Director's Report to the National Advisory Mental Health Council

February 4, 2005

Director's Opening Remarks

I am pleased to welcome members of the National Advisory Mental Health Council (NAMHC), and other participants and guests to our 208th Council meeting. Since we last met in September 2004, we have made progress on several fronts, which I will share with you in this report. First let me welcome five new members to the NAMHC:

Jonathan Cohen, PhD, Professor, Department of Psychology, Princeton University. Dr. Cohen's research centers on the neurobiological mechanisms underlying cognitive control.

Raquel Gur, MD, Professor and Vice Chair for Research Development, Departments of Psychiatry, Neurology and Radiology, and Director, Neuropsychiatry Section, University of Pennsylvania Medical Center. Dr. Gur is internationally known for her research on brain function in schizophrenia.

Peter Hollenbeck, PhD, Professor of Biological Sciences, Purdue University. His work focuses on how nerve cells convey messages and how the process goes awry in neurodegenerative diseases. He also serves as a scientific advisor and speaker for the national Tourette Syndrome Association.

Jeffrey Kelly, PhD, Professor of Psychiatry and Behavioral Medicine and Director, Center for AIDS Intervention Research, Medical College of Wisconsin. Dr. Kelly conducts research on the development, conduct, and evaluation of new strategies to prevent HIV among persons most vulnerable to the disease, as well as the prevention of adverse health and mental outcomes among persons living with HIV infection and their loved ones.

Helena Kraemer, PhD, Professor, Department of Psychiatry, Nancy Pritzker Laboratory, Stanford University. Dr. Kraemer is an expert in research methodology as it relates to the intersection of biological and behavioral factors, in psychiatric research as well as cardiology, pediatrics, and other fields in which behavioral research is becoming ever more relevant.

On behalf of the entire NIMH, I want to thank you for your willingness to serve the Institute and the many millions of Americans affected by mental illness for whom we work.

NIH-Wide Update

The NIMH is one of 27 Institutes and Centers that comprise the NIH. One of the most exciting developments over the past two years at the NIH has been the cross-institute Roadmap for accelerating discoveries to improve health. This effort is not disorder-specific or limited to a particular organ system. The goal of the Roadmap is to overcome the shared impediments to progress faced by all fields of biomedical research. Roadmap initiatives are divided into three general categories: new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise. NIMH has been involved deeply in all three categories of the Roadmap, in terms of intellectual commitment, staff effort, and dollars. In FY05, NIMH has committed $8,926,000 to the NIH Roadmap. More recently,

NIMH has joined with 14 other Institutes and Centers to launch an analogous effort in neuroscience. The Neuroscience Blueprint will focus on resources, tools, and training that can accelerate progress on our understanding of the nervous system and its diseases. In FY05, each participating Institute and Center has committed 0.15% of its neuroscience budget toward this shared project. Below, I describe recent progress on a few initiatives from the NIH Roadmap and the Neuroscience Blueprint.

NIH Roadmap

New Pathways to Discovery: Molecular Libraries Initiative of the NIH Roadmap
NIMH shares the lead with the National Human Genome Research Institute (NHGRI) on the Molecular Libraries Initiative of the Roadmap. The goal is to develop tools for investigating the biology of the thousands of genes being revealed in this genomic era. The Molecular Library program will include a large repository of small molecules, a network of both intramural and extramural screening centers using high throughput assays to screen thousands of small molecules, a comprehensive database for sharing results (http://pubchem.ncbi.nlm.nih.gov/), and a technology development arm to accelerate chemical diversity and predictive toxicology. Since our last Council meeting, we have awarded a contract for building the small molecule repository to Discovery Partners International (DPI). In addition, we have reviewed applications in response to the Molecular Libraries Screening Center Network (MLSCN) Request for Application (RFA-RM-04-017). These applications were from both the public and private sectors and covered a broad range of expertise and skills in molecular screening. We anticipate that six to eight centers will be funded in March/April 2005 as cooperative agreements for the next three years. In addition, a plan for a collaborative research network of extramural centers and the intramural NIH Chemical Genomics Center (NCGN) has been established (http://www.genome.gov/12512295). Each screening center will conduct 10-20 high throughput assays annually, and a variety of biological assays to be used within the MLSCN will be solicited from the scientific community through a Program Announcement. Finally, the molecular libraries database, Pubchem, is now live and servicing the scientific community with a daily average of 1,300 new users and 37,000 hits.

Research Teams of the Future: NIH Pioneer Award
Early in the course of developing the Roadmap, we recognized that one of the challenges to progress is identifying and supporting innovation. The Pioneer Award was designed to "support scientists of exceptional creativity who take innovative approaches to major challenges in biomedical research," according to NIH Director Elias Zerhouni. The NIH adopted a novel approach to proposals and review for the Pioneer Award (up to $500,000 in direct costs per year for five years). The first nine Pioneer Awardees were announced in September 2004, including two NIMH grantees: Dr. Steven McKnight of UT Southwestern School of Medicine and Dr. Larry Abbott of Brandeis University. In September 2005, NIH expects to present five to ten new Pioneer Awards (http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-05-021.html).

Re-engineering the Clinical Research Enterprise
In the past two decades, as the number of medical school graduates has doubled, the number of physicians involved in clinical research has fallen by 6%. Consistent with the NIH Roadmap goal of expanding the pipeline of students entering clinical research, training future leaders, and creating viable career pathways for clinical researchers, two

requests for applications were recently issued. Predoctoral Clinical Training Programs (http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-05-015.html) will support programs that promote training for medical, dental, nursing, and other allied health students and provide efficient entry of interested students into clinical research careers. Multidisciplinary Clinical Research Career Development Programs (http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-05-016.html) has been reissued due to the success of last year's announcement. This program now supports seven institutions in the clinical research career development of post-doctoral-level scholars and young faculty members from a variety of scientific and medical disciplines. These scholars will learn how to conduct patient oriented research, translational research, small- and large-scale clinical investigation and trials, and epidemiologic and natural history studies. While this is an investment on the part of NIH in clinical research in general, enlarging the pool of students in the clinical research pipeline is likely to increase the number of clinical investigators in psychiatric disorders.

Neuroscience Blueprint

The 15 Institutes and Centers of the NIH involved in neuroscience research have developed a blueprint that will help coordinate key research initiatives to speed progress and ease the burden of disorders of the nervous system. One example of the collaborative spirit reflected in the Blueprint is the Porter Neuroscience Research Center on the NIH campus in Bethesda. The first wing of the facility opened in mid-June and more than 50 investigators from eight different institutes (11 from NIMH) moved in this fall, providing a unique inter-disciplinary research facility at NIH without Institute boundaries. The Blueprint, which seeks to cultivate a similar spirit in the extramural environment, was launched by several of the Institute directors at a special session of the Society for Neuroscience meeting in October. In FY05, the Blueprint plans to (a) complete a comprehensive inventory of shared resources and infrastructure programs for neuroscience both within and outside of the NIH, (b) expand the GENSAT project (a mouse neurogenomics effort currently funded by NINDS, NIMH, and NIDA), and (c) fund supplements for "neurobiology of disease" courses in neuroscience training programs. Other initiatives being considered for FY05 include broadening efforts in neuroimaging brain development in children and enhancing microarray resources used in neuroscience research. The planned budget for FY05 (approximately $7 million) will be increased in FY06 to permit several new initiatives under development. Mike Huerta and Mayada Akil have taken the lead at NIMH, with Marlene Guzman from NIMH and Rebecca Farkas from NINDS providing key administrative support.

Conflict of Interest

As discussed at our last NMHAC meeting, revelations in media articles and at Congressional hearings over the past year have caused NIH to be concerned about both real and perceived conflicts of interest involving NIH employees, including most specifically scientists and scientist-administrators within intramural and extramural research programs. Earlier this week, the Department of Health and Human Services released new employee ethics regulations, designed to reduce conflict-related problems and to restore the integrity of NIH staff. The new regulations would (a) prohibit stock holdings in "substantially affected organizations" by NIH employees who file either public or confidential financial disclosure reports, while restricting such holdings among other employees to stock valued at no more than $15,000, (b) prohibit a range of outside activities (whether remunerated or not), and (c) prohibit acceptance of many non-Federal awards by NIH employees. NIH

scientists will continue to be able to conduct academic activities such as teaching, writing, and speaking at scientific meetings as well as practicing medicine, provided that these activities receive prior approval and adhere to guidelines for "outside activities." While these new regulations are generally consistent with current policies affecting extramural staff, our intramural scientists previously have been permitted to interact more freely with both grantee institutions and private industry. With the proposed policy, intramural and extramural faculty will be required to follow the same rules for outside activities.

NIMH Update

Intramural Program

The NIMH intramural program, which represents roughly 11% of the NIMH budget, is home to more than 50 independent investigators leading some of the most innovative research programs funded by the Institute. In the past six months, the NIMH intramural program has lost three of its leaders. The Scientific Director, Bob Desimone, has left the NIMH to serve as director of the McGovern Institute at MIT. Desimone, a world-class neurophysiologist with a passion for translation, has been the ideal scientific leader for NIMH for the past seven years. The search for his replacement has identified several outstanding candidates who will be visiting in the near future. I am serving as acting Scientific Director until Bob's replacement arrives. Dennis Charney, director of the Mood and Anxiety Disorder Program, left to become Dean for Research at the Mt Sinai School of Medicine. Richard Nakamura chairs the search committee for his replacement. In the interim, we are fortunate that Husseini Manji has provided superb leadership for the Mood and Anxiety Disorders Program. Finally, the Institute and the world at large have lost one of its greatest scientists on December 27, 2004 with the sudden death of Dr. Julius Axelrod. For more than four decades, Julie was a scientific icon at the NIH. He was not only one of the intellectual fathers of modern neurochemistry and neuropharmacology, he was quite literally the academic father of many of the leaders of the current generation. Solomon Snyder, Jacques Glowinski, Steven Paul, Joseph Coyle, Michael Brownstein, and many others trained with Julie at the NIMH. He received the 1972 Nobel Prize for his research on the pathways of catecholamine biosynthesis. Although the NIMH intramural program will always be known as the scientific home of Julie Axelrod, for all of us who knew him or worked with him, the program will not be the same without his keen and curious mind just down the hall.

Extramural Program

The reorganization of extramural programs presented at recent NAMHC meetings is now virtually complete. This is the first Council meeting in which we will be presenting grants from five instead of three divisions, with an emphasis on moving discoveries from bench to bedside to practice. The new Division Directors have been working together as a team to discuss research opportunities and priorities. I have been delighted by the support of the entire staff through this period of change and the willingness of the NIMH program officers to accept new responsibilities. Priority areas for each of the new divisions are on the NIMH website at http://www.nimh.nih.gov/researchfunding/reorganization.cfm. Several new program officers are being hired in key areas (see "Staff Changes" below).

At the same time that we have increased the number of divisions, we have been consolidating select programs to ensure a more coordinated approach. With Steve Koslow's departure, the Office of Neuroinformatics, which has been the home of the Human Brain Project, has been moved from under the Office of the Director to become a program within the Division of Neuroscience and Basic Behavioral Science under Michael Huerta. Clarissa Wittenberg, NIMH Director of Communications for the past 6 years, has accepted a new position in the HHS Office of Global Health with the Assistant Secretary for International Affairs. Jean Baum has graciously agreed to serve as acting Director of the Office of Communications. The Institute will evaluate its overall internal and external communication strategy, which is now spread across several offices in the OD. While we develop a coordinated communication strategy, the Office of Communications will report to Della Hann, Office of Science Policy and Program Planning, who will help set the orientation and priorities for the office.

Science of Note

New Neurons Born in Adult Rat Cortex

Recent evidence suggesting that antidepressants may act by triggering the birth of new neurons in the adult hippocampus has heightened interest in adult neurogenesis and raised the question: Could new neurons also be sprouting up in the parts of the adult brain involved in depression and anxiety? NIMH intramural scientists Heather Cameron, Alexander Dayer, and colleagues have found newly born neurons in adult rat cortex, seat of higher order "executive" functions, and in the striatum, site of habits, reward, and motor skill learning. In the cortex, the new neurons appear to arise from previously unknown precursor cells native to the area, rather than from cells migrating in from another area. Their discovery adds to the scientific debate over adult neurogenesis, which has potential implications for recovery from a variety of brain disorders and injuries. The researchers found that the cortex and striatum were giving birth to new, widely scattered small cells, called interneurons, which make and secrete GABA, a neurotransmitter that dampens neuronal activity. Interneurons are thought to play a role in regulating larger types of neurons that make long-distance connections between brain regions and predominate in these areas. The researchers suggest that since antidepressants increase neurogenesis in the adult hippocampus, they might have similar effects in the cortex, the region probably responsible for mood dysregulation in depression. Further studies are needed to answer such questions about regulation and possible functions of the new neurons.

Dayer AG, Cleaver KM, Abouantoun T, Cameron HA. New GABAergic interneurons in the adult neocortex and striatum are generated from different precursors. Journal of Cell Biology. 2005 Jan 31;168(3):415-427.

Discovery of Altered Growth Factor Gene Expression in Major Depressive Disorder

Brain areas such as the dorsolateral prefrontal cortex and the anterior cingulate cortex have been implicated in the development of major depressive disorder (MDD) and bipolar disorder (BPD). This spurred Simon Evans, Huda Akil, and their colleagues at the University of Michigan to study changes in gene expression in these brain areas in individuals with these disorders. Using microarray technology and postmortem brain samples, the scientists found significant differences in the levels of gene expression of a family of fibroblast growth factors (FGFs) in the brains of people with MDD, but not BPD, relative to controls. These findings were then confirmed by a different method and in a different cohort of individuals with MDD. Growth factors are known to be important in

development and maintenance of the CNS. In the adult brain, they are critical in neuronal survival, axonal branching, and synaptic plasticity. The differences the investigators found in FGF levels were not an effect of antidepressant therapy; rather, they were partially reversed by SSRIs. Therefore, the results implicate members of the FGF family for the first time in the etiology of MDD and show potential involvement in the mechanism of action of SSRIs. Further genomic analysis is needed to determine whether they represent vulnerability genes for severe depression. These findings may lead to a new understanding of severe depression and the development of new strategies for treating mood disorders.

Evans SJ, Choudary PV, Neal CR, Li JZ, Vawter MP, Tomita H, Lopez JF, Thompson RC, Meng F, Stead JD, Walsh DM, Myers RM, Bunney WE, Watson SJ, Jones EG, Akil H. Dysregulation of the fibroblast growth factor system in major depression. Proceedings of the National Academy of Sciences USA. 2004 Oct 26;101(43):15506-11. Epub 2004 Oct 13.

Brain Circuitry Revealed for Decision-making

Two recent publications pinpoint brain areas involved in the interrelated processes of perception, decision-making, and action. NIMH intramural scientists Hauke Heekeren, Leslie Ungerleider, and colleagues used functional magnetic resonance imaging (fMRI) to observe brain activity during a decision-making task that required participants to distinguish between images of faces and houses at varying degrees of clarity. Their results suggest that the dorsolateral prefrontal cortex may be responsible for decision-making tasks that involve perceptual differentiation. This model and the mechanisms involved may also help explain more complex decisions confronted in everyday life. In a similar study, Edwin Clayton and colleagues at the University of Pennsylvania, along with Princeton University's Jonathan Cohen, have discovered a surprising new role for an area of the brain called the locus coeruleus. By recording the activity of neurons in the locus coeruleus while monkeys performed a cognitive task involving simple decisions, investigators found that this brain area was most active just before the behavioral response. Their results suggest that the locus coeruleus is activated by the decision-making process and the commitment to act, and then facilitates the behavioral response.

Heekeren HR, Marrett S, Bandettini PA, Ungerleider LG. A general mechanism for perceptual decision-making in the human brain. Nature. 2004 Oct 14;431(7010):859-62.

Clayton EC, Rajkowski J, Cohen JD, Aston-Jones G. Phasic activation of monkey locus coeruleus neurons by simple decisions in a forced-choice task. Journal of Neuroscience. 2004 Nov 3;24(44):9914-20.

Habit Learning in Tourette Syndrome Affected by Caudate Nucleus

Reductions in the size of the caudate nucleus, a subcortical structure with rich connections to the frontal lobe, have implicated this structure in the pathophysiology of Tourette syndrome (TS). To better understand the functional implications of this anatomical finding, researchers at Columbia University, Texas A&M University, and Yale University tested two types of memory and learning in children and adults with TS: habit learning, known to be dependent on the striatum, and declarative memory, subserved primarily by the medial temporal lobe. Compared to controls, both children and adults with TS showed significant deficits in habit learning, while showing normal declarative memory. These deficits in habit learning correlated significantly with symptom severity (number and severity of tics), lending further support to the important role of the caudate in the pathophysiology of TS. These findings were independent of comorbid obsessive-compulsive disorder (OCD) or attention deficit hyperactivity disorder (ADHD) frequently associated with TS. In addition, an evaluation of medication effects indicated that neuroleptic treatment for TS was associated with improved habit learning, while medications used to treat OCD and ADHD

(selective serotonin reuptake inhibitors and alpha-adrenergic agonists) showed no such relationship.

Marsh R, Alexander GM, Packard MG, Zhu H, Wingard JC, Quackenbush G, Peterson B. Habit learning in Tourette syndrome. Archives of General Psychiatry. 2004 Dec;61(12):1259-1268.

High Risk of Major Depression Linked Across Three Generations

Family studies on early-onset major depressive disorder (MDD) have pointed to an increased risk for adults with parents who have MDD, but none of the previously published research had gone beyond two generations. A study of familial aggregation of psychiatric disorders across three generations revealed that the risk of MDD, anxiety disorders, and other psychiatric disorders were highest in children with parents and grandparents who had moderately to severely impairing depression. For all three generations studied, anxiety disorders in childhood were observed to be an early indicator that an individual would develop depression later in life. These results indicate that early intervention is warranted in the offspring of two generations affected with moderately to severely impairing MDD. The study was conducted by Myrna Weissman, Gerard Bruder, and colleagues at Columbia University.

Weissman MM, Wickramaratne P, Nomura Y, Warner V, Verdeli H, Pilowsky DJ, Grillon C, Bruder G. Families at high and at low risk for depression: a 3-generation study. Archives of General Psychiatry. 2005 Jan;62(1):29-36.

PET Scans Provide New Clues to Treating Depressed Elderly

Many studies on depression have implicated the regulation mechanism of the neurotransmitter serotonin in the development of disease as well as influencing a patient's response time to treatment with SSRIs. Using positron emission tomography (PET), researchers at the University of Pittsburgh led by Carolyn Meltzer observed changes in brain chemistry in elderly people with depression. Specifically, they focused on the activity of binding sites for serotonin 1A ($5\text{-}HT_{1A}$) in an area of the brainstem called the dorsal raphe nucleus (DRN). By observing DRN binding patterns before and after antidepressant treatment, researchers detected reduced binding in untreated, depressed, elderly patients compared to healthy control subjects. These findings suggest possible mechanisms for severe depression as well as a potential method for determining treatment outcomes with SSRIs.

Meltzer CC, Price JC, Mathis CA, Butters MA, Ziolko SK, Moses-Kolko E, Mazumdar S, Mulsant BH, Houck PR, Lopresti BJ, Weissfeld LA, Reynolds CF. Serotonin 1A receptor binding and treatment response in late life depression. Neuropsychopharmacology. 2004 Dec;29(12):2258-65.

Early Results of Practical Trials

The *Systematic Treatment Enhancement Program for Bipolar Disorder* (STEP-BD), currently underway, is one of the largest modern surveys of bipolar disorder. Investigators have identified a 20% incidence of rapid cycling – defined as four or more mood episodes within one year – among the first 500 patients enrolled in the study. Participants with rapid cycling reported a younger age of onset of bipolar disorder than non-rapid cycling patients, and were more severely ill on a number of clinical measures at the outset of their participation in the trial. A separate assessment of the first 1,000 STEP-BD participants confirmed clinical impressions that comorbid conditions, which are known to worsen the course of bipolar disorder, are common but under-treated. Nearly three-quarters of survey participants had a lifetime diagnosis of at least one comorbid mental disorder, most often a substance-use disorder (48%), and pharmacotherapy was inadequate.

The recently concluded *Sequenced Treatment Alternatives to Relieve Depression* (STAR*D) trial focused on treating non-psychotic major depressive disorder in adults who are seen in outpatient settings. In the Yates study, investigators evaluated the initial 1,500 STAR*D outpatients and found that 53% had significant concurrent physical illness, a relatively common but often overlooked comorbidity. Concurrent significant medical comorbidity was associated with a number of defining features, including older age, lower income, limited education, and absence of self-reported family history of depression. Those without comorbid medical illness had higher rates of impaired mood reactivity, distinct mood quality, and interpersonal sensitivity. Another study of this STAR*D cohort found that major depressive disorder that begins before age 18 is a particularly severe and chronic condition with a distinct set of demographic and clinical correlates, including female gender, more episodes, more suicidality, greater symptom severity, and atypical symptom features. Moreover, in this sample, early-onset major depression was associated with significant psychosocial consequences, specifically lower educational attainment and marriage rates.

Schneck CD, Miklowitz DJ, Calabrese JR, Allen MH, Thomas M, Wisniewski SR, Miyahara S, Shelton M, Ketter TA, Goldberg JF, Bowden CL, Sachs GS. Phenomenology of rapid cycling bipolar disorder: Data from the first 500 participants in the systematic treatment enhancement program for bipolar disorder. American Journal of Psychiatry 2004 Oct; 161:1902-1908.

Simon NM, Otto MW, Weiss RD, Bauer MS, Miyahara S, Wisniewski SR, Thase ME, Kogan J, Frank E, Nierenberg AA, Calabrese JR, Sachs GS, Pollack MH. Pharmacotherapy for bipolar disorder and comorbid conditions: Baseline data from STEP-BD. Journal of Clinical Psychopharmacology 2004 Oct; 24: 512-520.

*Yates WR, Mitchell J, Rush AJ, Trivedi MH, Wisniewski SR, Warden D, Hauger RB, Fava M, Gaines BN, Husain MM, Bryan C. Clinical features of depressed outpatients with and without general medical conditions in STAR*D. General Hospital Psychiatry 2004 Nov-Dec; 26(6):421-429.*

Zisook S, Rush AJ, Albala A, Alpert J, Balasubramani GK, Fava M, Husain M, Sackeim H, Trivedi M, Wisniewski S. Factors that differentiate early vs. later onset of major depressive disorder. Psychiatry Research 2004 Dec 15; 129(2):127-140.

Mutant Gene Linked to Treatment-Resistant Depression

A mutant gene that starves the brain of serotonin, a mood-regulating neurotransmitter, has been discovered and found to be 10 times more prevalent in depressed patients than in control subjects, according to researchers funded by NIMH and National Heart Lung and Blood Institute (NHLBI). Patients with the mutation failed to respond well to the most commonly prescribed class of antidepressant medications, which work via the serotonin system, suggesting that the mutation may underlie a treatment-resistant subtype of the illness. The mutant gene codes for the brain enzyme, tryptophan hydroxylase-2, which makes serotonin; it results in an 80 percent reduction of the neurotransmitter. The mutant gene was carried by nine of 87 depressed patients, three of 219 healthy controls and none of 60 bipolar disorder patients. Marc Caron, Xiaodong Zhang, and colleagues at Duke University announced their findings in the January 2005 *Neuron.* If confirmed, the discovery could lead to a genetic test for vulnerability to depression and a way to predict which patients might respond best to serotonin-selective antidepressants.

Zhang X, Gainetdinov RR, Beaulieu JM, Sotnikova TD, Burch LH, Williams RB, Schwartz DA, Krishnan KR, Caron MG. Loss-of-function mutation in tryptophan hydroxylase-2 identified in unipolar major depression. Neuron. 2005 Jan 6;45(1):11-6.

Psychotherapy and Medications Best for Youth with Obsessive Compulsive Disorder
Children and adolescents with obsessive compulsive disorder (OCD) respond best to a combination of both psychotherapy and antidepressant medication, a major clinical trial has found. The Pediatric OCD Treatment Study (POTS) study recommends that treatment begin with cognitive behavior therapy (CBT), either alone or with a serotonin reuptake inhibitor (SSRI) antidepressant. The research, led by John March at Duke University and Edna Foa at University of Pennsylvania, spotlights the need for improved access to CBT, since most young people with OCD currently receive only antidepressant medication, often combined with an antipsychotic medication. Ninety-seven 7-17 year-olds with OCD completed 12 weeks of treatment with either CBT, the SSRI sertraline, the combination treatment, or a placebo. Combining sertraline and CBT was more effective than treatment with just one or the other. CBT alone did prove superior to sertraline, which, in turn, was better than a placebo.

Pediatric OCD Treatment Study (POTS) Team. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. Journal of the American Medical Association.2004 Oct 27;292(16): 1969-76.

Treating Depression in the Workplace is Cost-Effective
Two publications by NIMH grantees at the Tufts-New England Medical Center and the University of Colorado Health Sciences Center clearly demonstrate the importance of recognizing depression in the workplace and the cost-effectiveness of treating those affected. In the first, employees with depression – even compared to employees with rheumatoid arthritis, a chronic illness that can impair job performance – were four to five times more likely to become unemployed, to have diminished productivity, and to exhibit increased absenteeism. However, appropriate treatment for depression resulted in positive changes in all three areas, suggesting a need for work accommodation programs to address this population. The second study provides evidence that offering appropriate, evidence-based depression treatment for employees is a cost-effective strategy for American businesses. Further information on cost effectiveness will become available at the completion of the ongoing NIMH-funded study, "*Outreach and Treatment for Depression in the Labor Force*," which is scheduled for completion in 2006.

Lerner D, Adler DA, Chang H, Lapitsky L, Hood MY, Perissinotto C, Reed J, McLaughlin TJ, Berndt ER, Rogers WH. Unemployment, job retention, and productivity loss among employees with depression. Psychiatric Services. 2004 Dec;55(12):1371-8.

Rost K, Smith JL, Dickinson M. The effect of improving primary care depression management on employee absenteeism and productivity. A randomized trial. Medical Care. 2004 Dec;42(12):1202-10.

HIV/AIDS

Genetic Trait Linked to AIDS Resistance
A team of investigators in the US, Great Britain, and Argentina showed that the likelihood of acquiring HIV and, once infected, of progressing to full-blown AIDS, is much greater in people who have a below-average number of copies of the gene that encodes for an immune system signaling chemical (chemokine) called CCL3L1. Researchers led by NIMH-supported Sunil Ahuja at the University of Texas Health Science Center selected CCL3L1 for study because it interacts with a receptor (CCR5) that is the main entry point of HIV into cells. CCL3L1 is also the most potent agonist for CCR5, giving it strong anti-HIV properties. Individuals who

possess both low numbers of the CCL3L1 gene and disease-accelerating CCR5 variants demonstrated a more than threefold greater risk of rapid progression to HIV-associated dementia and opportunistic infections, such as cytomegalovirus (CMV), which are associated with mental health disorders. These studies highlight a possible means to stratify, based on genetics, the susceptibility of individuals for disorders such as HIV-associated dementia.

Gonzalez E, Kulkarni H, Bolivar H, Mangano A, Sanchez R, Catano G, Nibbs RJ, Freedman BI, Quinones MP, Bamshad MJ, Murthy KK, Rovin BH, Bradley W, Clark RA, Anderson SA, O'Connell RJ, Agan BK, Ahuja SS, Bologna R, Sen L, Dolan MJ, Ahuja SK. The influence of CCL 3L1 gene-containing segmental duplications on HIV-1/AIDS susceptibility. Science. 2005 Jan 6; Epub ahead of print

Cost-Effectiveness Study Supports Expanded US HIV Screening

Although US guidelines recommend routine HIV counseling, testing, and referral (HIVCTR) in clinical settings with one percent or more HIV prevalence, roughly 280,000 Americans remain unaware that they are infected. The implication is that current guidelines, originally created by the CDC for high-risk populations (pregnant women, STD clinic workers and clients), may not be rigorous enough to provide the most cost-effective screening. Investigators led by David Paltiel at the Yale School of Medicine developed a computer simulation to compare routine, voluntary HIVCTR to current practice (background testing and detection upon presenting with an opportunistic infection). They evaluated these practices in three target populations: "high-risk," "CDC threshold," and "US population." In the "high-risk" population, adding one-time screening to current practice was associated with earlier diagnosis of HIV and increased average survival time among HIV-infected patients. In all study populations, testing every three to five years increased the cost-effectiveness per quality-adjusted life year (QALY). The investigators concluded that in all but the lowest-risk populations, routine, voluntary HIV screening once every 3 to 5 years is justified on both clinical and cost-effectiveness grounds.

Paltiel AD, Weinstein MC, Kimmel AD, Seage GR, Losina E, Zhang H, Freedberg KA, and Walensky RP. Expanded HIV screening in the United States – a cost-effectiveness analysis. New England Journal of Medicine. (in press, Feb 2005).

Intervention Reduces HIV Transmission and STDs among HIV-Infected Women

HIV transmission prevention strategies that focus on HIV-positive women may be key in controlling the spread of the disease. Given such need, researchers led by Emory University's Gina Wingood and Ralph DiClemente created the WiLLOW (women involved in life learning from other women) intervention, which emphasizes gender pride, communication and safer sex skills, and healthy sexual and social relationships. In a randomized controlled trial of 366 women living with HIV, researchers evaluated the efficacy of WiLLOW in reducing HIV transmission risk behaviors and the occurrence of sexually transmitted diseases (STDs), as well as in enhancing HIV-preventive psychosocial and social support factors. Over the 12-month follow-up, women in the WiLLOW intervention, relative to the comparison group, reported positive results, including fewer episodes of unprotected intercourse, lower incidence of bacterial STDs, greater HIV knowledge and condom-using skill, larger social support networks, and fewer partner-related barriers to condom use. This is the first trial to demonstrate that tailoring HIV transmission prevention strategies to the specific psychosocial needs of HIV-positive women can lead to reductions in risky sexual behavior and incident bacterial STDs.

Wingood GM, DiClemente RJ, Mikhail I, Lang DL, McCree DH, Davies SL, Hardin JW, Hook EW 3rd, Saag M. A randomized controlled trial to reduce HIV transmission risk behaviors and sexually transmitted

diseases among women living with HIV: The WiLLOW Program. Journal of Acquired Immune Deficiency Syndromes. 2004 Oct 1;37:S58-S67.

Online Training Provides Support for International HIV Intervention Efforts
Despite the need to transfer science advances to AIDS service providers globally, most providers have little access to scientific developments relevant to their programs. However, the Internet provides an important new avenue for technology transfer. Jeffrey Kelly and colleagues at the Medical College of Wisconsin conducted an international intervention study on nongovernmental HIV prevention organizations in 78 countries, which were randomized to be either a control site or an experimental technology transfer site. All organizations were given basic technology and training, while the experimental sites also received an interactive distance learning computer training curriculum and individualized distance consultation. Of the 42 organizations in the experimental group, 29 adopted the intervention in their communities or trained other agencies to also use it. The researchers concluded that advanced communication technologies can create a cost-effective infrastructure to disseminate new intervention models to service providers worldwide.
Kelly JA, Somlai AM, Benotsch EG, McAuliffe TL, Amirkhanian YA, Brown KD, Stevenson LY, Fernandez MI, Sitzler C, Gore-Felton C, Pinkerton SD, Weinhardt LS, Opgenorth KM. Distance communication transfer of HIV prevention interventions to service providers. Science. 2004 Sep 24;305(5692):1953-5.

NIMH Publications

Schizophrenia Bulletin
The last issue of the *Schizophrenia Bulletin* features a special section on mental illness stigma, "Building Mental Illness Stigma Research," edited by Emeline Otey and Wayne Fenton. Three of the papers are reports based on commissioned white papers recommended by the NIMH Stigma Working Group as a means of facilitating research on mental illness stigma and discrimination. A fourth paper reports the results of a field test of "The Science of Mental Illness," a five-module educational curriculum supplement for middle school students that will be distributed free of charge from the NIH to teachers around the country to foster interest in science and to improve science literacy. The field test indicated that exposure to a science-based educational module yielded short-term improvements in both knowledge about mental illness and mental illness stigma attitudes. Effects were most significant for students holding the most stigmatizing attitudes at baseline.
Schizophrenia Bulletin. 2004 Dec;30(3):477-677.

Progress on NIMH Initiatives

NIMH-Administered RFAs
Research on Interventions for Anorexia Nervosa
NIMH seeks applications to evaluate interventions for treating anorexia nervosa (AN). The aim of this grant is to support the development of a collaborative network of qualified institutions that will have the capacity to conduct moderate to large-scale evaluations of promising interventions for AN, as well as long-term follow-up of research participants. Establishing a Research in Anorexia Nervosa (RIAN) network will facilitate future research efforts on treating and preventing this rare and poorly understood disease.
Release date: January 7, 2005; Expiration date: March 12, 2005
http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-05-009.html

Scientific Program Director: Linda Street, PhD, Division of Services and Intervention Research, National Institute of Mental Health

Identifying Autism Susceptibility Genes

NIH and an international public/private partnership of government health agencies and private advocacy organizations committed more than $21 million for research to identify the genes and gene variants that confer susceptibility to autism. NIH is spearheading the coalition, whose members include the Canadian and Irish governments and three private autism foundations Applications are encouraged to focus on complex modes of inheritance that include multiple risk factors (e.g., environmental, multigenic, and epigenetic effects). The research may provide a means to subdivide autism spectrum disorders into identifiable, distinct disorders, with different molecular mechanisms. Data and biomaterials analyzed in projects supported by this initiative will be included in a data management and cell repository facility maintained under the NIMH Human Genetics Initiative (http://nimhgenetics.org/) and broadly distributed to the scientific community.

Release date: December 13, 2004; Expiration date: April 20, 2005

http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-05-007.html

Scientific Program Director: Steven O. Moldin, PhD, Division of Neuroscience & Basic Behavioral Science, National Institute of Mental Health

Psychosocial Needs of Children Affected by AIDS in Low-Resource Countries

The NIMH and NINR are looking for grant applications that address critical gaps in research on the mental health and psychosocial needs of children in low-resource countries facing the loss of parents or caretakers due to HIV/AIDS. This initiative will support the development, implementation, evaluation, and dissemination of research to minimize the adverse mental health problems associated with loss of parents and other close acquaintances to AIDS. It is hoped that such research will encourage new collaborations between US- and foreign-based principal investigators that effectively augment existing HIV treatment, care, and support programs with empirically-supported, sustainable interventions.

Release date: November 29, 2004; Expiration date: April 23, 2005

http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-05-008.html

Scientific Program Director: Andrew D. Forsyth, PhD, Division of Mental Disorders, Behavioral Research & AIDS, National Institute of Mental Health

Collaborative RFAs

Pediatric HIV/AIDS Cohort Study (PHACS)

NICHD, NIAID, NIDA, and NIMH are partnering to facilitate research efforts addressing the long-term safety of fetal and infant exposure to prophylactic antiretroviral chemotherapy, and the effects of perinatally acquired HIV infection in adolescents. The institutes are soliciting interest in a cooperative agreement to create a body of data to understand more fully the effect of HIV on sexual maturation, pubertal development, and socialization of perinatally HIV-infected pre-adolescents and adolescents, and to acquire more definitive information regarding long-term safety of antiretroviral agents when used during pregnancy or in newborns.

Release date: December 3, 2004; Expiration date: March 11, 2005

http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-05-018.html

Scientific Program Director: Jack Moye, Jr, MD, Pediatric, Adolescent and Maternal AIDS Branch, National Institute of Child Health and Human Development

Building Interdisciplinary Research Careers in Women's Health

The NIH Office of Research on Women's Health (ORWH) and its cosponsors (AHRQ, NICHD, NIAAA, NIAID, NIDA, NIDDK, NIEHS, NIMH, and ODS) invite institutional career development award applications for Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Career Development Programs. These awards will support research career development of junior faculty members, known as Interdisciplinary Women's Health Research (IWHR) Scholars, who have recently completed clinical training or postdoctoral fellowships, and who are commencing basic, translational, behavioral, clinical and/or health services research relevant to women. The goal of this initiative is to promote interdisciplinary research and the transfer of findings that will benefit women's health, including sex/gender similarities or differences in biology, health or disease.

Release date: November 24, 2004; Expiration date: February 24, 2005

http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-05-002.html

Scientific Program Director: Joan Davis, MD, MPH, Center for Population Research, National Institute of Child Health and Human Development

Adolescent Medicine Trials Network for HIV/AIDS Interventions

NIDA and NIMH are seeking applications for a cooperative agreement to sustain the Adolescent Medicine Trials Network (ATN). This network's primary mission is to conduct research, independently and collaboratively, on HIV-infected and HIV-at-risk pre-adolescents, adolescents, and young adults. Further funding will allow the ATN to continue expanding the infrastructure required to support a network of research sites with the capacity for developing and conducting selected behavioral, community-based translational, prophylactic, therapeutic, and vaccine trials.

Release date: November 24, 2004; Expiration date: March 26, 2005

http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-04-025.html

Scientific Program Director: Audrey Smith Rogers, PhD, MPH, Pediatric, Adolescent, and Maternal AIDS Branch, National Institute of Child Health and Human Development

Leadership for HIV/AIDS Clinical Trials Networks

The NIAID and co-sponsoring institutions (NIAAA, NCI, NICHD, NIDCR, NIDA, NIMH, FIC, and NINR) are calling for applications to help establish the leadership for three to six HIV/AIDS Clinical Trials Networks to carry out the NIAID research agenda in a variety of areas, including vaccine research and development, and prevention of HIV infections. Each network will be expected to give high priority to joint research efforts in order to effectively develop and implement a clinically relevant, interdisciplinary, and cost-efficient research program.

Release date: November 19, 2004; Expiration date: May 12, 2005

http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-05-001.html

Scientific Program Director: Office of the Director, Division of AIDS, National Institute of Allergy and Infectious Diseases

International Cooperative Biodiversity Groups (ICBG)

In alliance with the National Science Foundation (NSF) and the USDA, several NIH institutes (FIC, NCI, NIAID, NIGMS, NHLBI, NIDA, NIMH, NCCAM, ODS) are inviting applications for the establishment of "International Cooperative Biodiversity Groups" (ICBG) to address issues of biodiversity conservation, economic capacity, and human health through discovery and development of therapeutic agents for major diseases in developing countries, as well as those important to developed countries. The focus is to

promote the conservation of biological diversity through the discovery of bioactive agents from natural products, and to ensure that benefits accruing from both the research process and any discoveries are shared with the country of origin.
Release date: October 26, 2004; Expiration date: February 16, 2005
http://grants1.nih.gov/grants/guide/rfa-files/RFA-TW-04-004.html
Scientific Program Director: Joshua Rosenthal, PhD, Division of International Training and Research, Fogarty International Center, National Institutes of Health

NIH Roadmap RFAs

NIMH continues to be actively involved in the many initiatives of the NIH Roadmap. Some new RFAs from the Roadmap include Predoctoral Clinical Training Programs and Multidisciplinary Clinical Research Career Development Programs. For a comprehensive list of NIH Roadmap initiatives, please visit the NIH website at http://nihroadmap.nih.gov/grants/index.asp.

NIMH Public Outreach

NIMH Alliance for Research

NIMH is committed to bringing the views of its stakeholders to bear on its activities, programs, and decision-making. The Institute is also dedicated to maintaining a transparency that includes communicating about NIMH processes and progress, and seeking input from the public about the direction of NIMH scientific priorities. The opportunity to hear constituent views and to maintain a vibrant dialogue is critical for the Institute. Thus, the Institute has convened organizations that represent people with mental illnesses and their families in a group called the *NIMH Alliance for Research Progress*. The first meeting of the *Alliance*, held in July 2004, featured an opening plenary session on NIMH research advances and future scientific directions. The rest of the day was devoted to dialogue and interaction between constituents and NIMH staff. A full report is available on the website at http://www.nimh.nih.gov/Outreach/roundtablemenu.cfm. In response to constituents' requests for more research updates, the second meeting in late January 2005 featured scientific presentations from key senior NIMH investigators, both extramural and intramural, as well as continued efforts to foster discussion. The discussion period allowed *Alliance* participants to highlight various pressing needs in the mental health field. A comprehensive report of the January meeting will soon be posted on the NIMH web site.

NIMH Outreach Partners Program

The National Institute on Drug Abuse (NIDA) and the Substance Abuse and Mental Health Services Administration's (SAMHSA) Center for Mental Health Services (CMHS) have recently joined the NIMH Outreach Partners Program (http://www.nimh.nih.gov/outreach/partners/partners.cfm). The Outreach Partners Program is a nationwide initiative of the NIMH that enlists national and state organizations in partnerships to help bridge the gap between research and clinical practice by disseminating the latest scientific findings, informing the public about mental disorders, alcoholism, and drug addiction, and reducing the stigma and discrimination associated with these illnesses. The annual meeting of the Outreach Partners will be held in Omaha, Nebraska, March 31 to April 3, 2005.

Real Men Real Depression
In October, the NIMH celebrated the overwhelming success of the Real Men Real Depression (RMRD) campaign with an honor ceremony at the Lawton Chiles International House on the NIH campus. NIMH staff members were joined by several of the men who first volunteered for the campaign as well as US Surgeon General Richard Carmona, NIH Deputy Director Raynard Kington, and other early supporters of the effort. NIMH recognized each of the participants for their service on the campaign, and debuted a mini-documentary highlighting how the Peoria, IL local Mental Health Association adopted the RMRD campaign as a community-wide project. Other recent highlights include:

- NIMH is working with Caterpillar Inc. to raise awareness of depression among their employees and their family members. The company began the program in January 2005, using RMRD posters, brochures, and fact sheets co-branded with the NIMH and Caterpillar logos. Materials will be distributed to each of their business units in the United States, reaching more than 50,000 employees.
- In January, the University of Michigan, Ann Arbor began promoting the RMRD campaign to their students and employees. The campaign will be a highlight of the third annual conference on depression on college campuses in March 2005. They plan to run the campaign again as the incoming freshman class arrives next fall.
- In January, the Portsmouth Regional Hospital in Portsmouth, New Hampshire launched a local RMRD campaign to run through March 2005, with print PSAs in local papers and broadcast PSAs on several seacoast radio stations.

Research Conferences

Scientific Advances in Trichotillomania and Related Repetitive Behaviors
NIMH and the Trichotillomania Learning Center, Inc. co-sponsored a workshop in November 2004 to identify promising approaches and opportunities applicable to clinical research in trichotillomania and to highlight potentially promising avenues that require further development. Highlights of the meeting included recent work on animal models of trichotillomania, and focused discussion on neurobiology and therapeutics. *For more information, please contact Regina James at: rjames@mail.nih.gov.*

Federal Child Neglect Research Consortium Meeting
In cooperation with NIDA and NICHD, NIMH hosted the fifth meeting of the Federal Child Neglect Research Consortium in January 2005. Other research partners of the consortium include NINDS, NIAAA, and NIDCR, as well as the Department of Education, Department of Justice, Children's Bureau, and Office of Child Abuse and Neglect. Guest speakers included NIMH grantees Seth Pollack, who spoke on "Emotion Processing and Neurobehavioral Correlates," and Mark Chaffin, who discussed Project SafeCare, the statewide prevention-effectiveness trial for child neglect. *For more information, please contact Cheryl Boyce at: cboyce@mail.nih.gov.*

NIH State-of-the-Science Conference: Preventing Violence and Related Health-Risking Social Behaviors in Adolescents
In October 2004, NIMH co-sponsored a state-of-the-science conference to review research accomplishments that can improve public health and to identify areas for progress in preventing violence and related behaviors among adolescents. The panel noted a number of

factors contributing to scientific and practice advances, such as identification of developmental antecedents of violence and related behaviors, interventions targeting developmental antecedents, and identification of some widely implemented programs shown to be ineffective and harmful. The conference panel also observed that additional progress requires forging new partnerships, as well as adapting established intervention protocols, in support of efforts of the Department of Education, Department of Justice, SAMHSA, CDC, and others. For more information, please see: http://consensus.nih.gov/ta/023/023youthviolencepostconfintro.htm.

Dysfunctional Appetitive Behavior: Developing Novel Interdisciplinary Approaches to Understanding Substance Abuse and Eating Disorders

In September 2004, NIMH sponsored a small, targeted workshop bringing together leaders in the fields of eating and substance use disorders to share methodological approaches and research findings that would identify interdisciplinary scientific opportunities. Workshop participants noted strategies to facilitate the development of novel interdisciplinary research approaches in substance abuse and eating disorders and articulated research questions that could inform the discovery of shared endophenotypes. *For more information, please contact Regina Dolan-Sewell at: rdolan@mail.nih.gov.*

North American Prodromal Longitudinal Study Investigators Meeting

The North American Prodromal Longitudinal Study Investigators Meeting, held in January 2005 and chaired by Robert Heinssen, was designed to resolve methodological difficulties that prohibit integrating prodromal schizophrenia research datasets. Tasks accomplished included finalizing the list of variables, resolving measurement discrepancies, outlining access rights to the master database and authorship of scientific papers, and developing a detailed work plan for 2005. Work will commence immediately to create the largest database of persons at high clinical risk for schizophrenia using data from 400 study participants who have been followed longitudinally through the initial years of vulnerability. *For more information, please contact Robert Heinssen at: heinsse@mail.nih.gov.*

MATRICS/TURNS Team Selects Compounds for Cognitive Deficits of Schizophrenia

Following a nationwide "call for nominations" in November 2004, the Treatment Units for Research on Neurocognition in Schizophrenia (TURNS) Compound Selection Committee reviewed over twenty nominations of novel therapeutic compounds for treating the cognitive deficits of schizophrenia and selected two for initial clinical efficacy trials. Now almost complete, the NIMH Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) cognitive battery development process was the focus of a December 2004 special issue of *Schizophrenia Research*. In January 2005, NIMH, FDA, and MATRICS held a meeting to review data relating to the design of clinical efficacy trials of agents targeting negative symptoms of schizophrenia. The meeting focused on a process for developing or identifying widely acceptable, evidence-based measures and methodologies to establish the efficacy of treatments that target these negative symptoms. *For more information, please contact Wayne S. Fenton at: wfenton@mail.nih.gov.*

12th NIMH Biennial Research Conference on the Economics of Mental Health

The Financing and Managed Care Research Program held a conference in September 2004 inviting original research papers addressing issues related to the theme, "Enhancing the Impact of Mental Health Services: Economic Incentives and Research." Participants concluded that economics research plays an important role in understanding why and under

what circumstances cost-effective practices have or have not been adopted. The new Program Announcement (PA-05-008) "Research on Mental Health Economics" will further encourage health economists to conduct research in these challenging areas. *For more information, please contact Agnes Rupp at*: *arupp@mail.nih.gov*.

Advancing the Science of Implementation

This October 2004 workshop was an effort to improve the fit between mental health interventions and the service delivery systems that use them. Small interdisciplinary groups of intervention researchers, organizational theorists, intervention implementers, clinicians, and methodologists discussed key topics in relation to individual and team-delivered psychosocial interventions, and medication management interventions. Discussions focused on critical questions such as: Can intervention trials incorporate systemic variables in the research designs to more effectively understand the likely fit of an intervention with the service system? Are current measures and designs either usable or adaptable for mental health intervention and services research? How can research designs more effectively study "noise" from real-world service systems? *For more information, please contact David Chambers at: dchamber@mail.nih.gov*.

Community Assessment of the Safety of Psychotropic Medications in Children and Adolescents

NIMH convened this meeting in November 2004 to hear experts in the evaluation of drug safety in children discuss possible approaches to utilizing data from the naturalistic community use of psychotropic medications to inform about their safety. Such approaches would complement information derived from controlled clinical trials, which are limited by a relatively small sample size and subject selection. A number of potential designs and methods were discussed that would utilize large databases of public and private health insurance organizations. *For more information, please contact Benedetto Vitiello at: bvitiell@mail.nih.gov*.

Latin American Journalists' Workshop on Reporting Science Findings on Mental Health and Related Issues

The past 20 years have seen a boom in science communication in Latin American countries, but reports on mental illness still reflect bias and stigma. To address this issue, NIMH joined three other NIH institutes in sponsoring a weeklong workshop in Panama in October 2004 for journalists from Central and South America. The objectives were to increase the accuracy of reporting on scientific discoveries, to familiarize journalists with available Internet resources, and to foster dialogue between scientists and journalists. Sergio Aquilar-Gaxiola, a member of the NAMHC, reported on the prevalence of mental illness in Latin American countries and stimulated questions and requests for interviews from the majority of reporters. Rob Taylor, the executive director of the International Center for Journalists, a co-organizer of the meeting, was so impressed with the interest in mental health issues that he has requested mental health presentations at other international journalism workshops. *For more information, please contact Karen Babich at: kbabich@mail.nih.gov*.

Third Biennial World Conference on the Promotion of Mental Health and Prevention of Mental and Behavioral Disorders

Moving research into effective practice was the major theme of this September 2004 conference that drew participants from around the globe. Presentations focused on promotion and prevention of mental disorders worldwide, evidence-based programs and

principles of practice, international exchange of research outcomes, advocacy, and improved training. Keynote presentations were made by Rosalyn Carter, the honorary chair of the conference, Tom Insel, Charles Curie of SAMHSA, Kathryn Power, Director of CMHS, and mental health administrators from New Zealand, England and the Netherlands. Dr. Insel's presentation on an animal model of the long-term benefit of nurturing on stress management was readily translated by the audience to their own work on prevention strategies. Proceedings of the conference will be available this summer. *For more information, please contact Karen Babich at: kbabich@mail.nih.gov.*

Project One Billion: International Congress of Ministers of Health for Mental Health and Post-Conflict Recovery

Project One Billion – the "billion" signifying the number of people worldwide suffering the psychological consequences of war, torture, and terrorism – brought together 40 ministers of health from post-conflict countries. The December 2004 meeting, organized by NIMH grantee Richard Mollica, director of the Harvard University Program in Refugee Trauma, focused on planning mental health policies for populations exposed to mass violence. The consensus of the ministers and those who had conducted research in conflict-torn areas was that the victims suffer from depression and anxiety, not post-traumatic stress, and their disorders are most appropriately handled through listening, assuring basic needs are met, not forcing talk (not debriefing), mobilizing family and community support, and using indigenous healers. A significant outcome of this meeting was the production of the *Book of Best Practices for Trauma and the Role of Mental Health in Post-Conflict Recovery,* edited by Mollica, et al. *For more information, please contact Karen Babich at: kbabich@mail.nih.gov*

Public Reviewer Orientation and Training Meeting

To ensure that the public health importance of research grant applications is adequately considered, NIMH invites members of the public to take part in intervention and service review groups. In an effort to increase the pool of potential public reviewers, the Division of Extramural Affairs (DEA) sponsored a daylong orientation and training meeting in November 2004 for individuals interested in serving as public reviewers. Presenting on their experiences as scientific reviewers were Katharine Phillips, Chairperson of the Interventions Review Committee, and Martha Bruce, Chairperson of the Services Research Review Committee. Several veteran public reviewers also spoke about their tasks in the review process. The meeting provided an opportunity for participants to learn about the role of the public reviewer and to participate in hands-on exercises and activities. *For more information, please contact David Sommers at: dsommers@mail.nih.gov.*

Methods in Intervention Research

The DEA and the Interventions Review Committee sponsored a full day workshop in October 2004 to discuss issues related to ways that NIMH program staff, clinical researchers, and statisticians can collaborate in assessing the overall merit of applications. Topics included the level of statistical sophistication appropriate to different funding mechanisms, best practices for weighting statistics/data analysis elements in an application's final priority score, and different ways in which statisticians conceptualize their role in an application's development and follow-through. Approximately 70 people attended the workshop, and a7-member panel of expert statisticians led the discussion. Participants were awarded continuing education credits (CME's and CEU's). *For more information, please contact David Sommers at: dsommers@mail.nih.gov.*

Identified Neuron Database Workshop
In December 2004, the NIMH Office on Neuroinformatics co-sponsored a workshop at Georgia State University for neuroscientists, computer scientists, and other information technologists to initiate plans for creating a publicly accessible web-based database where information about identified neurons or neuronal classes and synapses can be published. The immediate goal was to develop a database of identified neurons in invertebrates that will serve as a test bed for understanding the issues involved in creating a complete wiring diagram of the mammalian brain. The group also collaborated to initiate plans for organizing a larger conference on the uses of databases for furthering neuroscience research. *For more information please contact Michael D. Hirsch at: mhirsch@helix.nih.gov.*

Meeting-based publications
The *Journal of Affective Disorders* devoted an October 2004 special issue to proceedings from the first annual **NIMH Pediatric Bipolar Disorder Conference**, which took place in Washington, DC, in March 2003, and was hosted in collaboration with Massachusetts General Hospital. The conference brought together physicians, parent advocates, and researchers from around the world to share information and discuss topics surrounding the recommendations from the 2001 NIMH research roundtable on bipolar disorder in children and adolescents.
Biederman J, James RS. The Proceedings of the National Institute of Mental Health (NIMH) Pediatric Bipolar Disorder Conference. Journal of Affective Disorders. 2004 Oct;82(1001):iii-S128.
Biederman J, James RS. Furthering the scientific foundation of pediatric bipolar disorder. Journal of Affective Disorders. 2004 Oct;82(1001):S1-S3.

The proceedings of the meeting on **Molecular Markers and Mechanisms of HIV-Induced Nervous System Disease** were published as a supplement to the *Journal of Neuroimmunology*. Jeymohan Joseph, Burt Sharp, Howard Fox and Howard Gendelman served as guest editors for this supplement.
Joseph J, Sharp B, Fox HS, Gendelman HE. Molecular markers and mechanisms of HIV-induced nervous system disease. Journal of Neuroimmunology.2004 Dec;157(1-2):1-208.

In November 2004, *Child Maltreatment* published a series on child neglect research, featuring various contributions from the **Federal Child Neglect Research Consortium** (composed of NIMH, NIDA, NICHD, NINDS, NIAAA, NIDCR, Dept of Education, Dept of Justice, Children's Bureau, and Office of Child Abuse and Neglect). Editors included Cheryl A. Boyce (DPTR) with Howard Dubowitz, Desmond Runyan, and Diane DePanfilis. The articles can be accessed online at http://cmx.sagepub.com/content/vol9/issue4.
Child Maltreatment. 2004 Nov 1;9(4):343-434.

Understanding and Treating Borderline Personality Disorder. A Guide for Professionals and Families is a January 2005 publication of the American Psychiatric Association edited by NIMH grantees John Gunderson and Perry Hoffman. The 15 chapters were originally presented at an annual meeting of the National Educational Alliance Borderline Personality Disorder for which the NIMH was a principal financial sponsor. Many of the chapters report findings from NIMH-funded research concerning this disorder.

New Prevention Interventions for People Living with AIDS
A special supplemental issue of the *Journal of Acquired Immunodeficiency Syndromes* published in October 2004 and guest-edited by Christopher Gordon of DAHBR focused on the state-of-the-science for prevention interventions for persons living with HIV/AIDS. The supplement follows up on a meeting sponsored by NIMH's Center for Mental Health Research on AIDS and the CDC, held in conjunction with the 2003 National HIV Prevention Conference in Atlanta. Dr. Gordon also authored the introductory article on progress and priorities.
Gordon CM, Stall R, Cheever LW. Prevention interventions with persons living with HIV/AIDS: challenges, progress, and research priorities. Journal of Acquired Immune Deficiency Syndromes. 2004 Oct 1;37:S53-S57.

Budget

FY 2005 Congressional Action
After three consecutive Continuing Resolutions held the National Institutes of Health to its FY 2004 funding level, the Congress passed an FY 2005 appropriation for the NIH as part of the FY 2005 Consolidated Appropriations Act on November 20, 2004. As indicated on Attachment 1, the Bill provides a total of $28.4 billion for the NIH. This total NIH amount represents an increase of $564 million or 2.0% over the FY 2004 NIH total of $27.8 billion. The final NIH total enacted appropriation of $28.4 billion was less than the amount in the President's Budget Request ($28.5 billion), the previous House action ($28.5 billion), and the previous Senate Committee action ($28.9 billion).

The FY 2005 President's Budget had proposed to reduce committed funding levels for ongoing Research Project Grants (RPGs) by about 1.1% and to allow no increase in the average cost of competing RPGs. The Congress rejected both these proposals – noncompeting RPGs will be paid at committed levels and the average cost of a competing RPG may increase by about 3.5% in FY 2005 over FY 2004.

The NIMH FY 2005 appropriation of $1.412 billion is an increase of $31 million or 2.2%over FY 2004. As shown on Attachment 2, NIMH currently projects to award approximately 559 competing RPGs in FY 2005, compared to 630 in FY 2004.

FY 2006 President's Budget Request
The FY 2006 President's Budget Request will become public when it is released on Monday, February 7, 2005.

Major NIMH Staff Awards

Richard K. Nakamura, PhD, Deputy Director of NIMH, received the Richard T. Louttit Award, which recognizes excellence in government service on behalf of mental health sciences. The award was presented by the Federation of Behavioral, Psychological, and Cognitive Sciences on December 4, 2004.

Molly Oliveri, PhD, Deputy Director of DPTR, received the Award for Distinguished Service on Behalf of Social-Personality Psychology from the Society of Personality and Social Psychology at the Society's annual meeting in January 2005.

Willo Pequegnat, PhD, of DAHBR, was presented the Meritorious Research Service Commendation of the American Psychological Association and the Board of Scientific Affairs at a meeting of the Board of Directors in December 2004. The commendation was given in recognition of her outstanding contributions to psychological science through service within the federal government in program development and research facilitation. An invited chapter by Dr. Pequegnat on AIDS behavioral prevention programs ("AIDS Behavioral Prevention: Unprecedented Progress and Emerging Challenges") was just published in *AIDS in the 21st Century* by Elsevier Publishing Company.

Staff Changes

Arriving:

Jing Bao, MD, PhD, joined DAHBR as a Scientific Program Analyst in November to work on HIV/AIDS therapeutic issues, having served previously at National Cancer Institute as a Research Fellow investigating the regulation of cell death pathways. In 2004, she started a new career as a Technology Transfer Specialist and received intensive training on the management of intellectual properties and various types of agreements, patents and licenses.

Andrea Beckel-Michener, PhD, has joined the Division of Neuroscience and Basic Behavioral Science as the Chief of the Functional Neurogenomics Program. Dr. Beckel-Mitchener received her PhD in biomedical sciences from the University of New Mexico. Her research has focused on mechanisms underlying transcriptional and post-transcriptional regulation of gene expression in the brain. She comes to NIMH from an academic appointment at the Beckman Institute, University of Illinois where she studied the expression and function of Fragile X Mental Retardation Protein (FMRP) in a mouse model of the syndrome.

Mary Farmer, MD, was detailed to the Extramural Review Branch in October from the Division of Neuroscience and Basic Behavioral Science where she served as Chief of the Human Genetics Initiative and Genomic Resources Program. Dr. Farmer is serving as a Scientific Review Administrator.

Shuang-Bao Hu, PhD, was detailed to the Extramural Review Branch in November to serve as a Scientific Review Administrator. Prior to his arrival at the branch, he was a Research Fellow in the Clinical Neuroendocrinology Branch, IRP, NIMH, where his work focused on gene expression patterns and unique gene expression changes in response to antidepressant treatment.

Michael Kozak, MD, has joined the Adult Psychopathology and Psychosocial Intervention Research Branch of DATR, where he is in charge of two new programs: the Affective Processes and Anxiety Disorders Research Program and the Psychosocial Intervention Efficacy Research Program. Dr. Kozak was formerly chief of the NIMH Review Branch.

Robert Munk joined the Grants Management Branch as a Grants Management Specialist in September 2004. Prior to his arrival at NIMH, Mr. Munk was a middle school math teacher in Carroll County, Maryland.

Elizabeth (Liz) Stillman, MSW, MPH, recently joined the Office of Constituency Relations and Public Liaison. She earned master's degrees in social work and public health and has worked as a mental health and substance abuse counselor. Before coming to NIMH, Liz worked in the Office of Communications and Public Liaison at National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Dawn Walker joined the Grants Management Branch in January as the Supervisory Grants Specialist (Team Leader) for the Division of Neuroscience and Basic Behavioral Science. Prior to her arrival at NIMH, Ms. Walker was a senior grants specialist with the National Heart, Lung, and Blood Institute.

Mark Walters joined the Grants Management Branch as a Grants Management Specialist in November 2004. Prior to his arrival at NIMH, he was an immigration specialist at the US Department of State's regional office in South Carolina.

Departing:

Joanna Chisar, RN, part of the Clinical Trials Operations and Biostatistics Unit in DSIR, responsible for the operations and safety oversight of multisite clinical trials (both within DSIR and across the two new translational divisions) left NIMH at the end of 2004.

Timothy Cuerdon, PhD, left his post as Chief, Adherence Research Program, Health and Behavioral Research Branch, DAHBR to pursue a career with the American College of Physicians in Philadelphia.

Dianne Grant, EEO assistant with the Office of Diversity and Employee Advocacy Programs, has left the Institute to devote more time to her undergraduate studies.

Timothy Hays, PhD, Director of the Outreach Partnership Program in the NIMH Office of Constituency Relations and Public Liaison, is moving on to the NIH Office of Policy for Extramural Research Administration (Office of Extramural Programs, OD) to serve as a health scientist administrator. Among his first tasks will be to work with staff as the Public Access Policy Project Manager.

Stephen Koslow, PhD, Director of NIMH's Neuroinformatics Program, retired from the federal government at the end of December 2004, after more than 30 years at the forefront of neuroscience research and its leadership at NIMH. Dr. Koslow will become Director of External Relations for the Allen Institute for Brain Science in Seattle, Washington, and Dr. Michael Huerta, Associate Director, DNBBS, will assume Dr. Koslow's responsibilities for the Human Brain Project. As part of the ongoing NIMH reorganization, the Office on Neuroinformatics (ONI) and its staff, Dr. Michael Hirsch, Deputy Director, and Kathryn Bognovitz, Program Assistant, will be transitioned to the DNBBS.

Izja Lederhendler, **PhD**, Chief of the Circadian Rhythms, Sleep and Regulation of Behavior Program in DNBBS, has accepted an offer to become Director of the NIH Office overseeing the NIH eRA efforts (Electronic Research Administration). eRA is NIH's infrastructure for conducting interactive electronic transactions for the receipt, review, monitoring, and administration of NIH grant awards to biomedical investigators

worldwide. With the departure of Dr. Lederhendler, national searches are currently being conducted to recruit new program chiefs for the Affect and Social Behavior Program and the Circadian Rhythms, Sleep and Regulation of Behavior Program. In the interim, Kevin Quinn, the Chief of this branch, will serve as the acting Program Officer for both programs.

Van Nguyen, who served as a Grants Program Specialist in DATR and DAHBR, left NIMH in January 2005 to serve as a Budget Analyst in the Financial Management Branch of the National Institute on Aging.

Clarissa Wittenberg, NIMH Director of Communications for the past six years, has accepted a new position in the HHS Office of Global Health with the Assistant Secretary for International Affairs. She and her staff made major contributions to NIMH and to the field of mental health. The Office of Communications created a series of award-winning educational materials about mental disorders and research: Science on our Minds; easy-to-read, plain language booklets; and Men and Depression. These materials continued to be reviewed, updated, reprinted, and disseminated through the recently redesigned website, which is earning awards for health communication. The Office of Communications has supported many other projects for the overall NIMH, including meetings and projects about children and violence, suicide prevention, autism, and school readiness. Clarissa Wittenberg was a creative force behind the landmark and highly successful Real Men Real Depression campaign. The Campaign increased the country's discussion of men and depression, and the issues related to depression.

Benjamin Xu, PhD, a Scientific Reviewer Administrator with the Extramural Review Branch, departed NIMH in January 2005.

In Memoriam

We deeply regret the passing of **Julius Axelrod, PhD**, a Nobel Laureate and NIMH researcher since 1955, who died in his sleep on December 29, 2004. Dr. Axelrod is probably best known for his work on brain chemistry in the early 1960's that led to modern-day treatments for depression and anxiety disorders. He inspired generations of neuroscientists during his long career at the National Institutes of Health (NIH). In 1996, NIH awarded him the title Scientist Emeritus. In 1970, Dr. Axelrod, known to his colleagues as "Julie," was awarded the Nobel Prize in Physiology or Medicine for his discoveries about how brain cells communicate with each other. He explained how neurotransmitters operate in the brain, forever altering the way modern antidepressant drugs are designed. Dr. Axelrod laid the groundwork for the treatment of anxiety and depression. He coined the phrase "re-uptake" inhibitors, referring to the "re-uptake" mechanism in brain cells that regulates the level of neurotransmitters available, influencing how neurons communicate. This revolutionary understanding of the brain's chemistry led to the modern generation of antidepressant medications—selective serotonin reuptake inhibitors (SSRIs). Dr. Axelrod had a remarkable approach to discovery, not only because of the breadth and depth of subject matter, but also his attitude in the lab. He mentored and trained more than 70 scientists, many of whom went on to become leaders in brain research. Dr. Axelrod was one of the giants upon whose shoulders today's neuroscientists stand. His contribution to the fields of mental health and neuroscience have made possible

current breakthroughs on mood and anxiety disorders, and myriad other areas. His legacy lives on in the work of others. He will be greatly missed.