Volume 1. Number 7 Spring 2011

IDARS NEWS

Newsletter of the International Drug Abuse Research Society

Volume 1 Issue 7

Spring 2011

Inside this issue:

I am happy to report that IDARS has continued to vigorously pursue its mission with our international conferences to foster an environment of intellectual exchange and dissemination of novel drug abuse research information not only between our members but also sharing this information with the general and scientific community. The challenges of understanding the global problem of substance abuse and drug addiction remain an IDARS focus.

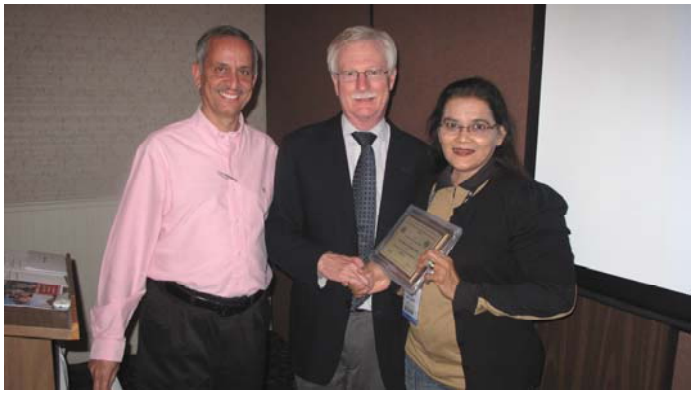
Dr. George F. Koob

It is with profound sadness that we remember the death of Dr. Charles (Bob) Schuster, a scientific pioneer, former Director of the National Institute on Drug Abuse and Distinguished Professor Emeritus of Psychiatry and Behavioral Neuroscience. He was our Guest Speaker at our IDARS social event during the 2009 Society for Neuroscience. We express our deepest sympathy to Bob's family (See more on Bob's passing on page 12 of this newsletter).

As we prepare for the 3rd IDARS/ISN/ESN satellite meeting in Istanbul-Turkey in August 23-26, 2011, we have already made major contribution in advancing IDARS initiative. We have therefore, continued the fundamental goal and mission of IDARS to focus on global drug abuse and sharing internationally new advances in substance related disorders and therapeutic approaches.

Yours Truly
George F. Koob, Ph.D.
President

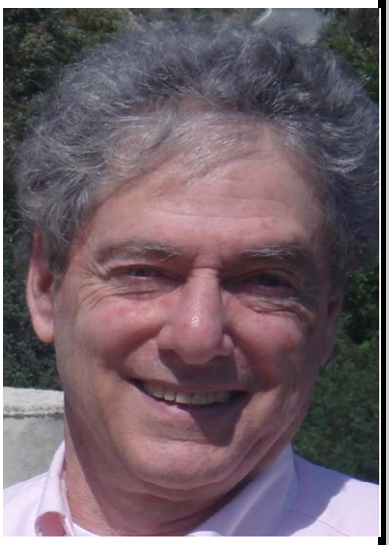
IDARS AWARDEES TO NIDA MINI-SYMPOSIUM AT SFN IN SAN DIEGO IN 2010.



During IDARS socials at SFN meeting in San Diego in 2010, Dr. Syed Ali announces and Dr. Koob presented the IDARS-NIDA awards, to: top left, Paula Aronne from Argentina, top right is Maria Estela Andres from Chile; Middle left, Kaneez Fatima Shad, from Brunei Darussalam, and middle right is Frank Meye, from The Netherland.

Bottom left panel, George Koob and the Guest Speaker, Dr. Eliot Gardner and bottom right Drs Ali, Mason, Koob and Gardner. (See page 3 for summary of Dr. Eliot Gardner's presentation).

Drug reward mechanisms– Past, Present & Future



Dr. Eliot Gardner

The IDARS social event at the Society for Neuroscience (SFN) meeting in San Diego in 2010 included a dinner party, at which Dr. Eliot Gardner gave a perspective on brain-stimulation reward (BSR) as a measure of hedonic state and reviewed past and present work using this animal model, together with observations and thoughts on drug reward mechanisms. Dr. Gardner is Chief of the Neuropsychopharmacology Section at the Intramural Research Program at the National Institute on Drug Abuse (NIH) in Baltimore, MD. Dr. Gardner reviewed early work from the 1950s and 1960s on positive reinforcement produced by direct electric stimulation of discrete brain loci, and noted that the behavioral paradigm - using a specific corner of a laboratory counter top as the spot the animals had to return to in order to receive the rewarding electrical stimulation - constituted a crude conditioned place preference (CPP) model. He also noted that early operant BSR self-stimulation studies were based on simple operant rate measures and were thus flawed by motoric artifacts produced by stimulant or sedative drugs. However, the strength of BSR as a reinforcer is undeniable - animals self-administer BSR at maximal rates, ignoring food, water and sexually receptive mates, and putting up with aversive consequences to obtain BSR. Initial studies with BSR in animals were directed at understanding the neuroanatomical and neurotransmitter substrates of BSR. Such studies soon implicated the medial forebrain bundle and its dopaminergic component. Dr. Gardner and co-workers developed an improved variant of the two-lever titrating threshold BSR model, and with this improvement were able to pioneer studies of BSR in non-human primates. Two series of human subjects were studied with electrical BSR, with subjective reports by the subjects of a euphoric state produced by BSR. More elaborate and sophisticated experiments have continued up to the present time to discover the underlying mechanistic substrates of BSR. Neurobehavioral evidence for both opponent/proponent processes underlying BSR and for hedonic allostasis with escalating cocaine use was demonstrated. BSR remains an effective research tool, with much current use focusing on the search for effective pharmacotherapies for drug addiction. Dr. Gardner concluded by noting that medication development for effective pharmacotherapy of drug addiction is currently taking a variety of approaches - dopamine D3 receptor antagonists, slow-onset long-acting dopamine transporter inhibitors, baclofen (a GABA-B agonist), drugs acting on the endocannabinoid and glutamate systems, and CRF antagonists to specifically target stress-provoked drug-seeking behavior.

MEMBERS NEWS

IDARS NEWSMAKERS

Dr. Michael Kuhar

Dr. Michael Kuhar is the winner of the prestigious, Eddy Award of College on Problems of Drug Dependence (CPDD), in 2011. Dr. Kuhar is clearly highly deserving of the prestigious award, stated Dr Evans, the Chairperson of the 2011 CPDD awards committee.

The Nathan B. Eddy Memorial Award was established by CPDD in memory of one of the pioneers in the field of drug dependence following his death in 1973. The Eddy Award is known as the Crown Jewel of CPDD and goes to the most valuable player of the field.

Dr. Kuhar is Candler Professor of Pharmacology, Georgia Research Alliance Eminent Scholar and Chief, Division of Neuroscience, Yerkes National Primate Research Center of Emory University. He previously was Chief, Neuroscience Branch, Addiction Research Center, NIDA-IRP in Baltimore and past Presidents of CPDD and IDARS. Dr. Kuhar serves on the editorial board of many journals and has record over 800 publications, including refereed papers, chapters, edited books, and patents and has active grants from NIH. Dr. Kuhar is deeply involved in the training of future scientists in the neurobiology of drug abuse and his on-going research is on the molecular mechanisms associated with cocaine and amphetamine regulated transcript (CART) peptide genes in mammalian physiology and in the effects psychostimulants. We congratulate Dr. Michael Kuhar.

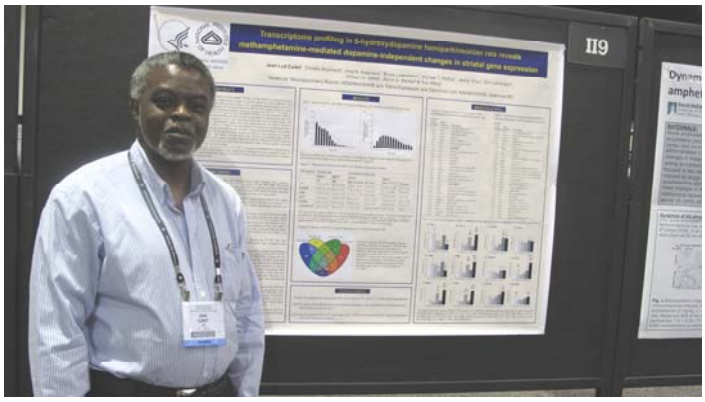
By O9V

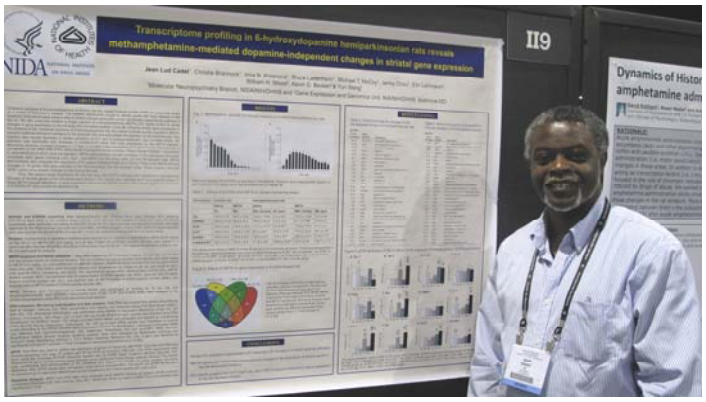
MEMBERS NEWS

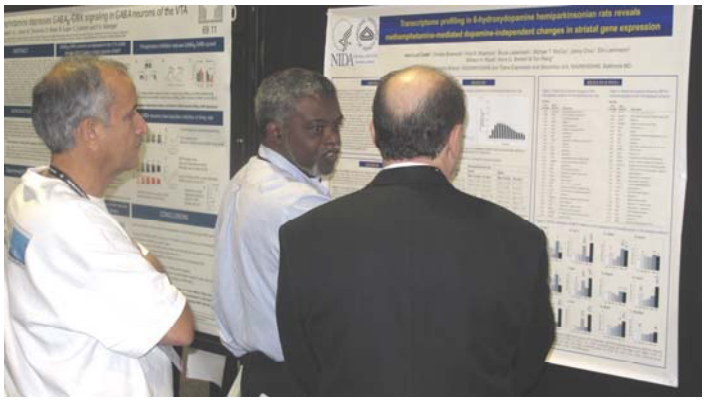
Scientist to Watch

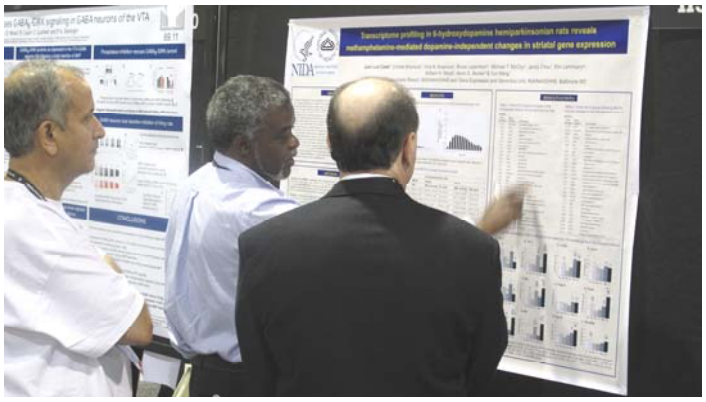
Focus on Jean Lud Cadet MD.

Dr. Cadet is the Chief of Molecular Neuropsychiatry branch at the NIDA-NIH intramural program. His branch uses both basic science and clinical approaches in drug abuse research. He is the Associate Director for Diversity and Outreach at NIDA IRP.









Pictures above shows Dr. Cadet at the society for neuroscience meeting in San Diego in 2010, presenting a poster and attended the IDARS dinner party.

MEMBERS NEWS

Member publications

Members of IDARS and associates from the Food and Drug Administration (FDA)NCTR were authors and co-authors in the book titled: Developmental Neurotoxicology: Principles, Models, Techniques, Strategies, and Mechanism edited by Drs. Cheng Wang and William Slikker. See http://www.wiley.com/WileyCDA/WileyTitle/productCd-0470426721.html

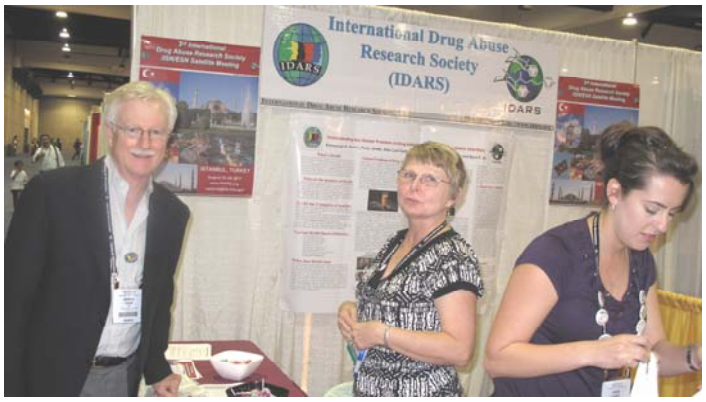
Selected Chapters

1. MODELS, APPROACHES, AND CHALLENGES IN NEUROTOXICITY RESEARCH DURING DEVELOPMENT *(Tucker A. Patterson).*
2. APPROACHES AND MODELS FOR EVALUATING THE TOXIC EFFECTS OF ANESTHETICS IN THE DEVELOPING NERVOUS SYSTEM *(William Slikker, Jr., Xuan Zhang, Fang Liu, Merle G. Paule, and Cheng Wang).*
3. SYSTEMS BIOLOGY APPROACHES TO NEUROTOXICITY STUDIES DURING DEVELOPMENT *(Tucker A. Patterson, Bradley J. Schnackenberg, William Slikker, Jr., and Cheng Wang).*
4. BEHAVIORAL APPROACHES FOR ASSESSING NERVOUS SYSTEM FUNCTION DURING DEVELOPMENT IN ANIMAL MODELS *(Merle G. Paule).*
5. STRATEGIES AND PROGRESS IN EPILEPSY RESEARCH *(Merle G. Paule).*

Selected IDARS Member Publications

1. M.G. Paule, M. Li , R.R. Allen, F. Liu, X. Zou, C. Hotchkiss, J.P. Hanig, T.A. Patterson, W. Slikker, Jr, C. Wang. Ketamine anesthesia during the first week of life can cause long-lasting cognitive deficits in rhesus monkeys: In press in Neurotoxicology and Teratology, 2011.
2. Imam SZ, Zhou Q, Yamamoto A, Valente AJ, Ali SF, Bains M, Roberts JL, Kahle PJ, Clark RA, Li S. Novel regulation of parkin function through c-Abl-mediated tyrosine phosphorylation: implications for Parkinson's disease. J Neurosci. 2011 Jan 5;31(1):157-63.
3. Ali SF and Bondy SC. Red wine but not ethanol at low doses can protect against the toxicity of methamphetamine. Brain res 1346: 247-250, 2010.
4. Onaivi ES. Endocannabinoid system, pharmacogenomics and response to therapy. Pharmacogenomics 11: 907-10, 2010.
5. Cleva RM, Hicks MP, Gass JT, Wischerath KC, Plasters ET, Widholm JJ, Olive MF. mGluR5 positive allosteric modulation enhances extinction learning following cocaine self-administration. Behav Neurosci. 2011 Feb;125 (1):10-9.
6. Cleva RM, Wischerath KC, Olive MF. Extinction learning and adult neurogenesis. Neuropsychopharmacology. 2011 Jan;36(1):360-1. (Hot topic paper).
7. Yao L, Fan P, Arolfo M, Jiang Z, Olive MF, Zablocki J, Sun HL, Chu N, Lee J, Kim HY, Leung K, Shryock J, Blackburn B, Diamond I. Inhibition of aldehyde dehydrogenase-2 suppresses cocaine seeking by generating THP, a cocaine use-dependent inhibitor of dopamine synthesis. Nat Med. 2010 Sep;16(9):1024-8.
8. Bolla KI, Lesage SR, Gamaldo CE, Neubauer DN, Wang NY, Funderburk FR, Allen RP, David PM, Cadet JL. Polysomnogram changes in marijuana users who report sleep disturbances during prior abstinence. Sleep Med. 2010 Oct;11(9):882-9.
9. Biezonski DK, Meyer JS. Effects of 3, 4-methylenedioxmethamphetamine (MDMA) on serotonin transporter and vesicular monamine transporter 2 protein and gene expression in rats: implication for MDMA neurotoxicity. J. Neurochemistry 112: 951-962, 2010.
10. Mackay RK, Colson NJ, Dodd PR, Lewohl JM. Differential expression of 14-3-3 isoforms in human alcoholic brain. Alcohol Clin Exp Res. Epub ahead of print, 2011.

IDARS Exhibition at the Society for Neuroscience meeting in 2010.



IDARS members took turns to man the IDARS booth and to introduce IDARS to SFN members. Top left panel is IDARS Executive Director, Syed Ali setting up the booth with Susan and Bonnie. Top right is the President of IDARS George Koob with Bonnie and Susan at IDARS booth. IDARS booth was strategically positioned near NIDA booth as seen in the middle panel. Lower left panel is Jean Lud Cadet and Syed Ali at the back-ground manning the booth and lower right panel is Syed Ali with Susan and Debra Mash.

IDARS dinner party at the Society for Neuroscience meeting in San Diego in 2010








Members of IDARS and guests at the dinner party during the Society for Neuroscience meeting in San Diego in 2010.

Neurobiology of use and abuse of γ-hydroxybutyric acid (GHB)

γ-hydroxybutyric acid (GHB) was developed in 1961 by Dr. Henri Laborit in France as an anesthetic agent but because of its serious side-effects and its abuse potential, it was soon withdrawn from human use. Therapeutically it continues to be used in the treatment of sleep disorders and alcohol withdrawal. In the 1980s, GHB gained popularity as a muscle builder and became readily available in health food stores. Its popularity increased among people as a "club drug" like other club drugs flunitrazepam (Rohypnol), ketamine and methamphetamine ("ice").

The 2009 Monitoring of the Future survey reported that 0.7 percent of 8th graders and 1.1 percent of 12th graders reported having used GHB within the past one year. Drug Administration has labeled GHB as a "dangerous drug," and made it a Schedule I controlled substance subject to regulation under the federal Controlled Substance Act. GHB is abused for it's euphorogenic, dysinhibiting, sedative and anabolic effects, and is usually used in combination with alcohol and other drugs. GHB overdose has been associated with seizures, cardiovascular and respiratory depression, coma and death. In humans, low doses of GHB are known to induce short-term anterograde amnesia, and this cognitive-impairing property makes this recreational drug a "date rape drug".

GHB occurs naturally in the brain. Several studies indicate that GHB acts as a putative neurotransmitter. GHB is both a precursor as well as a metabolite of g-aminobutyric acid (GABA). Multiple mechanisms appear to contribute to the effects of GHB. In the brain, GHB is located within presynaptic terminals. GHB-binding sites have been shown to have a distinct anatomical distribution pattern. Hippocampus including dentate gyrus, frontal cortex, septum, nucleus accumbens and caudate-putamen, have high densities of GHB binding sites, and areas such as the cerebellum, hypothalamus, pons-medulla are devoid of any GHB binding. In rats, sedative effects of GHB are counteracted by the GHB-specific antagonist NCB-382. At high doses, GHB has anxiolytic effects, similar to GABAergic depressant drugs, and $GABA_B$ antagonists attenuate the anxiolytic effects of GHB.

Although GHB use and abuse is most prevalent among adolescents and young adults, the literature on the neurobehavioral effects of GHB exposure in adolescent humans and animals remains sketchy at best. In adolescent rat GHB administration has been shown to impair the acquisition of memory, and these cognitive-impairing effects of GHB are thought to be mediated by the NMDA class of glutamate receptors. More detailed cellular, molecular, behavioral studies are needed to determine the neurobiology of GHB, in the hope of development of better identification and treatment of GHB addiction.

Ratna Sircar, PhD
Head, Neuropsychopharmacology Laboratory
Department of Neuroscience
The Feinstein Institute for Medical Research
350 Community Drive, Manhasset, NY 11030
(516) 56-1068

Ecstasy and Marijuana Co-Use: Prevalence and Consequences

Ecstasy (3,4-methylenedioxymethamphetamine; MDMA) is an amphetamine congener that is consumed recreationally by many adolescents and young adults. MDMA is often associated with the "rave" scene, although it may also be taken on other occasions. MDMA consumption acutely produces mild euphoria, heightened feelings of well-being, increased sociality (closeness with others), and enhanced visual and auditory perception. Adverse physiological and behavioral effects may also occur, such as hyperthermia, tachycardia, hypertension, tremor, trismus (jaw tightening), and bruxism (teeth grinding). British researchers have reported that heavy MDMA use on the weekend is sometimes associated several days later with a temporary dysphoric state consisting of mild depression, anxiety, and irritability. This negative mood state, which has been termed the "mid-week blues", usually resolves by the following weekend, although there are reports that repeated MDMA exposure may lead to more persistent mood alterations. Equally importantly, there is substantial evidence that heavy MDMA users suffer from significant cognitive deficits compared to non-MDMA using control subjects.

Animal studies have shown that the acute effects of MDMA are mediated by a massive release of serotonin (5-HT) throughout the brain accompanied by a smaller but still significant release of dopamine and norepinephrine. On the other hand, high doses of MDMA administered to rats or nonhuman primates lead to a long-lasting depletion of forebrain serotonin as well as reductions in other biochemical markers of serotonergic neurons such as tryptophan hydroxylase and the plasma membrane serotonin transporter (SERT). Brain imaging studies have shown that SERT binding potential is also significantly decreased in heavy MDMA users, which raises the possibility that serotonergic deficits may underlie the cognitive and affective disturbances observed in these subjects.

Despite the strong evidence for cognitive impairment in MDMA users, there has been a debate in the literature as to whether these effects are actually due to MDMA consumption. The reason for this controversy is that heavy MDMA users typically also smoke marijuana, and regular marijuana use has itself been associated with cognitive deficits. Consequently, it has been difficult to tease apart the relative contributions of MDMA and marijuana to the cognitive differences between the MDMA and control groups. It is possible that MDMA and marijuana exert mechanistically independent effects on the neural circuitry underlying various cognitive functions. However, there are at least two different neural mechanisms by which these substances could interact. First, CB1 cannabinoid receptors are present on serotonergic nerve terminals, and THC (the major psychoactive component of marijuana) has been shown to inhibit 5-HT release from these terminals. Second, THC and several other cannabinoids possess significant antioxidant activity. This is important because MDMA-induced serotonergic neurotoxicity is thought to be mediated by increased oxidative stress, and thus marijuana's antioxidant effects could actually attenuate MDMA neurotoxicity.

It seems clear that properly designed animal studies are needed to determine the separate and combined influences of MDMA and THC on neural and cognitive function. Previous studies demonstrated that low doses of MDMA and THC that, by themselves, had no effect on working memory when given acutely, produced a synergistic memory deficit when given together. ***See page 11***

Editorial Corner: Welcome to our Newsletter*

Emmanuel Onaivi, Ph.D., Newsletter Editor IDARS is delighted to publish our electronic newsletter, with information about the society, seeking ideas about our journal, and opportunities for our members. The intention of this newsletter is not only to communicate to you, but also, for you to be able to respond with suggestions for how IDARS may increase its role in your research. Please send us feedback, and get involved! As editor of this newsletter, I invite you to contact me with ideas for articles in future editions, or to volunteer to write an article yourself.

EDITORIAL COMMENTS ON ECSTASY (MDMA):

Increase in Ecstasy (MDMA) -related emergency department visits has recently been high-lighted by SAMHSA—the Substance Abuse and Mental Health Services Administration in USA. Ecstasy is known for its psychostimulant and psychedelic effects and used in social settings such as in parties. In many situations, it is used with other drugs such as cannabis, or alcohol as is one of the focus of IDARS biomedical report as described by Dr. Meyer on Ecstasy and marijuana co-use. Yet there are campaigns for MDMA-assisted psychotherapy for post traumatic stress disorders (PTSD) in many parts of the world. So it is important to separate the medicinal and recreational use of MDMA and cannabis.

Continued from page 10

Ecstasy and Marijuana Co-Use: Prevalence and Consequences

By Dr. Jerrold S. Meyer

However, these results still leave open the question of whether MDMA and THC produce longer-lasting effects when given repeatedly over time to adolescent and young adult animals. Studies are currently underway in my laboratory using a rat model of adolescent MDMA and THC co-exposure to determine the cognitive and neurochemical effects of this treatment regimen. Hopefully our findings will help to resolve the current controversy over the relative contributions of MDMA and marijuana to the cognitive impairment observed in heavy MDMA users.

Jerrold S. Meyer, Ph.D.
Professor, Department of Psychology
Director, Neuroscience and Behavior Program
University of Massachusetts Amherst
135 Hicks Way
Amherst, MA 01003 USA
(413) 545-2168.

Newsletter Editor*:
Emmanuel S. Onaivi
Onaivie@wpunj.edu

Home Web Site
www.idars.org

Office email
Syed.ali@fda.hhs.gov
Office Telephone
870-543-7123

Office Fax
870-543-7745

Office Mailing address
IDARS
Syed F. Ali, Ph.D.
Neurochemistry Laboratory,
Division of Neurotoxicology,
HFT-132, National Center for
3900 NCTR Road
Jefferson, AR 72079-9502,
USA

IDARS-NIDA AWARDEES

- *Paula Aronne Luna*
  Argentina
- *Maria Estela Andres*
  Chile
- *Kaneez Fatima Shad*
  Pakistan
- *Frank Julius Meye*
  Netherlands

OBITUARY

Dr. Charles (Bob) Schuster

Neuroscientist who contributed widely to Behavioral Pharmacology and Addiction Research—An Emeritus member of IDARS.

It is with deep sorrow that the scientific community in drug abuse and addiction research remember Dr. Charles (Bob) Schuster who died on February 21, 2011, from stroke. As noted by Dr. Koob, on the President's page, Bob was a scientific pioneer who was committed to the elimination of drug abuse and addiction, and his impact in our field will continue to be remembered as a champion who touched many lives.

Bob until his death was Distinguished Professor Emeritus of Psychiatry and Behavioral Neuroscience at Wayne State University's School of Medicine. At the society for Neuroscience meeting in Chicago in 2009, Bob who is also an Emeritus member if IDARS gave a historical review of drug self administration and we got to know that in his early days he was also a jazz musician.

Bob founded the University of Chicago's Drug Abuse Research Center and served as the director of NIDA from 1986-1992. He was also a past President and a Nathan B. Eddy awardee of CPDD. He was author and co-author in over 200 articles as well as book chapters and books. He leaves a rich legacy and his loss is deeply felt by so many in substance abuse and addiction research…..*by O9V.*