, level of prenatal care for pregnant HIV-infected women, history of untreated maternal drug abuse, and mother's and child's anti-retroviral and prophylactic drug treatment), analyses of over 2,000 pregnancies have shown that very few HIV-infected women received adequate prenatal care (20% reported no prenatal care and an additional 45% reported too few visits). These findings have important implications for the translation of clinical findings into actual practice, e.g., clinical trial findings of a two-thirds reduction in the rate of mother-to-infant HIV transmission by women treated with zidovudine during pregnancy (with short-term treatment of the infant after delivery). The project has also shown that prenatal care was associated with reduced adverse birth outcomes (e.g., low birth weight and preterm birth). Further analyses are examining associations of health care patterns and clinical factors with the child's clinical course. This study is the largest population of pregnant, HIV-infected women to be analyzed to date, and constitutes the first detailed analysis of prenatal care to be conducted for this population (Turner, BJ; Markson, LE; Hauck, W; et al. Prenatal care of HIV-infected women: Analysis of a large New York State cohort. J Acquir Immune Defic Syndr, 1995, in press.)

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Research Findings

Epidemiology, Etiology and Prevention Research

1994 Monitoring the Future Study.

Dr. Lloyd Johnston and his colleagues at the University of Michigan, in their Monitoring the Future study, found that overall, the percentage of young people who report using drugs and/or alcohol is level or increasing. After peaking in 1979, with 60.4 percent of seniors reporting having tried marijuana at least once in their lives, use steadily declined through 1992. An increase in marijuana use was first observed for all three grades in 1993. These earlier increases were confirmed by dramatic increases in use again in 1994. Lifetime use in 1994 was 38.2 percent among seniors and 30.4 percent among tenth graders. For eighth graders, 1994 was the third year of marijuana use increases, rising from 11.2 percent in 1992 to 12.6 percent in 1993 and then to 16.7 percent in 1994. While the sharpest rises in drug use were reported for marijuana use, other substances showed statistically significant increases as well. After remaining level between 1992 and 1993, cocaine use increased among 8th and 10th graders. There were also significant increases observed for hallucinogens, particularly among 10th graders. The most frequently reported hallucinogen is LSD. The percent of students reporting being drunk in the month prior to survey has remained level between 1991 and 1994. However, these rates are very high. Among seniors, 30.8 percent reported being drunk in the past 30 days. For tenth graders, 20.3 percent reported this behavior and among eighth graders, 8.7 percent reported being drunk in the past month. The data collected on students' attitudes related to drug use revealed more bad news for all three grades. This is of major concern because there has been an inverse relationship between the attitude questions and the proportions of students reporting substance since the survey was initiated. In 1994, the proportion of students who perceive risk of harm from use and social disapproval of people who use marijuana substantially declined in all three grade levels. Two measures of high school seniors' attitudes are at the lowest levels since the survey began in 1975 -- the percentage of 12th graders who perceive great risk in trying LSD once or twice and the percentage of seniors who disapprove of people who try LSD. These erosions in attitude are accompanied by more than half of seniors saying it is very or fairly easy to get LSD. Perceived risk associated with experimentation with alcohol, daily drinking, or weekend binge drinking declined in all grades in 1994. Also, students in all grades reported declines in social disapproval of these drinking behaviors.

National Pregnancy and Health Survey.

Data from the National Pregnancy and Health Survey, found that 5.5 percent, or 221,000 of the 4 million women who gave birth in 1992, used some illicit drug during pregnancy. The survey also estimated that the number of babies born to women who used drugs during pregnancy was 222,000 (a number slightly higher than the number of mothers due to multiple live births). These estimates show that, at some time during their pregnancy, 119,000 women (2.9%) reported use of marijuana and 45,000 women (1.1%) reported use of cocaine; the two most frequently used illicit drugs. The survey also found that 757,000 women (18.8%) used alcohol and 820,000 women (20.4%) smoked cigarettes at some time during pregnancy. Only 6% of those who reported no use of any drug used alcohol and cigarettes during pregnancy, while 32% of those who reported use of one drug also smoked cigarettes and drank alcohol. Conversely, of those who reported no use of alcohol or cigarettes, only 0.2% used marijuana, and 0.1% used cocaine. However, of those who reported use of both alcohol and cigarettes, 20.4% also used marijuana, and 9.5% also used cocaine. This has tremendous public health implications and reinforces the need for health practitioners to continually monitor the status of smoking, drinking and illicit/nonmedical drug use during pregnancy. A final report

will be available June 1995.

Validity of Illicit Drug Use Reports in Juvenile Arrestees.

Dr. Michael Fendrich and Yanchun Xu have completed a study of over 3,000 juvenile arrestees. Using urine test results as a gold standard, this report evaluates the validity of illicit drug use reports for five illicit substances provided in a multisite, national interview study of the juvenile arrestees. Willingness to report substance use varied according to the type of substance, the time frame for substance use reports, and the characteristics of the juveniles asked to provide the reports. Youth were particularly reluctant to disclose recent use of cocaine and heroin. Race/ethnicity and willingness to disclose other substance use were the most important predictors of cocaine use disclosure among those testing positive for this drug. Race/ethnicity differences in validity were evaluated in the context of other recent epidemiological findings from surveys of drug use in the United States. Implications for the measurement of drug use in criminal justice samples are discussed. Fendrich M, Yanchun X The Validity of Drug Use Reports from Juvenile Arrestees. International Journal of the Addictions, 29(8),971-985,1994.

Consistency in Symptom and Substance Abuse Reporting.

Drs. Michael Fendrich and Virginia Warner have reported on symptom and substance use reporting consistency for offspring at high and low risk for depression. They examined two year recall of reports of lifetime symptomatology and substance use questions on the K-SADS-E in a sample of offspring at high and low risk for depression. Comparisons were made between those who forgot and those who remembered reports of screening symptoms made at the initial interview. In general, recall for symptoms of internalizing disorders (depression and anxiety disorder) was much worse than recall for symptoms of externalizing disorders (conduct disorder and substance use). Less than two-thirds of those initially meeting the lifetime depression screening criteria provided reports which met the lifetime screening criteria at follow up. Significant correlates of screening criteria recall included the following variables (measured at the initial interview): history of treatment for any disorder, impairment on the GAS (a score less than 61), and the presence of hypersomnia and suicidal symptoms (thoughts or ideation). Logistic regression suggested that a prior report of suicidal symptoms (including thoughts, ideation, or behavior) was the most important correlate of screen recall. Fendrich M, Warner V. Symptom and Substance Use Reporting Consistency over Two Years for Offspring at High and Low Risk for Depression. Journal of Abnormal Child Psychology, Vol. 22, No.4, 1994.

Prevention Research

Role of Caffeine in Early Substance Use Onset.

Drs. Linda M. Collins, John W. Graham, and William B. Hansen have just completed a study titled "Does Caffeine Play a Role in Very Early Substance Use Onset? An Illustration of Latent Transition Analysis". This study had two objectives. First it demonstrated the usefulness for prevention research of a relatively new methodology, Latent Transition Analysis (LTA). LTA allows the researcher to estimate and test models of stage-sequential development. Stage sequential models of substance use onset have been investigated in a wide variety of studies. The results indicate that alcohol and tobacco play a role relatively early in the onset process. However, these substances may not initiate the onset process in every case. Another drug that is usually considered harmless, caffeine, is tried by most children before they try either tobacco or alcohol. This study used LTA to examine whether heavy caffeine use played a role very early in the substance use onset process. It was found that children who used large amounts of caffeine were more likely to start the onset process (i.e., begin their substance use experience) before the seventh grade than subjects who used none or moderate amounts. In addition, there was evidence that the early part of the onset process was accelerated for heavy caffeine users. These results suggest that children who use large amounts of caffeine should be watched carefully for signs of increasing substance use. Data came from 4,325 subjects who completed a survey as seventh graders and again one year later as eighth graders. (In press as a chapter in an American Psychological Association Book).

Adolescent Transitions Program.

The Adolescent Transitions Program (ATP), a multicomponent psycho-educational program, was designed to prevent the emergence of problem behaviors in young teens by building both parent and teen skills as well as altering school environments for participating students. A cognitive-behavioral intervention strategy was developed and tested in a

clinical setting with parents and teens and was then adapted for implementation within the middle school context. The program consisted of two coordinated interventions, one of which was focused on parents and the other on teens. The basic components of ATP were evaluated using 158 families. Teens recruited were from middle schools and were recruited at the end of the 6th grade school year. Information on program effectiveness was gathered from teens, parents, and teachers. Information included program engagement, skill acquisition, improvement in family interaction, and reductions in problem behavior. Comparisons were made with control families who did not participate. The basic components of ATP were found to be effective in engaging students and their parents, teaching them skills, and improving parent-child relations. The Teen Focus curriculum, while enhancing parent-child relations, did not influence problem behavior in short term evaluations. In fact, teens seemed to escalate in their problem behavior after experiencing the intervention. Although the ATP has proven effectiveness on building individual skills, the efficacy of changing school contexts is being investigated. There is a need to work with schools to change the school environment to (a further increase parent involvement and home-school communication, and b) work to develop more heterogeneous peer environments to counter the effects of deviant peer groups. David W. Andrews, Lawrence H. Soberman and Thomas J. Dishion (Oregon) "The Adolescent Transitions Program: A School-Based Program for High-Risk Teens and Their Parents." Published in Banff Conference for Behavioral Therapy.

Research on Risk/Resiliency Factors

Drs. Lawrence Scheier, Michael Newcomb, and Rodney Skager of the University of California at Los Angeles examined the role of risk and protective factors in predicting teenage drug use (DU) for three age groups separated by gender. Using data from California's biennial survey of students, they applied latent-variable modeling to address the question of how protective factors may inoculate youth from initiating or escalating their DU. A vulnerability latent construct was reflected in three unit-weighted indexes: risk for initiation to DU, risk for problem DU, and protection from DU. A polydrug use construct was reflected in eight measures of alcohol, tobacco, and drug use. Structural equation modeling revealed that, regardless of age and gender, vulnerability was strongly related to polydrug use and other specific DU measures. The number of specific effects between protective factors and DU remained stable with increasing age, although effects between vulnerability and DU were more numerous for 7th and 11th grade students than for 9th grade students. The results underscore two important principles: (1) that DU prevention programs must consider age-related developmental phenomena, and (2) programs should continue to emphasize risk reduction while simultaneously developing and reinforcing protective agents. Scheier, L., Newcomb, M. and Skager, R. Risk, Protection, and Vulnerability to Adolescent Drug Use: Latent-Variable Models of Three Age Groups. Journal of Drug Education, 24(1): 49-82, 1994.

Adolescent Substance Abuse Among Children of Alcoholics (COAs).

Dr. Laurie Chassin and her associates at Arizona State University have investigated factors associated with adolescent substance abuse among children of alcoholics (COAs) and non-COAs. In earlier work, these investigators had found that parental alcoholism affected early adolescent substance use through stress and negative affective mechanisms and through impairments in parental monitoring, both of which increased the probability of associations with peer networks that supported substance use. They also found that parental alcoholism was associated with higher levels of temperamental emotionality in adolescents, which raised the risk of experiencing negative affect. Subsequent investigation using structural equation modeling revealed that parental monitoring and negative affective mechanisms influenced adolescent substance use for both COAs and non-COAs. This finding suggests that programs aimed at teaching coping skills or at improving parental management could be useful regardless of parents' alcoholism history. Molina, B., Chassin, L. and Curran, P. A Comparison of Mechanisms Underlying Substance Use for Early Adolescent Children of Alcoholics and Controls. Journal of Studies on Alcohol, 55(3):269-275, 1994.

Novelty-Seeking, Risk-Taking, and Related Constructs as Predictors of Adolescent Substance Use.

Dr. Thomas Wills and his colleagues tested Cloninger's theory, which posits that substance abuse is related to novelty seeking, harm avoidance, and reward dependence. The investigators used a school-based, self-administered questionnaire (on 7th and 8th grade students) that assessed ten related constructs, including affective states, anger, competence, impulsivity, major negative life events, optimism, self-control, sensation seeking, tolerance for deviance, value on independence/achievement, substance use, and friends' substance use. Cluster analysis identified five groups: (1) "problem teens" characterized by poor self-control; high levels of novelty seeking, risk taking, anger, independence, life events, tolerance for deviance, and negative affect; and low levels of orderliness, achievement

orientation, optimism, positive affect, and behavioral competence; (2) "conventional teens," who had opposite levels for all these attributes; (3) "controlled risk-takers," who were high on risk taking and novelty seeking but average on self-control and achievement orientation; (4) "stressed nondeviants," who had average to moderate levels of achievement orientation and self-control but high levels of life events, negative affect, and social anxiety; and (5) "withdrawn youth," who had low levels of both negative and positive characteristics and low levels of peer competence and social orientation. "Problem teens" were found to have the highest levels of substance use and "conventional teens" had the lowest levels. The study findings were interpreted as providing general support for Cloninger's theory but also showing a substantial relationship of substance use to other constructs considered in paradigms such as problem behavior theory, stress-coping theory, and personality models. Wills, T., Vaccaro, D., and McNamara, G. Novelty Seeking, Risk Taking, and Related Constructs as Predictors of Adolescent Substance Use: An Application of Cloninger's Theory. Journal of Substance Abuse, 6(1):1-20, 1994.

Individual, Family, and Peer Risk Factors of Substance Use.

In a prospective longitudinal study conducted at the Center for Education and Drug Abuse Research at the University of Pittsburgh, early onset of alcohol and drug use was investigated among sons of substance-abusing and normal fathers. Hierarchical regression analyses were used to test models to identify risk characteristics associated with sons' perception of family dysfunction, unconventional activities among peers, and affiliation with peers engaged in delinquent behaviors. Logistic regression analyses showed that individual, family, and peer risk factors obtained when the boys were 10-12 years old correctly predicted alcohol and/or drug use by the time the boys were 12-14 years old in 84 percent of cases. The findings support a model of alcohol and drug abuse liability that includes individual, family, and peer risk factors. The findings also suggest that temperament phenotypes influence family interaction patterns, which in turn influence the psychosocial development of the child. Parents tend to take out their anger more often on children with difficult temperaments, and in the presence of a dysfunctional family, high abuse potential and maladaptive discipline practices in parents, children are likely to disengage prematurely from the parental sphere of influence to peer influence. In the presence of conflicted parent-child and sibling relationships, this disengagement from parental influence may increase involvement in unconventional activities among peers, tolerance for deviance, and liability for a host of problems including substance abuse. Blackson, T. and Tarter, R. Individual, Family, and Peer Affiliation Factors Predisposing to Early-Age Onset of Alcohol and Drug Use. Alcoholism: Clinical and Experimental Research, 18(4)813-821, 1994.

Novelty-Seeking Behavior and Dopaminergic Effects.

Dr. Bardo from the University of Kentucky has been involved in exciting research on novelty seeking behavior and dopaminergic effects. Volammetry with electrochemically pretreated carbon fibers is a new technology which provides a distinct signal of catechols with in-vivo implantation. A signal coming from the nucleus accumbens primarily reflects DOPAC, a major dopamine metabolite. The researchers used this technique to assess possible sub-second changes in accumbal dopamine transmission in rats exposed to a novel environment. Following habituation to one compartment of a behavior chamber, rats were allowed to explore an adjacent novel compartment when the partition was removed. All rats either peered into or entered the novel compartment. These behaviors occurred in close temporal association with a marked (more than 70%) but short-lived (less than one minute) rise in the DOPAC signal above the habituated baseline level. Random motor activity in either compartment failed to alter DOPAC, arguing against a simple motor-dependent effect. The authors state that their results add to growing evidence for the involvement of mesolimbic dopamine in novelty-seeking behavior and highlight the value of voltammetric techniques in elucidating this role. G.V. Rebec, C.P. Grabner, R.C. Pierce, M.T. Bardo, "Voltammetry in Freely Moving Rats: Novelty-Dependent Increases in Accumbal DOPAC." Paper presented at the Society for Neuroscience Annual Meeting, Miami Beach, Florida, November 13-18, 1994.

Drugs and Aggression.

While it is widely believed that drugs and violent behavior are associated, it has been difficult to show that drugs actually produce aggression under controlled scientific conditions. A recent study from McLean Hospital in Massachusetts1 showed that athletes reported significantly more fights, verbal aggression and violence toward their wives and significant others during periods in which they were using anabolic-androgenic steroids. A study from the University of Texas Health Science Center2 recently contradicted often-reported findings that marijuana reduces aggressive behavior. When poly-drug users with antisocial personality disorder were studied instead of the usual college students, they increased their aggression toward other laboratory subjects immediately after smoking marijuana. The increased aggression was directly related to the THC content of the marijuana cigarettes.

Victims of criminal aggression and other forms of stress have been found to suffer from a number of behavioral disorders loosely collected under the term "post-traumatic stress disorder". The idea that traumatic stress may bring about drug use in otherwise drug-naive people has been controversial, but has now found some support in the animal laboratory. Researchers at the Louisiana State University Medical Center2 have shown that animals who experience random, unpredictable stress learn to self-administer intravenous cocaine much faster than animals who had some measure of control over their stress experiences.

These studies taken together suggest that aggression and stress may produce drug-taking, and that drug-taking in turn can produce aggression and violence. Further studies will help to identify persons at most risk, and those drugs and drug combinations that produce such dangerous behavioral effects. (1. Choi, P.Y. and Pope, H.G. Jr. Violence toward women and illicit androgenic-anabolic steroid use. Annals of Clinical Psychiatry, 6:21-5, 1994; 2. Cherek, D.R., Roache, J.D., Egli, M., Davis, C., Spiga, R., and Cowan, K. Acute effects of marijuana smoking on aggressive, escape and point-maintained responding of male drug users. Psychopharmacology, 111:163-8, 1993; 3. Goeders, N. E. and Guerin, G.F. Non-contingent electric foot shock facilitates the acquisition of intravenous cocaine self-administration in rats. Psychopharmacology, 114: 63-70, 1994.)

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Research Findings

Intramural Research

Neuroimaging Section - Edythe London, Ph.D.

Scientists in NDAS reported that the spontaneous electroencephalogram (EEG) shows specific alterations in response to acute morphine administration. Morphine increased alpha and theta power. Most important was the finding that changes in EEG spectral power predict the subjective response to morphine. Thus, changes in alpha and beta power can predict the magnitude of positive affect, as measured by subjective self-reports. Findings such as these provide a basis for understanding the role of changes in the spontaneous EEG in brain function and behavior. (RL Phillips, R Herning, ED London (1994): Morphine effects on the spontaneous electroencephalogram in polydrug abusers: Correlations with subjective self-reports: Neuropsychopharmacol. 10:171-181.)

The N-methyl-D-aspartate (NMDA) receptor is major excitatory neurotransmitter receptor in the brain. Scientists in NDAS have discovered that a variety of cations, including polyamines that are present in high concentrations in the brain, cause a shift in the affinity state of the NMDA receptor. Understanding factors that modulate this receptor can lead to important advances in therapeutics aimed at drug abuse, epilepsy, and neurodegeneration. (ED London, A Mukhin: Polyamines as endogenous modulators of the N-methyl-D-aspartate receptor. Ann. N.Y. Acad. Sci., in press.)

A major approach to assessment of brain function noninvasively involves measurement of regional cerebral glucose metabolism by positron emission tomography (PET) scanning. Quantitative determinations using this procedure involve repeated sampling of arterial blood. Investigators in NDAS have developed a mathematical model that may revolutionize cerebral metabolic studies using PET scanning by simplifying the procedure. The model requires only four to six samples of venous blood to estimate the integral of the arterial concentration of the radiotracer during the measurement. (RL Phillips, CY Chen, DF Wong, ED London: An improved method to calculate metabolic rates for glucose using PET. J. Nucl. Med., in press.)

Previous work by investigators in NDAS has demonstrated that inhibitors of nitric oxide synthase, the enzyme that catalyzes formation of nitric oxide, ameliorates the opioid withdrawal syndrome in rats. Although most known inhibitors of nitric oxide produce hypertension, that may be an unwanted side-effect in a treatment medication, recent studies by these investigators have shown that 7-nitroindazole, a selective inhibitor of the neuronal form of the enzyme, ameliorates opioid withdrawal without pressor effects. This compound may lead to development of new approaches to treat opioid dependence. (DB Vaupel, AS Kimes, ED London: Comparison of 7-nitroindazole with other nitric oxide synthase inhibitors as attenuators of opioid withdrawal. Psychopharmacol. in press.)

Investigators in NDAS have demonstrated that the pattern of cerebral glucose metabolism is different in polydrug abusers than in control subjects matched for gender, age, and education. The drug abusers have a lower metabolic rate in the visual association cortex and higher metabolism in the orbitofrontal cortex. It is not know to what extent these differences in drug abusers reflect the effects of chronic drug abuse rather than pre-existing differences that may be pre-disposing factors that confer vulnerability to drug abuse. Future studies directed at testing other measures of function in the orbitofrontal cortex in drug abusers are planned. (JM Stapleton, MJ Morgan, RL Phillips, DF Wong, BCK Yung, EK Shaya, RF Dannals, X Liu, RL Grayson, and ED London: Cerebral glucose utilization in polysubstance abuse. Neuropsychopharmacol., in press.)

Psychobiology Section - Jonathan Katz, Ph.D.

A series of benztropine analogs has been prepared as probes for the dopamine transporter. Several of these 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 and yet are not efficacious locomotor stimulants nor are they recognized as being cocaine-like in a drug discrimination paradigm. These compounds represent an unprecedented class of dopamine uptake inhibitors that will provide important tools for further exploration into the role of the dopamine transporter in mediating the behavioral effects of cocaine that lead to abuse. One significant question that may be addressed with these compounds is why some dopamine uptake inhibitors are abused and others are not. Further, these compounds may have potential as cocaine-abuse therapeutics.

Clinical Trials Section - Kenzie Preston, Ph.D.

Cocaine use among patients participating in methadone maintenance programs is a widespread problem for which no reliable treatment solutions currently exist. Division of Intramural Research (DIR) scientists evaluated the effectiveness of a novel voucher-based reinforcement contingency in producing sustained cocaine abstinence. A randomized controlled trial compared a voucher-based reinforcement contingency for cocaine abstinence to noncontingent voucher presentation in the treatment research clinic of the NIDA Intramural Research Program, Baltimore, MD. Patients were selected from 52 intravenous heroin abusers in methadone maintenance treatment; thirty seven of the 52 patients who used cocaine consistently during the first 5 weeks of treatment participated. Patients exposed to voucher-based reinforcement received a voucher for each cocaine-free urine sample (i.e., negative for benzoylecgonine) provided during a 12-week period; the vouchers had monetary values that increased as the number of consecutive cocaine-free urines increased. Control patients received noncontingent vouchers that were matched in rate, pattern, and amount to the vouchers received by patients in the contingent group. Primary outcome measures were cocaine abstinence by study week and the longest duration of sustained cocaine abstinence as determined by qualitative urinalysis. Patients receiving voucher reinforcement achieved significantly more weeks of cocaine abstinence (P=.007) and significantly longer durations of sustained cocaine abstinence (P=.001) than controls. Nine patients (47%) receiving voucher reinforcement achieved between 7 and 12 weeks of sustained cocaine abstinence; only 1 control patient (6%) achieved more than 2 weeks of sustained abstinence. Patients receiving voucher reinforcement rated the overall treatment quality significantly higher than controls (P=.002). Decreases in cocaine use were not associated with increases in use of alcohol or other drugs. Voucher-based reinforcement contingencies can produce sustained cocaine abstinence in inner-city intravenous polydrug abusers.

In addition to establishing the efficacy of contingency management procedures for treatment of cocaine abuse, the usefulness of quantitative urinalysis for cocaine metabolite and creatinine correction techniques and the relationship between these data and self-reported drug use were evaluated with data collected in the clinical trial. Rules were developed to differentiate between occasions of new use and carry-over in positive qualitative urine tests. These data were compared to self-reported drug use to evaluate the concordance between objective and subjective measures of drug use. Preliminary analyses suggest: qualitative and quantitative urine testing show greater rates of drug use than that shown by self report; quantitative testing provides a means of differentiating incidences of new drug use from residual carry-over; the identification of new use with quantitative testing may help to reconcile (by elimination of positives due to carry-over) differences between rates of drug use indicated by qualitative urine screens and self-report. In addition, quantitative testing of urine specimens in the contingency management study suggests that individuals who responded to treatment (i.e. stopped their cocaine use) had lower cocaine metabolite concentrations during baseline compared to those who did not respond to treatment. Thus, urine cocaine metabolite concentrations revealed through quantitative testing may be useful for predicting treatment outcome.

This study showed that voucher-based reinforcement of drug abstinence is an effective means of decreasing illicit cocaine use in polydrug abusers. The generalized effects of providing financial support to patients in the form of vouchers was controlled for in the study, clearly establishing the importance of the contingent nature of voucher distribution. It is particularly significant that efficacy was established in the context of otherwise standard methadone treatment, suggesting that this procedure may be readily exportable to community-based treatment programs. The work is further significant in the potential for identification of subject characteristics (e.g., demographic, physiological and behavioral) that are relevant to prediction of treatment outcome.

Buprenorphine has been reported to have the same efficacy as methadone in the treatment of narcotic abusers, but with lower abuse/dependence liability and greater safety than methadone. Naltrexone has been marketed in the United States for treatment of narcotic addiction; it blocks the euphoriant and analgesic effects of opioids and prevents the development of physical dependence and tolerance in patients who continue to use opioids. Researchers

at the NIDA DIR have been working to develop a treatment regimen for short term inpatient detoxification and transition to outpatient naltrexone treatment. The safety and effectiveness of buprenorphine alone or in combination with naltrexone was evaluated in an 8-day inpatient medically supervised withdrawal single-blind study. Naltrexone 12.5, 25 or 50 mg was administered on days 3 & 4, 3 to 8, 5 to 8, or not at all; placebo was given on all days when active naltrexone was not given. All subjects received one sublingual buprenorphine dose daily in the following order: 4 mg (day 1), 6 mg (day 2), 4 mg (day 3), 2 mg (day 4), and 0 mg (day 5 to 8). The study was being conducted under a double-blind, controlled, randomized, parallel group design. The primary outcome variables are: 1) opioid withdrawal; 2) changes in craving for opioids; 3) results from screening of urine samples for opioids and cocaine during outpatient treatment; and 4) outpatient treatment compliance. Forty-five subjects who met DSM-IIIR criteria for opioid dependence consented to be studied. The group on buprenorphine alone (n=33) had equal or less withdrawal from day 2 through 4 compared to the group that started naltrexone on day 2 (n=8). However, from day 5 through day 7 the naltrexone-treated group had less withdrawal than the group with buprenorphine alone. All subjects who started receiving naltrexone on day 5 (n=4) had severe opiate withdrawal and recruitment of subjects for this group was stopped. These results suggest that administration of naltrexone on day 2 may increase opiate withdrawal at the beginning of treatment but lead to decreased withdrawal thereafter, compared to treatment with naltrexone placebo. This result may bear on the hypothesis that antagonists may produce partial resetting of the opiate receptor, resulting in a shorter duration of withdrawal. These data also support the development of cost-effective short-term inpatient opiate detoxification and early transition to opiate-free treatment using naltrexone.

Oral ingestion is the primary route by which cocaine has been used throughout most of history. Cocaine has been self-administered orally for over 3000 years, first by Indians of South America who began the practice of chewing coca leaves, and later by members of a number of cultures who orally ingested cocaine in a variety of vehicles, particularly beverages such as coca tea, soft drinks (i.e., Coca Cola) and coca wine. Recent estimates indicate that today over four million Indians in Peru and Bolivia chew coca leaves regularly, and coca tea is still sold widely and legally in many areas of South America. Despite this remarkable longevity and current-day prevalence, relatively little is known about the behavioral pharmacology of oral cocaine, particularly at low doses that approximate those commonly ingested by the oral route. The study was conducted to characterize the behavioral pharmacology of low-dose oral cocaine in humans as a potential screening tool for identifying pharmacological treatments of cocaine abuse.

Seven volunteers with histories of regular cocaine use were taught to distinguish 50 mg of oral cocaine from placebo using a drug discrimination procedure. During daily training sessions, under double-blind conditions, the volunteers ingested a capsule containing 50 mg cocaine or placebo. For 2 hours after capsule ingestion, subjects guessed whether they had received "Drug" or "Placebo." At the end of each session, subjects were told which compound they had received. Subjects earned money for correct guesses and lost money for incorrect guesses. One subject who quickly acquired the cocaine vs. placebo discrimination was exposed to 3 doses of oral cocaine (6.25 mg, 12.5 mg, and 25 mg) in test sessions in random order across days to determine the lowest doses of cocaine he could detect. No feedback was provided at the end of test sessions. Test sessions were randomly intermixed among training sessions identical to the ones described above in which subjects received either 50 mg cocaine or placebo. Throughout all of these administrations cardiovascular, performance, and self-reported mood measures were collected.

In the last 20 sessions of the initial training condition, 50 mg cocaine produced significant discriminative stimulus and rate increasing performance effects, and increases in "liking" ratings in five of seven subjects. It also produced a profile of mood effects characteristic of cocaine administered by other routes. The onset of the behavioral effects was between 30 and 40 minutes after capsule ingestion. Fifty mg cocaine produced only minor cardiovascular effects. Interestingly, two subjects showed significant behavioral effects without significant tachycardic effects. The subject exposed to 25 mg, 12.5 mg, and 6.25 mg showed clear discriminative stimulus and rate-increasing performance effects at 25 mg and to a lesser extent at 12.5 mg. Cardiovascular effects were minimal or absent at those lower doses.

This study demonstrated the behavioral activity of doses of oral cocaine that are lower than those previously shown to affect human behavior. Oral cocaine produced a similar profile of self-reported mood and performance effects and cocaine administered by other routes. These methods revealed important behavioral effects of oral cocaine at doses that produced minimal or no detectable cardiovascular effects. The results of this study suggest that these procedures may be useful in studying the behavioral pharmacology of cocaine under conditions that minimize risk to subjects.

Pharmacotherapy Section, David Gorelick, M.D., Ph.D.

Much research on the neuropharmacology of cocaine abuse has focused on brain dopamine systems, but there is

growing evidence from animal studies that cocaine also influences brain opiate systems, especially mu-opiate receptors. Researchers at the NIDA DIR, in collaboration with scientists at the Johns Hopkins School of Medicine, recently completed a study showing that chronic cocaine users, compared with healthy controls, have increased mu-opiate receptor binding in certain brain regions, and this increase persists in most subjects even after four weeks of cocaine abstinence. Receptor binding in several brain areas was also significantly correlated with subjects' self-reported craving for cocaine. These findings suggest that brain mu-opiate receptors changes associated with chronic cocaine use may play a role in cocaine abuse, and provide a basis for the study of opiate medications, e.g., buprenorphine, as possible treatments for cocaine abuse.

Numerous animal studies have shown that calorie deprivation increases drug self-administration, but this phenomenon has never been demonstrated in human drug users. Researchers at the NIDA DIR have recently completed a study showing that a 700-calorie deficit diet significantly increased drug self-administration in human subjects, using cigarette smoking as the target drug. This is the first experimental demonstration of this phenomenon in humans, and suggests that dietary changes induced by drug abuse could themselves influence further drug use.

Researchers at the NIDA DIR are exploring several new approaches to the pharmacological treatment of cocaine abuse. One approach is the use of combinations of medications which act on a neurotransmitter system by different mechanisms, thus possibly producing additive or synergistic therapeutic effects while minimizing side-effects. The first such study, recently completed, used two dopaminergic medications, bromocriptine, a dopamine receptor agonist, and bupropion, a presynaptic reuptake inhibitor, in an open-label outpatient clinical trial. The first phase of the study used a very slow dose escalation regimen to establish the safety of this medication combination, even in subjects who use cocaine while in treatment. The second phase used a more rapid dose escalation regimen that achieved putative therapeutic doses earlier in treatment. This phase also established safety, and gave promising efficacy results as compared with the first phase. NIDA DIR now plans a double-blind clinical trial to follow-up this promising approach.

Molecular Neurobiology Section, George R. Uhl, M.D., Ph.D.

Recent studies continuing this laboratory's work characterizing the rat and human mu opiate receptors and their genes have identified surprising findings that add to the diversity of opiate receptor actions in the brain. In studies expressing the rat and human mu receptor genes, sequences were identified that dramatically alter levels of expression of the receptor protein in several model expression systems. These findings, coupled with recent observations of mu receptor gene splice variants, have uncovered, for the first time, a novel mode of possible regulation of the mu receptor's expression. Mechanisms of this regulation and its implications for receptor regulation in brain are currently being explored.

Studying mu receptor localization with selective antisera reveals striking localizations in pathways associated with reward and reinforcement. Densities of mu receptor immunoreactive nerve fibers and terminals patterns in the ventral tegmental area contrast with strongly-immunopositive cell bodies, fibers and terminals in the nucleus accumbens. These studies provide, for the first time, a precise anatomic picture of the ways in which mu opiate activation by morphine and other drugs directly influences both ends of putative dopaminergic reward pathways in the brain.

Recent studies continued this laboratory's work characterizing the rat and human dopamine transporters that form the major brain cocaine receptors. In studies expressing mutants of this transporter, amino acids selectively contributing to cocaine affinity were identified in previous studies. In current work, the exact functional side-chains of these amino acids that contribute to cocaine-selectivity were identified by selective amino acid substitutions. These findings provide new and important clues in efforts to develop dopamine-sparing cocaine antagonist drugs.

Genetics Section, Lucinda Miner, Ph.D. (Acting Chief)

There are large individual differences among humans and animals in behavioral, physiological and toxicological responses to drugs of abuse. Transgenic mouse models with only modest regional overexpression of the dopamine transporter showed greater sensitivity to the rewarding properties of cocaine in the conditioned place preference paradigm.

QTL analyses have located candidate regions for the psychomotor stimulant effects of cocaine to segments of murine chromosomes 4, 5, 9 and 13, several of which have reasonable syntenic matches with human chromosomal segments. This information underscores the possibility that genetic determination of human interindividual differences in drug abuse vulnerability may be oligogenic, caused chiefly by effects of a limited number of genes.

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Program Activities

Historically Black Colleges and Universities Initiative

Under our HBCU initiative, two contracts were awarded in September to Howard University. The first, Drug Abuse Research Technical Assistance Project (DARTAP), awarded to Dr. Ernest Quimby in the Dept. of Sociology is to provide assistance to HBCUs in developing drug abuse researchers and research programs. The second awarded to Dr. William West in the College of Medicine is to establish a drug abuse research center on the campus. Both are three year awards with two option years.

NIH Office of AIDS Research

The Office of AIDS Research, NIH, has begun the planning process for FY1997. NIDA staff are participating in this process to identify programmatic initiatives for 1997 in the areas of etiology and pathogenesis, epidemiology and natural history, behavioral research, vaccine development, and information dissemination.

Using Case-Mix Adjusted Client Outcomes in a Quality Assurance System: The Methadone Treatment Quality Assurance System (MTQAS) Feasibility Study

The Methadone Treatment Quality Assurance System (MTQAS) feasibility study supported by NIDA and being conducted by the Research Triangle Institute, was designed as a performance-based reporting and feedback system for narcotic addiction treatment programs. Its purpose is to develop client outcome information that can be used to improve the quality of treatment services delivered. After a period of client level data collection, each of the 25 clinics participating in the MTQAS project were sent individualized feedback reports that gave them information about client characteristics and rankings on a variety of outcomes. With the increase in numbers and span of managed care organizations, the ability to collect and use outcome data will be crucial to substance abuse treatment agencies.

NIDA/NIAID Collaboration to Conduct WITS II Study

By means of a recent Memorandum of Understanding (MOU), NIDA and the National Institute of Allergy and Infectious Diseases (NIAID) have formalized their collaborative research efforts regarding the impact of HIV infection in pregnant, drug-using women and their offspring. NIDA will provide support for one of the sites (Columbia University) of the NIAID-supported Women and Infants Transmission Study II (WITS II), a multi-center study of factors related to maternal-infant HIV transmission and to disease progression among the women and their infected children. NIDA funds will enable continued development of Columbia as the core site for enhancing research on the drug use related aspects of the WITS II agenda, and will allow for continued follow-up of a cohort of pregnant HIV-infected women, the majority of whom are drug users.

Medications Development Research Centers

Five (5) P50 Medications Development Research Centers were funded in last quarter of 1994. Each award is for 5 years. Awards were made to the following sites: Yale University, The University of Minnesota, The University of Texas

at Houston, Columbia University, and the Los Angeles Addiction Treatment Research Center to study cocaine and opiate pharmacotherapies. Approximately 80% of the funds awarded under these grants was identified as dedicated for studying new cocaine therapies.

Contracts for Medicinal Chemistry Design and Synthesis

In September 1994, 6 contract awards were made to provide medicinal chemistry design and synthesis, with the aim of discovering a treatment agent for cocaine abuse, to MDD/NIDA. A total of 121 new compounds have been proposed from the 6 contracts. This program is somewhat unique in that it is a multi-award contract program which requires the offerors to provide 1 gram quantities of compounds and to work in certain R&D areas of medicinal chemistry development of specific interest to the Medications Development Division. However, once they have satisfied the direct requests of MDD, they are free to propose and pursue a range of structural approaches of their own choosing. This makes the program somewhat of a hybrid of the contract and grant mechanisms. The response to this solicitation was unusually large (11 received, 6 funded) and the productivity has been exceptionally high in terms of numbers of compounds received.

Biostatistical Support Center

A biostatistical support center has been established at Palo Alto VA/Stanford University under direction of Philip Lavori. The center will provide statistical consultation for NIDA VA sites, review data provided to MDD from clinical trials, and analyze and report safety and efficacy data to NIDA's Data Safety Monitoring Board.

Outpatient Study of Selegilene

An out-patient study of selegilene to reduce cocaine use has been reviewed/approved, an IND obtained, and the study begun under clinical trial agreement with Pharmavene, Inc. Four sites are participating (DCVA, Brentwood VA, Philadelphia VA, and UCSF). To date, 20 patients have been enrolled (expected to recruit 140 patients). No adverse events have been reported to date.

New Program Announcements/RFAs

On November 18, 1994, a program announcement (PA-95-005) was released on **"AIDS, Drug Abuse and Neurobiology."** The purpose of this program announcement is to enhance knowledge regarding drug modulation of the HIV infectivity and progression to AIDS by understanding how drug abuse affects HIV-related disease states.

The Program Announcement (PA 95-008) entitled **"Innovative Methods for Screening Drugs to Treat Cocaine and Opiate Abuse"** was published in the NIH Guide on November 25, 1994. The purpose of this announcement is to encourage research to develop innovative preclinical methods and model systems, for example, in rodents or non-human primates for the identification of potential treatment agents for the entire spectrum of cocaine and opiate abuse, from pre addiction through abstinence, relapse, and recovery. The methods may be based upon behavioral, neurophysiologic, neurochemical, or other approaches as long as a strong case is made that they will be relevant to human cocaine and opiate abuse and their pharmacologic treatment. These methods should be novel or they should significantly expand other undeveloped or unrecognized methods or models as tools for evaluating pharmacotherapies for drug abuse disorders.

On January 20, 1995, NIDA released a program announcement (PA 95-022) soliciting proposals for **"Drug Abuse Health Services Research and HIV/AIDS"** which will support a program of research on health services to drug abusers at high risk for HIV/AIDS at the client, program and service system level.

An addendum to the Behavioral Therapies Development Program Announcement (PA 94-078) was issued to encourage the incorporation of HIV risk reduction strategies as an integral component in the development of behavioral therapies for drug abuse and dependence treatment and to encourage the use of HIV risk measures and the provision of HIV testing and counseling to participating subjects.

NIDA, in conjunction with 7 other NIH Institutes issued a program announcement on "**Basic and Clinical Research on Sleep and Wakefulness"** (PA-95-014) on December 23, 1994 to stimulate, foster, and coordinate a wide range of basic and clinical studies on sleep and wakefulness as they relate to the missions of these Institutes.

On February 3, 1995, a program announcement entitled **"HIV Disease Progression in Drug Users"** was published in the NIH Guide. The purpose of this announcement is to stimulate research on the biological and behavioral factors influencing HIV disease progression in populations of drug users both in- and out-of drug abuse treatment, in order to facilitate prevention and treatment efforts. An RFA on "**Neuroscience Networks in Basic Drug Abuse Research"** (DA-95-001) was published on January 13, 1993. This initiative is intended to stimulate novel insights and innovative approaches in drug abuse research through the establishment of national, collaborative networks of investigators active in the neurosciences; to encourage and enable neuroscientists not currently focused on drug abuse research to explore applications of their expertise to the field; and to develop experimental prototypes of research enterprises which exploit emerging communication and information technologies to form "virtual research centers" in the drug abuse field.

An RFA entitled **"Human Basic and Clinical Neuroscience of Drug Addiction"** was published on February 3, 1995. This announcement is intended to stimulate research using noninvasive technologies to study the human brain and the etiology and consequences of drug abuse and to translate this information into novel prevention, diagnostic, and treatment strategies.

NIDA HIV/AIDS Counseling and Testing Policy.

The policy, which will require grantees and contractors to provide HIV preventive services, is in the final stages of Institute review.

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Congressional Affairs

104th Congress

The 104th Congress convened at noon on January 4. Like the House, the Senate remained in session through January -- forgoing the tradition of adjourning until after the President's late January State of the Union address.

The House opened its first session of the 104th Congress by electing Newt Gingrich (R-GA) Speaker by a vote of 228-202. Changes to House rules were then adopted with mostly bipartisan support:

1. limit to six consecutive years the length of time a Representative can be Chairman of a committee [committee chairman could serve unlimited terms during previous sessions] and to eight years for Speakers;
2. cut committee staffs by one-third;
3. ban proxy voting in committees;
4. require the Congressional Budget Office to use actual spending levels, not inflation-adjusted ones, in preparing budget estimates;
5. to open committee meetings to the public;
6. take away budgets, staffs and offices from 26 groups including the Democratic Study Group and caucuses of Black, Hispanic and female lawmakers; and
7. abolish the District of Columbia, Post Office and Civil Service, and Merchant Marine and Fishers committees.

The Senate's first session of the 104th Congress was opened by Senate Majority Leader Bob Dole (R-KS). He stated that Federal programs from A to Z will be placed under Senate scrutiny during the 104th Congress with the guiding question being: Is this program a basic function of a limited government, or is it an example of how government has lost faith in the judgments of our people and the potential of our markets? He also said "I believe that, more often than not, the answer to this question will justify less Federal involvement, fewer Federal rules and regulations, a reduction in Federal spending, and more freedom and opportunity for our States and our citizens".

In the House, some of the topics currently drawing most of the attention are revisions to the welfare system, proposals to prevent Federal unfunded mandates, and legislation for a constitutional balanced-budget amendment [all of which are part of the GOP Contract with America]. House Republicans have promised only a vote within 100 days on all 10 parts of the Contract. Even though many of the proposals included in the Contract have bi-partisan support, various divisions are emerging and it appears as if the [April 13] deadline will be difficult to meet.

Hearings/Briefings

Senator Carl Levin requested a briefing on medications development and other treatment issues. On December 20, 1994, NIDA Director, Dr. Alan Leshner presented this briefing. Other attendees included: Jackie Parker, legislative assistant to the Senator; Drs. Charles Grudzinskas and Frank Vocci, MDD; Mary McLaughlin, congressional affairs, SPB, OSPC; and Anne Houser of the NIH legislative office.

On January 17, Representative John Porter (R-IL), Chairman of the Labor/HHS Appropriations Subcommittee, visited NIH and brought some of his appropriations subcommittee members and staff. Subcommittee members accompanying the Chairman included Representatives Ernest Istook (R-FL), Henry Bonilla (R-TX), Dan Miller (R-FL), Jay Dickey (R-Ark), and Roger Wicker (R-Miss). Congressional staff included Marty Reiser (Miller), Brian Williams (Dickey), Eric Fox (Bonilla), Bill Duncan (Istook), Steve Morin (Pelosi), Christine Hamilston (Obey), and Kevin Burke of the Office of the Assistant Secretary for Legislation.

The NIH Office of AIDS Research (OAR) is developing plans for a series of congressional briefings on advances in AIDS research and treatment, with presentations by leading intramural and extramural experts in AIDS. A date had been set for the first briefing. However, it was postponed and no new date has yet been set.

Bills of Interest

By vote of 300 ayes to 132 noes, the House passed a Constitutional amendment calling for a balanced budget [H.J. Res. 1] **minus the controversial three-fifths majority requirement for tax increases.** The Senate continues to deliberate, with the Minority Leader, Tom Daschle (D-SD), joining the strong opposition headed by Bob Byrd (D-WV).

H.R. 11 - Introduced (as part of the Contract with America) by Representative Barbara Vucanovich, to strengthen the rights of parents. Included under Title IV of the bill is a provision (Section 401 which concerns family privacy protection) requiring Federal departments and agencies receive written parental consent before a minor submits to a survey, analysis or evaluation that reveals certain information. Specifically, the bill requires parental consent for the participation of a minor in any federally funded survey or analysis regarding (1) parental political affiliations; (2) any mental or psychological problems in the family; (3) family or individual sexual behavior and attitudes; (4) any illegal or self-incriminating behavior; (5) privileged relationships with lawyers, physicians or clergymen; (6) any household income information other than that required by law for federal program participation; (7) religious beliefs; and (8) appraisals of other individual with whom the minor has had a familial relationship. The outcome of this provision is of keen interest to researchers.

Representative Gerald Solomon (R-NY) has introduced a number of drug-testing bills including H.R. 153, a bill to amend the Public Health Service Act to establish Federal standards to ensure quality assurance of drug testing programs.

S. 18 - Introduced by Senator Arlen Specter (R-PA), entitled Health Care Assurance Act of 1995, which includes a provision authorizing $120M for FY 96 which authorizes the NIH Director to establish and implement a program for the conduct of clinical trials with respect to new drugs and disease treatments determined to be promising to the Director. In making this determination priority is to be given to those drugs and disease treatments determined (l) to be most costly to treat; (2) to have the highest mortality; or (3) to affect the greatest number of individuals. It also would establish a trust fund for medical treatment outcomes research. It would be funded through taxes relating to health insurance policies. These amounts are to be made available to the DHHS Secretary to pay for research activities related to medical treatment outcome.

S. 38 - Introduced by Senator Orrin Hatch (R-UT), new Chairman of the Judiciary Committee, to amend the Violent Crime Control and Law Enforcement Act of 1994. Section 701, Elimination of Ineffective Programs, repeals certain subtitles, under Title III which include in part, Residential Substance Abuse Treatment for State Prisoners. It also repeals Title V, Drug Courts, and Title XXVII, Presidential Summit on Violence and National Commission on Crime Prevention and Control.

S. 59 - Introduced by Daniel Inouye (D-HI), to amend the Public Health Service Act to provide health care practitioners in rural areas with training in preventive health care, including both physical and mental care.

S. 142 - Introduced by Senator Nancy Kassebaum (R-KS), new Chairman of the Labor and Human Resources Committee, to strengthen the capacity of state and local public health agencies to carry out core functions of public health, by eliminating administrative barriers and enhancing State flexibility.

Health Care Reform

Though there was no mention of health care reform included in the GOP "Contract with America," the Republicans may take up health care reform during this Congress.

New Commerce Committee Chairman, Thomas Bliley (R-VA), has said that he hopes to get a modest health care reform bill out of the House by the end of the year. He favors a bill similar to the proposal introduced during the

103rd Congress (as H.R. 3955) by the new Health & Environment Subcommittee Chairman Michael Bilirakis (R-FL). This proposal would have, in part: assured portability of health insurance coverage, allowed people to remain insured if they change jobs, but would not protect people who lose their jobs; and limited insurance companies' ability to deny coverage to applicants with pre-existing medical conditions.

On the Senate side, both Senate Finance Committee Chairman Bob Packwood (R-OR) and Majority Leader Bob Dole (R-KS) have had a longstanding interest in health care reform. Senator Dole said that he and Packwood would offer a scaled-back version of the bill they proposed in the 103rd Congress.

In this first session of the 104th Congress, Senator Phil Gramm (R-TX) has introduced S. 121, to guarantee individuals and families continued choice and control over their doctors and hospitals, to ensure that health coverage is permanent and portable, to provide equal tax treatment for all health insurance consumers, to control medical cost inflation through medical savings accounts, to reform medical liability litigation, and to reduce paperwork. Senator Tom Daschle (D-SD) introduced S. 7 to provide for health care reform through health insurance market reform and assistance for small business and families.

Other Items of Interest

Indirect Costs

Representatives from some of the nation's largest research institutions are said to be intensely concerned about possible limitations on Federal reimbursements of university "indirect costs." It has been reported in the specialty press that universities also fear reductions in indirect costs as part of any budget rescission package.

Administration's Budget

President Clinton is scheduled to submit his budget on February 7.

War on Drugs

Included in the Extensions of Remarks in the January 4 Congressional Record, is a statement by Representative Gerald Solomon (R-NY) that a war on drugs be re-declared. He said that the "Republican-controlled Congress will play a major role in the war on drugs. . .As a result of the Clinton administration's half-hearted effort to fight the drug war we have witnessed a dramatic increase in the use of drugs." He went on to cite statistics from the Partnership for a Drug-Free America and further stated that additional legislation was necessary. Some of this legislation included a bill to deny Federal benefits upon conviction of certain drug offenses, a bill to require mandatory drug testing for all Federal job applicants, and a bill to prohibit Federally-sponsored research involving the legalization of drugs.

Methadone Recommendations

The Institute of Medicine, an arm of the National Academy of Sciences, convened drug experts to study the issue of methadone. In a report released in late December, the panel concluded that methadone significantly reduces heroin use and related crime and AIDS infection transmitted by infected needles. It urged the DHHS to relax methadone restrictions and require the States to follow the rules. The report states:
"Current policy. . .puts too much emphasis on protecting society from methadone and not enough on protecting society from the epidemics of addiction, violence and infectious diseases that methadone can help reduce."

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International Activities

Richard Millstein, Deputy Director, represented NIDA at the Israel-U.S. Binational Working Group on Adolescent Health in November. Three major themes of the meeting addressing adolescent risk behaviors were: injuries; substance use (including alcohol, tobacco and drugs); and sexual behavior. In post-symposium discussions, the group chaired by Mr. Millstein recommended the establishment of a collaborative working group to develop a joint research protocol for a longitudinal study of resiliency and protective factors in preventing or delaying the initiation and progression of substance abuse.

Through a Memorandum of Agreement between the Bureau of Oceans and International, Environmental, and Scientific Affairs (OES), Department of State, and NIDA, plans have been initiated to host a joint U.S.-China symposium on research on drug abuse and drug-related HIV/AIDS. Support has also been provided by the Bureau of International Narcotics Matters, Department of State. Dr. Patricia Needle, International Program Acting Director, visited China in October for discussions with the Ministry of Health, Chinese Academy of Sciences, Chinese Academy of Traditional Medicine and other agencies, in preparation for the meeting, tentatively scheduled for August 1995 in Beijing.

Research cooperation has already been initiated as outcomes from the Second Regional Central Europe/U.S. Symposium on Drug Dependence held in Poland last summer. NIDA grantees Dr. Steven Specter, Dr. Clyde McCoy, and Dr. Burt Sharp have begun formal discussions and/or implemented plans for collaborative research with Polish and Russian drug abuse scientists.

As part of its role as a WHO Collaborating Center, NIDA provided relevant medical and scientific information on eight psychotropic compounds being considered by the WHO Expert Committee on Drug Dependence for international drug control pursuant to the 1971 Psychotropic Convention. These compounds were aminorex, brotizolam, etryptamine, flunitrazepam, mesocard, methcathinone, zipeprol, and triazolam. NIDA also provided additional information on other drugs being considered for future WHO review. Dr. Yng-shiuh Sheu, Division of Clinical and Services Research (DCSR), prepared the critical review of these compounds and also served as temporary adviser to the Secretariat at the 29th annual meeting in Geneva, Switzerland during September.

During November, NIDA sponsored an International Work Group meeting on postgraduate medical education in addiction in collaboration with New York University. Dr. Dorynne Czechowicz, DCSR, and Dr. Marc Galanter, New York University, organized and co-chaired the meeting. Objectives were to develop ways to disseminate and enhance the utilization of drug abuse treatment research findings to improve medical education and clinical practice and to facilitate on-going communication between the International Working Group and NIDA.

Dr. Maria Majewska, Medications Development Division (MDD), has established research collaborations with scientists and pharmaceutical companies in Germany, Belgium, Poland, Japan, Netherlands, France, and Hungary, testing a variety of compounds as potential medications for cocaine addiction. She also participated in the International Conference on Steroids in Dallas.

The Medications Development Division announced continued CRADA collaboration with Reckitt & Colman, Ltd. and its U.S. subsidiary in development efforts for buprenorphine and for buprenorphine-naloxone combination products.

Drs. Charles Grudzinskas, Carol Hubner and David McCann, MDD, visited Basel, Switzerland in September to meet with representatives of Sandoz Research Institute, Ciba-Geigy, and Hoffman LaRoche and to make formal presentations of NIDA's Medications Development Program (preclinical and clinical cocaine and opiate). These

companies were selected because they are very active players in the development of drugs to treat CNS disorders. The majority of their research efforts in this area are conducted by their European divisions, and they were likely to have compounds of interest to the Cocaine Treatment Discovery Program and the Opiate Treatment Discovery Program for preclinical efficacy testing. It was also hoped that they could have potential clinical candidate compounds for evaluation by MDD.

Mr. Nicholas Kozel, Division of Epidemiological and Prevention Research (DEPR), attended the 15th International Federation of Non-Government Organizations Conference in Hong Kong in December and participated in a symposium on "Community-Based Epidemiologic Approaches and their Use in the Development of Prevention, Treatment and Public Health Interventions."

The semi-annual meeting of NIDA's Community Epidemiology Work Group (CEWG) held in New Orleans in December included a special program focus on the epidemiology of drug abuse among selected Caribbean island countries. In conjunction with the CEWG, DEPR staff (Dr. Zili Sloboda, Nicholas Kozel, Moira O'Brien) and representatives from the World Health Organization, the Organization of American States and the Pan American Health Organization met to discuss the establishment of a periodic International Drug Abuse Epidemiology Network Conference. Moira O'Brien, then International Office, and Dr. Ralph Tarter, University of Pittsburgh, traveled to Turkey in September to provide technical assistance in the development of a strategy for the assessment and monitoring of drug abuse in Turkey and to explore opportunities for binational research cooperation.

NIDA's International Program and DEPR, in conjunction with the Department of State, conducted a workshop with drug abuse researchers from Bolivia, Colombia, Ecuador, Peru and Venezuela in Rockville during September. Participants summarized epidemiologic research, identified research priorities and generated recommendations for follow-up collaborative activities.

Dr. Steven Goldberg, Intramural Program, ARC, served as a guest editor for a December 1994 supplement to Clinical Pharmacology & Therapeutics" titled "Abuse Liability of 1-Deprenyl: Examination of the Clinical and Preclinical Pharmacological Data." This special publication was a record of the proceedings of a special symposium held at the Ninth General Meeting of the European Society for Neurochemistry in 1992.

As a result of Indo-US collaboration projects, a number of conferences were organized by Dr. Rao S. Rapaka (NIDA) and Dr. B.N. Dhawan (Central Drug Research Institute (CDRI, India, 1991) at several research institutes in India. A number of NIDA grantees participated in these conferences and the proceedings of the conferences have been recently published as a monograph entitled "Recent Advances in the Study of Neurotransmitter Receptors" (1994), edited by Drs. B.N. Dhawan, R.C. Srimal, R. Raghubir (CDRI, India) and Dr. Rao S. Rapaka.

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Meetings/Conferences

NIDA Technical Reviews

A technical review entitled **"Laboratory Behavioral Studies of Vulnerability to Drug Abuse"** co-chaired by Dr. Cora Lee Wetherington of the Behavioral Sciences Research Branch, DBR, and Council member, Dr. John Falk was held August 2-3, 1994 in Bethesda, MD.

Other Meetings

Constituency Groups Meeting

NIDA's Office of Science Policy and Communications convened a one and a half day meeting of constituent organizations on November 21 and 22 at Westfield's Conference Center in Chantilly Virginia. The meeting, chaired by Dr. Alan Leshner and Mr. Richard Millstein, was convened for the Director to solicit advice on NIDA's research agenda from senior representatives of these groups. Dr. Leshner stated in his remarks that, " One of my top priorities as the new Director of NIDA is to obtain the advice of the users of our research." Some 36 organizations sent one or two representatives, in most cases the President and/or the Executive Director to this, the first in a series of meetings with constituent organizations. A report of the deliberations and recommendation is being prepared and should be finalized shortly.

Treatment Researchers Meeting

On October 24, 1994, Dr. Leshner, in conjunction with NIDA DCSR staff, convened a group of eminent treatment researchers to discuss new and innovative strategies that have shown promise, both within and outside the drug abuse and addiction field. The primary objective of these discussions was to generate creative ideas that could lead to quantum improvements in drug addiction treatment.

Prevention Researchers Meeting

On January 11, 1995, Dr. Leshner convened a meeting with prominent drug abuse prevention researchers to discuss innovative and exciting new approaches to drug abuse prevention that should be considered in future NIDA prevention research program development. The charge to the group was to explore uncharted, yet promising new research areas and propose novel and salient prevention theories to test, highly creative prevention interventions to assess, and challenging new research paradigms to pursue in future research.

AIDS Researchers Meeting

NIDA hosted a workshop on January 19, 1995 on its AIDS-related research. Participants included representatives of basic, clinical, and applied research as well as other NIH Institutes, the Office of AIDS Research, and the American Foundation for AIDS Research.

The Role of Resilience in Drug Abuse, Alcohol Abuse, and Mental Illness

Although resilience to drug involvement is a critical phenomenon, it has received little attention in research and intervention efforts. To address some of the important issues surrounding resilience, on December 5 and 6, 1994, the National Institute on Drug Abuse, in collaboration with the Center for Mental Health Services, the Center for Substance Abuse Prevention, the National Institute of Alcohol Abuse and Alcoholism, the National Institute of Mental Health, and the National Association for Children of Alcoholics, jointly sponsored a conference on **"The Role of Resilience in Drug Abuse, Alcohol Abuse, and Mental Illness"**. The meeting brought together researchers,

educators, and practitioners in the field who considered the research and applied experiences related to different perspectives on resilience. The conference covered five separate areas: Models and Definitions of Resilience, Measurement of Resilience, What Resilience Predicts, Interventions in Resilience, and Applications of Resilience. Comprehensive literature reviews in these five separate areas were written and presented by experts and discussed by panels of experienced researchers and practitioners; the papers and discussions will be published in the next year.

Promising Prevention Program Models
NIDA sponsored a 1-day meeting on October 3, 1994, to increase awareness about three prevention program models and to provide an opportunity for prevention practitioners to dialogue with researchers, program administrators and program participants on implementation and evaluation issues. The more than 150 practitioners, who attended the forum, were also briefed on the new prevention research dissemination and application package and had an opportunity to participate in a community readiness exercise.

Drug Addiction Research and the Health of Women
A NIDA-sponsored conference entitled **"Drug Addiction Research and the Health of Women"**, held September 12-14, 1994 in Tysons Corner, VA, was intended to assess the current state of scientific knowledge about addiction and women's health. In addition to showcasing what is known about women and drug abuse, NIDA hosted the conference to identify the many gender related issues that the field of drug abuse research needs to address to meet the health needs of women. For two and a half days, scientists and practitioners from a wide range of disciplines presented gender-related findings from epidemiologic, basic, clinical, and health services research studies and discussed the implications of these findings for the prevention and treatment of drug abuse, addiction, and related diseases such as HIV/AIDS among women.

Recent Special Populations Meetings
On January 18-19, 1995 NIDA's Special Populations Office convened meeting of research scholars, federal employees, and others to discuss strategies to improve drug abuse research training for ethnic minorities.

NIDA's Special Populations Office held a meeting of the African American workgroup (to discuss drug abuse research and research training concerns of African American populations) on Sept. 26-27, 1994.

NIDA cosponsored a meeting entitled **"AIDS and African Americans: Community-based Approaches"** part of their series, Black Survival 2000 at the University of Maryland (College Park), September 28-30, 1994.

On January 11-12, 1995 NIDA's Hispanic Drug Abuse and AIDS Research and Technology Transfer Workgroup met in Rockville, MD to develop an Action Plan for Policy Report Recommendations.

Boston Museum of Science Exhibit
NIDA, the Division on Addictions at Harvard Medical School, and the Boston Museum of Science, hosted the opening of a new museum exhibit, **"Changing Your Mind: Drugs in the Brain"** on November 29, 1994. Dr. Alan Leshner spoke on the importance of these types of exhibits in serving to enlighten the public about addiction and drug abuse as a public health problem and to teach our children about science. The museum project, part of NIDA's Science Education Program, was developed with primary funding from a NIDA Science Education Drug Abuse Partnership Award from the Office of Science Policy and Communications. After a stay of approximately one year at the Boston Museum, the exhibit will be available to travel throughout the United States.

Family-Focused Therapy Meeting
On January 12 and 13, 1995, the Treatment Research Branch, Division of Clinical and Services Research, held a meeting on family-focused behavioral therapy development. Experienced clinical investigators in this area reviewed accomplishments of past NIDA-supported studies and suggested future research initiatives. The meeting was co-chaired by Drs. Elizabeth Rahdert and Jack Blaine.

Stage 1 Behavioral Therapy Development Program Research Projects
Drs. Lisa Onken and Jack Blaine chaired a meeting of the Principal Investigators of NIDA and NIMH-funded "Stage 1" behavioral therapy research projects on January 24 and 25. Stage 1 projects involve the development, manualization, and pilot testing of new and innovative behavioral therapies. The goal of the meeting was to further clarify and define Stage 1 and to exchange ideas in order to maximize the productivity of existing Stage 1 research projects. The PIs at the meeting are essentially "pioneers" in that they are the first ever to receive Federal support for early behavioral therapy development projects. One of the purposes of this meeting was to provide direction and structure for the evolving behavioral therapy research field.

Dr. Timothy P. Condon, Acting Deputy Director, Office of Science Policy and Communications, was invited to address the Research Training Committee of the American Psychiatric Association. Dr. Condon discussed with the Committee

NIDA's research training opportunities and novel ways to increase the training of psychiatrists in drug abuse research.

In December, 1994, Dorynne Czechowicz, M.D., DCSR presented data from the recently completed MTQAS Phase I field trial at the State Systems Development Conference in Seattle, Washington and met with 10 state methadone authorities in collaboration with CSAT to address ways in which performance based outcome data can be integrated into existing quality assurance systems to improve the quality of care in narcotic addiction treatment programs.

Dr. Dorynne Czechowicz and Dr. Jag Khalsa presented a workshop on NIDA's research programs on Medical/Health Consequences and Prescription Drug Use/Abuse, respectively, at a recent AMERSA meeting, October 1994, Washington, DC.

Dr. Lula Beatty moderated a session on Substance Abuse Disorders, at the "Second Annual conference on Psychopathology, Psychopharmacology, Substance Abuse and Culture" in Los Angeles, October 20, 1995.

Dr. Lula Beatty presented a session on, **"Future Directions in Drug Abuse Research on Underserved Populations"** at the "Second Annual Conference on Psychopathology, Psychopharmacology, Substance Abuse and Culture" in Los Angeles, October 20, 1995.

Dr. Lula Beatty presented a session on **"African Americans and Drug Abuse: Research Needs"**, at North Carolina Central University, October 26, 1994, for MARC students and others.

Dr. Lula Beatty presented a session on Drug Abuse Research Needs in African American Communities and Research Opportunities at NIDA, for the Association of Black Psychologists, DC chapter, November 30, 1994.

Dr. Lula Beatty presented a session on Drug Abuse Research Opportunities at NIDA for psychiatry staff, Howard University Hospital, November 30, 1994.

Dr. Lula Beatty served on the African American Women and Family Life panel and gave a presentation entitled **"Family and Love in the Lives of African American Women"** at the 1st conference of African American Women's Research Institute, Howard University, November 18, 1994.

George Uhl, Acting Scientific Director and Chief of the Molecular Neurobiology Branch, was invited to speak at the Wellcome Trust meeting on Substance Abuse near London, UK; at the Japanese Society for Neuropharmacology in Okayama, Japan; the Movement Disorders Society in Orlando, FL; the Society for Neuroscience in Miami Beach, FL; at Osaka, Okayama, Virginia Commonwealth, and Johns Hopkins Universities; and at Dupont-Merck and Guilford Pharmaceutical companies.

Dr. Uhl worked with the CPDD to establish a half-day symposium and dinner celebrating the 60th anniversary of the Addiction Research Center. The predecessor of NIDA's Division of Intramural Research opened in Lexington, KY in May, 1935.

David A. Gorelick, M.D., Ph.D., DIR, ARC presented psychiatry grand-rounds at West Los Angeles VA Medical Center, and George Washington University.

Jonathan Katz, Chief of the Psychobiology Section, Behavioral Pharmacology Branch at the Addiction Research Center, was invited to present a paper entitled: **"Behavioral Pharmacology of Cocaine and Treatments for Cocaine Abuse"** at the *Symposium on Addictive Behavior* held as part of the Annual meeting of the American Psychological Association, Science Weekend Program, 1994.

Sari Izenwasser, a Senior Staff Fellow in the Psychobiology Section, was invited to present a seminar entitled: **"Neurochemical Mechanisms of Tolerance and Sensitization to Cocaine."** Department of Pharmaceutical Sciences, School of Pharmacy, University of Maryland at Baltimore.

Dr. Edythe London participated in round-table discussions at the Wellcome Frontiers Meeting on **"The Biological, Social and Clinical Bases of Drug Addiction"** in Broadway, England, Sept. 16-21, 1994.

Dr. Edythe London presented lectures on brain imaging in studies of substance abuse at University of Maryland, Towson State University, and Johns Hopkins Medical Institutions, Baltimore, MD.

Dr. Edythe London presented a lecture entitled, **"Functional Assessment of Opiate Actions by Brain Imaging"** at the eleventh annual Einstein Symposium in Psychiatry entitled "Opiate Addiction and its Treatment: Impact of Science on Clinical Practice, New York, NY, Nov. 4, 1994.

Drs. Bruce Vaupel and Edythe London attended a NIDA Technical Review on **"The Role of Glutamatergic Systems in the Development of Opiate Addiction"**, Gaithersburg, MD, Oct. 17-18, 1994. Dr. Vaupel presented findings

from NDAS on the use of inhibitors of nitric oxide to antagonize the opioid withdrawal syndrome. Dr. London served as a discussant of the clinical implications of the presented research for the treatment of opiate addiction.

Dr. Edythe London presented a lecture entitled, **"Positron Emission Tomography in Studies of Substance Abuse"** to the German Society for Research on Drugs and Addiction, Frankfurt, Germany, Dec. 2-4, 1994.

Drs. Steven Grant and Edythe London attended the American College on Neuropsychopharmacology held in San Juan, PR, Dec. 12-16, 1994, where they presented recent findings of a study aimed at mapping the neuroanatomical substrates of cocaine craving in human volunteers, using PET scanning.

Drs. Rao S. Rapaka (NIDA), Nora Chiang (NIDA) and Billy Martin (Virginia Commonwealth University, Richmond, VA) organized a symposium entitled **"Metabolism, Pharmacokinetics and Pharmacodynamics of Drugs of Abuse"** on November 4-5, 1994, in San Diego, CA. It is expected that proceedings of the meeting will be published as a NIDA Research Monograph.

Dr. Charles Grudzinskas, and Dr. Frank Vocci, of the Medications Development Division, attended the **Third Annual State Systems Development Conference** in Seattle Washington December 6-8, 1994, where they conducted a workshop discussing the role of pharmacotherapeutic interventions in drug abuse treatment, and describing medications currently approved or under development. Mr. Joel Egertson joined Drs. Grudzinskas and Vocci in meetings with state officials, and staff of the Center for Substance Abuse Treatment (CSAT), to discuss issues of how to expand the use of current and future medications.

On September 23, 1994, Mr. Robert Walsh, Dr. Lynda Erinoff and Dr. Frank Vocci co-hosted a group of neurologists and neurosurgeons in a workshop discussing neurological measures and standardization of ataxia for a draft protocol of the compound, ibogaine.

On December 12, 1994, Drs. Christine Ollo and Barbara Schwartz of the NIDA/VA unit at the D.C. Veterans Administration Medical Center and Dr. Frank Vocci co-hosted a workshop discussing neuropsychological and cognitive measures to be incorporated into a draft Phase I protocol for ibogaine.

NIDA's Medications Development Division (MDD) hosted a meeting with the Italian pharmaceutical company "Pharmacia" on Jan 31, 1995 to discuss its Cocaine Treatment Discovery Program and request submission of potential candidate compounds for testing.

Dr. Frank Vocci presented at an advisory meeting of a CSAT workshop on opiate addiction treatment improvement on November 29, 1994.

Dr. Bennett Fletcher was a panel speaker on **"Financing of Drug Abuse Treatment: Impact on Service Delivery"**, at the CSAT State Systems Development Program meeting, in Seattle, WA, held December 6-8, 1994.

Dr. Peter Delany participated in a Therapeutic Communities of America Planning Conference on Substance Abuse and Youth, held January 4-6, 1995.

Dr. Peter Delany made a presentation to the American Corrections Association on **"Developing a Working Relationship Between NIDA and the Corrections Community,"** on January 14, 1994.

Dr. Frank Tims chaired a panel on NIDA's Health Services Research portfolio at the Annual Meeting of the American Public Health Association, November 1-4, 1994.

Ms. Carol Cowell co-presented a paper, **"Dynamic Measures of Drug Treatment System Capacity"** at the Annual Meeting of the American Public Health Association, November 1-4, 1994.

Dr. Bennett Fletcher chaired a panel on **"Mediators of Client Change in Substance Abuse Treatment,"** at the annual meeting of the American Evaluation Association, November 2-6, 1994.

Dr. Elizabeth Rahdert presented a paper entitled **"Reliability and Validity Evidence for the Problem Oriented Screening Instrument for Teenagers (POSIT),"** at the October 1994 meeting of the American Public Health Association held in Washington, D.C. Reported results were from a NIDA-supported validation study that demonstrated the psychometric properties of the POSIT, a drug-related multi-problem screening tool designed specifically for use with adolescents, 12-19 years of age.

At the 1994 Annual Meeting of the American Public Health Association in Washington, DC, the week of October 30-November 3, Dr. James Colliver, DEPR, presented a paper entitled **"Factors Associated with Discontinuation of Marijuana and Cocaine Use"**; Andrea Kopstein, DEPR, presented a paper entitled **"The Association Between**

Drug Use and Aggressive and Violent Behaviors"; Arthur Hughes, DEPR, presented **"Trends in the Number of Drug-Related Emergency Room Episodes"**; Marc Brodsky, DEPR, presented **"Relative Risk of Drug Use and Dependence;"** and Elizabeth Lambert, DEPR, gave a presentation entitled **"The Washington, D.C. Metropolitan Area Drug Study (DC*MADS): Overview and Challenges."** Ms. Lambert also participated in a poster presentation entitled **"Comparison of Illicit Drug Use Among the Homeless and the Household Populations in the Washington, D.C. MSA, 1991".**

Andrea Kopstein and Dr. William Bukoski participated in a December 14, 1994 meeting designed to develop new recommendations for goals and objectives for the 1995 Drug Control Strategy. At this meeting, sponsored by the Office of National Drug Control Policy, participants also reviewed last year's long-term goals and two-year objectives.

On November 29, 1994 Arthur Hughes presented findings from the National Pregnancy and Health Survey at the NCADI In-Service Training Seminar.

On December 20, 1994 Andrea Kopstein presented findings from the 1994 Monitoring the Future Study at the NCADI In-Service Training Seminar.

On September 21, 1994 Arthur Hughes presented findings on NIDA's survey research at the Louisiana State Epidemiology Workgroup in New Orleans.

Nick Kozel, DEPR, chaired the semi-annual meeting of NIDA's Community Epidemiology Work Group (CEWG) which was held on December 13-16 in New Orleans.

Richard H. Needle, Ph.D., M.P.H., served as a panelist at the Kaiser Science Committee meeting, **"HIV Prevention: Looking Back, Looking Ahead,"** sponsored by the Center for AIDS Prevention Studies at the University of California in San Francisco on October 6-7, 1994.

Richard H. Needle, Ph.D., M.P.H., gave a presentation on NIDA's prevention research in a session entitled **"Prevention Research: Meeting the Challenges,"** at the NIAID/NIH Conference on Advances in AIDS Vaccine Development in Reston, Virginia, on November 10, 1994.

Richard H. Needle, Ph.D., M.P.H. served as a discussant on a panel entitled **"Contributions of Anthropological Research to Successful HIV/AIDS Interventions"** at the American Anthropological Association Annual Conference in Atlanta, Georgia on December 2, 1994.

Dr. Needle was also a panelist in a Conference workshop session on Federal funding, sponsored by the AIDS and Anthropology Research Group.

Peter Hartsock, Ph.D., DEPR, and Don Vereen, M.D., M.P.H., OD, represented NIDA at the White House Conference, **"Meeting the Challenge: Health, Safety, and Food for America,"** on November 21-22, 1994. During the conference, emphasis was given to the significance of epidemiology and prevention for understanding and reducing substance abuse, HIV/AIDS, and violence.

Peter Hartsock, Ph.D., represented NIDA at the Seniors Meeting of the Interagency Arctic Research Policy Council on December 8, 1994. The meeting focused on preparation of the biennial report to Congress on Arctic research accomplishments and new initiatives, which include establishment of a State Epidemiologic Work Group (SEWG) in Alaska.

Peter Hartsock, Ph.D., represented NIDA at the second meeting of the New Mexico SEWG, Las Cruces, New Mexico on October 24-25, 1994. The purpose of the meeting was to solidify the SEWG process begun under NIDA auspices in New Mexico last July and to develop a New Mexico-Mexico border surveillance and research capability for drug abuse and related correlates, including HIV/AIDS and violence. Special representation and assistance at the meeting came from the U.S.-Mexico Border Health Association.

Helen Cesari, M.Sc., DEPR, served as a panelist on **"Training Guidelines on Women and Minorities in Research"** during the extramural training sessions on inclusion guidelines, conducted by the NIH Office of Research on Women's Health on September 28, 1994.

Elizabeth Lambert, M.Sc., DEPR, represented NIDA at the Maryland SEWG at the University of Maryland in College Park on November 4, 1994. The semiannual Maryland SEWG has expanded so that every county in Maryland is now represented; the SEWG agenda includes topics of special interest to Marylanders, such as alcohol and drug use among shock trauma patients admitted to the University of Maryland's Shock Trauma Center and longitudinal research on psychoactive drug use in specific counties.

Arnold Mills, M.S.W., DEPR, served as a panelist in the Nationwide Evaluation of TASC Programs Workshop at the 46th Annual Meeting of the American Society of Criminology, in Miami, Florida November 8-12, 1994. Among others, panelists included NIDA grantees Duane McBride, Ph.D. and James Inciardi, Ph.D.

Dr. Lana Harrison and Andrea Kopstein coauthored a paper entitled **"A Twenty Year Perspective on Adolescent Drug Use"** which was presented at the American Society of Criminology meeting.

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Director's Report to the National Advisory Council on Drug Abuse
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Media and Education Activities

Press Conferences/Briefings

NIDA has participated in the following Press Conferences/Briefings since the September 1994 Advisory Council meeting:

- NIDA coordinated a press conference for the release of the 1994 Monitoring the Future Study (MTF). The data were released on December 12, 1994, by HHS Secretary Donna Shalala, ONDCP Director, Lee Brown, Education Secretary, Richard Riley and Lloyd Johnston, Principal Investigator for MTF.
- NIDA assisted in press coverage for the November 29, 1994 opening of a NIDA-funded exhibit at the Boston Museum of Science. Dr. Leshner and Dr. David Ellis, Museum of Science Director, Dr. Steven Hyman, Director of Addictions, Harvard Medical School, and Dr. Bertha Madras, the director of the project participated in the opening ceremony. The exhibit, **"Changing Your Mind: Drugs in the Brain,"** is a multimedia project consisting of a free-standing exhibit with artifacts and information on various aspects of drugs; a 25-minute play that describes the lives of two drug users and shows what cocaine does to the brain; and workstations with an interactive computer program that includes detailed information on neurobiology, treatment, and drug users.
- On September 27, 1994, NIDA and the Johns Hopkins Medical Institutions held a seminar for science writers. The seminar, **"Understanding Addiction,"** featured a team of experts from NIDA and Hopkins who presented knowledge on the biological and psychological nature of addiction, including such topics as scientifically defining craving, the biology of addiction, and treating drug addiction with other drugs.
- On September 12, 1994, NIDA held a press briefing to release findings from the National Pregnancy and Health Survey. The survey found that approximately 221,000 or 5.5 percent of the 4 million women who gave birth in 1992 had used some illicit drug during pregnancy. Dr. Alan Leshner and Dr. Loretta Finnegan spoke at the press briefing, which resulted in significant press coverage on the survey.

Media Advisories

The NIDA Press Office has issued the following Media Advisories in the past several months:

- NIDA Releases Data on Practices of Chronic Drug Abusers (November 25, 1994) - Announcing release of the publication entitled **Drug Procurement Practices of the Out-Of-Treatment Chronic Drug Abuser**.
- NIDA Issues Findings on HIV Risk Among Drug Users and their Partners (November 23, 1994) - Announcing the release of **Research Monograph 143: Context of HIV Risk Among Drug Users and Their Sexual Partners**.
- NIDA Survey Examines Extent of Women's Drug Use During Pregnancy (September 6, 1994) - Announcing the release of findings from the **National Pregnancy and Health Survey**
- NIDA Drug Use Surveys: Experts Seek to Improve Accuracy (August 26, 1994) - Announcing a NIDA Technical Review on **"The Validity of Self-Reported Drug Use: Improving the Accuracy of Survey Estimates."**
- NIDA Symposium on 20 Years of Progress and Discovery (August 18, 1994) - Announcing a full-day symposium covering the research on the neuroscience of addiction, the nature and extent of drug addiction and abuse, and

prevention and treatment of drug problems.

NIDA hosted its annual information exchange meeting with the Executive Committee of the National Prevention Network (NPN) December 1 and 2, 1994. The agenda included briefings by the NPN on committee activities and the annual research conference, and by NIDA staff on the following programs: Prevention Research Branch, Division of Epidemiology and Prevention Research, Public Information Branch, and Office of Special Populations. Additionally, several hours were devoted to receiving the NPN's comments on the draft of the *Prevention Research Dissemination and Application Package*. The NPN also agreed to aggressively market NIDA's drug abuse and AIDS campaign materials as well as the research dissemination videos for practitioners.

The Union of Pan Asian Communities (UPAC) is developing culturally and linguistically appropriate drug prevention flyers for the following communities: Vietnamese, Chinese, Cambodian, Laotian, Hmong, and Thai. Each flyer (a folding postcard with a map of the appropriate country on the front) contains basic information on the health consequences of alcohol, tobacco, and other drugs of abuse.

Videos

The following videotapes have been produced and released in recent months (or are soon to be released):

- **"Drug Abuse Treatment in Prison - A New Way Out."** This 27-minute video, based on NIDA supported research, presents two approaches to prison-based treatment of drug abusers in State and Federal prisons. One is a modified Therapeutic Community approach and the other is a form of cognitive therapy. Each is linked to transitional care programs in the community and stresses the importance of a continuum of care from institutionalization to freedom.
- A shorter 10-minute version of the Prisons video has also been prepared for policymakers (e.g., legislators, corrections officials, etc.), and it will be accompanied by a companion manual. The manual will discuss such issues as cost-effectiveness and implementation.
- **"Drug Abuse and HIV - Reaching Those at Risk"** is a 16-minute video, based on the outreach/intervention models developed from NIDA's National AIDS Demonstration Research. The video focuses mostly on the indigenous leader outreach model, developed at the University of Illinois at Chicago, to demonstrate the common elements of outreach and intervention with injection drug abusers who are not in treatment. NIDA plans to market it to public health, as well as drug abuse treatment providers.
  These videos are soon to be released:
- A video on LAAM for methadone maintenance providers, clients and their families. This video will explain how LAAM works and how it can serve as an additional agonist medication to methadone in the treatment of heroin addiction.
- A video, targeted at health care providers and child development personnel, on the effects of drug abuse on pregnant and postpartum women, their babies, and the mother-child relationship.

NIDA Exhibits

In the past several months NIDA has exhibited at the following meetings:

- **Third Annual State Development Program**; December 6-8; Seattle, Washington
- Meeting of the **Association of Medical Education and Research in Substance Abuse (AMERSA)**; November 17-20; Bethesda, Maryland
- Conference of the **American Public Health Association (APHA)**; October 30-November 3; Washington, D.C.
- Community Anti-Drug Coalition of America's **National Leadership Forum**; October 27-29; Washington, D.C.
- Annual Meeting of the **National Association of Social Workers (NASW)**; October 19-22; Nashville, Tennessee
- NIDA's **20th Anniversary Symposium**, September 22, NIH Campus

Office of AIDS Research's **National Minority HIV/AIDS Conference**, September 15-18, Washington, D.C.

- NIDA's Conference on **Drug Addiction Research and the Health of Women**, September 12-14, Tysons Corner, Virginia
- **Meeting of the Society for Neuroscience**, November 13-18; Miami Beach, Florida
- NIDA's presence at the annual meeting of the Society for Neuroscience has increased progressively over the past decade. Originally, the Institute had a small cardboard sign with "NIDA Monograph Series" written on it. This was placed on a small table in the exhibit area along with a few monographs and some program announcements. This year NIDA greeted the neuroscientists (and tropical storm "Gordon") with a 40 foot long exhibit booth, an illuminated backdrop highlighting significant NIDA research areas, a demonstration of our video series, monographs, buttons, and program announcements. In addition, there was a special NIDA Anniversary Poster Session as well as several scientific sessions specifically focused on drug abuse research.

Planned Meetings

NIDA will be co-sponsoring a workshop on sterile needles and syringes for drug users who continue injecting, on February 15 and 16, 1994 at Johns Hopkins University. The purpose of the workshop is to review issues related to this concept.

NIDA will be co-sponsoring a conference **"HIV Infection in Women: Setting a New Agenda"**, to be held February 21-24 in Washington D.C. This represents the first national scientific meeting of its kind on HIV infection in adult and adolescent women.

On April 3-4, 1995, NIDA will be sponsoring a workshop on **"HIV Disease Progression: Opioids and Immune Function."** This meeting will bring together basic and clinical scientists and epidemiologists to discuss the lack of concurrence between animal data on immune effects of drugs of abuse, principally opioids, and the lack of accelerated disease progression seen in longitudinal studies of HIV infected drug abusers.

NIDA is sponsoring a satellite conference on **"AIDS and Drug Abuse,"** which will be held at the Princess Hotel in Scottsdale, Arizona, on June 9-10, 1995, prior to the opening of the College on Problems of Drug Dependence annual meeting. The purpose of the satellite conference is to bring together investigators from the biomedical and behavioral sciences to review the state of research on AIDS and drug abuse, to discuss future research priorities, and to foster scientific collaborations.

A March 8 meeting of outside consultants is planned to review the safety data and information current known about human experiences with ibogaine to advise the institute on the risks of proceeding with a Phase I study.

On March 6-7, 1994, NIDA's Behavioral Sciences Research Branch will sponsor a workshop entitled **"Behavioral Sciences: New Research Directions."** Participants in the workshop--fourteen eminent behavioral scientists who represent diverse areas of behavioral and cognitive science research--will be "brainstorming" about new ideas and promising research directions that relate to drug abuse.

NIDA's Prevention Research Branch and Division of Epidemiology and Prevention Research will be involved in the activities of the third annual meeting of the newly formed Society of Prevention Research. The Society is a professional association of researchers and scholars engaged in the study and advancement of preventive intervention methods as applied to topics in the fields of substance use, mental health, and social behavior and is multidisciplinary in nature. This year's meeting will be in Scottsdale, Arizona on June 15-17, 1995. The deadline for submission of presentations and posters is April 1, 1995.

The National Prevention Network (NPN) will be holding its Eighth Annual Prevention Research Findings Conference at the Skamania Lodge in Stevenson, Washington, September 10-13, 1995. Objectives for the conference include:

1. linking state and regional alcohol, tobacco and other drug (ATOD) prevention program funders and program administrators with prevention researchers in dialogue around research-proven effective prevention efforts,
2. assisting ATOD prevention program leaders and administrators in identifying those approaches, programs, models and strategies that can be easily adapted to their particular services areas, be they statewide, regional, national or at the local community level,
3. focusing the attentions of both prevention researchers and prevention program administrators and funders on the

needs of diverse communities in dealing with the issues around alcohol, tobacco and other drug demand reduction efforts,

4. sharpening the awareness of both prevention researchers and prevention program administrators and funders about the need to conduct and disseminate the findings of prevention research in such a way as to respond to the needs of prevention programs and their administrators, and
5. providing an opportunity for the country's best prevention researchers and prevention program directors to showcase their expertise in preventing ATOD problems.

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Publications

Outreach/Risk Reduction Strategies for Changing HIV Related Risk Behaviors Among Injection Drug Users (1994) € NCADI #BKD145

Describes the effectiveness of HIV intervention and prevention services in changing the HIV-related risk behaviors among out-of-treatment injection drug users and their sexual partners.

Women and Drug Abuse (1994) € Brochure € NCADI #PHD669

Addresses issues that are of particular importance to drug abusing women: HIV/AIDS and maternal exposure to drugs. Encourages women and their families and friends to seek treatment for drug addiction and provides information on where to go for help.

Women and Drug Abuse: You and Your Community Can Help. (1994) € NCADI #PHD668

Provides guidance for policymakers and community leaders who wish to establish programs to help women and families affected by drug abuse. Addresses issues such as the effects of drug abuse on children and families and the economic, social, and personal costs to women who use drugs.

National Survey Results on Drug Use from the Monitoring The Future Study, 1975-1993; Volume I, Secondary School Students (1994) € NCADI #BKD149

Discusses the prevalence of drug use among American secondary students (specifically eighth, tenth and twelfth graders) and trends in use by those students (seniors, since the study began in 1975 and eighth and tenth graders, since 1991). Examines important demographic distinctions among subgroups in these populations. Includes data on grade at first use, intensity of drug use, attitudes and beliefs among students concerning various types of drug use, and the students' perceptions of certain relevant aspects of the social environment.

National Survey Results on Drug Use from the Monitoring the Future Study, 1975-1993, Volume II: College Students and Young Adults (1994) € NCADI # BKD150

Discusses the prevalence of drug use among American young adults and college students. Examines important demographic distinctions among subgroups in these populations. Includes data on the intensity of drug use, attitudes and beliefs among young adults and college students concerning various types of drug use, and their perception of certain relevant aspects of the social environment.

Drug Procurement Practices of the Out-of-Treatment Chronic Drug Abuser (1994) € NCADI #BKD154

Examines the patterns of drug use, methods of obtaining drugs and income sources and expenditures for drugs by noninstitutionalized out-of-treatment populations.

Research Monographs

NIDA Research Monograph 142: Advances in Data Analysis for Prevention Intervention Research (1994) € NCADI #M142

Discusses state-of-the-art statistical techniques and methodological issues relevant to prevention intervention research. Provides general, introductory as well as technically detailed descriptions for a variety of methodological procedures applicable to prevention intervention as well as other forms of research.

Research Monograph 143: The Context of HIV Risk Among Drug Users and Their Sexual Partners (1994) € NCADI #M143

Reviews current research on drug-using and sexual behaviors of drug users associated with HIV transmission, focussing on the effect of the social and environmental context on risk behaviors and risk avoidance. Develops directions for future research.

Research Monograph 144: Therapeutic Community: Advances in Research and Application (1994) € NCADI #144

Discusses and examines research on the therapeutic community (TC) approach to substance abuse treatment. TC emphasizes a social treatment perspective that focuses on resocializing the client and the use of the community as an agent of personal change.

Research Monograph 145: Neurobiological Models for Evaluating Mechanisms Underlying Cocaine Addiction (1994) € NCADI #M145

Presents models used in animal and human studies for evaluating the neurobiological basis of cocaine addiction. Among the models discussed are self-administration, brain-stimulation reward, discriminative stimulus effects, and conditioned effects. Evidence for the role of dopamine and serotonin in mediating different components of addiction is also critically evaluated.

Research Monograph 146: Hallucinogens: An Update (1994) € NCADI #M146

Presents a complete survey of state-of-the-art hallucinogen research including both animal and human studies. Discusses the regulatory issues involved in human investigations. Highlights challenges and opportunities and identifies future research needs.

NIDA NOTES

Volume 9, No. 3 , September/October NCADI No. NN0004

Discusses the most recent research on Nicotine and Nicotine Addiction. Articles included are: "NIDA Nicotine Research Helps Smokers Kick the Habit", "How Nicotine Replacement Treatment Works", and "NIDA, FDA and Nicotine Research."

Volume 9, No. 4 November/December NCADI No. NN0005

Articles include discussions on the long-term benefits of methadone treatment; NIDA's Perinatal-20 projects--treating drug abusing pregnant and parenting women, school-based drug abuse prevention programs, and drug abuse among the homeless in Washington, D.C.

New Videos

Drug Abuse Treatment in Prisons: A New Way Out (1994) € NCADI #VHS72

Goes behind the gates of two prison-based drug abuse treatment programs, one for men and one for women, to demonstrate an effective option for intervening with drug addicts who are involved in the criminal justice system. One utilizes a therapeutic community model and the other is based on pro-social skills building and rational-behavioral therapy. The impact on inmates, staff, and administrators is explored, and stress is placed on the importance of continuity of care between prison and the community.

Other Publications

Fletcher, B.W., J.A. Inciardi, and A.M. Horton, Eds. (1994) Drug Abuse Treatment. Volume II: The Implementation of Innovative Approaches, Westport, CT: Greenwood Press.

Delany, P., Fletcher, B. and Lennox, R. (1994) "Analyzing Shelter Organizations and the Services They Offer: Testing a Structural Model Using a Sample of Shelter Programs," Evaluation and Program Planning, 17:4, 391-398.

Brown, B.S. and Needle, R.H. Modifying the Process of Treatment to Meet the Threat of AIDS. The International Journal of the Addictions; 29(13), 1739-1752, 1994.

The Washington, D.C. Metropolitan Area Drug Study (DC*MADS): Homeless and Transient Population Study, 1991 User Guide for Microcomputers; (and datafile on diskette). NTIS Order Number: PB95-500351GEI; NIDA Program Official: Elizabeth Lambert, M.Sc.

Haverkos, H.W., Kopstein, A.N., Wilson, H. and Drotman, P. Nitrite Inhalants: History, Epidemiology and Possible Links to AIDS, Environmental Health Perspectives, Journal of the National Institute of Environmental Health Sciences, Volume 102, Number 10, October 1994.

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Staff Highlights

Staff Changes

On December 30, 1994, Dr. Charles R. Schuster, NIDA's Director from 1986 to 1992, retired from Federal service to assume a position as Professor of Psychiatry and Behavioral Neurosciences at Wayne State University. After leading the Institute for 6 years, Dr. Schuster moved to the Addiction Research Center to resume his research career as a Senior Scientist in the Office of the Director.

On December 30, 1994, Dr. Marvin Snyder, retired from the Federal Government after 27 years of government service and 20 years at NIDA. During Dr. Snyder's tenure at NIDA, he held numerous leadership positions including: Director, Division of Research; Director, Division of Preclinical Research; Acting Deputy Director, NIDA; Director, Office of Science Policy, Education, and Legislation; and most recently, Director, Office of Science Policy and Communications. Dr. Snyder's extraordinary contributions to NIDA ranged from articulating the concept of drug addiction as a brain disease, fostering the development of NIDA's AIDS research program, conceptualizing and developing the Medications Development Program at NIDA, and formulating NIDA's Clinical Neuroscience initiative.

On December 11, 1994, Dr. Loretta Finnegan, NIDA's Special Expert on Women's Health Issues and Director of NIDA's Office on Women's Health, left the Institute to assume the position of Director of the NIH Women's Health Initiative.

Dr. Christine Hartel, Associate Director for Clinical Neuroscience, DCSR, retired from Federal service on December 9, 1994 to assume a position with the American Psychological Association. During her tenure at NIDA, Dr. Hartel served in a number of key roles including Special Assistant to the Director, NIDA, Deputy Director, DBR and Acting Director, DBR.

Dr. Chris Ellyn Johanson, Chief of the Etiology Research Branch at the Addiction Research Center, retired from Federal Service on December 30, 1994 to assume a position at Wayne State University.

On September 30, 1994, Dr. Richard Lindblad retired from his position as Director of NIDA's International Program. During his tenure at NIDA, Dr. Lindblad was instrumental in developing the International Visiting Scientists and Technical Exchange Program (INVEST), a key component of the Institute's program of international activities.

Dr. Michael Backenheimer, Deputy Director of NIDA's Office of Extramural Program Review (OEPR), retired from 33 years of Federal Government service on December 30, 1994. Dr. Backenheimer served in the armed forces before joining the Public Health Service. He was one of the original NIDA staff, moving from NIMH's Psychopharmacology Research Branch to NIDA's Division of Epidemiology and Statistical Analysis in 1974.

On December 30, 1994, Ursula Evans, a Contract Review Specialist with NIDA's Office of Extramural Program Review retired after 28 years of Federal service.

Dr. Lisa Onken has been serving as the Acting Deputy Director, Division of Clinical and Services Research, since October 17, 1994.

Robin I. Kawazoe is serving as the Acting Director, Office of Science Policy and Communications.

Dr. Timothy P. Condon is serving as the Acting Deputy Director, Office of Science Policy and Communications.

Dr. M. Patricia Needle is currently serving as the Acting Director of NIDA's International Program.

On December 25, 1994, Mr. Joel Egertson joined the Medications Development Division as a senior advisor to the Director. In this position, Mr. Egertson will concentrate on developing strategies to facilitate the expanded use of current and future medications in treating drug abuse dependence.

Two new staff members have or will soon join the Office on AIDS (OA). Mr. Noble Jones, formerly in the Office of Extramural Program Review, will become a Health Science Administrator in the OA. Ms. Deborah Crump has joined the Office as a Program Assistant.

Jaylan S. Turkkan, Ph.D. joined the Division of Basic Research in November as Chief of the new Behavioral Sciences Research Branch. Dr. Turkkan most recently was a Grants Associate at NIH where she spent last year learning about science program administration, review, and policy at NIDA and at other agencies. She comes to NIDA from the Johns Hopkins School of Medicine where she is an Associate Professor of Behavioral Biology.

Awards

Dr. Dorynne Czechowicz received an award from CSAT for "extraordinary collaboration between NIDA and CSAT and her dedicated service as Technical Advisor to the Treatment Improvement Project". The award was presented on December 6, 1994 at the State Systems Development Conference in Seattle, Washington.

Amy H. Newman, Senior Staff Fellow in the Psychobiology Section, was appointed to tenure track status.

Beth Geter-Douglass, an IRTA in the Psychobiology Section, received an American College of Neuropsychopharmacology/NIMH Minority Travel Award.

David A. Gorelick, M.D., Ph.D., Chief, Treatment Branch and Pharmacotherapy Section has been named to the editorial board of Substance Abuse, the official journal of the Association for Medical Education and Research in Substance Abuse and is serving as section editor for Principles of Addiction Medicine, a new textbook published by the American Society of Addiction Medicine.

Richard Nelson, M.D., a Clinical Associate at the ARC won an NIH AIDS loan repayment award (first NIDA staffer to do so).

Dr. Rao S. Rapaka, Associate Director for Research Technology, Division of Basic Research, has been elected as Program Vice-Chair Elect for the Medicinal and Natural Products Chemistry Section of the American Association of Pharmaceutical Scientists

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Grantee Honors

Howard Hughes Medical Institute
NIDA grantee Susan G. Amara of Vollum Institute has recently been selected as an associate investigator of Howard Hughes Medical Institute. Currently there are only 225 investigators at 53 US institutes in the existing Hughes network.

Most-Cited Paper in Neuroscience
In the October 31, 1994 issue of Current Contents, the "Nature" publication of NIDA grantee Philip Seeman and his coworkers: **"Cloning of the Gene for a Human Dopamine D5 Receptor with Higher Affinity for Dopamine than DI"**, Roger K. Sunahara, Hong-Chang Guan, Brian F. O'Dowd, Philip Seeman, Lisanne G. Laurier, Gordon Ng, Susan R. George, Joseph Torchia, Hubert H. M. Van Tol & Hyman B. Niznik, Nature, 350:614-9, 1991, was ranked number one of the most-cited papers in neuroscience, 1988-1992.

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