November-December 2005
Volume 20, Number 6
The Education Issue

ASAM News

Newsletter of The American Society of Addiction Medicine

Inside

***See the new NIAAA Clinical Guidelines for Alcohol Use, enclosed with this issue of* ASAM NEWS!**

www.asam.org

ASAM's MRO, Drug Testing Courses Meet in Washington, DC

A comprehensive review of Federal drug-free workplace requirements, as well as the clinical aspects of MRO practice, was presented at ASAM's Medical Review Officer Training Course, December 9-11, 2005, at the Westin Embassy Row Hotel in Washington, DC. **Subsequent MRO courses will be offered July 21-23, 2006, in Phoenix, Arizona, and December 8-10, 2006, in Washington, DC.** Under the direction of course chair James L. Ferguson, D.O., an expert faculty reviewed the impact of the Federal Part 40 rule and recent developments in alcohol and drug testing technologies in terms of their implications for the work of Medical Review Officers. The course, which is approved for 18 Category 1 CME credits, also prepares candidates to sit for the MROCC certifying examination.

The MRO course was preceded by a workshop on Best Practices: Clinical Drug Testing in Addiction Treatment, on December 8th, also at the Westin Embassy Row Hotel in Washington, DC. Chaired by Louis E. Baxter, Sr., M.D., FASAM, the Best Practices workshop examined the legal, ethical and procedural aspects of drug testing in clinical practice, with an emphasis on cutting-edge issues such as the civil and criminal law. It is approved for 7.5 Category 1 CME credits.

For additional information on any of ASAM's courses, visit the ASAM website at WWW.ASAM.ORG or contact ASAM's Department of Meetings and Conferences at 301/656-3920. *(Conference coverage continues on page* **14***)*

ASAM Launches CME Course on Treatment of Alcohol Use Disorders

Elizabeth F. Howell, M.D., FASAM, President

As part of its ongoing commitment to help members translate the latest scientific breakthroughs to their own practices, ASAM has announced a new series of CME courses on the treatment of alcohol disorders. To be offered in 10 locations around the country, the 4-hour courses are free to participants. They are underwritten by an unrestricted educational grant from Forest Laboratories, manufacturers of acamprosate, and cosponsored by ASAM's state affiliates in California, Florida, Illinois, New Jersey, New York, Maryland, Michigan, Pennsylvania, Texas and Wisconsin.

The new courses are designed to meet the needs of addiction specialists who seek a succinct review and update on the latest strategies for identifying and managing alcohol use disorders. Each course is approved for 4 Category 1 CME credits.

See page 15 for course dates and locations. For additional information, visit the ASAM website at WWW.ASAM.ORG or contact project manager Angela Warner by phone at 301/656-3920, ext. 6010, or by email at AWARNER@ASAM.ORG. To register for one of the courses, contact Maureen Donohue by email at ASAM@RXPERIENCE.COM or by phone at 914/372-1960.

ASAM Members Respond to Katrina Victims' Call for Help

Eileen McGrath, J.D., Executive Vice President/CEO

Eileen McGrath, J.D.

In response to a request from the Center for Substance Abuse Treatment for physician volunteers to treat victims of Hurricane Katrina, 24 ASAM members signed up for a two-week relief mission in the Gulf Coast states. Sarz Maxwell, M.D., of the Illinois Society of Addiction Medicine, delivered a moving account of her experiences in the Gulf at ASAM's State of the Art Course. Another volunteer, who wishes to remain anonymous, has described his experiences in a blog that can be accessed at HTTP://WWW.HURRICANEADDICTS.BLOGSPOT.COM. Dr. Maxwell and Dr. Anton Bizzell, Medical Advisor in CSAT's Division of Pharmacologic Therapies, provided the photos below.

ASAM would like to acknowledge all of the wonderful members and other health care workers who responded to the call for help. Their generosity exemplifies the selfless commitment to patient care that is the spirit of ASAM. *(See page 6 for more news on Hurricane recovery efforts.)*

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ASAM is a specialty society of physicians concerned about alcoholism and other addictions and who care for persons affected by those illnesses.

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Web Site
For members visiting ASAM's web site (WWW.ASAM.ORG), entrance to the on-line Membership Directory requires the Username "asam" and the password "asam" (in lower case letters).

HOUSE REJECTS HHS FUNDING BILL

In a Congressional rarity, the full House of Representatives has defeated a spending bill for the Departments of Labor, Health and Human Services, and Education, even though the measure represented a compromise hammered out by a joint House-Senate conference committee. The bill included FY 2006 funding for a majority of the Federal government's addiction treatment and prevention programs. JoinTogether Online reports that the bill failed to pass when about two dozen House Republicans joined all the Democrats in voting against the bill, many because they were upset that negotiators had stripped all "earmarks" — also known as "pork" projects — from the final bill.

The compromise measure would have level-funded the Substance Abuse Prevention and Treatment Block Grant, maintaining spending at the FY 2005 level of $1.775 billion. President Bush's Access to Recovery voucher program also would have received no increase over 2005's $100 million budget. Overall funding for the Center for Substance Abuse Prevention (CSAP) would have been cut by $3.8 million from FY 2005, to $194.9 million, while the Center for Substance Abuse Treatment (CSAT) budget would have been trimmed by $19.4 million, to $402.9 million (some of the cuts represented deleted earmarks).

The budget for the National Institute on Drug Abuse (NIDA) would have increased by a modest $3.3 million, to $1.01 billion, while the budget of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) would have gained $1.8 million, to $440 million.

Addiction field leaders had called for $1.7 billion for the block grant, $422 million for CSAT, $202 million for CSAP, $400 million for SDFS, $1.035 billion for NIDA, and $452 million for NIAAA. Despite their disappointment at the compromise numbers, some field leaders are breathing a sigh of relief, noting that other programs were cut even more deeply or eliminated. One funding expert even joked that, in the current budget environment, level funding for the addiction block grant represented a "Good Housekeeping Seal of Approval."

That said, the fact that the conference report was defeated means it is back to the drawing board for the HHS budget. And while some advocates may see this as another opportunity to press lawmakers for higher funding levels for addiction-related programs, others are concerned that more scrutiny by conferees could just as easily lead to deeper cuts. Other possible budget scenarios being discussed include an across-the-board cut for all non-defense programs — which the Legal Action Center notes would mean that "our programs that are being level funded, including the Substance Abuse Prevention and Treatment Block Grant, are in jeopardy" — or simply keeping all programs at FY 2005 funding levels. *Source: Curley R, JoinTogether Online, November 18, 2005.*

GAO Says U.S. "Distracted" from Cocaine Problem

In a newly released report, the Government Accountability Office (GAO) warns that competing priorities, such as the war on terror, have distracted the U.S. from the battle against cocaine smuggling. The GAO report acknowledges that "in-transit" cocaine seizures rose 68 percent between 2000 and 2004, but notes that reprogramming of resources to the wars in Iraq and Afghanistan and dealing with the aftermath of Hurricane Katrina could undo any progress made by U.S. law enforcement. By way of example, the report describes the Coast Guard as increasingly hampered by lack of resources for interdicting drugs. The Pentagon cited "war-fighting requirements" as the reason for fewer anti-drug flights, while the Department of Homeland Security acknowledged that "unforeseen events such as Hurricane Katrina relief efforts may temporarily impact asset availability."

The report also says that the number of U.S. cocaine users remains stable at about two million, and that the greater number of drug seizures may reflect more supply in the pipeline. "Sen. Charles Grassley (R-IA), who commissioned the GAO study, commented: "We need to be more effective and better prepared because these are routes that not only move illicit drugs today, but can easily move other more dangerous commodities such as terrorists in the future."

Advertising Campaign Called Irresponsible

The National Association of Addiction Treatment Providers (NAATP) has called on RJ Reynolds, Inc., to discontinue its marketing efforts targeting 21-year-olds, the content of which links "coming of age" with the ability to use tobacco and alcohol.

In a statement calling the ad campaigns "irresponsible," NAATP's Board of Directors said that "when the costs to provide and to deliver quality health care are skyrocketing…[and] corporations (perhaps even RJ Reynolds) are finding it increasingly difficult to provide health care coverage to their employees, we know that a significant cost factor is the result of alcohol and nicotine addiction." The statement goes on to say that a sense of social responsibility requires that we "do all we can to reduce the costs associated with alcohol and nicotine addiction."

NAATP called on Reynolds to immediately halt the campaign, which involved mailing promotional materials — including coupons for $1.75 discounts on packs of Camel cigarettes — directly to young people. Dr. Ken Ramsey, who chairs NAATP's Board of Directors, said in the letter to Reynolds that, "As executives of organizations that deliver addiction treatment, we deal on a daily basis with the damaging effects of addiction: families are ruined; jobs are lost and health care cost rise."

NAATP is a trade association representing nearly 300 of the largest and best known providers of addiction treatment, both in the U.S. and internationally. Additional information on this issue or on the work of NAATP is available from the Executive Director, Dr. Ronald Hunsicker, at 717/392-8480 or at the association's website, HTTP://NAATP.ORG.

Clinical Support Network Seeks Volunteer Mentors

Elizabeth F. Howell, M.D., FASAM

The Physician Clinical Support System (PCSS), now entering its second year of operation, fosters support and communication among physicians who provide office-based buprenorphine treatment. The system, whose goal is to increase access to addiction treatment by expanding the network of physicians who provide buprenorphine in office-based settings, provides free peer-to-peer consultation in response to physicians' questions and concerns

Physician mentors are the backbone of the PCSS. Mentors are practicing physicians who volunteer to provide consultation by telephone, email, or in person. Mentors' advice covers a range of topics, including strategies for patient selection, induction. dosing and patient monitoring, as well as treatment of polysubstance addiction and management of co-occurring medical and psychiatric disorders.

At present, the national mentoring network has 45 physician members, who are organized in five regional groups, with each group supported by a Clinical Expert in the use of buprenorphine. The Clinical Experts are Paul Casadonte, M.D., Judith Martin, M.D., Elinore F. McCance-Katz, M.D., Ph.D., John A. Renner, Jr., M.D., and Andrew J. Saxon, M.D. The Clinical Expert group is chaired by PCSS Medical Director David Fiellin, M.D.

Mentor Martin Doot, M.D., says, "The strength of the program is the support and reassurance we are able to provide to physicians getting started with this new treatment." Dr. Doot adds that "being available to colleagues in our specialty by phone or email has been reassuring to them and brings out the `old teacher' in me. Experience with patients keeps me prescribing the medication; passing on hope, reassurance and a little of my experience gives a new prescriber the confidence to begin. Good therapeutic outcomes keep them involved after their initial experiences."

Dr. Elizabeth F. Howell

As part of the PCSS project, 14 chapters of the American Academy of Family Physicians and the American College of Physicians will offer workshops on office-based treatment of opioid addiction as part of their 2005 or 2006 annual scientific meetings. Three such workshops have already taken place. ASAM member James Flowers, M.D., addressed 75 family medicine physicians and residents at a Nevada workshop sponsored by AAFP in August 2005. The Nevada Academy's Executive Director said, " [Dr. Flowers] did a great job and we appreciate your organization providing such an informative lecture at our conference."

ASAM member Rolly Sullivan, M.D., presented at the West Virginia College of Physicians meeting in October. He reports that about 75 physicians attended.

Mark Publicker, M.D., spoke to the Maine Chapter of the American Academy of Family Physicians. He reports that there were about 70 attendees and adds, "I had a terrific reception and I'm sure that I'll be invited back next year."

Mentor Adam Gordon, M.D., notes that "One of the main strengths of the PCSS program is that it encourages one-to-one dialogue between the physician in the community and the PCSS mentor." Explaining that many physicians are interested in using buprenorphine, but are not confident that it can be managed in their practice settings, Dr. Gordon concludes that "The PCSS program encourages facilitation of this treatment and minimizes barriers by applying general principles of treatment to real-world, often chaotic and unique clinical practice settings…. The PCSS and its mentors often are thought of as clinical champions for addiction treatment. Through their example, we hope that more clinicians will engage in the treatment of opioid addiction."

The Physician Clinical Support System is funded by the Center for Substance Abuse Treatment (CSAT) of the Substance Abuse and Mental Health Services Administration (SAMHSA) and is administered by ASAM, with the help of a Steering Committee composed of representatives of the participating organizations. Steering Committee members (such as the AAAP, AAFP, AAPM, AATOD, AMA, AMERSA, AOAAM, APA, APS, ASAM, ATTC, CPDD, CSAT, HRSA, NIDA Clinical Trials Network, NYAM, PAETC, and SGIM) oversee the development, implementation and evaluation of the PCSS network; promote the integration of office-based treatment of opioid addiction into the ongoing practice of medicine; and promote research on buprenorphine treatment in office-based practice.

Becoming involved in this free nationwide network is easy: simply contact the PCSS staff to find a mentor, to become a mentor, or to obtain more information about the project. Visit the PCSS website at www.PCSSmentor.org, phone the staff at 877/630-8812, email PCSSproject@asam.org, or fax 301/576-5156.

Board Revises ASAM's Policy on Rapid and Ultra Rapid Opioid Detoxification

Mark L. Kraus, M.D., FASAM, and Petros Levounis, M.D., Co-Chairs, ASAM Public Policy Committee

ASAM's Board of Directors has approved a revision of the Society's Public Policy Statement on the use of rapid and ultra rapid opioid detoxification to reflect recent research on the use of the technique and to underscore ASAM's position that detoxification is only one component of treatment and does not, in itself, constitute a course of treatment. The new policy statement revises one adopted in 2000, entitled "Opioid Antagonist Agent Detoxification under Sedation or Anesthesia (OADUSA)." A copy of the revised statement is provided with this issue of **ASAM News**.

POLICY RECOMMENDATIONS

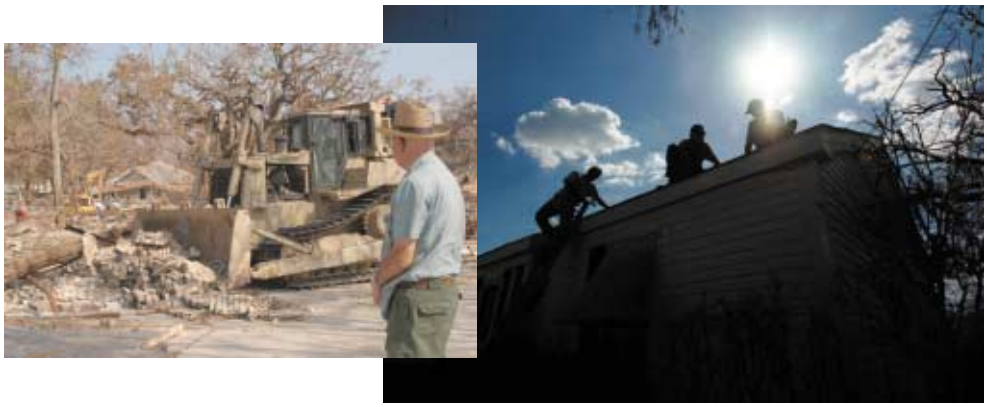
After reviewing the current literature on rapid and ultra rapid detoxification, the policy statement offers the following recommendations:

1. Opioid detoxification alone is not a treatment of opioid addiction. ASAM does not support the initiation of acute opioid detoxification interventions unless they are part of an integrated continuum of services that promote ongoing recovery from addiction.
2. Ultra-Rapid Opioid Detoxification (UROD) is a procedure with uncertain risks and benefits, and its use in clinical settings is not supportable until a clearly positive risk-benefit relationship can be demonstrated. Further research on UROD should be conducted.
3. Although there is medical literature describing various techniques of Rapid Opioid Detoxification (ROD), further research into the physiology and consequences of ROD should be supported so that patients may be directed to the most effective treatment methods and practices.
4. Prior to participation in any particular modality of opioid detoxification, a patient should be provided with sufficient information by which to provide informed consent, including information about the risks of termination of a treatment plan of prescribed agonist medications such as methadone or buprenorphine, as well as the need to comply with medical monitoring of their clinical status for a defined period of time following the procedure to ensure a safe outcome. Patients should also be informed of the risks, benefits and costs of alternative methods of treatment available.

ACCESSING POLICY STATEMENTS

ASAM's entire body of Public Policy Statements, which date back to a statement on abstinence, adopted in 1974, can be accessed on the Society's website at www.asam.org. The website features a topical listing of all policy statements, with links to each statement in a given category. The statements can be printed out for use as a reference and may be cited in speech or writing.

To protect the integrity of ASAM's public policies and discourage misquotations and inappropriate attributions, the Board of Directors also decided to apply copyright protections to all of the Society's policy statements when they are reproduced, published, or cited in various electronic or print forums. Such copyrights also prohibit reproduction of abbreviated forms of the statements without the express written permission of the Society. Since a number of Public Policy Statements have been revised over the years — some more than once — the copyright also requires that interested parties use only the latest versions.



Help Slowly Reaches Hurricane Victims

The response to hurricane victims with addiction problems in Louisiana, Mississippi and elsewhere has been marked by an outpouring of support from the private sector, mixed with criticism of government efforts in a time of crisis.

In the wake of the storms, public and private treatment programs have offered assistance ranging from volunteer counselors to treatment beds for hurricane victims. The National Council on Alcoholism and Drug Dependence immediately began mobilizing its affiliates to help storm victims, while the National Association of Addiction Treatment Providers (NAATP) — which happened to be holding its annual meeting in Florida when Hurricane Katrina hit — pulled together its membership to pledge a total of $5 million worth of primary inpatient and other treatment services for Katrina victims. "When a crisis of this magnitude hits, and there is no funding available, it's critical for the private sector to take action," said NAATP President Ronald J. Hunsicker.

In other cases, the response came from individuals. Dr. Al Mooney, a North Carolina physician, persuaded pharmaceutical manufacturers to donate medications needed to manage withdrawal and drove to Baton Rouge in a motor home to provide care. Many physicians and other health care workers volunteered. *(See the related story on page 2.)*

At the Federal level, the Congress quickly appropriated $50 billion in emergency relief funds. Asked how much of this would go toward addiction services, H. Westley Clark, M.D., J.D., M.P.H., Director of SAMHSA's Center for Substance Abuse Treatment, replied, "We have to work with local communities to prioritize how that's allocated." Immediately after the storms, SAMHSA announced that it was sending $600,000 in emergency mental health grants to the affected region. Dr. Clark added that CSAT also has funded hotlines in Louisiana (1-877/664-2248 in the state or 1-800/662-4357 from out of state) for persons seeking addiction treatment.

He noted that past experience has shown that different populations tend to be affected by disasters like Katrina. "In the general population, there are people who use alcohol in an acceptable fashion, but because of the magnitude of the storm may engage in dysfunctional coping," he said, adding that the primary response to this population should be prevention materials and messages. Over time, he said, alcohol and other drug use among this population could be expected to drop to pre-storm levels.

By contrast, individuals who previously were treated for addictive disorders might relapse and need services, Dr. Clark said, while those currently in active treatment who were displaced by the storm have a clear need for immediate help. He also warned that the sizeable population who meet the criteria for abuse or dependence but deny they have a problem may have to confront their drug or alcohol addiction when they are cut off from their suppliers. "Those people could cause a rush for detox beds if they suddenly…start going through withdrawal," he noted.

Dr. Clark pointed out that after the Oklahoma City bombing, researchers found a measurable increase in alcohol use, while benzodiazepine use rose in New York in the aftermath of 9/11. But those were one-off events and use tended to decline over time, he said. "We don't have any accurate epidemiological data on this," he said, "[but] we know about one million people have been affected." Prior to the storms, Louisiana's Office of Addictive Disorders estimated that 600,000 state residents met the criteria for substance dependence, while 1,200 to 1,800 were on waiting lists for treatment. *Note: SAMHSA's Disaster Technical Assistance Center can be accessed online at* HTTP://WWW.MENTALHEALTH.SAMHSA.GOV/DTAC/.

Congress Urged to Earmark Addiction Services in Disaster Response

Funds for addiction treatment would be included as a distinct component of emergency services delivered to disaster victims if a pair of recent Katrina-related bills pass. The "Louisiana Katrina Reconstruction Act," introduced in both the House and Senate, would provide $400 million to the Louisiana Department of Health and Hospitals' mental health division, including $100 million earmarked for addiction assessment, early intervention, prevention, and treatment. The "Emergency Health Care Relief Act of 2005," introduced by Sen. Charles Grassley (R-IA), calls for treatment of addictive disorders determined to result from the hurricane and its aftermath.

Meanwhile, the Addiction Leadership Group has asked Congressional leaders to amend Section 416 of the Stafford Act, which establishes the Federal Emergency Management Agency's Crisis Counseling Training and Assistance Program (CCP), to specifically include substance abuse services. In its letter to Rep. Joe Barton (R-TX), chair, and Rep. John Dingell (R-MI), ranking minority member of the House Committee on Energy and Commerce, the group said the change "will strengthen our collective response to future disasters by distinctly acknowledging in statute the fact that trauma is a significant risk factor in substance use."

Congress Hears Arguments for Parity

Reducing discrimination against persons with addictive disorders and those in recovery not only would save society millions, perhaps billions, of dollars, advocates told members of Congress.

A panel of the *American Bar Association's Standing Committee on Substance Abuse* appeared at an October briefing called by the *Congressional Addiction, Treatment and Recovery Caucus,* to discuss "the millions of dollars the failure to allow appropriate treatment is costing the American public," said attorney and ABA substance abuse committee chair Barbara Howard.

"One of the hardest steps for any addict or alcoholic to take is to ask for help," said Rep. Jim Ramstad (R-MN), who co-chairs the bipartisan caucus with Rep. Patrick Kennedy (D-RI), as he opened the hearing. "All too often, doors are slammed in their face, or basic public services are denied. It's time to end the discrimination against people who need treatment for chemical addiction." Ramstad called on Congress and the Bush administration to pass parity legislation for addiction treatment and improve access to care.

The ABA has adopted a pair of policies to address parity, including a position against discrimination and a call to repeal state insurance laws — known as UPPL provisions — that effectively bar emergency physicians from screening patients for alcohol abuse and referring them to treatment.

Study: Treatment Saves Medicaid Funds

Medicaid patients who received addiction treatment experienced a 30 percent decrease in their overall medical costs under the program, according to a new study from researchers at Kaiser Permanente.

Dr. Lawrence Walter and colleagues in Kaiser's Division of Research compared a group of 197 Medicaid patients with a group of non-Medicaid patients. Each group was tracked for one year before and three years after receiving addiction treatment at Kaiser's Vallejo Chemical Dependency Recovery Program in Oakland, Calif. They found that patients who received treatment through a managed behavioral health program saw their Medicaid costs fall from an average of $5,402 per year to an average of $3,627 per year. The researchers also calculated that Medicaid patients with substance use disorders had medical costs that were 60 percent higher than non-Medicaid patients prior to entering treatment.

"Previous studies have shown similar reductions in health care costs as a result of providing substance abuse treatment, but this study also showed that the reductions in medical costs are across all areas, including hospital stays, visits to the emergency room, and medical clinics," said Dr. Walter, adding that "The reductions in cost are not because of a shift in costs from one area to another."

The study, which was funded by the Robert Wood Johnson Foundation, is reported in the July 2005 issue of the *Journal of Behavioral Health Services and Research*.

Alcohol Screening Yields 2-to-1 Savings

Employers can save $2 for every dollar they spend on screening patients for alcohol problems and referring them to treatment, according to a research group at the George Washington University Medical Center.

Ensuring Solutions to Alcohol Problems said companies' return on investment for alcohol screening — 215 percent — is comparable to that from heart disease management programs (278 percent). Savings come from increased productivity, lower medical costs, and fewer days of work missed due to alcohol problems. Said Ensuring Solutions director Eric Goplerud, Ph.D., "Employers and health plans need to do a better job screening and treating employees who suffer from alcohol-related problems because it saves money and it's the right thing to do."

Ensuring Solutions has developed an online Alcohol Treatment Return on Investment Calculator that employers can use to determine their own potential savings. The calculator can be accessed at WWW.ENSURINGSOLUTIONS.ORG.

Screening Could Save Hospitals Billions

Hospitals could save $2 billion each year by screening emergency patients for alcohol use and offering them brief interventions, according to Larry Gentilello, M.D., professor of surgery at the University of Texas Southwestern Medical Center in Dallas. "Alcohol is by far the leading risk factor for injuries," Dr. Gentilello said, and patients are most likely to consider changing a harmful behavior when that behavior has caused a crisis or a severe problem in their lives. He adds that an injury makes patients with an alcohol problem much more responsive to counseling. If brief interventions were offered routinely to emergency patients nationwide, therefore, the annual net savings to hospitals and insurers could be up to $1.82 billion. The study appeared in the April 2005 issue of *Annals of Surgery.*

Cost-Effectiveness of Treatment Modalities Reviewed

Researchers at the University of Pennsylvania's Treatment Research Institute have published a review of cost-effectiveness data undertaken to evaluate various treatment modalities for specific populations. The report also includes an analysis of the costs and benefits associated with improved outcomes.

Findings reported in *"Economic Benefits of Drug Treatment: A Critical Review of the Evidence for Policymakers"* include:

- Evidence-based practices achieve clinically significant reductions in alcohol and drug use and improvements in clients' health and social functioning.
- Residential programs may be more effective than outpatient ones for high-risk populations, although outpatient programs reduce substance use at a lower cost.
- Enhanced outpatient programs are more cost-effective than standard ones.
- Brief interventions for clients who use alcohol may be more effective in some settings than in others.
- Prison treatment is cost-effective when combined with post-release aftercare services.

The full report can be accessed at WWW.TRESEARCH.ORG.

Treat the Condition

Opioid Dependence Is a Chronic Medical Condition

Long-term, fundamental changes to structure and function of the brain occur.[1,2]

Intravenous misuse of buprenorphine, usually in combination with benzodiazepines or other CNS depressants, has been associated with significant respiratory depression and death.

SUBOXONE has potential for abuse and produces dependence of the opioid type with a milder withdrawal syndrome than full agonists.

Cytolytic hepatitis and hepatitis with jaundice have been observed in the addicted population receiving buprenorphine.

There are no adequate and well-controlled studies of SUBOXONE (a category C medication) in pregnancy.

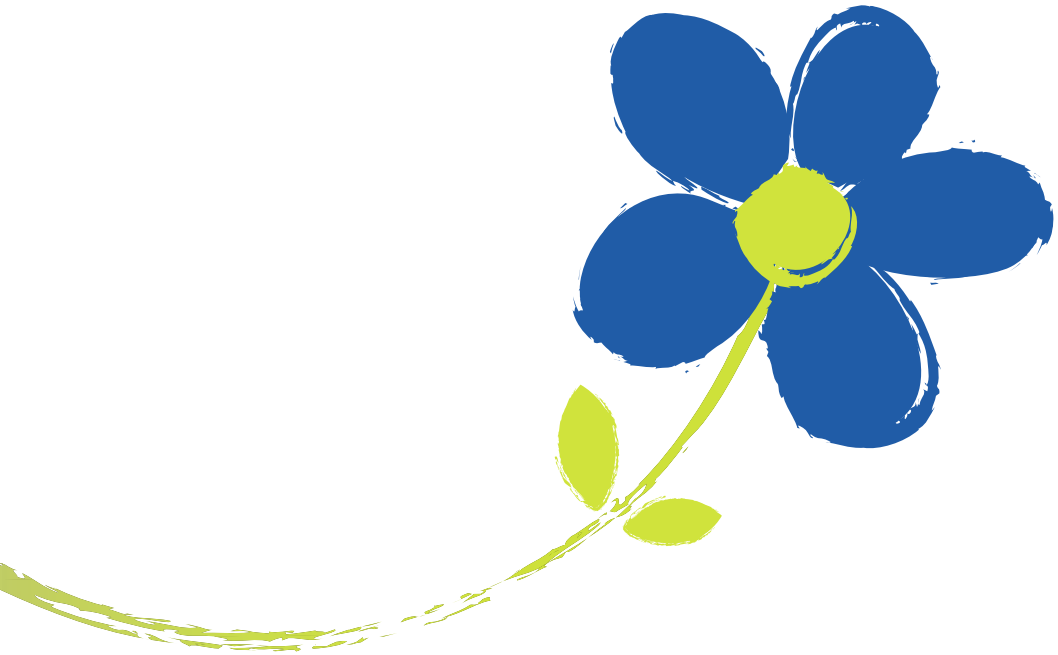
Due caution should be exercised when driving cars or operating machinery.

The most commonly reported adverse events with SUBOXONE include: headache (36%, placebo 22%), withdrawal syndrome (25%, placebo 37%), pain (22%, placebo 19%), nausea (15%, placebo 11%), insomnia (14%, placebo 16%), and sweating (14%, placebo 10%).

Please see adjacent Brief Summary of Prescribing Information.

References: 1. Leshner AI, Koob GF. Drugs of abuse and the brain. *Proc Assoc Am Physicians.* 1999;111(2):99-108. 2. Leshner AI. Addiction is a brain disease, and it matters. *Science.* 1997;278:45-47.

Transform the Life



In the Privacy and Convenience of Your Office

SUBOXONE, combined with counseling, can be used to treat opioid-dependent patients with privacy,* as other chronic, medical conditions are treated.

Target the Biological Basis of Opioid Dependence

SUBOXONE suppresses withdrawal symptoms, decreases cravings, and improves treatment retention. With the support of pharmacotherapy and counseling, patients may gain control over opioid dependence and be able to address other aspects of their lives.

To learn more, call 1-877-SUBOXONE or visit suboxone.com

*Under the Drug Addiction and Treatment Act of 2000 (DATA 2000), physicians who meet certain qualifying requirements may prescribe SUBOXONE. **Visit OpioidDependence.com** for information about qualifying.

Suboxone®
(buprenorphine HCl/naloxone HCl dihydrate) C III sublingual tablets

Because Treatment Transforms Lives

SUBOXONE (CIII)
(buprenorphine HCl and naloxone HCl dihydrate sublingual tablets)
SUBUTEX (CIII)
(buprenorphine HCl sublingual tablets)
Rx only

Brief Summary: Consult the SUBOXONE package insert for complete prescribing information.

Under the Drug Addiction Treatment Act of 2000 (DATA) codified at 21 U.S.C. 823(g), prescription use of this product in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements, and have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe this product for the treatment of opioid dependence.

INDICATIONS AND USAGE

SUBOXONE and SUBUTEX are indicated for the treatment of opioid dependence.

CONTRAINDICATIONS

SUBOXONE and SUBUTEX should not be administered to patients who have been shown to be hypersensitive to buprenorphine, and SUBOXONE should not be administered to patients who have been shown to be hypersensitive to naloxone.

WARNINGS

Respiratory Depression: Significant respiratory depression has been associated with buprenorphine, particularly by the intravenous route. A number of deaths have occurred when addicts have intravenously misused buprenorphine, usually with benzodiazepines concomitantly. Deaths have also been reported in association with concomitant administration of buprenorphine with other depressants such as alcohol or other opioids. Patients should be warned of the potential danger of the self-administration of benzodiazepines or other depressants while under treatment with SUBUTEX or SUBOXONE.

IN THE CASE OF OVERDOSE, THE PRIMARY MANAGEMENT SHOULD BE THE RE-ESTABLISHMENT OF ADEQUATE VENTILATION WITH MECHANICAL ASSISTANCE OF RESPIRATION, IF REQUIRED. NALOXONE MAY NOT BE EFFECTIVE IN REVERSING ANY RESPIRATORY DEPRESSION PRODUCED BY BUPRENORPHINE.

SUBOXONE and SUBUTEX should be used with caution in patients with compromised respiratory function (e.g., chronic obstructive pulmonary disease, cor pulmonale, decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression).

CNS Depression: Patients receiving buprenorphine in the presence of other narcotic analgesics, general anesthetics, benzodiazepines, phenothiazines, other tranquilizers, sedative/hypnotics or other CNS depressants (including alcohol) may exhibit increased CNS depression. When such combined therapy is contemplated, reduction of the dose of one or both agents should be considered.

Drug Abuse and Dependence: SUBOXONE and SUBUTEX are controlled as Schedule III narcotics under the Controlled Substances Act.

Buprenorphine is a partial agonist at the mu-opioid receptor and chronic administration produces dependence of the opioid type, characterized by moderate withdrawal upon abrupt discontinuation or rapid taper. The withdrawal syndrome is milder than seen with full agonists, and may be delayed in onset.

Neonatal withdrawal has been reported in the infants of women treated with SUBUTEX during pregnancy (See PRECAUTIONS).

SUBOXONE contains naloxone and if misused parenterally, is highly likely to produce marked and intense withdrawal symptoms in subjects dependent on other opioid agonists.

Hepatitis, Hepatic Events: Cases of cytolytic hepatitis and hepatitis with jaundice have been observed in the addict population receiving buprenorphine both in clinical trials and in post-marketing adverse event reports. The spectrum of abnormalities ranges from transient asymptomatic elevations in hepatic transaminases to case reports of hepatic failure, hepatic necrosis, hepatorenal syndrome, and hepatic encephalopathy. In many cases, the presence of pre-existing liver enzyme abnormalities, infection with hepatitis B or hepatitis C virus, concomitant usage of other potentially hepatotoxic drugs, and ongoing injecting drug use may have played a causative or contributory role. In other cases, insufficient data were available to determine the etiology of the abnormality. The possibility exists that buprenorphine had a causative or contributory role in the development of the hepatic abnormality in some cases. Measurements of liver function tests prior to initiation of treatment is recommended to establish a baseline. Periodic monitoring of liver function tests during treatment is also recommended. A biological and etiological evaluation is recommended when a hepatic event is suspected. Depending on the case, the drug should be carefully discontinued to prevent withdrawal symptoms and a return to illicit drug use, and strict monitoring of the patient should be initiated.

Allergic Reactions: Cases of acute and chronic hypersensitivity to buprenorphine have been reported both in clinical trials and in the post-marketing experience. The most common signs and symptoms include rashes, hives, and pruritus. Cases of bronchospasm, angioneurotic edema, and anaphylactic shock have been reported. A history of hypersensitivity to buprenorphine is a contraindication to SUBUTEX or SUBOXONE use. A history of hypersensitivity to naloxone is a contraindication to SUBOXONE use.

Use in Ambulatory Patients: SUBOXONE and SUBUTEX may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery, especially during drug induction and dose adjustment. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that buprenorphine therapy does not adversely affect their ability to engage in such activities. Like other opioids, SUBOXONE and SUBUTEX may produce orthostatic hypotension in ambulatory patients.

Head Injury and Increased Intracranial Pressure: SUBOXONE and SUBUTEX, like other potent opioids, may elevate cerebrospinal fluid pressure and should be used with caution in patients with head injury, intracranial lesions and other circumstances where cerebrospinal pressure may be increased. SUBOXONE and SUBUTEX can produce miosis and changes in the level of consciousness that may interfere with patient evaluation.

Opioid Withdrawal Effects: Because it contains naloxone, SUBOXONE is highly likely to produce marked and intense withdrawal symptoms if misused parenterally by individuals dependent on opioid agonists such as heroin, morphine, or methadone. Sublingually, SUBOXONE may cause opioid withdrawal symptoms in such persons if administered before the agonist effects of the opioid have subsided.

PRECAUTIONS

General: SUBOXONE and SUBUTEX should be administered with caution in elderly or debilitated patients and those with severe impairment of hepatic, pulmonary, or renal function; myxedema or hypothyroidism, adrenal cortical insufficiency (e.g., Addison's disease); CNS depression or coma; toxic psychoses; prostatic hypertrophy or urethral stricture; acute alcoholism; delirium tremens; or kyphoscoliosis.

The effect of hepatic impairment on the pharmacokinetics of buprenorphine and naloxone is unknown. Since both drugs are extensively metabolized, the plasma levels will be expected to be higher in patients with moderate and severe hepatic impairment. However, it is not known whether both drugs are affected to the same degree. Therefore, dosage should be adjusted and patients should be watched for symptoms of precipitated opioid withdrawal.

Buprenorphine has been shown to increase intracholedochal pressure, as do other opioids, and thus should be administered with caution to patients with dysfunction of the biliary tract.

As with other mu-opioid receptor agonists, the administration of SUBOXONE or SUBUTEX may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Drug Interactions: Buprenorphine is metabolized to norbuprenorphine by cytochrome CYP 3A4. Because CYP 3A4 inhibitors may increase plasma concentrations of buprenorphine, patients already on CYP 3A4 inhibitors such as azole antifungals (e.g., ketoconazole), macrolide antibiotics (e.g., erythromycin), and HIV protease inhibitors (e.g., ritonavir, indinavir and saquinavir) should have their dose of SUBUTEX or SUBOXONE adjusted.

Based on anecdotal reports, there may be an interaction between buprenorphine and benzodiazepines. There have been a number of reports in the post-marketing experience of coma and death associated with the concomitant intravenous misuse of buprenorphine and benzodiazepines by addicts. In many of these cases, buprenorphine was misused by self-injection of crushed SUBUTEX tablets. SUBUTEX and SUBOXONE should be prescribed with caution to patients on benzodiazepines or other drugs that act on the central nervous system, regardless of whether these drugs are taken on the advice of a physician or are taken as drugs of abuse. Patients should be warned of the potential danger of the intravenous self-administration of benzodiazepines while under treatment with SUBOXONE or SUBUTEX.

Information for Patients: Patients should inform their family members that, in the event of emergency, the treating physician or emergency room staff should be informed that the patient is physically dependent on narcotics and that the patient is being treated with SUBOXONE or SUBUTEX.

Patients should be cautioned that a serious overdose and death may occur if benzodiazepines, sedatives, tranquilizers, antidepressants, or alcohol are taken at the same time as SUBOXONE or SUBUTEX.

SUBOXONE and SUBUTEX may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery, especially during drug induction and dose adjustment. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that buprenorphine therapy does not adversely affect their ability to engage in such activities. Like other opioids, SUBOXONE and SUBUTEX may produce orthostatic hypotension in ambulatory patients.

Patients should consult their physician if other prescription medications are currently being used or are prescribed for future use.

Carcinogenesis, Mutagenesis and Impairment of Fertility: *Carcinogenicity.* Carcinogenicity data on SUBOXONE are not available. Carcinogenicity studies of buprenorphine were conducted in Sprague-Dawley rats and CD-1 mice. Buprenorphine was administered in the diet to rats at doses of 0.6, 5.5, and 56 mg/kg/day (estimated exposure was approximately 0.4, 3 and 35 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis) for 27 months. Statistically significant dose-related increases in testicular interstitial (Leydig's) cell tumors occurred, according to the trend test adjusted for survival. Pair-wise comparison of the high dose against control failed to show statistical significance. In an 86-week study in CD-1 mice, buprenorphine was not carcinogenic at dietary doses up to 100 mg/kg/day (estimated exposure was approximately 30 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis).

Mutagenicity: SUBOXONE: The 4:1 combination of buprenorphine and naloxone was not mutagenic in a bacterial mutation assay (Ames test) using four strains of *S. typhimurium* and two strains of *E. coli*. The combination was not clastogenic in an *in vitro* cytogenetic assay in human lymphocytes, or in an intravenous micronucleus test in the rat.

SUBUTEX: Buprenorphine was studied in a series of tests utilizing gene, chromosome, and DNA interactions in both prokaryotic and eukaryotic systems. Results were negative in yeast (*Saccharomyces cerevisiae*) for recombinant, gene convertant, or forward mutations; negative in *Bacillus subtilis* "rec" assay, negative for clastogenicity in CHO cells, Chinese hamster bone marrow and spermatogonia cells, and negative in the mouse lymphoma L5178Y assay. Results were equivocal in the Ames test: negative in studies in two laboratories, but positive for frame shift mutation at a high dose (5 mg/plate) in a third study. Results were positive in the Green-Tweets (*E. coli*) survival test, positive in a DNA synthesis inhibition (DSI) test with testicular tissue from mice, for both *in vivo* and *in vitro* incorporation of [^{3}H]thymidine, and positive in unscheduled DNA synthesis (UDS) test using testicular cells from mice.

Impairment of Fertility: SUBOXONE: Dietary administration of SUBOXONE in the rat at dose levels of 500 ppm or greater (equivalent to approximately 47 mg/kg/day or greater; estimated exposure was approximately 28 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis) produced a reduction in fertility demonstrated by reduced female conception rates. A dietary dose of 100 ppm (equivalent to approximately 10 mg/kg/day; estimated exposure was approximately 6 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis) had no adverse effect on fertility.

SUBUTEX: Reproduction studies of buprenorphine in rats demonstrated no evidence of impaired fertility at daily oral doses up to 80 mg/kg/day (estimated exposure was approximately 50 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis) or up to 5 mg/kg/day *im* or *sc* (estimated exposure was approximately 3 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis).

Pregnancy: *Pregnancy Category C:*

Teratogenic effects: SUBOXONE: Effects on embryo-fetal development were studied in Sprague-Dawley rats and Russian white rabbits following oral (1:1) and intramuscular (3:2) administration of mixtures of buprenorphine and naloxone. Following oral administration to rats and rabbits, no teratogenic effects were observed at doses up to 250 mg/kg/day and 40 mg/kg/day, respectively (estimated exposure was approximately 150 times and 50 times, respectively, the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis). No definitive drug-related teratogenic effects were observed in rats and rabbits at intramuscular doses up to 30 mg/kg/day (estimated exposure was approximately 20 times and 35 times, respectively, the recommended human daily dose of 16 mg on a mg/m^2 basis). Acephalus was observed in one rabbit fetus from the low-dose group and omphacele was observed in two rabbit fetuses from the same litter in the mid-dose group; no findings were observed in fetuses from the high-dose group. Following oral administration to the rat, dose-related post-implantation losses, evidenced by increases in the numbers of early resorptions with consequent reductions in the numbers of fetuses, were observed at doses of 10 mg/kg/day or greater (estimated exposure was approximately 6 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis). In the rabbit, increased post-implantation losses occurred at an oral dose of 40 mg/kg/day. Following intramuscular administration in the rat and the rabbit, post-implantation losses, as evidenced by decreases in live fetuses and increases in resorptions, occurred at 30 mg/kg/day.

SUBUTEX: Buprenorphine was not teratogenic in rats or rabbits after *im* or *sc* doses up to 5 mg/kg/day (estimated exposure was approximately 3 and 6 times, respectively, the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis), after *iv* doses up to 0.8 mg/kg/day (estimated exposure was approximately 0.5 times and equal to, respectively, the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis), or after oral doses up to 160 mg/kg/day in rats (estimated exposure was approximately 95 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis) and 25 mg/kg/day in rabbits (estimated exposure was approximately 30 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis). Significant increases in skeletal abnormalities (e.g., extra thoracic vertebra or thoraco-lumbar ribs) were noted in rats after *sc* administration of 1 mg/kg/day and up (estimated exposure was approximately 0.6 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis), but were not observed at oral doses up to 160 mg/kg/day. Increases in skeletal abnormalities in rabbits after *im* administration of 5 mg/kg/day (estimated exposure was approximately 6 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis) or oral administration of 1 mg/kg/day or greater (estimated exposure was approximately equal to the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis) were not statistically significant.

In rabbits, buprenorphine produced statistically significant pre-implantation losses at oral doses of 1 mg/kg/day or greater and post-implantation losses that were statistically significant at *iv* doses of 0.2 mg/kg/day or greater (estimated exposure was approximately 0.3 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis).

There are no adequate and well-controlled studies of SUBOXONE or SUBUTEX in pregnant women. SUBOXONE or SUBUTEX should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.

Non-teratogenic effects: Dystocia was noted in pregnant rats treated *im* with buprenorphine 5 mg/kg/day (approximately 3 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis). Both fertility and peri- and postnatal development studies with buprenorphine in rats indicated increases in neonatal mortality after oral doses of 0.8 mg/kg/day and up (approximately 0.5 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis), after *im* doses of 0.5 mg/kg/day and up (approximately 0.3 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis), and after *sc* doses of 0.1 mg/kg/day and up (approximately 0.06 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis). Delays in the occurrence of righting reflex and startle response were noted in rat pups at an oral dose of 80 mg/kg/day (approximately 50 times the recommended human daily sublingual dose of 16 mg on a mg/m^2 basis).

Neonatal Withdrawal: Neonatal withdrawal has been reported in the infants of women treated with SUBUTEX during pregnancy. From post-marketing reports, the time to onset of neonatal withdrawal symptoms ranged from Day 1 to Day 8 of life with most occurring on Day 1. Adverse events associated with neonatal withdrawal syndrome included hypertonia, neonatal tremor, neonatal agitation, and myoclonus. There have been rare reports of convulsions and in one case, apnea and bradycardia were also reported.

Nursing Mothers: An apparent lack of milk production during general reproduction studies with buprenorphine in rats caused decreased viability and lactation indices. Use of high doses of sublingual buprenorphine in pregnant women showed that buprenorphine passes into the mother's milk. Breast-feeding is therefore not advised in mothers treated with SUBUTEX or SUBOXONE.

Pediatric Use: SUBOXONE and SUBUTEX are not recommended for use in pediatric patients. The safety and effectiveness of SUBOXONE and SUBUTEX in patients below the age of 16 have not been established.

ADVERSE REACTIONS

The safety of SUBOXONE has been evaluated in 497 opioid-dependent subjects. The prospective evaluation of SUBOXONE was supported by clinical trials using SUBUTEX (buprenorphine tablets without naloxone) and other trials using buprenorphine sublingual solutions. In total, safety data are available from 3214 opioid-dependent subjects exposed to buprenorphine at doses in the range used in treatment of opioid addiction.

Few differences in adverse event profile were noted between SUBOXONE and SUBUTEX or buprenorphine administered as a sublingual solution.

In a comparative study, adverse event profiles were similar for subjects treated with 16 mg SUBOXONE or 16 mg SUBUTEX. The following adverse events were reported to occur by at least 5% of patients in a 4-week study (Table 1).

Table 1. Adverse Events (≥5%) by Body System and Treatment Group in a 4-week Study

	N (%)	N (%)	N (%)
Body System /Adverse Event (COSTART Terminology)	**SUBOXONE 16 mg/day N=107**	**SUBUTEX 16 mg/day N=103**	**Placebo N=107**
Body as a Whole			
Asthenia	7 (6.5%)	5 (4.9%)	7 (6.5%)
Chills	8 (7.5%)	8 (7.8%)	8 (7.5%)
Headache	39 (36.4%)	30 (29.1%)	24 (22.4%)
Infection	6 (5.6%)	12 (11.7%)	7 (6.5%)
Pain	24 (22.4%)	19 (18.4%)	20 (18.7%)
Pain Abdomen	12 (11.2%)	12 (11.7%)	7 (6.5%)
Pain Back	4 (3.7%)	8 (7.8%)	12 (11.2%)
Withdrawal Syndrome	27 (25.2%)	19 (18.4%)	40 (37.4%)
Cardiovascular System			
Vasodilation	10 (9.3%)	4 (3.9%)	7 (6.5%)
Digestive System			
Constipation	13 (12.1%)	8 (7.8%)	3 (2.8%)
Diarrhea	4 (3.7%)	5 (4.9%)	16 (15.0%)
Nausea	16 (15.0%)	14 (13.6%)	12 (11.2%)
Vomiting	8 (7.5%)	8 (7.8%)	5 (4.7%)
Nervous System			
Insomnia	15 (14.0%)	22 (21.4%)	17 (15.9%)
Respiratory System			
Rhinitis	5 (4.7%)	10 (9.7%)	14 (13.1%)
Skin and Appendages			
Sweating	15 (14.0%)	13 (12.6%)	11 (10.3%)

The adverse event profile of buprenorphine was also characterized in the dose-controlled study of buprenorphine solution, over a range of doses in four months of treatment. Table 2 shows adverse events reported by at least 5% of subjects in any dose group in the dose-controlled study.

Table 2. Adverse Events (≥5%) by Body System and Treatment Group in a 16-week Study

	Buprenorphine Dose*				
Body System/Adverse Event (COSTART Terminology)	**Very Low* (N=184)**	**Low* (N=180)**	**Moderate* (N=186)**	**High* (N=181)**	**Total* (N=731)**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Body as a Whole					
Abscess	9 (5%)	2 (1%)	3 (2%)	2 (1%)	16 (2%)
Asthenia	26 (14%)	28 (16%)	26 (14%)	24 (13%)	104 (14%)
Chills	11 (6%)	12 (7%)	9 (5%)	10 (6%)	42 (6%)
Fever	7 (4%)	2 (1%)	2 (1%)	10 (6%)	21 (3%)
Flu Syndrome	4 (2%)	13 (7%)	19 (10%)	8 (4%)	44 (6%)
Headache	51 (28%)	62 (34%)	54 (29%)	53 (29%)	220 (30%)
Infection	32 (17%)	39 (22%)	38 (20%)	40 (22%)	149 (20%)
Injury Accidental	5 (3%)	10 (6%)	5 (3%)	5 (3%)	25 (3%)
Pain	47 (26%)	37 (21%)	49 (26%)	44 (24%)	177 (24%)
Pain Back	18 (10%)	29 (16%)	28 (15%)	27 (15%)	102 (14%)
Withdrawal Syndrome	45 (24%)	40 (22%)	41 (22%)	36 (20%)	162 (22%)
Digestive System					
Constipation	10 (5%)	23 (13%)	23 (12%)	26 (14%)	82 (11%)
Diarrhea	19 (10%)	8 (4%)	9 (5%)	4 (2%)	40 (5%)
Dyspepsia	6 (3%)	10 (6%)	4 (2%)	4 (2%)	24 (3%)
Nausea	12 (7%)	22 (12%)	23 (12%)	18 (10%)	75 (10%)
Vomiting	8 (4%)	6 (3%)	10 (5%)	14 (8%)	38 (5%)
Nervous System					
Anxiety	22 (12%)	24 (13%)	20 (11%)	25 (14%)	91 (12%)
Depression	24 (13%)	16 (9%)	25 (13%)	18 (10%)	83 (11%)
Dizziness	4 (2%)	9 (5%)	7 (4%)	11 (6%)	31 (4%)
Insomnia	42 (23%)	50 (28%)	43 (23%)	51 (28%)	186 (25%)
Nervousness	12 (7%)	11 (6%)	10 (5%)	13 (7%)	46 (6%)
Somnolence	5 (3%)	13 (7%)	9 (5%)	11 (6%)	38 (5%)
Respiratory System					
Cough Increase	5 (3%)	11 (6%)	6 (3%)	4 (2%)	26 (4%)
Pharyngitis	6 (3%)	7 (4%)	6 (3%)	9 (5%)	28 (4%)
Rhinitis	27 (15%)	16 (9%)	15 (8%)	21 (12%)	79 (11%)
Skin and Appendages					
Sweat	23 (13%)	21 (12%)	20 (11%)	23 (13%)	87 (12%)
Special Senses					
Runny Eyes	13 (7%)	9 (5%)	6 (3%)	6 (3%)	34 (5%)

*Sublingual solution. Doses in this table cannot necessarily be delivered in tablet form, but for comparison purposes:
"Very low" dose (1 mg solution) would be less than a tablet dose of 2 mg
"Low" dose (4 mg solution) approximates a 6 mg tablet dose
"Moderate" dose (8 mg solution) approximates a 12 mg tablet dose
"High" dose (16 mg solution) approximates a 24 mg tablet dose

OVERDOSAGE

Manifestations: Manifestations of acute overdose include pinpoint pupils, sedation, hypotension, respiratory depression and death.

Treatment: The respiratory and cardiac status of the patient should be monitored carefully. In the event of depression of respiratory or cardiac function, primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated.

IN THE CASE OF OVERDOSE, THE PRIMARY MANAGEMENT SHOULD BE THE RE-ESTABLISHMENT OF ADEQUATE VENTILATION WITH MECHANICAL ASSISTANCE OF RESPIRATION, IF REQUIRED. NALOXONE MAY NOT BE EFFECTIVE IN REVERSING ANY RESPIRATORY DEPRESSION PRODUCED BY BUPRENORPHINE.

High doses of naloxone hydrochloride, 10-35 mg/70 kg may be of limited value in the management of buprenorphine overdose. Doxapram (a respiratory stimulant) also has been used.

Manufactured by: Reckitt Benckiser Healthcare (UK) Ltd, Hull, UK, HU8 7DS

Distributed by: Reckitt Benckiser Pharmaceuticals, Inc., Richmond, VA 23235

#138274BS July 2005

WHAT'S NEW AT NCADI

The following resources have been added to the catalogue of the National Clearinghouse on Alcohol and Drug Information (NCADI). They can be ordered online at WWW.NCADI.GOV or by phone at 1-800/729-6686. Unless indicated otherwise, single copies are available at no charge.

Acamprosate: A New Medication for Alcohol Use Disorders

This SAMHSA Treatment Advisory (Vol. 4, Issue 1) profiles acamprosate, a new medication for alcohol use disorders. The advisory covers what acamprosate is, how it works, how it compares to other medications, what its side effects may be, and how treatment providers can incorporate it into their practices.

Source: Center for Substance Abuse Treatment/SAMHSA
Publication Number: MS974

Medication-Assisted Treatment for Opioid Addiction (TIP 43)

Opioid addiction is a problem with high costs to individuals, families, and society. This *Treatment Improvement Protocol (TIP 43)* provides a detailed description of medication-assisted treatment for opioid addiction, including optional approaches such as comprehensive maintenance treatment, detoxification, and medically supervised withdrawal.

Source: Center for Substance Abuse Treatment/SAMHSA
Publication Number: BKD524

Substance Abuse Treatment for Persons With Co-Occurring Disorders (Quick Guide for Clinicians Based on TIP 42)

This brief guide was developed to accompany *Substance Abuse Treatment for Persons With Co-Occurring Disorders*, Number 42 in the Treatment Improvement Protocol (TIP) series. It is designed to meet the needs of the busy clinician for concise, easily accessed "how-to" information.

Source: Center for Substance Abuse Treatment/SAMHSA
Publication Number: QGCT42

Use of Buprenorphine in the Treatment of Opioid Addiction (Quick Guide for Physicians Based on TIP 40)

This small handbook addresses the pharmacology of buprenorphine, along with associated treatment protocols, policies, and procedures.

Source: Center for Substance Abuse Treatment/SAMHSA
Publication Number: QGPT40

Methamphetamine Abuse and Addiction

This NIDA Research Report describes the pharmacology of methamphetamine, as well as the drug's effects and the scope of methamphetamine abuse in the United States. It also explains how the drug is abused and how it differs from other stimulants, as well as the medical complications of methamphetamine abuse and current effective treatments.

Source: National Institute on Drug Abuse/NIH
Publication Number: PHD756

Prescription Drug Abuse and Addiction

This volume in the NIDA Research Report series describes the dangers of prescription drug abuse and reviews recent research on the subject. The report reviews most commonly abused prescription medications and outlines approaches providers and patients can take to avoid such misuse and abuse.

Source: National Institute on Drug Abuse/NIH
Publication Number: PHD866

Do I Have a Problem With Alcohol or Drugs? (Patient Booklet)

This patient education booklet helps patients to assess the role alcohol and drugs play in their lives as they follow the stories of five individuals from different backgrounds who also have a problem with substance abuse. Contains a change plan worksheet and contact information.

Source: Center for Substance Abuse Treatment/SAMHSA
Publication Number: PHD1103

Beverly Watts Davis

Beverly Watts Davis to Leave CSAP Post

BEVERLY WATTS DAVIS, Director of the Center for Substance Abuse Prevention (CSAP), is expected to resign that post to become a senior advisor to Charles G. Curie, M.S.W., Administrator of CSAP's parent agency, the Substance Abuse and Mental Health Services Administration (SAMHSA).

Ms. Davis was appointed CSAP Director in May 2003. Prior to joining SAMHSA, she was the Senior Vice President of United Way of San Antonio and Bexar County, Texas, as well as Executive Director of the San Antonio Fighting Back Anti-Drug Community Coalition. Ms. Davis has extensive experience with multi-site community grant programs and comprehensive prevention and early intervention projects targeted to children and adolescents, ethnic minorities, pregnant and postpartum women, and ex-prisoners reentering society.

She led CSAP at a time when the Center's charge was to identify prevention programs that are effective and can be replicated across the country. Her portfolio also included preventing substance abuse in the workplace and promoting state activities to prevent the sale of tobacco to minors.

Ms. Davis received her bachelor's degree in economics, political science, and social sciences from Trinity University in San Antonio and is pursuing her M.A. in management and human resources from Webster University in Jeffersonville, Indiana.

Her immediate replacement at CSAP is expected to be Richard T. Kopanda, Ph.D., who currently serves as Deputy Director of the Center for Substance Abuse Treatment (CSAT), another SAMHSA agency.

Mady Chalk to Join Treatment Research Institute

MADY CHALK, Ph.D., who recently retired as Director of the Division of Services Improvement at the Center for Substance Abuse Treatment, has joined the Treatment Research Institute (TRI) as Director of the Center for Performance-based Policy. In announcing the appointment, TRI co-founder A. Thomas McLellan, Ph.D., said that Dr. Chalk will lead a new TRI initiative to assist state and local governments to adopt evidence-based changes in their financing, regulatory, licensing and information requirements toward the broader goal of improving the delivery of addiction treatment.

Two premises will guide the new Center, according to Dr. McLellan. The first is that evidence should be the foundation for government practices as well as clinical practices. The second premise is that evidence of effectiveness can come from systematic evaluation of city, county and state government procedures and policies.

Dr. Chalk's extensive experience with Federal policy and administration of addiction treatment combines well with the clinical research and evaluation experience of the Treatment Research Institute, Dr. McLellan noted. "She will work with other TRI researchers to develop the Center as an "incubator" where state and local policy makers, fiscal managers, elected officials and treatment providers can meet with clinical and policy researchers to exchange ideas and develop testable strategies," he added. The Center's inaugural project will be a series of forums showcasing evidence of existing administrative practices that have produced better treatment efficiency and accountability.

AMERICAN SOCIETY OF ADDICTION MEDICINE

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ASAM's State of the Art Course Wins Praise From Clinicians, Researchers

Nobel Laureate Paul Greengard, Ph.D. (second from left) chats with audience members (from left) Chris Linden, M.D., Brabielle Batzer, M.D., and Kevin Kunz, M.D, who traveled from Hawaii to attend ASAM's 2005 State of the Art course in Washington, DC. Dr. Kunz pronounced the 2005 course "the best ever." Dr. Batzer is a founding member of the Hawaii Society of Addiction Medicine, and Dr. Linden chairs HSAM's CME Committee.

"The best scientific course I've ever attended!" This sentiment was widely heard from the more than 400 participants in ASAM's 2005 course on The State of the Art in Addiction Medicine. Held October 27-29th in Washington, DC, the course attracted physicians, medical students and residents, psychologists, nurses, counselors and social workers from across the U.S. and Canada. Designed for physicians and other professionals who seek an advanced level of understanding of the scientific underpinnings of addiction practice, the course provides an important translational link between cutting-edge scientific research and patient care.

Co-chairs Shannon C. Miller, M.D., FASAM, CMRO, and Martha J. Wunsch, M.D., FAAP, designed this year's program around the theme "Addiction Across the Lifespan." As in years past, ASAM partnered with the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), the Center for Substance Abuse Treatment (CSAT), and the Center for Substance Abuse Prevention (CSAP) in designing and offering the course. In acknowledging the importance of the partnership, Dr. Miller and Dr. Wunsch said: "The agencies make a real investment in deepening and disseminating the knowledge base of addiction practice. The intellectual capital that derives from their efforts is what makes the course shine."

Like the four State of the Art courses that preceded it, the 2005 course showcased the most recent findings in addiction research, reported by the nation's leading addiction researchers. Led by Nobel Laureate Paul Greengard, Ph.D., of the Rockefeller University, the distinguished faculty provided a concentrated review of recent scientific advances and their implications for clinical care.

In addition, keynote addresses were delivered by the leaders of the Federal addiction agencies: NIAAA Director Ting-Kai Li, M.D., NIDA Director Nora Volkow, M.D., CSAT Director H. Westley Clark, M.D., J.D., M.P.H., FASAM, and CSAP's Kevin P. Mulvey, Ph.D.

Course registrants also received a 700-page Syllabus and a CD-Rom featuring articles from the scientific literature selected by Terry K. Schultz, M.D., FASAM. Under Dr. Schultz' editorship, the Syllabus has come to be a popular feature of the course and is regarded as an essential reference by many registrants.

The next ASAM State of the Art Course is scheduled for the Hyatt Regency Capitol Hill Hotel,Washington, DC, October 25-27, 2007. The course alternates with ASAM's Review Course in Addiction Medicine, which will meet in Chicago on October 26-28, 2006. Information on all of ASAM's educational activities is available on the ASAM website or from EMAIL@ASAM.ORG.

A sampling of the presentations follows:

BIOLOGICAL PLASTICITY

Mechanism of Action of Drugs of Abuse: Cellular and Molecular Studies

Paul Greengard, Ph.D., Vincent Astor Professor, Laboratory of Molecular and Cellular Neuroscience, The Rockefeller University

Nerve cells communicate with each other through two mechanisms, referred to as fast and slow synaptic transmission. Fast-acting neurotransmitters, e.g., glutamate (excitatory) and GABA (inhibitory), achieve effects on their target cells within one millisecond, by virtue of opening ligand-operated ion channels. In contrast, all of the effects of the biogenic amine and peptide neurotransmitters, as well as many of the effects of glutamate and GABA, are achieved over hundreds of milliseconds to minutes, by slow synaptic transmission. The latter process is mediated through an enormously more complicated sequence of biochemical steps, involving second messengers, protein kinases, and protein phosphatases. The elucidation of the signaling pathways underlying synaptic transmission has led to a vastly increased understanding of the mechanisms of action of various drugs of abuse, including cocaine, amphetamine, LSD, PCP, opiates, marijuana, alcohol, nicotine, and caffeine.

Clinical Implications of Biological Plasticity: How Can Pharmacological or Behavioral Therapies Affect Synaptic Plasticity in Addiction?

Peter W. Kalivas, Ph.D., Professor and Chair, Department of Neurosciences, Medical University of South Carolina

A fundamental hypothesis in addiction research is that the pharmacological properties of drugs serve as important environmental events for inducing neuroplasticity and thereby creating drug-related memories. These processes are thought to mediate the development of pathological behaviors such as habitual drug use and the overwhelming drive to get drugs (e.g., relapse). Our understanding of the cellular and circuitry mechanisms underlying drug-induced neuroplasticity is an area of explosive growth in neurobiology. This fulminating landscape is beginning to yield consistent sequelae of change in neuron function, such that it may be possible to begin to rationally design pharmacotherapies to treat addicts. In order to do so, it is important to recognize that neuroplasticity occurs in a

temporal sequence, with early changes mediating the transition from social to habitual use, and the late, relatively permanent changes underlying vulnerability to relapse. In approaching neuroplasticity as a target for behavioral and pharmacologic therapies, it is also important to recognize that in addition to reversing or counteracting negative drug-induced neuroplasticity, it also will be useful to promote drug-induced plasticity that is compensatory or protective.

Relapse Vulnerability: Neuronal Mechanisms and Clinical Implications

Yavin Shaham, Ph.D., Section Chief, Neurobiology of Relapse Section, Behavioral Neuroscience Branch, NIDA Intramural Research Program

Using a rat model of drug relapse and craving, we found time-dependent increases in cocaine-seeking induced by exposure to drug cues after withdrawal from the drug, suggesting that cocaine craving incubates over time. In subsequent studies, we found that the time-dependent increases in cocaine-seeking are associated with increases in the peptide levels of the plasticity-related growth factor BDNF in the nucleus accumbens, amygdala and ventral tegmental area (VTA), and that a single intra-VTA infusion of BDNF induces long-lasting increases (up to 30 days) in cocaine-seeking after withdrawal. A series of experiments led us to conclude that the central — but not the basolateral — amygdala ERK signaling pathway mediates the incubation of cocaine craving. These preclinical findings have implications for the treatment of relapse in humans.

ADDICTION ACROSS THE LIFESPAN

Genetic and Environmental Influences in the Addiction Life Cycle

Michael A. Nader, Ph.D., Professor of Physiology/Pharmacology and Radiology, Wake Forest University

My laboratory is interested in identifying factors that predispose an individual to drug abuse. Our research utilizes two models of drug abuse in monkeys: drug self-administration and drug discrimination. In drug self-administration, monkeys are surgically prepared with chronic indwelling intravenous catheters and they are trained to make an operant response that results in the delivery of cocaine. In drug discrimination, responding is differentially reinforced in the presence or absence of cocaine. In both animal models, the effects of potential pharmacotherapies on the behavioral effects of cocaine are examined. In addition, when combined with PET imaging, the effects of cocaine on brain function can be assessed at all phases of drug abuse, from acquisition through maintenance and into withdrawal. Overall, these studies are providing evidence that combining behavioral pharmacology with brain imaging provides valuable information about the interactions between drugs, the environment, and the organism. This approach should aid in the understanding of variables that mediate cocaine's high abuse liability, and ultimately in identifying effective behavioral and pharmacological treatment strategies.

Neuropsychological Testing Data for Fetal Alcohol Syndrome

Sandra W. Jacobson, Ph.D., Professor, Department of Psychiatry and Behavioral Neurosciences, and Joseph L. Jacobson, Ph.D., Professor, Departments of Psychiatry and Behavioral Neurosciences, Obstetrics & Gynecology, and Psychology, Wayne State University School of Medicine

This talk presents new findings demonstrating the utility of identifying core deficits with known brain/behavior linkages as well as moderators and a new biomarker that facilitate identification of which children are at greatest risk. The data come from two prospective, longitudinal cohort studies, one in Detroit, Michigan, and the other in Capetown, South Africa. Data from both cohorts provide evidence of effects on fundamental components of numerosity ("number sense") that have been shown to be mediated by activity in the inferior parietal cortex. Moreover, data from both sites point to markedly increased vulnerability in children born to older mothers and in children born to mothers who lack a variant of the ADH1B allele, a polymorphism that regulates speed of alcohol metabolism. Measurement of fatty acid ethyl esters (FAEEs) of alcohol in meconium provide a biomarker of maternal heavy alcohol use to confirm maternal report of alcohol consumption during pregnancy. Focus on these endpoints and moderators has considerable potential to enhance diagnosis, prevention, and treatment of fetal alcohol spectrum disorders.

Functional Neuroimaging and Executive Functioning in Children with Prenatal Cocaine Exposure

Stephen Sheinkopf, Ph.D., Assistant Professor of Psychiatry, Infant Development Center, Brown Medical School

Prenatal cocaine exposure (CE) may affect brain systems related to cognitive planning, impulse control, and organization. Effects on such executive functions may place children at risk for cognitive and behavioral disorders, including risk for psychopathology and substance abuse. Animal studies indicate that prenatal exposure to cocaine disproportionately affects dopaminergic systems in the brain. This research also has demonstrated long-term effects of prenatal CE on brain development, attention, and learning. Emerging literature from ongoing follow-up studies has begun to demonstrate such effects of prenatal CE in children, including effects on overall IQ, executive functioning, and behavior problems in the school age period. Functional neuroimaging (e.g., fMRI) is a potentially powerful research tool with which to identify brain regions that may be affected by prenatal CE and, ultimately, identify brain mechanisms that mediate the effects of prenatal cocaine on cognitive and behavioral outcomes. Results from our lab indicate that prenatal CE affects functioning in the right frontal and striatal regions of the brain, which has implications for risk of substance use in adolescence.

Emerging Attitudes Toward and Patterns of Substance Abuse Among Adolescents and Young Adults: Results of a National Survey

Stephen Pasierb, M.Ed., President & CEO, Partnership for a Drug-Free America.

Patterns of youth substance abuse are undergoing a "sea change" — essentially moving from a base of agricultural products (cannabis, coca, and poppies) to myriad prescription and over-the-counter medications. Findings from annual national surveys conducted by the Partnership for a Drug-Free America show widespread awareness among young people of both general categories and specific pharmaceutical products that can be misused for psychoactive effect; a significantly lowered perception of the risks or social disapproval of such behavior (including respondents reporting that they see actual benefits); and a belief that the products are very easy to access. Through discriminant function analysis that compared attitudinal sets of non-users and users, a population of vulnerable adolescents nearly equal in size to current users was identified, suggesting the potential for the total number of users to double. A similar mapping study among parents indicated similarly weak attitudinal sets, the perception that the problem is not significant in size, and both misunderstanding and a lack of parent-child communication on the issue. We concluded that misuse and abuse of prescription and over-the-counter products demands a research-based, national education and prevention effort to address weak consumer understanding of risks and change consumer behavior.

PTSD and SUD in Military Personnel Returning from Operation Enduring Freedom and Operation Iraqi Freedom

Charles W. Hoge, M.D, Col, MC, USA, Department of Psychiatry and Behavioral Sciences, Walter Reed Army Institute of Research

A recent study showed that among U.S. military personnel, mental disorders were the leading medical correlate of separation from military service. The reasons for this association have not been determined. The current combat operations in Iraq and Afghanistan have involved U.S. military personnel in major ground combat and hazardous security duty. Studies are needed to systematically assess the mental health of members of the armed services who have participated in these operations and to inform policy with regard to the optimal delivery of mental health care to returning veterans. We studied members of four U.S. combat infantry units (three Army units and one Marine Corps unit), using an anonymous survey that was administered to the subjects either before their deployment to Iraq (n=2,530) or three to four months after their return from combat duty in Iraq or Afghanistan (n=3,671). The outcomes included major depression, generalized anxiety, and post-traumatic stress disorder (PTSD).

Late Life Drug and Alcohol Misuse: A Spectrum of Behaviors and Implications for Prevention

David W. Oslin, M.D., Associate Professor, Geriatric and Addiction Psychiatry, University of Pennsylvania Medical Center

Significant cohort shifts are occurring among older adults, with the result that addictive disorders no longer are rare or inconsequential. Alcohol misuse use remains one of the principal concerns among older adults, but illicit drug use and prescription drug misuse are becoming common. To address the needs of an aging population, a broad array of services will be needed to address the equally broad spectrum of problems. Effective interventions can range from brief advice to residential treatment. Many of the strategies that have been developed and delivered for younger adults need to be reassessed for their appropriateness for older adults. The promising news is that treatment appears to be even more effective for older adults than for younger adults. However, specific competencies and knowledge will be necessary to provide the best care to these individuals.

NEW AND PIPELINE ANTI-ADDICTION MEDICATIONS

Emerging Medications: From the Bench to the Clinic

Frank Vocci, Ph.D., Director, Division of Treatment Research and Development, National Institute on Drug Abuse

This review will concentrate on the development of pharmacotherapies for opiate, cocaine, methamphetamine, and cannabis addiction. The NIDA Medications Development Program has had success in developing, with pharmaceutical partners, levomethadyl acetate, buprenorphine, and buprenorphine/naloxone for opiate addiction. Moreover, several marketed medications have shown promise in reducing cocaine use. Of interest, these medications likely operate through diverse neurochemical mechanisms, suggesting that combination therapy may be a rational next step that could increase treatment gains further in cocaine-addicted patients. The Medications Development Program also has identified multiple neuronal mechanisms that are altered by chronic administration of drugs of abuse, including changes in conditioned cueing, drug priming, stress-induced increases in drug intake, and reduced frontal inhibitory mechanisms — all of which suggest possible avenues for the development and maintenance of, and possible relapse to — addiction.

Selecting the Right Medication for Alcoholism: A Clinically Significant Endophenotype.

Charles P. O'Brien, M.D., Ph.D., Kenneth Appel Professor and Vice Chair of Psychiatry, University of Pennsylvania

Since 2004, American physicians have had a choice among three entirely different medications as an aid in the treatment of alcoholism. Disulfiram, which has been available for almost 50 years, still has a place for specific patients in whom adherence to the medication regime can be assured. Acamprosate, which has been available for over 10 years in Europe and only recently in the United States, has a unique mechanism of action and early indications are that it may be helpful to a different group of patients. Naltrexone, which was approved by the FDA for the treatment of alcoholism 10 years ago, has been the subject of over 25 double-blind controlled clinical trials and thus, there is a large amount of information regarding which patients are naltrexone responders and which patients do not respond. A retrospective analysis of genotypes in clinical trials of naltrexone indicate that the A118G allele, which codes for a m receptor with increased sensitivity to b-endorphin, influences the treatment response to alcohol. In a population study, the risk of developing alcoholism was increased in people carrying this allele. In clinical trials, alcoholics with the gene for the sensitive form of the mu receptor did poorly when randomized to placebo but exceptionally well when randomized to naltrexone. A prospective study is in progress to determine

whether treatment response to naltrexone among alcoholics can be predicted according to genotype.

Depot Naltrexone: A First in Pharmacotherapy for Alcoholism

Helen M. Pettinati, Ph.D., Professor, Department of Psychiatry, and Chair, Treatment Research Division, University of Pennsylvania Medical School

Efforts to improve naltrexone compliance have included the development of injectable, long-acting depot formulations. We conducted a multicenter trial in 315 subjects who were randomly assigned to receive an intramuscular injection of a depot formulation containing naltrexone (n=158) or a placebo formulation (n=157) monthly for 3 months. All patients received five sessions of manual-guided motivational enhancement therapy during the 12 weeks of the study. The outcomes of interest were based on self-reported alcohol use and gamma-glutamyl transpeptidase level (missing data or data from subjects who discontinued the study were conservatively treated as heavy-drinking days). The two groups were comparable on pretreatment demographic and clinical measures. The medication was well tolerated; 73.7% of subjects received all injections. The time to the first heavy-drinking day, the percentage of subjects with no heavy drinking throughout the study, and gamma-glutamyl transpeptidase levels favored the naltrexone depot, although the effects did not reach statistical significance. There was a significant advantage for naltrexone depot treatment on the time to the first drinking day. Naltrexone depot subjects also had significantly fewer drinking days during treatment and a significantly greater abstinence rate than the placebo group (18% vs. 10%).

Rimonabant for Tobacco Cessation

Robert M. Anthenelli, M.D., Associate Professor of Psychiatry & Neuroscience, and Director, Tri-State Tobacco and Alcohol Research Center, Addiction Sciences Division, University of Cincinnati College of Medicine

In addition to directly stimulating dopamine release in the brain's reward circuitry, chronic nicotine use overactivates the endocannabinoid system (ECS) — an important modulator of nicotine reinforcement, food intake and energy balance. In this presentation, we examine how blockade of type 1 cannabinoid (CB1) receptors appears to be a promising treatment for tobacco dependence and other major cardiovascular risk factors. The first selective antagonist of the CB1 receptor, rimonabant, has been found in randomized clinical trials to promote smoking abstinence, prevent relapse to smoking, and markedly reduce post-cessation weight gain.

Vaccine Therapies for Addiction: Targeting the Drug Instead of the Brain

Paul Pentel, M.D., Professor of Medicine and Pharmacology, University of Minnesota

Immunization against heroin, cocaine, methamphetamine, phencyclidine and nicotine is being studied as an adjunct to existing therapies for treating or preventing addiction. Considerable animal data are available, and candidate vaccines for cocaine and nicotine addiction are in Phase II and III clinical trials. These vaccines elicit the production of drug-specific antibodies, which circulate in blood, bind drug, and reduce its distribution to the brain. Because these pharmacokinetic processes are key determinants of the behavioral effects of addictive drugs, they provide novel targets for intervention. Vaccination of rats against cocaine, methamphetamine or nicotine reduces drug-induced locomotor activity, conditioned place preference, drug discrimination and drug self-administration. Clinical trials of cocaine and nicotine vaccines have shown them to be safe and immunogenic. Early data from analysis of secondary endpoints of three nicotine vaccine trials are consistent with enhanced abstinence from smoking in subjects receiving the highest vaccine doses, but additional data are needed to establish their efficacy. Because the antibodies elicited by vaccination are highly specific (e.g., they bind only to the target drug) and do not enter brain, they circumvent the side effects that limit the use of most other medications for addiction. Vaccines are best suited to reducing the acute effects of drugs, e.g. reinforcement, but are not expected to reduce effects that occur when drug is no longer present, e.g. withdrawal or craving. As such, vaccines will likely be most effective if combined with medications or behavioral measures to address these additional components of addiction. In addition, practical aspects of vaccination, such as infrequent dosing and long-lasting effects, may prove attractive for improving treatment compliance.

ASAM's New CME Course on Treatment of Alcohol Disorders To Be Offered at 10 Sites

ASAM's new CME course on treatment of alcohol use disorders will be offered at 10 sites around the country, under the co-sponsorship of State Societies and Chapters in California, Florida, Illinois, New Jersey, New York, Maryland, Michigan, Pennsylvania, Texas and Wisconsin. Each course is approved for 4 Category 1 CME credits.

CALIFORNIA (Los Angeles — Hotel TBD), February 2006

FLORIDA (Marriott St. Mary, Orlando), March 23, 2006

ILLINOIS (Hilton Garden Inn — Downtown, Chicago), December 3, 2005

MARYLAND (Sheraton Hotel, Columbia), January 14, 2006

MICHIGAN (Marriott Dearborn Inn, Dearborn), January 14, 2006

PENNSYLVANIA (Crowne Plaza, Valley Forge), March 18, 2006

NEW JERSEY (Chauncey Conference Center, Princeton), December 3, 2005

NEW YORK (Sheraton Hotel and Towers, New York City), January 28, 2006

TEXAS (Marriot Riverwalk, San Antonio), February 4, 2006

Wisconsin (Hilton Garden Inn, Green Bay), January 28, 2006

There is no charge to register for the courses, which are underwritten by an unrestricted educational grant from Forest Laboratories. To review a course description, visit the ASAM website at WWW.ASAM.ORG. For additional information, contact project manager Angela K. Warner by phone at 301/656-3920, ext. 6010, or by email at AWARNER@ASAM.ORG. To register for one of the courses, contact Maureen Donohue by phone at 914/372-1960 or by email at ASAM@RXPERIENCE.COM.

ONDCP Report Calls for Improved Medical Education in Substance Abuse

The Office of National Drug Control Policy (ONDCP) has released the report of its Leadership Conference on Medical Education in Substance Abuse, describing specific strategies to enhance the training of physicians in the prevention, diagnosis and management of alcohol and drug use disorders.

The conference — which brought together leaders of private sector organizations, Federal agencies, organized medicine, and licensure and certification bodies — was co-sponsored by the Center for Substance Abuse Treatment of the Substance Abuse and Mental Health Services Administration, as well as the National Institute on Alcohol Abuse and Alcoholism and the National Institute on Drug Abuse, with the assistance of the Robert Wood Johnson Foundation. ASAM was represented by Immediate Past President Lawrence S. Brown, Jr., M.D., and a number of ASAM members were involved in planning the event.

Surgeon General Richard H. Carmona, M.D., M.P.H., told the conferees that the medical community has a pivotal role to play in helping to identify patients who may have substance use disorders and guiding them to appropriate treatment. For this to occur, he said, medical students, residents, and practicing physicians need more and better training about the disease of addiction and the impact it can have on many other medical and psychiatric disorders.

ONDCP Director John P. Walters asked the participants to develop action plans to improve physicians' knowledge and skills through enhanced training in undergraduate, graduate, and continuing medical education. Director Walters pledged that, in return, his office and other Federal agencies will continue to support scientific research and clinical education that bring the medical community better tools to identify, prevent, and treat those who are at risk for or experiencing such disorders, including problems with prescription drugs.

In response to Director Walters' call to action, the conferees agreed on a series of specific recommendations and action steps. They pointed to nutrition and geriatrics as good examples of how cross-cutting ideas have been incorporated into medical education and practice, and suggested that they be used as models. Their recommendations included strategies specific to undergraduate, graduate, and continuing medical education, as well as the following action steps:

1. Ask the Surgeon General to convene a working group of medical organizations to draft a strong ethics policy stating that physicians may not ignore the signs or symptoms of alcohol and drug problems, on the grounds that substance use disorders are medical illnesses and may not be left untreated.
2. Work with medical student organizations to help students and residents advocate for better education in the identification and management of substance use disorders, which afflict one in 10 patients in primary medical practice.
3. Develop collaborative projects to design useful clinical models and tools. Involve multiple government agencies and private-sector organizations.
4. Work with the Federal health agencies to develop and fund a program (similar to the Career Teacher program of the 1980s) that would support the recruitment and training of medical school faculty to become experts on SUDs. Experience shows that such faculty members go on to become "champions" for adding addiction-related content to the curriculum in undergraduate and graduate medical education.
5. Establish an expert panel to assist the National Board of Medical Examiners and the National Board of Osteopathic Medical Examiners in developing test questions on substance use disorders for licensure and certification exams.
6. Teach about prescribing and prescription drug abuse in the same way other areas of clinical knowledge and skills are taught. Employ multiple focused interventions, which research shows are more effective at changing behaviors than single exposures.
7. Amend medical licensure and certification/recertification standards to require competency in prescribing controlled drugs. For example, DEA could require that, at the time of re-registration, physicians present evidence of CME credits and/or focused self-assessment to achieve competence in this vital area.
8. Address patients' health literacy needs by working through public-private partnerships to evaluate and/or develop educational materials that physicians can give to patients for whom they prescribe drugs with abuse potential.

The conferees also recommended that ONDCP schedule a follow-up meeting in 2006 to revisit the objectives, strategies, and action steps and to measure progress toward implementing them. In the interim, they pledged to continue the dialogue.

The full report of the Leadership Conference outlines the rationale for greater physician involvement in recognizing and treating patients with SUDs, describes current barriers to education in this field, and evaluates the impact of prior initiatives to improve physician education about SUDs. In addition, it proposes core clinical competencies for all physicians, based on important work that has been done by a number of organizations over the past 30 years. The report can be accessed on ONDCP's website at WWW.WHITEHOUSEDRUGPOLICY.GOV.

Defining the Core Competencies

Leadership Conference participants agreed that the critical core competencies for physicians encompass a thorough understanding of the basic biomedical sciences (e.g., molecular biology, genetics, anatomy, physiology, pharmacology, and pathology), as well as knowledge and skills in the following areas:

1. *Screening, Prevention, and Brief Intervention.* All physicians should know how and when to screen patients for SUDs. Such screening may involve (1) direct questioning by a physician or other health care professional; (2) self-administered questionnaires; or (3) laboratory tests. Physicians also should be able to provide preventive counseling to patients at risk for SUDs, as well as brief interventions to those who screen positive for such disorders.
2. *Co-Occurring Medical and Psychiatric Disorders.* Physicians should understand the medical and psychiatric comorbidities and complications of substance use disorders. They also should be able to evaluate patients with such co-occurring disorders and complications and refer them to specialized treatment services that match the patients' individual treatment needs.
3. *Prescribing Drugs with Abuse Potential.* Physicians should have a thorough understanding of the clinical, legal, and ethical considerations involved in prescribing medications with abuse potential. Such knowledge encompasses drug selection, communicating the treatment program to the appropriate individuals (patient, family, and other health professionals), correctly executing the prescription order, and monitoring the treatment program to determine whether changes are needed to achieve optimum effectiveness and safety of drug therapy. It also involves avoiding undermedication (underprescribing), overmedication (overprescribing), and drug misuse or abuse.

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*The mechanism of action of acamprosate in the maintenance of abstinence is not completely understood. Chronic alcohol exposure is hypothesized to alter the normal balance between neuronal excitation and inhibition. *In vitro* and *in vivo* studies in animals have provided evidence to suggest acamprosate may interact with neurotransmitter systems centrally, and has led to the hypothesis that acamprosate restores this balance. The clinical significance in humans is unknown.

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CAMPRAL (acamprosate calcium) is indicated for the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation. Treatment with CAMPRAL should be part of a comprehensive management program that includes psychosocial support. The efficacy of CAMPRAL in promoting abstinence has not been demonstrated in subjects who have not undergone detoxification and not achieved alcohol abstinence prior to beginning CAMPRAL treatment. The efficacy of CAMPRAL in promoting abstinence from alcohol in polysubstance abusers has not been adequately assessed.

CONTRAINDICATIONS
CAMPRAL is contraindicated in patients who previously have exhibited hypersensitivity to acamprosate calcium or any of its components. CAMPRAL is contraindicated in patients with severe renal impairment (creatinine clearance ≤30 mL/min).

PRECAUTIONS
Use of CAMPRAL does not eliminate or diminish withdrawal symptoms. **General: Renal Impairment** Treatment with CAMPRAL in patients with moderate renal impairment (creatinine clearance of 30-50 mL/min) requires a dose reduction. Patients with severe renal impairment (creatinine clearance of ≤30 mL/min) should not be given CAMPRAL (see also CONTRAINDICATIONS). **Suicidality** In controlled clinical trials of CAMPRAL, adverse events of a suicidal nature (suicidal ideation, suicide attempts, completed suicides) were infrequent overall, but were more common in CAMPRAL-treated patients than in patients treated with placebo (1.4% vs. 0.5% in studies of 6 months or less; 2.4% vs. 0.8% in year-long studies). Completed suicides occurred in 3 of 2272 (0.13%) patients in the pooled acamprosate group from all controlled studies and 2 of 1962 patients (0.10%) in the placebo group. Adverse events coded as "depression" were reported at similar rates in CAMPRAL-treated and placebo-treated patients. Although many of these events occurred in the context of alcohol relapse, no consistent pattern of relationship between the clinical course of recovery from alcoholism and the emergence of suicidality was identified. The interrelationship between alcohol dependence, depression and suicidality is well-recognized and complex. Alcohol-dependent patients, including those patients being treated with CAMPRAL, should be monitored for the development of symptoms of depression or suicidal thinking. Families and caregivers of patients being treated with CAMPRAL should be alerted to the need to monitor patients for the emergence of symptoms of depression or suicidality, and to report such symptoms to the patient's health care provider. **Information for Patients** Physicians are advised to discuss the following issues with patients for whom they prescribe CAMPRAL. Any psychoactive drug may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that CAMPRAL therapy does not affect their ability to engage in such activities. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Patients should be advised to notify their physician if they are breast-feeding. Patients should be advised to continue CAMPRAL therapy as directed, even in the event of relapse and should be reminded to discuss any renewed drinking with their physician. Patients should be advised that CAMPRAL has been shown to help maintain abstinence only when used as a part of a treatment program that includes counseling and support. **Drug Interactions** The concomitant intake of alcohol and CAMPRAL does not affect the pharmacokinetics of either alcohol or acamprosate. Pharmacokinetic studies indicate that administration of disulfiram or diazepam does not affect the pharmacokinetics of acamprosate. Co-administration of naltrexone with CAMPRAL produced a 25% increase in AUC and a 33% increase in the Cmax of acamprosate. No adjustment of dosage is recommended in such patients. The pharmacokinetics of naltrexone and its major metabolite 6-beta-naltrexol were unaffected following co-administration with CAMPRAL. Other concomitant therapies: In clinical trials, the safety profile in subjects treated with CAMPRAL concomitantly with anxiolytics, hypnotics and sedatives (including benzodiazepines), or non-opioid analgesics was similar to that of subjects taking placebo with these concomitant medications. Patients taking CAMPRAL concomitantly with antidepressants more commonly reported both weight gain and weight loss, compared with patients taking either medication alone. **Carcinogenicity, Mutagenicity and Impairment of Fertility** A carcinogenicity study was conducted in which Sprague-Dawley rats received acamprosate calcium in their diet at doses of 25, 100 or 400 mg/kg/day (0.2, 0.7 or 2.5-fold the maximum recommended human dose based on an AUC comparison). There was no evidence of an increased incidence of tumors in this carcinogenicity study in the rat. An adequate carcinogenicity study in the mouse has not been conducted. Acamprosate calcium was negative in all genetic toxicology studies conducted. Acamprosate calcium demonstrated no evidence of genotoxicity in an *in vitro* bacterial reverse point mutation assay (Ames assay) or an *in vitro* mammalian cell gene mutation test using Chinese Hamster Lung V79 cells. No clastogenicity was observed in an *in vitro* chromosomal aberration assay in human lymphocytes and no chromosomal damage detected in an *in vivo* mouse micronucleus assay. Acamprosate calcium had no effect on fertility after treatment for 70 days prior to mating in male rats and for 14 days prior to mating, throughout mating, gestation and lactation in female rats at doses up to 1000 mg/kg/day (approximately 4 times the maximum recommended human daily oral dose on a mg/m^2 basis). In mice, acamprosate calcium administered orally for 60 days prior to mating and throughout gestation in females at doses up to 2400 mg/kg/day (approximately 5 times the maximum recommended human daily oral dose on a mg/m^2 basis) had no effect on fertility. **Pregnancy Category C Teratogenic Effects** Acamprosate calcium has been shown to be teratogenic in rats when given in doses that are approximately equal to the human dose (on a mg/m^2 basis) and in rabbits when given in doses that are approximately 3 times the human dose (on a mg/m^2 basis). Acamprosate calcium produced a dose-related increase in the number of fetuses with malformations in rats at oral doses of 300 mg/kg/day or greater (approximately equal to the maximum recommended human daily oral dose on a mg/m^2 basis). The malformations included hydronephrosis, malformed iris, retinal dysplasia, and retroesophageal subclavian artery. No findings were observed at an oral dose of 50 mg/kg/day (approximately one-fifth the maximum recommended human daily oral dose on a mg/m^2 basis). An increased incidence of hydronephrosis was also noted in Burgundy Tawny rabbits at oral doses of 400 mg/kg/day or greater (approximately 3 times the maximum recommended human daily oral dose on a mg/m^2 basis). No developmental effects were observed in New Zealand white rabbits at oral doses up to 1000 mg/kg/day (approximately 8 times the maximum recommended human daily oral dose on a mg/m^2 basis). The findings in animals should be considered in relation to known adverse developmental effects of ethyl alcohol, which include the characteristics of fetal alcohol syndrome (craniofacial dysmorphism, intrauterine and postnatal growth retardation, retarded psychomotor and intellectual development) and milder forms of neurological and behavioral disorders in humans. There are no adequate and well controlled studies in pregnant women. CAMPRAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nonteratogenic Effects** A study conducted in pregnant mice that were administered acamprosate calcium by the oral route starting on Day 15 of gestation through the end of lactation on postnatal day 28 demonstrated an increased incidence of still-born fetuses at doses of 960 mg/kg/day or greater (approximately 2 times the maximum recommended human daily oral dose on a mg/m^2 basis). No effects were observed at a dose of 320 mg/kg/day (approximately one-half the maximum recommended human daily dose on a mg/m^2 basis). **Labor and Delivery** The potential for CAMPRAL to affect the duration of labor and delivery is unknown. **Nursing Mothers** In animal studies, acamprosate was excreted in the milk of lactating rats dosed orally with acamprosate calcium. The concentration of acamprosate in milk compared to blood was 1.3:1. It is not known whether acamprosate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when CAMPRAL is administered to a nursing woman. **Pediatric Use** The safety and efficacy of CAMPRAL have not been established in the pediatric population. **Geriatric Use** Forty-one of the 4234 patients in double-blind, placebo-controlled, clinical trials of CAMPRAL were 65 years of age or older, while none were 75 years of age or over. There were too few patients in the ≥65 age group to evaluate any differences in safety or effectiveness for geriatric patients compared to younger patients. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (See CLINICAL PHARMACOLOGY, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS
The adverse event data described below reflect the safety experience in over 7000 patients exposed to CAMPRAL for up to one year, including over 2000 CAMPRAL-exposed patients who participated in placebo-controlled trials. **Adverse Events Leading to Discontinuation** In placebo-controlled trials of 6 months or less, 8% of CAMPRAL-treated patients discontinued treatment due to an adverse event, as compared to 6% of patients treated with placebo. In studies longer than 6 months, the discontinuation rate due to adverse events was 7% in both the placebo-treated and the CAMPRAL-treated patients. Only diarrhea was associated with the discontinuation of more than 1% of patients (2% of CAMPRAL-treated vs. 0.7% of placebo-treated patients). Other events, including nausea, depression, and anxiety, while accounting for discontinuation in less than 1% of patients, were nevertheless more commonly cited in association with discontinuation in CAMPRAL-treated patients than in placebo-treated patients. **Common Adverse Events Reported in Controlled Trials** Common, non-serious adverse events were collected spontaneously in some controlled studies and using a checklist in other studies. The overall profile of adverse events was similar using either method. Table 1 shows those events that occurred in any CAMPRAL treatment group at a rate of 3% or greater and greater than the placebo group in controlled clinical trials with spontaneously reported adverse events. The reported frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed, without regard to the causal relationship of the events to the drug.

Table 1. Events Occurring at a Rate of at Least 3% and Greater than Placebo in any CAMPRAL Treatment Group in Controlled Clinical Trials with Spontaneously Reported Adverse Events

Body System/ Preferred Term	CAMPRAL 1332 mg/day	CAMPRAL 1998 mg/day[1]	CAMPRAL Pooled[2]	Placebo
Number of Patients in Treatment Group	**397**	**1539**	**2019**	**1706**
Number (%) of Patients with an AE	**248 (62%)**	**910 (59%)**	**1231 (61%)**	**955 (56%)**
Body as a Whole	**121 (30%)**	**513 (33%)**	**685 (34%)**	**517 (30%)**
Accidental Injury*	17 (4%)	44 (3%)	70 (3%)	52 (3%)
Asthenia	29 (7%)	79 (5%)	114 (6%)	93 (5%)
Pain	6 (2%)	56 (4%)	65 (3%)	55 (3%)
Digestive System	**85 (21%)**	**440 (29%)**	**574 (28%)**	**344 (20%)**
Anorexia	20 (5%)	35 (2%)	57 (3%)	44 (3%)
Diarrhea	39 (10%)	257 (17%)	329 (16%)	166 (10%)
Flatulence	4 (1%)	55 (4%)	63 (3%)	28 (2%)
Nausea	11 (3%)	69 (4%)	87 (4%)	58 (3%)
Nervous System	**150 (38%)**	**417 (27%)**	**598 (30%)**	**500 (29%)**
Anxiety**	32 (8%)	80 (5%)	118 (6%)	98 (6%)
Depression	33 (8%)	63 (4%)	102 (5%)	87 (5%)
Dizziness	15 (4%)	49 (3%)	67 (3%)	44 (3%)
Dry mouth	13 (3%)	23 (1%)	36 (2%)	28 (2%)
Insomnia	34 (9%)	94 (6%)	137 (7%)	121 (7%)
Paresthesia	11 (3%)	29 (2%)	40 (2%)	34 (2%)
Skin and Appendages	**26 (7%)**	**150 (10%)**	**187 (9%)**	**169 (10%)**
Pruritus	12 (3%)	68 (4%)	82 (4%)	58 (3%)
Sweating	11 (3%)	27 (2%)	40 (2%)	39 (2%)

*includes events coded as "fracture" by sponsor; **includes events coded as "nervousness" by sponsor
[1] includes 258 patients treated with acamprosate calcium 2000 mg/day, using a different dosage strength and regimen. [2] includes all patients in the first two columns as well as 83 patients treated with acamprosate calcium 3000 mg/day, using a different dosage strength and regimen.

Other Events Observed During the Premarketing Evaluation of CAMPRAL
Following is a list of terms that reflect treatment-emergent adverse events reported by patients treated with CAMPRAL in 20 clinical trials (4461 patients treated with CAMPRAL, 3526 of whom received the maximum recommended dose of 1998 mg/day for up to one year in duration). This listing does not include those events already listed above; events for which a drug cause was considered remote; event terms which were so general as to be uninformative; and events reported only once which were not likely to be acutely life-threatening.
Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring in at least 1/100 patients (only those not already listed in the summary of adverse events in controlled trials appear in this listing); infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients. **Body as a Whole** – *Frequent:* headache, abdominal pain, back pain, infection, flu syndrome, chest pain, chills, suicide attempt; *Infrequent:* fever, intentional overdose, malaise, allergic reaction, abscess, neck pain, hernia, intentional injury; *Rare:* ascites, face edema, photosensitivity reaction, abdomen enlarged, sudden death. **Cardiovascular System** – *Frequent:* palpitation, syncope; *Infrequent:* hypotension, tachycardia, hemorrhage, angina pectoris, migraine, varicose vein, myocardial infarct, phlebitis, postural hypotension; *Rare:* heart failure, mesenteric arterial occlusion, cardiomyopathy, deep thrombophlebitis, shock. **Digestive System** – *Frequent:* vomiting, dyspepsia, constipation, increased appetite; *Infrequent:* liver function tests abnormal, gastroenteritis, gastritis, dysphagia, eructation, gastrointestinal hemorrhage, pancreatitis, rectal hemorrhage, liver cirrhosis, esophagitis, hematemesis, nausea and vomiting, hepatitis; *Rare:* melena, stomach ulcer, cholecystitis, colitis, duodenal ulcer, mouth ulceration, carcinoma of liver. **Endocrine System** – *Rare:* goiter, hypothyroidism. **Hemic and Lymphatic System** – *Infrequent:* anemia, ecchymosis, eosinophilia, lymphocytosis, thrombocytopenia; *Rare:* leukopenia, lymphadenopathy, monocytosis. **Metabolic and Nutritional Disorders** – *Frequent:* peripheral edema, weight gain; *Infrequent:* weight loss, hyperglycemia, SGOT increased, SGPT increased, gout, thirst, hyperuricemia, diabetes mellitus, avitaminosis, bilirubinemia; *Rare:* alkaline phosphatase increased, creatinine increased, hyponatremia, lactic dehydrogenase increased. **Musculoskeletal System** – *Frequent:* myalgia, arthralgia; *Infrequent:* leg cramps; *Rare:* rheumatoid arthritis, myopathy. **Nervous System** – *Frequent:* somnolence, libido decreased, amnesia, thinking abnormal, tremor, vasodilatation, hypertension; *Infrequent:* convulsion, confusion, libido increased, vertigo, withdrawal syndrome, apathy, suicidal ideation, neuralgia, hostility, agitation, neurosis, abnormal dreams, hallucinations, hypesthesia; *Rare:* alcohol craving, psychosis, hyperkinesia, twitching, depersonalization, increased salivation, paranoid reaction, torticollis, encephalopathy, manic reaction. **Respiratory System** – *Frequent:* rhinitis, cough increased, dyspnea, pharyngitis, bronchitis; *Infrequent:* asthma, epistaxis, pneumonia; *Rare:* laryngismus, pulmonary embolus. **Skin and Appendages** – *Frequent:* rash; *Infrequent:* acne, eczema, alopecia, maculopapular rash, dry skin, urticaria, exfoliative dermatitis, vesiculobullous rash; *Rare:* psoriasis. **Special Senses** – *Frequent:* abnormal vision, taste perversion; *Infrequent:* tinnitus, amblyopia, deafness; *Rare:* ophthalmitis, diplopia, photophobia. **Urogenital System** – *Frequent:* impotence; *Infrequent:* metrorrhagia, urinary frequency, urinary tract infection, sexual function abnormal, urinary incontinence, vaginitis; *Rare:* kidney calculus, abnormal ejaculation, hematuria, menorrhagia, nocturia, polyuria, urinary urgency. **Serious Adverse Events Observed During the Non-US Postmarketing Evaluation of CAMPRAL (acamprosate calcium)** Although no causal relationship to CAMPRAL has been found, the serious adverse event of acute kidney failure has been reported to be temporally associated with CAMPRAL treatment in at least 3 patients and is not described elsewhere in the labeling.

DRUG ABUSE AND DEPENDENCE
Controlled Substance Class Acamprosate calcium is not a controlled substance. **Physical and Psychological Dependence** CAMPRAL did not produce any evidence of withdrawal symptoms in patients in clinical trials at therapeutic doses. Post marketing data, collected retrospectively outside the U.S., have provided no evidence of CAMPRAL abuse or dependence.

OVERDOSAGE
In all reported cases of acute overdosage with CAMPRAL (total reported doses of up to 56 grams of acamprosate calcium), the only symptom that could be reasonably associated with CAMPRAL was diarrhea. Hypercalcemia has not been reported in cases of acute overdose. A risk of hypercalcemia should be considered in chronic overdosage only. Treatment of overdose should be symptomatic and supportive.

Manufactured by: Merck Santé s.a.s.
Subsidiary of Merck KGaA, Darmstadt, Germany
37, rue Saint-Romain
69008 LYON FRANCE

Manufactured for FOREST PHARMACEUTICALS, Inc.
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NEW SURVEYS PROVIDE INSIGHT INTO TREATMENT NEEDS

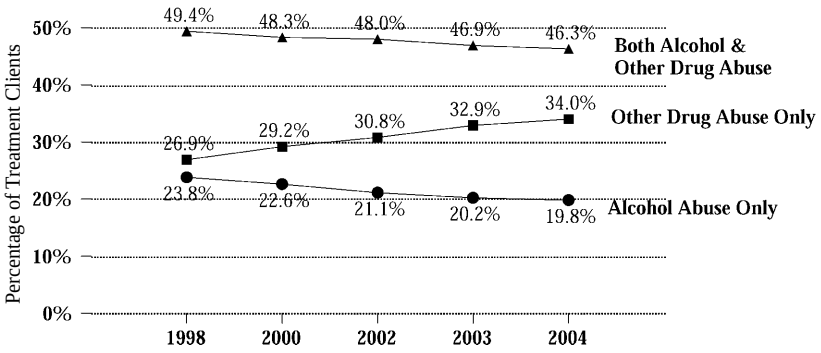
The proportion of patients being treated for both drug and alcohol abuse is decreasing, while a growing number of patients come to treatment solely for drug abuse, according to the National Survey of Substance Abuse Treatment Services (N-SSATS): 2004. Sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA), N-SSATS surveys all 14,000 public and private U.S. treatment facilities each year.

Results of the 2004 survey, which were released by SAMHSA in October, show that the proportion of patients in treatment for both drug and alcohol problems declined from 49 percent in 1998 to 46 percent in 2004. Over the same period, the number of patients treated solely for problems with alcohol declined from 23.8 percent to 19.8 percent.

The 2004 survey, which captures data on the location, characteristics, and use of addiction treatment facilities and services throughout the U.S. and its territories, found that 1,072,251 persons were enrolled in treatment. For purposes of the survey, persons were defined as "in treatment" if they were (1) hospital inpatients or non-hospital residential clients receiving addiction treatment at a facility on March 31, 2004, or (2) outpatients who were seen at a facility for addiction treatment or detoxification services at least once during the month of March 2004 and who were still enrolled in treatment as of March 31, 2004. A total of 14,167 facilities responded to the 2004 survey — a response rate of 96 percent.

It is unclear whether the survey findings reflect actual changes in substance use patterns or other factors, such as changes in insurance policies or access to treatment.

TYPE OF SUBSTANCE ABUSE PROBLEM TREATED AMONG CLIENTS IN U.S. TREATMENT FACILITIES, 1998 TO 2004



Further insights into treatment needs are provided by a new report from the Treatment Episodes Data Set (TEDS), which shows that admissions for problems related to methamphetamine and prescription opioids jumped sharply from 2002 to 2003.

Admissions to treatment for methamphetamine as primary drug of abuse increased by 10 percent, from 105,754 in 2002 to 116,604 in 2003. Similarly, treatment admissions for prescription opioids as primary drug of abuse increased by 12 per cent between 2002 and 2003, from 43,377 to 48,457.

Specifically, admissions for treatment of methamphetamine use rose 10 percent, from 105,754 in 2002 to 116,604 in 2003, while admissions related to abuse of prescription opioids rose by 12 percent — from 43,377 to 48,457 — during the same period. On a state level, more than 20 percent of treatment admissions in Arkansas, California, Hawaii, Idaho, Nevada, Oklahoma, and Utah were related to methamphetamine use, while 10 percent of treatment admissions in Maine, Tennessee, and West Virginia were for problems related to prescription opioids.

Commenting on the data, John Walters, Director of National Drug Control Policy, said the reports show "the terrible harms that dangerous drugs like meth inflict upon our country. Addiction is a treatable disease and through the expansion of programs like Access to Recovery, we are helping more Americans who are suffering from this disease."

Calling the N-SSATS and TEDS data a "snapshot of the treatment service system," SAMHSA Administrator Charles Curie said the survey data help SAMHSA and state and local governments assess the nature and extent of services provided in state-supported and other treatment facilities, and forecast treatment resource requirements. They also are used to update SAMHSA's Substance Abuse Treatment Facility Locator, available at HTTP://FINDTREATMENT.SAMHSA.GOV. The locator service provides the phone numbers and locations of all state-approved treatment facilities. Both the N-SSATS and TEDS reports can be accessed online at WWW.OAS.SAMHSA.GOV. *Source: Treatment Episode Data Set (TEDS) Highlights 2003; National Survey of Substance Abuse Treatment Services (N-SSATS): 2004. Substance Abuse and Mental Health Services Administration, October 2005. Available online at http://oas.samhsa.gov/dasis.htm#nssats2.*

Ruth Fox Memorial Endowment Fund

DIRECTOR, PHYSICIANS HEALTH PROGRAM

The Washington Physicians Health Program (WPHP) is seeking candidates for the position of Director. WPHP's mission is to facilitate the rehabilitation of health professionals who have medical conditions that could compromise public safety and to monitor their recovery.

Qualifications include leadership and managerial ability as well as clinical experience. Addiction certification and specialization in Addiction Psychiatry are desirable.

Submit curriculum vitae to
Shannon McGeoy
Washington Medical
State Medical Association
2033 6th Avenue, Suite 1100
Seattle, WA 98121
or email SLM@WSMA.ORG.

Please express your interest by January 2, 2006.

Dr. Ruth Fox

Dear Colleague:

As another year draws to a close, we extend to you and your family our warmest wishes for a wonderful holiday season and a happy, prosperous and peaceful New Year.

With the Ruth Fox Memorial Endowment Fund now in its 25th year, we are only $18,000 shy of our goal of $4 million. We want to take this opportunity to thank those whose generosity and continued support have helped toward this goal which we are sure will be reached before the end of this year. Please let us know if you have included the Endowment in your estate plans so that we can acknowledge your generosity now.

One of our newest activities — the Ruth Fox Scholarship Program — has become a great success since its launch in 2002. Through the program, interest income from the Endowment Fund is used to sponsor scholarships for physicians-in-training to attend ASAM's Medical-Scientific Conference and Ruth Fox Course. To date, 24 such scholarships have been awarded.

The next Ruth Fox Donor Reception is scheduled for Friday evening, May 5, 2006, in San Diego. It is by invitation only, so if you have not already contributed or pledged to the Endowment, please do so now and help us reach our goal. Pledges can be paid over five years. Also, now may be an opportune time to examine the amount and timing of your gifts in order to maximize your tax savings this year. All contributions to the Endowment Fund are completely tax-deductible to the full extend provided by law.

For information about making a contribution or pledge, or to discuss other types of gifts in confidence, contact Claire Osman by phone at 1-800/257-6776 or 718/275-7766, or by e-mail: asamclaire@aol.com.

Max A. Schneider, M.D., FASAM
Chair, Ruth Fox Memorial Endowment Subcommittee

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NIAAA Releases New Clinician's Guide

Dr. Mark Willenbring

*[**Editor's Note:** This issue of ASAM News is accompanied by a new publication from the National Institute on Alcohol Abuse and Alcoholism, titled "Helping Patients Who Drink Too Much: A Clinician's Guide." The Guide was developed under the leadership of Dr. Mark Willenbring, Director of NIAAA's Division of Treatment and Recovery Research, with input from primary care and mental health clinicians. Dr. Willenbring answers questions about the Guide in the following interview.]*

***ED:** Dr. Willenbring, why did NIAAA revise the Guide?*

Dr. Willenbring: Our overall goal was to make it more physician-friendly. A number of ASAM members gave us feedback, which we found very valuable. For example, they recognized that the physician's time is limited, so they supported our efforts to simplify the screening process. Another reality is that mental health patients are more likely to have alcohol problems than are patients in the general population, so we expanded the audience beyond primary care to include mental health clinicians.

In addition, since screening identifies not only at-risk drinkers but also alcohol-dependent patients, we provided more tools for managing those patients in the context of general medical or psychiatric practice. A lot can be accomplished in those settings even with dependent patients, especially if their medical or psychiatric problems are related to drinking. Finally, we wanted to provide information about anti-craving medications and encourage non-addiction specialists to consider their use.

***ED:** How was the screening process simplified?*

Dr. Willenbring: The new single screening question about heavy drinking days is easy to remember and use: **How many times in the past year have you had 5 or more drinks** (for men) **or 4 or more drinks** (for women)**?**

***ED:** The new screen is positive with just one heavy drinking day in the past year — isn't that casting a very broad net?*

Dr. Willenbring: Several studies support the use of a single screening question, and two nationwide epidemiologic studies show that individuals who never have a heavy drinking day rarely have an alcohol-related problem.

I commonly hear, "Everybody's going to meet this [limit], at least occasionally." My response is: "Well, that's an opportunity to educate people about safe drinking limits, and say `Watch it — make sure this doesn't become more frequent'." You can let them know that the fewer heavy drinking days, the better, since the relationship between the number of heavy drinking days and the rate of complications is similar to that between blood pressure levels and complications — it's essentially linear. This takes just a few minutes, and then you go on.

***ED:** What was the thinking behind adding a diagnostic assessment for alcohol use disorders?*

Dr. Willenbring: The old model was "screen and refer," but we recognized that it no longer responds to the reality of medical practice today. Clinicians often are concerned about what to do with a patient identified with a problem, especially one who is alcohol-dependent. Such patients often refuse referrals or do not have access to treatment, or go to treatment but don't respond. We wanted to empower the physician to assess and manage these patients, not just the at-risk drinkers. So, in addition to a diagnostic assessment, the new *Guide* emphasizes long-term medical management of alcohol problems. This should be useful not only to physicians, but also to counselors, social workers, nurses, and others who see patients over extended periods of time.

***ED:** You mentioned that this revision also contains more information on pharmacotherapies than earlier editions of the Guide. What's been added?*

Dr. Willenbring: There's a chart in both the full *Guide* and the pocket version that presents information about the three currently approved medications, including how to prescribe them, their contraindications, interactions, and common side effects. These charts will be continually updated as we gain more experience, so users should check the NIAAA website regularly.

***ED:** Considering that ASAM members are specialists in addiction medicine, will the Guide be of use to them?*

Dr. Willenbring: We hope they find some of the new tools helpful, such as the single question screen, the medications chart, and the patient progress forms. Also, a lot of ASAM members teach non-specialists, and we encourage them to use the *Guide* for that purpose. To help with this, we'll soon be posting a PowerPoint presentation to accompany the *Guide* on NIAAA's website (WWW.NIAAA.NIH.GOV). We also encourage ASAM members to order copies for colleagues, including nurses and counselors.

***ED:** So ASAM members can be important in spreading the word about the new Guide?*

Dr. Willenbring: Yes — we're much more likely to be effective if all of us are advancing the same idea. Even if we have minor disagreements about approach, the *Guide* is a good resource: it's been carefully vetted, it's free, and people can get as many copies as they need. We would like this to become a national standard.

***ED:** What's next?*

Dr. Willenbring: This is an active project, not a one-shot publication. We're now working on a single-page update that condenses the medical management manual from Project COMBINE, which we will make available to nurses and counselors. Future updates will focus on topics such as disease management, comorbid conditions, and screening in emergency departments and OB/Gyn practice.

We'd also like to hear from ASAM members with ideas about other products that may be helpful to them and their colleagues, and we welcome feedback on the *Guide* itself. I can be reached at MLW@NIAAA.NIH.GOV.

To order additional copies of *Helping Patients Who Drink Too Much: A Clinician's Guide*, phone NIAAA at 301/443-3860 or visit WWW.NIAAA.NIH.GOV/GUIDE2.HTM.

ASAM Conference Calendar

ASAM

May 4, 2006
Ruth Fox Course for Physicians
San Diego Sheraton Hotel & Marina
San Diego, California
[8 Category 1 CME Credits]

May 5-7, 2006
37th Annual
Medical-Scientific Conference
San Diego Sheraton Hotel & Marina
San Diego, California
[21 Category 1 CME Credits]

July 21-23, 2006
Medical Review Officer (MRO)
Training Course (Basic)
Ritz Carlton Phoenix Hotel
Phoenix, Arizona
[8 Category 1 CME Credits]

October 29, 2006
Course on Pain & Addiction
Westin O'Hare Hotel
Chicago, Illinois
[8 Category 1 CME Credits]

December 8-10, 2006
Medical Review Officer (MRO)
Training Course (Basic & Advanced)
Marriott Metro Center Hotel
Washington, DC
[8 Category 1 CME Credits]

April 26-29, 2007
38th Annual
Medical-Scientific Conference
Marriott Doral Resort and Spa
Miami, Florida
[21 Category 1 CME Credits]

OTHER EVENTS OF NOTE

December 8-9, 2005
Second Annual Joint Commission
National Conference on
Behavioral Health Care:
Focusing on Outcomes Research
and Using Data
Sponsored by the Joint Commission
on Accreditation of Healthcare
Organizations (JCAHO)
Hotel Le Meridien, Chicago, Illinois
[Contact: 877/223-6866
or visit WWW.JCRINC.COM]

March 28-29, 2006
Managing Individual and
Program Liability Risk
Sponsored by the Center for
Substance Abuse Treatment (CSAT)
Wilshire Grand Hotel
Los Angeles, California
[12.5 Category 1 CME Credits]
[Contact: 240/645-4136
or email JGIBBS@JBS.BIZ]

BUPRENORPHINE TRAINING

For information or to register for a Buprenorphine Training Course, contact 1-888/362-6784 or visit the website: WWW.DOCOPTIN.COM. All courses are approved for 8 Category 1 CME credits.

January 6, 2006
Anaheim, California
Sponsored by ASAM & the
California Society of Addiction
Medicine

March 4, 2006
Seattle, Washington
Sponsored by ASAM & the
Washington Society of Addiction
Medicine

March 11, 2006
Grand Rapids, Michigan
Sponsored by ASAM & the
Michigan Society of Addiction Medicine

April 22, 2006
Atlanta, George
Sponsored by ASAM & the
Georgia Society of Addiction Medicine

May 6, 2006
Augusta, Maine
Sponsored by ASAM & the
Maine Society of Addiction Medicine

May 7, 2006
San Diego, California
Sponsored by ASAM & the
California Society of Addiction
Medicine

May 10, 2006
Madison, Wisconsin
Sponsored by ASAM & the
Wisconsin Society of Addiction
Medicine

June 3, 2006
Columbia, Maryland
Sponsored by ASAM & the
Maryland Society of Addiction Medicine

Except where otherwise indicated, additional information is available on the ASAM web site (WWW.ASAM.ORG) or from the ASAM Department of Meetings and Conferences at 4601 No. Park Ave., Suite 101, Chevy Chase, MD 20815-4520; phone 301/656-3920; fax 301/656-3815; email EMAIL@ASAM.ORG.

ASAM MEMBERS: *Expand your network of contacts and colleagues!*
Recruit new members between October 1, 2005 and April 15, 2006 and you could receive one complimentary registration for ASAM's 2006 Medical-Scientific Conference, or a one-year membership renewal, or a copy of* Principles of Addiction Medicine. *Find out more at WWW.ASAM.ORG.