ADDICTION TREATMENT Forum NEWS & UPDATES

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#91 – May 2004

Does MMT Affect Male Sexual Function?

Washington, DC; ASAM Conference Abstracts; April 22-25, 2004 -- Males engaged in methadone maintenance treatment (MMT) have been reported to have higher levels of sexual dysfunction than the general population. However, the prevalent types of and potential etiologies for sexual dysfunction in this population are still unclear.

A total of 87 male MMT patients participated in this study; 76 had been on methadone maintenance for a period of 6 months or longer. To provide a comparison group, the remaining 11 were recruited and participated at the time of MMT admission, and repeated the study protocol after 60 days of continuous methadone treatment.

Significant findings included erectile dysfunction and libido dysfunction that increased with increasing age of the patient. Duration of methadone treatment was not associated with increasing levels of dysfunction. Methadone dose was significantly correlated with increased orgasm dysfunction, even after adjusting for duration of treatment. Depression, as measured by the Beck Depression Inventory, was significantly associated with increased erectile and orgasm dysfunction. Ongoing substance abuse and alcohol use were not directly associated with sexual dysfunction, but were associated with depression.

This study indicates that, while methadone may account for some degree of orgasm dysfunction, it is unlikely to account for other types of sexual dysfunction which may occur in methadone maintained men. The evaluation of sexual dysfunction in this population should, therefore, mirror that which occurs in the general male population.

Source: Abstract 3A. Brown R, Mundt M, Plahn S. Methadone maintenance and male sexual dysfunction.

Factors Influencing Retention in MMT

Drug and Alcohol Dependence; May 10, 2004 -- This study examined factors associated with retention in methadone maintenance, defined as remaining in treatment for a minimum of 90 days, among street recruited injection drug users (IDUs) in Denver, Colorado.

A total of 577 IDUs were randomly assigned to either a risk reduction intervention -- focusing on safer injection and sex behaviors -- or motivational interviewing, which addressed more sweeping lifestyle changes including drug treatment. All subjects who wanted methadone maintenance treatment were provided transportation, rapid intake, and a waiver of the intake fee. In addition, 50% were randomly assigned a coupon for 90 days of free treatment.

Overall, one third entered MMT and of these, 60% remained for at least 90 days. Factors associated with retention included higher methadone dose, free treatment, greater contacts with the clinic, and counselor rating of patient cooperation. Although desire for treatment, or motivation, was associated with greater retention, there were no differences observed between the motivational interviewing and risk reduction interventions.

See: Booth RE, et al. Factors associated with methadone maintenance treatment retention among street-recruited injection drug users. *Drug Alcohol Depend*. 2004;74(2):177-185.

Tenure in MMT a Critical Factor for Opioid Abstinence

Washington, DC; ASAM Conference Abstracts; April 22-25, 2004 -- Despite the fact that many opioid treatment programs (OTPs) stress an abstinence-oriented approach, with the eventual withdrawal of methadone to a drug free state, clinical research has demonstrated the following:

> The relapse rate for patients withdrawn from methadone is extremely high (70-90%), even with well-designed withdrawal regimens under close medical supervision.

> Patients enrolled in OTPs for a longer length of stay (LOS ≥ 3 months to 1 year) are more likely to have negative opiate toxicology results.

> Patients on higher doses of methadone (80-120 mg/day) are more likely to have negative opiate toxicology results.

Surprisingly, however, there is a dearth of literature that looks at the interrelationships between LOS (or tenure in MMT) and methadone dosage. These 2 variables were examined, based on opiate toxicology results during a 12-month period for nearly 3,000 adults attending 7 OTPs in the New York area. It was found that longer LOS (≥ 1 year) significantly correlated with negative opiate toxicology results, and patients with LOS greater than 1 year also received significantly higher methadone doses. At comparable methadone doses, patients with longer LOS had significantly greater negative opiate toxicology results than those with less tenure in MMT. These findings demonstrate that LOS predominates over methadone dosage in yielding negative opioid toxicology results.

Source: Abstract 2A. Brown Jr LS, Kritz S, Chu M, et al. The interrelationships between length of stay and methadone dosage at an urban opioid treatment program.

Impact of Environment & SSRIs in Depressed MMT Patients

Drug and Alcohol Dependence; May 10, 2004 -- Psychiatric comorbidity, particularly depressive disorders, is associated with continued substance use and poor social functioning among MMT patients. Evidence suggests similar neurochemical and environmental pathways may link the two disorders and it is reasonable to hypothesize that pharmacological and environmental factors play important roles in treating comorbid depression and substance use. The present study tested the efficacy of sertraline for treating depressive disorders among non-abstinent MMT patients. Ninety-five patients were randomized in a 12-week, double-blind, placebo-controlled trial of sertraline, a serotonin-selective reuptake inhibitor. There was no main effect of sertraline on either depression or substance use outcomes. However, the odds of being abstinent from heroin and cocaine were greater for patients on sertraline in environments with relatively less adversity. The findings support the hypothesis that contextual factors moderate the efficacy of pharmacological treatment for depression among methadone patients. They also suggest future research should examine pharmacological treatments that are combined with behavioral interventions reducing the impact of aversive environmental interactions.

See: Carpenter KM, et al. The effect of sertraline and environmental context on treating depression and illicit substance use among methadone maintained opiate dependent patients: a controlled clinical trial. *Drug Alcohol Depend*. 2004;74(2):123-134.

Gender Differences in MMT Patients

Washington, DC; ASAM Conference Abstracts; April 22-25, 2004 -- To study gender differences related to drugs of abuse in MMT patients all 470 patients who were admitted to the Adelson MMT Clinic in Israel between July 1993-December 2002 were prospectively followed-up until July 2003. Patient's urine specimens were analyzed for cocaine, opiates, benzodiazepines, THC, amphetamines, and methadone. Changes in numbers of patients with positive or negative urine screens for cocaine between admission (first month) and after 1 year (13th month) were evaluated.

Females represented 27.9% (n = 131) and males 72.1% (n = 339) of the sample, and females were significantly younger (mean age on admission = 34.5 years) compared with males (37.3 years). Retention in treatment after one year was similar in both groups: 76.3% females, 72.6% males. Positive urine screens for cocaine during the first month of admission were significantly higher in females (20%) compared with males (11.3%); however, both groups showed a net decrease after one year. No differences in the proportion of opiates, benzodiazepines, THC, and amphetamines on admission and after one year were found between groups. In sum, compared to males, females started MMT at a younger age and with a higher proportion of cocaine abuse. Both gender groups showed high retention rates after one year and a net decrease in cocaine abuse.

Source: Abstract 26A. Peks E, Adelson M. Gender differences in methadone maintenance treatment (MMT) patients.

Medical Maintenance: Next Step for Methadone Patients

Albany, NY; Capital News TV-9; May 10, 2004 -- For patients who no longer need the rigid regulations of methadone maintenance clinics, New York offers a new medical-maintenance program that provides methadone prescriptions via private, one-on-one consultations with a physician.

Joseph LaCoppola of the Whitney M. Young Jr. Health Center in Albany, said patients who meet behavioral requirements and have made a four-year commitment to methadone maintenance are eligible for the program. "It's office-based privacy. A prescription is written. You are no longer going to a dispensing window to be observed drinking your medication or take your medication home. All those policies and procedures, and regulations are waived," he said. This medical-maintenance program is one of the first in the nation to be offered through a community health center.

MMT Prevents Crime: Study

Sydney Morning Herald (Australia); April 19, 2004 (Paola Totaro) -- methadone maintenance has been shown to be an extremely effective crime prevention tool and can significantly reduce robbery, break-and-enter, and car theft incidents.

Research studying the criminal offense rates of 11,000 opiate users revealed that people on a methadone program committed significantly fewer crimes than those using heroin. The study, by the Bureau of Crime Statistics and Research and the National Drug and Alcohol Research Centre in New South Wales (Australia), analyzed the court appearance records of patients on the state's public methadone program over 12 months. After adjusting for time spent in custody, offending rates were found to be significantly lower for most patients when they were on methadone treatment than when they were off it. The report found a reduction in offending rates for all age groups and both sexes, although the drop was much larger for young women.

The bureau's director, Don Weatherburn, said the study provided the first conclusive evidence in Australia, outside an experimental setting, that methadone could control crime. "The research not only vindicated the state's methadone program but provided support for programs such as the Drug Court, which coerces offenders into treatment," he said.

Chronic Cocaine Use Lowers Brain's Dopamine Neurons

Medical Post; April 13, 2004 -- A postmortem brain-tissue study found that individuals who were chronic cocaine users suffered damage to their brain's dopamine system.

"This is the clearest evidence to date that cocaine dependency results in deleterious changes in dopamine neurons," said Dr. Karley Little, chief of the Ann Arbor VA Medical Center's Affective Neuropharmacology Laboratory and associate professor of psychiatry at the University of Michigan medical school. Little led a team of researchers in a study that compared the dopamine system of 35 cocaine users and 35 non-users with the same age, sex, race, and cause of death.

The study was published in the *American Journal of Psychiatry*.

Cocaine May Compromise Immune System, Increase Infection

NIDA Notes; reported April 23, 2004 (Patrick Zickler) -- Cocaine abusers are more likely than nonusers to suffer from HIV, hepatitis, sexually transmitted diseases, and other infections. Most of this increased incidence is the result of conditions and behaviors -- for example, injecting drugs, poor nutrition, and unsafe sex -- that often are associated with drug abuse.

NIDA-supported investigators at the McLean Hospital Alcohol and Drug Abuse Research Center in Belmont, Massachusetts, found that cocaine itself has a direct biological effect that may decrease an abuser's ability to fight off infections. Researchers found that a key immune system component, a protein called interleukin-6 (IL-6), responded less robustly to an immunological challenge in male and female abusers injected with cocaine than in those who received a placebo. "This research suggests a link between cocaine use and compromised immune response and could help explain the high incidence of infectious disease among drug abusers," said Dr. Steven Grant of NIDA's Division of Treatment Research and Development. "It reminds us that the health consequences of drug abuse reach far beyond disruption of the brain systems involved in abuse and addiction."

See: Halpern, JH, et al. Diminished interleukin-6 response to proinflammatory challenge in men and women after intravenous cocaine administration. *J Clin Endocrinology Metab*. 2003;88(3):1188-1193. Or, *NIDA Notes*. 2004;18(6).

Mayo Clinic Launches Research to Predict, Prevent Addictions

Rochester, Minn., PRNewswire; April 16, 2004 -- Mayo Clinic has established a landmark research program in the genomics of addiction with the long-term goal of predicting and preventing alcoholism and other chemical dependencies.

The first step in the research will be to identify human genes that contribute to someone's vulnerability to alcoholism. The next step will be to develop ways to use the genetic information to protect someone from becoming addicted. Ultimately, people who are at increased risk of becoming addicted could receive personalized therapy that could change their lives. The total investment needed over five years to support this research is nearly $20 million, and much of it will be funded by the Samuel C. Johnson family of Racine, Wisconsin, and the SC Johnson Fund. In honor of this significant support, the program will be named the Samuel C. Johnson Program in the Genomics of Addiction.

More information about Mayo Clinic's genomics research can be found at http://www.mayo.edu/research.

Many Patients Choose Not to Comply With Medication Regimens

Drug Benefit Trends; April 2004 (Vol. 16, No. 3, pp. 107-108) -- Most patients who fail to comply with their medication regimens do not simply forget but are actively choosing to disregard their physicians' directives. Thus, solutions to the problem of noncompliance need to address this more complex underlying issue.

Thirty percent of persons for whom medication was prescribed reported that they took the indicated amount less often than directed during the previous 12-month period, according to findings of a survey, "The Hidden Epidemic: Finding a Cure for Unfilled Prescriptions and Missed Doses," conducted by The Boston Consulting Group (BCG) in conjunction with Harris Interactive.

Among those patients who received prescriptions in the prior 12 months but acknowledged not taking the medications as prescribed, only 24% cited forgetfulness as the reason. Instead, most patients who didn't take their medication as prescribed actively chose not to comply with their physicians' treatment plan. Common reasons cited for not taking medication as directed included undesirable or debilitating side effects (20%), medication was too costly (17%), patients deciding they didn't need the drug (14%), and difficulties in getting the prescription filled (10%). The study was based on responses from more than 9,000 persons aged 18 years and older for whom medication was prescribed in the prior 12 months.

More information is available at the BCG Web site: http://www.bcg.com.

Free Directory of U.S. Drug & Alcohol Treatment Programs

SAMHSA News Release; April 27, 2004 -- The Substance Abuse and Mental Health Services Administration's (SAMHSA) updated guide to finding local substance abuse treatment programs is now available. The guide, *National Directory of Drug and Alcohol Abuse Treatment Programs 2004*, provides information on thousands of alcohol and drug treatment programs located in all 50 states, the District of Columbia, Puerto Rico, and four U.S. territories.

The new directory includes public and private facilities that are licensed, certified, or otherwise approved by substance abuse agencies in each of the states. The directory is a nationwide inventory of substance abuse and alcoholism treatment programs and facilities that is organized and presented in a state-by-state format for quick-reference by health care providers, social workers, managed care organizations, and the general public. This latest and improved edition of the SAMHSA directory of treatment programs provides a listing of the most current information available on more than 11,000 substance abuse treatment programs at the community level.

To order a free copy of the directory, see: http://store.health.org/catalog/productDetails.aspx?ProductID=16816. Or, call SAMHSA's National Clearinghouse on Alcohol and Drug Information (NCADI) at 800-729-6686

NCADD Seeks to Change Attitudes About Addiction

Alcoholism & Drug Abuse Weekly; March 22, 2004 -- The National Council on Alcoholism and Drug Dependence Inc. (NCADD) has hired a public-relations firm to plan and implement a multi-year public-education campaign aimed at changing attitudes about alcohol and other drug addiction.

"Nobody has yet launched a multi-year, professionally created and managed national communication campaign utilizing new methodologies and a new language in order to break through the clutter and change the way people and institutions think and act," said Roger Bensinger, an NCADD board member. The Council selected Burson-Marsteller, a public-relations firm in New York, to plan and

implement the campaign. The initiative will include print, television, radio, and the Internet and target 7 audiences: government officials, the clergy, the medical community, business leaders, the recovery community, education leaders, and the general public. NCADD is currently working to raise money for the campaign

Med Students Create Website for Addiction Training

Alcoholism & Drug Abuse Weekly; April 19, 2004 --A group of medical-school students have created a Website -- http://www.hpssat.org -- to provide healthcare professionals with basic information on addiction.

The students from medical schools, nursing schools, and pharmacy and physician assistant programs throughout the country formed Health Professional Students for Substance Abuse Training (HPSSAT) to help those looking for educational and advocacy information pertaining to addiction. The Website provides information on curriculum development, state and national news developments, educational resources, training tools, and educational opportunities in the addiction field.

FDA Warns About Harmful Supplements

Associated Press; April 12, 2004 -- The U.S. Food and Drug Administration (FDA) is warning consumers against using 8 liquid products promoted as providing a "safe legal high" as an alternative to illegal street drugs. The products are Trip2Night, Invigorate II, Snuffadelic, Liquid Speed, Solar Water, Orange Butterfly, Schoomz, and Green Hornet Liquid.

Although the products contain various herbal ingredients, an FDA investigation also found two drugs, diphenhydramine and dextromethorphan, as ingredients. The substances are generally used separately in over-the-counter cold medicines. The investigation also revealed the presence of other dangerous chemicals, including ephedrine and the controlled substance GHB.

#92 – June 2004

Performance During MMT Similar in Pregnant and Non-pregnant Patients

Journal of Substance Abuse Treatment; June 2004 -- This is a first of its kind controlled study comparing pregnant with non-pregnant heroin-addicted women in methadone maintenance treatment (MMT).

Researchers examined treatment outcomes among 51 pregnant and 51 non-pregnant participants enrolled in a metropolitan MMT program between 1994 and 2003. Groups were compared on demographic characteristics, psychiatric comorbidity, urinalysis results, and retention rates.

The groups were comparable in terms of most demographic characteristics and severity of addiction at intake. They did not differ significantly in terms of urinalysis results or retention rates. While most women reduced their drug use, many patients in both groups continued to use illicit drugs at least occasionally. Psychiatric comorbidity was significantly different, with the non-pregnant group being more psychiatrically disordered.

See: Crandall C, et al. Does pregnancy affect outcome of methadone maintenance treatment? *J Subst Abuse Treat*. 2004; 26(4):295-303.

Starting MMT Safely

Heroin Addiction and Related Clinical Problems; released June 2004 -- Patient deaths most often have been reported during the induction (start-up) phase of methadone maintenance treatment (MMT). In this article, J. Thomas Payte, MD, shares his many years of experience in safely providing MMT for thousands of patients.

The induction phase begins with the initial dose of methadone and ends when the medication reaches a steady-state blood level and the patient is at a stable dose. Payte stresses that safe induction is based on several principles: 1) carefully diagnosing current opioid physical dependence, 2) assessing the extent or degree of opioid tolerance, 3) daily assessments of patient response during induction, 4) dose adjustments made with a full understanding of the pharmacokinetics of methadone, particularly the "build-up" of methadone as it rises toward steady-state. At steady-state level, the amount of methadone eliminated each day is in balance with the amount remaining in the body.

Payte offers several examples of induction dosing routines in patients with differing degrees of initial opioid tolerance. Among the helpful pointers, or "clinical pearls," he provides are: a) very severe withdrawal signs/symptoms do not denote a very high tolerance or the need for higher start-up doses of methadone, b) consider the use of instant opioid screens on admission with a 2000 ng cut-off point, c) document signs/symptoms of withdrawal with at least 2

objective signs, d) document daily assessments during induction, including the basis for decisions to increase methadone dosing. "When things go wrong," he writes, "a detailed record of daily assessments with justification and reasons for dose changes can be extremely valuable."

See: Payte TJ. Methadone treatment. Safe induction techniques. *Heroin Add & Rel Clin Probl*. 2004;6(1):35-42.

Also see the special *AT Forum* report "Methadone Dosing & Safety" for which Payte was an advisor. It is available online at: http://www.atforum.com/SiteRoot/pages/rxmethadone/dosingandsafety.shtml.

Costs of MMT versus Outpatient Non-Methadone Treatment

SAMHSA News Release; May 25, 2004 -- The average cost for treatment of alcohol or drug abuse in *outpatient* facilities was an estimated $1,433 per course of treatment in 2002, according to a new report by the Substance Abuse and Mental Health Services Administration (SAMHSA).

The report -- "Alcohol and Drug Services Study Cost Study" -- noted that *residential* treatment for alcohol or drug abuse cost $3,840 per admission and *outpatient* methadone maintenance treatment (MMT) cost $7,415 per admission in 2002. It should be noted, however, that the costs reflect different lengths of stay: 520 days for MMT, compared with only 45 days for non-hospital residential treatment and 114 days for outpatient non-methadone treatment. Estimated costs per outpatient visit in 2002 were approximately $18 for methadone treatment versus $27 for outpatient non-methadone therapy. For non-hospital residential treatment, the average cost per day was $76.

Personnel costs comprised the largest component of costs for all types of treatment programs. These costs amounted to 63% of non-hospital residential care, 65% of MMT, and 79% of outpatient non-methadone treatment.

"Treatment is a bargain compared to expenditures for jails, foster care for children, and health complications that often accompany addiction," SAMHSA Administrator Charles Curie said. "Rarely do we have public initiatives that can save society as much as substance abuse treatment and recovery support services. Treatment provides an opportunity for recovery for the individual, better homes for children, and improved safety for our communities."

The report was based on site visits to 280 facilities that were chosen following a telephone survey of a nationally representative sample of 2,395 treatment facilities. The site visits collected details on costs, patients served, staffing, and services provided.

For the full report, see: http://www.oas.samhsa.gov.

Ongoing MMT More Advantageous Than Methadone Withdrawal

Addiction; June 2004 -- A study of 179 patients compared the cost and cost-effectiveness of methadone maintenance treatment (MMT) with a 180-day methadone withdrawal program enriched with psychosocial services.

This was a randomized controlled study conducted from May 1995 to April 1999. Patients were assigned either to methadone maintenance (n = 91), which required monthly 1 hour/week psychosocial therapy visits during the first 6 months, or 180-day withdrawal (n = 88), which required 3 hours/week of psychosocial therapy and 14 education sessions during the 6 month period.

MMT produced significantly greater reductions in illicit opioid use than 180-day withdrawal. Study costs were significantly higher for MMT than withdrawal patients; however, patients undergoing methadone withdrawal incurred significantly higher costs for substance abuse and mental health care received outside the study.

The authors concluded that, compared with enriched methadone withdrawal services, ongoing MMT is more effective, has a cost-effectiveness ratio within the range of many accepted medical interventions, and may provide a survival advantage. Results provide additional support for the use of sustained MMT as opposed to methadone withdrawal for treating opioid addiction, they noted.

See: Masson CL, et al. Cost and cost-effectiveness of standard methadone maintenance treatment compared to enriched 180-day methadone withdrawal. *Addiction*. 2004;99(6):718-726.

Vermont Methadone Clinics Won't Need Hospital Affiliation

WCAX-TV (Burlington, VT); May 24, 2004 -- As previously projected in *Addiction Treatment Forum* (Winter 2004;13[1]), methadone clinics in Vermont will no longer need the backing of hospitals to open.

The legislature did not extend the state's law that required hospital affiliation. That means federal rules will be in effect that allow for clinics away from hospitals and the change could make it easier to open methadone centers around the

state. Vermont has only one methadone clinic located at Fletcher Allen Health Care in Burlington, and the state says more are needed. However, due to community resistance to opening new clinics, the Vermont Health Department is organizing a mobile methadone unit scheduled to be up and running by the end of summer.

Methadone Deaths Focus of Maryland Study

Baltimore Sun; May 18, 2004 (Erika Niedowski) -- The number of deaths in Maryland associated with methadone more than tripled between 1998 and 2002, from 24 to 76. However, very few Marylanders who died from methadone-related overdoses between 2000 and 2002 were known to be in drug treatment programs at the time of their deaths, new research shows.

The study by the Center for Substance Abuse Research at the University of Maryland did not explain the reasons for the recent increase in methadone deaths; however, in reviewing the medical records of 56 deaths from 2000 through 2002, the researchers found that only 16% were known to be in treatment programs in which they would be given methadone. Twenty percent were known to have obtained the medication illegally, while 5% had a prescription for methadone to treat pain. In 59% of the cases the source of how the methadone was obtained was not known.

Methadone sales jumped 167% in Maryland between 1998 and 2002, the report said. By contrast, admissions to methadone treatment programs climbed only 30% during the same period. “We didn’t see any indication that this was diverted methadone from treatment programs,” said Erin Artigiani, deputy director of policy for the Center for Substance Abuse Research.

NTA Releases Briefings on Achieving Effective MMT

The National Treatment Agency for Substance Misuse (NTA) in the United Kingdom has released three “Briefings” for addiction treatment providers focusing on the effectiveness of methadone maintenance treatment (MMT) and providing suggestions for achieving optimal results. Here is a synopsis of each:

“Methadone Dose and Methadone Maintenance Treatment”

Decisions about the dose of methadone to be used for methadone maintenance treatment, and how practitioners and services make these decisions for individual service users, are crucial questions for effective management of care. Adequately high methadone doses for individual need, as well as responsive and flexible individualized decisions on dosing, may be key factors that assist practitioners in achieving improved outcomes.

The Briefing notes that in British MMT programs, methadone doses average less than 50 mg/day and only just over a quarter of patients receive more than 60 mg/day. Yet, it stresses, higher doses have been consistently shown to increase treatment retention and reduce illicit drug use. While not providing mandates for specific doses, the Briefing uses evidence largely from U.S. studies demonstrating that many patients need 100 mg/day or more, with some requiring in excess of 200 mg/day for ongoing stability in MMT.

This document is available at:
http://www.nta.nhs.uk/publications/briefing3.pdf

“More Than Just Methadone Dose”

This briefing discusses enhancing outcomes of methadone maintenance treatment with counseling and other psychosocial and “ancillary” services. Most opioid users seeking treatment present to services with a range of problems including severe family and social problems, employment difficulties, and use of other illicit drugs. Many have comorbid psychiatric disorders or other comorbidity (e.g., HIV or hepatitis C infection). These problems may impede the progress of service users and work against their retention in treatment. Retention is acknowledged as having a major association with good outcomes.

It has been found that the more successful MMT programs are those that reflect good organizational management, providing a range of services that maximize the effectiveness of methadone for improving patient outcomes. These include counseling, other psychosocial interventions, and the provision of adjunctive support services. This briefing focuses on the evidence demonstrating the importance of this range of offerings.

Available at:
http://www.nta.nhs.uk/publications/briefing4.pdf

“Engaging and Retaining Clients in Drug Treatment”

This research summary suggests that practitioners and MMT programs have a wide range of responses available to minimize poor engagement and retention of patients. Rapid

intake to treatment, motivational interventions, intensive ongoing support, as well as practical measures to encourage attendance are all approaches that research suggests can impact positively on patient engagement. Factors such as empathic, positive staff approaches and flexible, responsive services have been associated with more positive outcomes for patients. The attitudes of the staff and key workers can also influence engagement of drug users in services positively. Poor response to treatment can be a legitimate response to poor treatment.

Much depends on the therapy and the setting. But much also depends on whether treatment is delivered quickly after presentation, and with understanding and optimism. The research suggests that low retention figures should appropriately lead to a review of the attitudes and characteristics of the service, among other factors. The simple assumption that such problems are only due to poorly motivated drug users is difficult to sustain. This Briefing paper looks at the evidence relating to these issues and at particular approaches aimed at improving engagement and retention in treatment.

Available at:
http://www.nta.nhs.uk/publications/briefing5.pdf

Predicting Effectiveness of Naltrexone in Treating Opioid Addiction

Heroin Addiction and Related Clinical Problems; released June 2004 -- Naltrexone is an effective opioid antagonist that can be useful in preventing relapse to heroin and other opioid abuse. However, it has been shown to have poor results in improperly selected patient populations and this article explores some of the factors that might predict more successful outcomes.

The authors report on 149 formerly heroin-addicted patients undergoing long-term naltrexone maintenance treatment. They were administered naltrexone under the supervision of a family member 3 times weekly (100 mg on Mondays and Wednesdays, 150 mg on Fridays). Drop-out risk was highest during the first few months of a patient's participation in the program, but fell to zero over time. At the time the program was evaluated, two thirds (98/149) of the initially enrolled patients were still on naltrexone maintenance: cumulatively, 43% of the subjects had been on naltrexone for a year, 21% for at least 2 years, and 5% for 3 years.

Patients successfully retained in the program were more likely to have no problems at work and to be psychosocially adjusted, with helpful family relationships. Those dropping out had greater psychopathological impairments relating to mood (depression), aggressiveness, and delusional thinking. Therefore, the authors conclude, naltrexone maintenance appears to be most suitable for a subgroup of patients with a low level of addictive disease -- i.e., stable remission of addictive behaviors -- and an absence of major mood disturbances, aggressive behaviors, and psychosis.

See: Maremmani I, et al. Naltrexone as maintenance therapy for heroin addiction: predictors of response. *Heroin Add & Rel Clin Probl*. 2004;6(1):43-52.

63% of Americans Affected by Addiction: Poll

Faces & Voices of Recovery (Press Release); May 14, 2004 -- A majority of Americans surveyed during April 19-22, 2004 -- 63% -- said there had been a great deal or some impact on their lives as a result of grappling with addiction, and for most of them (72% of those who were affected) the addiction involved a family member.

Peter D. Hart Research Associates and Robert M. Teeter's Coldwater Corporation conducted the poll, which surveyed a nationally representative sample of 801 American adults. Faces & Voices of Recovery, a Washington, DC-based national recovery advocacy campaign, commissioned the poll.

Two thirds of the public believes that a stigma exists toward people in recovery from addiction to alcohol or other drugs. Such stigma was defined as "something that detracts from the character or reputation of a person, a mark of disgrace." A significant minority (27%) admits they would be less likely to hire someone who was in long-term recovery from addiction, and strong majorities (up to 80%) say that discrimination in the workplace and the availability of health insurance for people seeking recovery is a problem in the United States today.

According to the poll, the public shows a strong preference for policies that treat addiction as a health rather than a law enforcement issue. For example, more than eight out of ten people say they would be more likely to vote for a Congressional candidate who favors reallocating what the government spends on the war on drugs to place more emphasis on drug prevention, education, treatment, and recovery programs. The same proportion would be more likely to vote for a candidate who expanded programs to get treatment for drug users rather than locking them up.

For more information, visit:
http://www.facesandvoicesofrecovery.org.

Many Need Addiction Treatment in U.S. But Do Not Receive It

SAMHSA Press Release; June 14, 2004 -- The Substance Abuse and Mental Health Services Administration (SAMHSA) unveiled a new report showing that, in 2002, 2.7% of persons 12 and older nationwide (about 6.3 million persons) needed, but did not receive treatment for an illicit drug problem. Meanwhile, 7.3% (17 million persons) needed but did not receive treatment for an alcohol problem.

The report, "State Estimates of Persons Needing But Not Receiving Substance Abuse Treatment," found that New Mexico had the highest percentage, 3.5% of its population aged 12 or older, who needed but did not receive treatment for an *illicit drug* use problem in 2002, while Wisconsin, at 2.2%, had the lowest percentage. Overall, the 10 states with the highest rates of persons needing but not receiving treatment for a drug problem were New Mexico, Arizona, Washington, Alaska, Oregon, Nevada, Montana, Vermont, Rhode Island, and the District of Columbia.

Nebraska had the highest percentage, 9.6% of population aged 12 or older, who needed but did not receive treatment for an *alcohol problem*, while West Virginia had the lowest percentage, 5.6%.

According to SAMHSA Administrator Charles Curie, "The fear and stigma surrounding substance abuse treatment is a major reason why people do not seek help. Fortunately, everyone can do something to help reduce stigma."

The Report on treatment need is based on data from SAMHSA's National Survey on Drug Use and Health, which asked questions to determine if people needed treatment for drug or alcohol abuse. The report deals with persons who needed and received treatment at drug or alcohol rehabilitation facilities (inpatient or outpatient), hospital inpatient units, or mental health centers. It does not include treatment at an emergency room, private doctor's office, self-help group, prison or jail, or by a hospital as an outpatient.

The report is available at: http://www.oas.samhsa.gov.

Also see: http://www.recoverymonth.gov for helpful materials to launch a community program focusing on addiction and recovery issues during the 15th Annual Recovery Month, September 2004.

Alcohol Abuse on Rise; Alcoholism Declines

Alcoholism & Drug Abuse Weekly; June 14, 2004 -- The number of American adults who abuse alcohol or are alcohol dependent rose from 13.8 million (7.4%) in 1991-1992 to 17.6 million (8.5%) in 2001-2002, according to results from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a study directed by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) involving interviews with 43,093 individuals.

However, the NESARC study showed that while the rate of alcohol abuse increased from 3.0 to 4.7% between 1992 and 2002, the rate of alcohol dependence [alcoholism] declined from 4.4 to 3.8%.

Overall, the NESARC data found that rates of alcohol abuse and dependence in 2001-2002 were substantially higher in men than women and among younger study participants aged 18-29 and 30-44 years. The prevalence of alcohol dependence alone declined across the decade for men but remained almost static for women, effectively narrowing the gender gap. Alcohol abuse is more prevalent among whites than among Hispanics, African Americans, and Asians, according to the study. Alcohol dependence is more prevalent among Native Americans, Hispanics, and whites than among Asians.

See: Grant BF, et al. The 12-month prevalence and trends in DSM-IV alcohol abuse and dependence: United States, 1991–1992 and 2001–2002. *Drug and Alcohol Dependence*. 2004;73(3):223-328. ***Available at:*** http://www.sciencedirect.com.

Treatment Admissions Increase for Opioids, Methamphetamine

SAMHSA News Release; May 17, 2004 -- The proportion of admissions to substance abuse treatment for abuse of opioid prescription medications, heroin, and methamphetamine has increased in the past ten years, while admissions for cocaine abuse declined. This data was released in the "Treatment Episode Data Set Summary of Findings 2002" by the Substance Abuse and Mental Health Services Administration.

The new data show that heroin abuse is the primary reason for admission to treatment in 15% of cases, up from 11% of admissions in 1992. For other opioids, largely prescription pain medications, admissions doubled from less than 1% of all admissions in 1992 to 2% in 2002.

Admissions for abuse of stimulants, mainly methamphetamine, increased from 1% to 7% between 1992 to 2002. Cocaine admissions, on the other hand, declined from 18% of admissions in 1992 to 13% in 2002.

Alcohol is still the most abused substance among those entering addiction treatment. The TEDS data show that it accounted for 43% of admissions in 2002, but this is down from 59% of admissions in 1992. Furthermore, 45% of persons admitted primarily for alcohol abuse in 2002 also reported secondary drug abuse.

The report is available on the web at: http://www.oas.samhsa.gov.

Addiction Treatment Counselor Salaries Rise

Counselor Magazine; June 2, 2004 -- Salaries are up among U.S. addiction treatment professionals, according to *Counselor Magazine's* recently-released second annual survey.

More than 56% of the 112 respondents said their salaries increased during the year; 12% even received bonuses. The average salary is approximately $40,000. However, many do not have health insurance, vacation, or other benefits. Thirty percent are without medical coverage, 40% do not have dental coverage, and 55% do not receive coverage for substance use or mental health services.

Despite the lack of benefits, more than 81% of respondents said they do not plan to seek a new job in the upcoming year. More than 50% reported feeling "generally" satisfied with their work, and 37% said they are "thoroughly" satisfied.

The survey also provides insights into several industry hot topics. For example, 75% of the respondents were older than age 46, lending credibility to concerns that younger people are not entering the field. Additionally, in the survey's feedback section, respondents wrote in comments on quality of care. One respondent said, "My company is very worried about getting paid and not as much about treatment." Another said, "Therapy seems to be taking a secondary place to medical management."

Causes of Death Among Injecting Drug Users, 1980-2001

Archives of Internal Medicine; June 2004 -- High mortality rates among drug users have been widely recognized and this study investigates whether there has been a change in specific causes of mortality over time.

Patients known to have ever injected drugs were recruited into a cohort study from 1980 until 2001, covering a large practice that treated 10,000 patients in Edinburgh, Scotland. Of 667 patients enrolled, there were 153 deaths at follow-up (110 men and 43 women). Average annual mortality rate was 2.3%. Death rate peaked in the early to mid-1990s, reflecting the development of advanced human immunodeficiency virus (HIV). Drug deaths and suicide were the same in both sexes but tended to occur in younger subjects. Principal cause of death was overdose in the early years and HIV/AIDS in later years. Toward the close of the study period, hepatitis C emerged as a significant cause of death.

The authors concluded that injecting drug users have a very high risk of mortality. Infectious diseases from nonsterile injecting are the most obvious preventable cause of death. Use of death certificate information alone is inaccurate in analyzing drug-related deaths and greatly underestimates the full impact of the HIV epidemic. They note that this study provides some of the most convincing evidence so far that harm minimization, in its broadest sense, is effective in reducing drug-related mortality.

See: Copeland L, et al. Changing Patterns in Causes of Death in a Cohort of Injecting Drug Users, 1980-2001. *Arch Intern Med*. 2004;164:1214-1220.

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Avoid Grapefruit During MMT, Study Recommends

Clinical Pharmacology and Therapeutics; July 2004 -- Cytochrome P450 (CYP) 3A4 is the main isozyme involved in methadone metabolism and researchers in Switzerland investigated the influence on methadone of grapefruit juice, which contains inhibitors of intestinal CYP3A. In 8 patients undergoing MMT and receiving either water or grapefruit juice both before and with their daily methadone dose, grapefruit juice administration was associated with a modest increase in methadone bioavailability; however, no symptoms of methadone overmedication were detected by the clinical staff or reported by the patients. Still, the authors concluded that a much stronger effect could occur in some patients and, thus, grapefruit juice intake is not recommended during MMT -- particularly in patients first initiating such a treatment.

See: Benmebarek M, Devaud C, Gex-Fabry M, Powell Golay K, Brogli C, Baumann P, Gravier B, Eap CB. Effects of grapefruit juice on the pharmacokinetics of the enantiomers of methadone. *Clin Pharmacol Ther*. 2004 Jul;76(1):55-63.

No Increase Seen in NY Methadone Mortality

Addiction; July 2004 -- Reports have suggested increases in methadone-induced overdose deaths in several locations in the U.S. and in Europe. This study investigated the role of methadone and opiates in accidental overdose deaths in New York City.

Researchers analyzed data from the Office of the Chief Medical Examiner to examine all accidental drug overdose deaths in New York City between 1990 and 1998. Of 7,451 total overdose deaths during this period, there were 1,024 methadone-induced overdose deaths, 4,627 heroin-induced overdose deaths, and 408 deaths attributed to both methadone and heroin. During this period, the proportion of accidental overdose deaths attributed to methadone did not change appreciably (12.6-15.8% of total overdose mortality), while the proportion of overdose deaths attributed to heroin increased significantly (53.5-64.2%). The authors concluded that there was no appreciable increase in methadone-induced overdose mortality in New York City during the 1990s; however, both heroin-induced overdose mortality and prescriptions of methadone increased during the same time interval.

See: Bryant WK, Galea S, Tracy M, et al. Overdose deaths attributed to methadone and heroin in New York City, 1990-1998. *Addiction*. 2004;99(7):846-854.

Does Methadone Protect the Heart?

American Journal of Cardiology; May 2004 -- Having previously observed an absence of cardiovascular disease in methadone maintained patients, a team of New York researchers investigated whether long-term exposure to opioid agents might be associated with decreased severity of coronary artery disease that is believed to precede most myocardial infarctions (heart attacks).

They compared autopsy results in 98 persons who had methadone or opioids in their blood compared with 97 matched decedents without such drugs present. Nearly all of the subjects in the opioid group (98%) had methadone in their blood, either alone (64/98) or with traces of another opioid (32/98; only 2 cases had opioids without methadone). Severe coronary artery disease (CAD) was found significantly *less often* in the opioid-group than control-group decedents. In fact, subjects with opioids (primarily methadone) in their systems were roughly 2½ times less likely to have moderate or severe CAD.

Exact reasons for these possible cardioprotective effects of methadone were unclear and require further research. However, the authors concluded that long-term opioid exposure, as with methadone, may lessen CAD severity and its often fatal consequences.

See: Marmor M, Penn A, Widmer K, Levin RI, Maslansky R. Coronary artery disease and opioid use. *Am J Cardiol*. 2004;93:1295-1297.

Report Suggests Heart Monitoring Needed in Certain MMT Patients

Journal of Clinical Pharmacology; August 2004 -- A case report from Switzerland of 10 patients on methadone maintenance therapy (MMT) who experienced heart rhythm disturbances points to a need for closer monitoring of certain patients with physical disorders and also taking medications that might interfere with methadone metabolism.

The authors observed QTc-interval prolongations in 8 males and 2 females receiving methadone maintenance doses ranging from 14 to 360 mg/d; however, serum methadone levels were not reported. Three patients experienced torsade de pointes (TdP), 2 had ventricular tachycardia, and 1 had an irregular heartbeat (bigeminy); the other 4 were asymptomatic. There were no deaths.

Cases were collected during a 3 year period and patient ages ranged from 31 to 42 years. QTc values ranged from 480 to 660 msec. It is important to note that *all* patients had comorbid medical conditions: Hepatitis, HIV, AIDS, electrolyte irregularities, and/or other conditions in combination. Furthermore, all patients were taking multiple medications for their illnesses; many of which were known to affect methadone metabolism and/or potentially produce cardiac dysrhythmias. Some patients would be expected to have compromised liver function affecting drug metabolism, and continued alcohol or drug abuse was noted in a few cases.

See: Piguet V, Desmeules J, Ehret G, Stoller R, Dayer P. QT interval prolongation in patients on methadone with concomitant drugs [letter]. *J Clin Psychopharmacology*. 2004[Aug];24(4):446-448.

Editor's note: This latest report of heart dysrhythmias associated with methadone-maintenance is a reminder of the need to assess physical health, cardiac function, and medication/drug history in all patients. Those patients in whom there might be concerns should be monitored more closely, including appropriate ECG studies. However, there still is insufficient evidence to recommend ECG assessments routinely in all patients. For further information see the following AT Forum *special research reports available in*

the "Addiction Resources" section at http://www.atforum.com:
Cardiac Considerations During MMT:
http://www.atforum.com/SiteRoot/pages/addiction_resources/CardiacPaper.pdf

Methadone-Drug Interactions:
http://www.atforum.com/SiteRoot/pages/addiction_resources/Drug_Interactions.pdf

HCV Treatments Effective in MMT Patients

Hepatology; July 2004 -- Researchers in Germany examined the feasibility of hepatitis C (HCV) treatment in patients on methadone maintenance.

One hundred patients with chronic hepatitis C -- 50 in MMT and 50 with no intravenous drug use or opioid maintenance for at least 5 years -- were prospectively matched to receive treatment with peginterferon alfa-2b and ribavirin for HCV. Within the first 8 weeks of therapy, discontinuation due to noncompliance or patient request was observed in 22% (11/50) in the methadone group versus 4% (2/50) in the control group. However, after this time, there was no significant difference in discontinuation due to noncompliance or patient request, nor were there differences between groups in discontinuation of therapy because of viral failure or adverse events.

At the end of treatment, half (25/50) in the methadone group and 76% (38/50) in the control group had undetectable HCV RNA; however, there was no significant difference between groups in sustained viral response: 42% (21/50) methadone; 56% (28/50) controls. No serious psychiatric events occurred in either group. The researchers concluded that peginterferon and ribavirin seem reasonably safe and sufficiently effective in patients on methadone maintenance. Patients discontinuing therapy due to noncompliance or request did so early, thereby limiting the cost of an unsuccessful approach to treatment.

See: Mauss S, Berger F, Goelz J, Jacob B, Schmutz G. A prospective controlled study of interferon-based therapy of chronic hepatitis C in patients on methadone maintenance. *Hepatology*. 2004 Jul;40(1):120-124.

MMT Reduces Heroin & Cocaine Relapse

Nature Publishing Group; July 2004 -- Although it is well established that methadone can be an effective treatment for opioid addiction, it is not clear how methadone maintenance treatment (MMT) affects cocaine use and cravings in individuals who illicitly self-administer both opioids and cocaine.

In an animal model, researchers in Canada explored the effects of cocaine in rats maintained on methadone. Essentially, they found that methadone blocked both cocaine- and heroin-induced relapse, but not stress-induced relapse. These results suggest that although MMT may not reduce the direct stimulatory effects of cocaine, it has the potential to reduce cocaine-seeking behavior.

See: Leri F, Tremblay A, Sorge RE, Stewart J. Methadone maintenance reduces heroin- and cocaine-induced relapse without affecting stress-induced relapse in a rodent model of poly-drug use. *Neuropsychopharmacology*. 2004;29(7):1312-1320.

Wide Variations in MMT Practices Reported at VA Programs

Drug & Alcohol Dependence; July 15, 2004 -- Methadone maintenance treatment (MMT) clinical practices often do not conform to evidence-based guidelines. The goal of the U.S. Veterans Administration (VA) OpiATE Initiative is to improve patient outcomes by implementing four evidence-based strategies: (1) long-term maintenance orientation, (2) adequate dosing, (3) adequate counseling, and (4) use of contingency management. As a part of this program, for each patient, counselors record methadone dose, recent counseling frequency, length of treatment, and urine toxicology results.

In their assessment of the VA programs the researchers used an algorithm to determine if the current dose was clinically appropriate for patients with sub-standard methadone doses, Maintenance orientation was measured using an abstinence orientation scale. The authors found that concordance with counseling recommendations was uniformly high, concordance with maintenance orientation and dosing recommendations varied widely across clinics, and concordance with contingency management principles was low.

As might be expected, abstinence orientation scores were negatively correlated with dose and patient retention. Dose was negatively correlated with percent of urine screens positive for non-medical opioids and other illicit substances. *[Essentially, this means that an orientation toward methadone as a short-term solution resulted in lower methadone doses, greater patient abuse of illicit substances, and reduced retention in treatment.]* The authors concluded that there was wide variability in clinical practices and

outcomes across VA clinics, which supports the importance of individualizing quality improvement strategies to address specific performance gaps.

See: Willenbring ML, Hagedorna HJ, Postiera AC, Kennya M. Variations in evidence-based clinical practices in nine United States Veterans Administration opioid agonist therapy clinics. *Drug and Alcohol Dependence*. 2004 July;75(1):97-106.

Doctors Slow to Embrace Buprenorphine

Associated Press; July 11, 2004 -- According to this news report, doctors in Maine have been slow to embrace the use of buprenorphine for the treatment of opioid addiction.

About two dozen Maine doctors have taken the eight-hour course required to prescribe buprenorphine, but only about half of them are treating any patients with the medication. "There is no other part of the country as devastated by narcotic addiction as northern New England," said Robert Lubran, Director of the Division of Pharmacologic Therapies at the Substance Abuse and Mental Health Services Administration in Washington, DC. "There and in Appalachia. It's really hard to understand."

But primary care physicians say addiction treatment is a complicated medical specialty. And, they say, the one-day substance abuse and addiction management course that they are required to take before prescribing buprenorphine is an inconvenience and does not provide solid clinical grounding. "On the surface, it doesn't sound like much of an impediment," said Gordon Smith, Director of the Maine Medical Association. "But I don't know of any other drug that you need to take a course for." He also noted that many Maine doctors have all the patients they can handle without opening their doors to the specialized population of narcotics abusers.

Expanding the network of physicians able to prescribe buprenorphine is essential to managing Maine's epidemic of drug addiction, said Kim Johnson, the Director of Maine's Office of Substance Abuse. "The methadone clinics are all full, and all the buprenorphine doctors can't take any more patients," she said. "There is simply no place left to send an opiate addict who needs medication to get control of his disease."

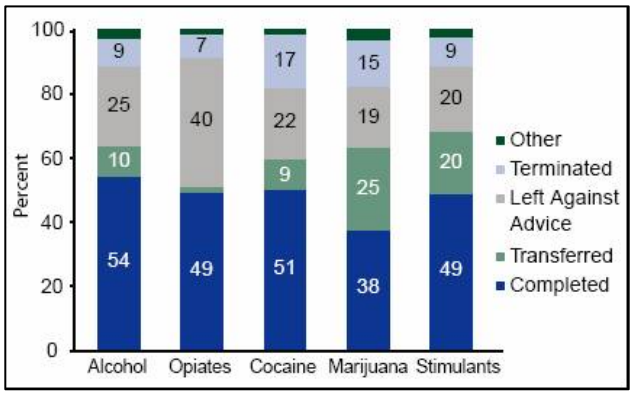
[This situation in Maine is of particular interest because the few existing methadone clinics have received a great deal of criticism and community resistance during the past couple of years, as reflected in numerous press reports. Yet, there is apparently a continuing and severe crisis of opioid addiction in Maine that is not being adequately addressed by all available means. -- Ed.]

Fewer Than Half Complete Opioid Detox

Washington, DC; July 9, 2004; DASIS Report -- Newly released data, from the Substance Abuse and Mental Health Services Administration's Drug and Alcohol Services Information System (DASIS), notes that less than half of persons entering an opioid detoxification program actually complete it.

The report examined discharge data in the Treatment Episode Data Set (TEDS) for year 2000. It noted that detoxification services are specifically intended to treat alcohol or drug *withdrawal*. Only 49% of persons entering an opioid detox program completed it and this modality had the greatest percentage (40%) leaving AMA (against medical advice). See ***Graph***. The median length of stay in opioid detox was rather brief -- 6 days -- but was the longest of the five modalities reported. Unfortunately, there were no data reported on how many persons completing detox resume substance abuse (relapse) or how soon.

For the report, see: http://www.oas.samhsa.gov.



Study: Women Hit Harder by Addiction

Hartford Courant; June 22, 2004 -- A new study by the University of Connecticut (UConn) Health Center and Yale University School of Medicine found that women experience more psychiatric, medical, and employment complications from alcohol and other drug addiction than men.

The study involved interviews with 271 participants (156 women, 115 men) at two drug-treatment centers in Connecticut. Although men and women appear to become addicted to drugs at the same age, and the severity of addiction is about the same, the researchers found that

women had more related problems and sought treatment sooner than men.

"The findings may help to support more aggressive prevention efforts among women at risk and create gender-specific treatment for drug and alcohol dependence," said Carlos Hernandez-Avila of UConn's Alcohol Research Center and lead author of the study.

The study was published in the June 11, 2004 issue of the journal *Drug and Alcohol Dependence*.

Many With Dual Diagnosis Unaware They Need Treatment

SAMHSA News Release; June 24, 2004 -- Many persons with co-occurring substance abuse and serious mental illness (dual diagnosis) are unaware that they need treatment, according to a report from the U.S. Substance Abuse and Mental Services Administration (SAMHSA).

The report -- "Adults with Co-Occurring Serious Mental Illness and a Substance Use Disorder" -- indicates that 17.5 million persons aged 18 or older (8% of adults in the U.S.) were estimated to have serious mental illness in 2002. Of these, 4 million (23% of adults with serious mental illness) were also dependent on or abused alcohol or an illicit drug -- called "dual diagnosis." More than half (52%) of those with dual diagnosis had received neither mental health nor specialty substance use treatment. An estimated 34% only received treatment for mental disorders, 2% only received specialty substance abuse treatment, and close to 12% received treatment for both mental and substance use disorders. Importantly, 61% of those with a dual diagnosis, and who had not received treatment for either illness, *perceived no unmet need for treatment.*

"The time has come to ensure that all Americans who experience co-occurring mental and substance use disorders have an opportunity for treatment and recovery." SAMHSA Administrator Charles Curie said. "Unfortunately, there continue to be many barriers to appropriate treatment and support services. Clearly our systems of services must continue to evolve to reflect the growing evidence base that promotes integrated treatment and supportive services. Both disorders must be addressed as primary illnesses and treated as such."

The report can be accessed at: http://www.oas.samhsa.gov.

Canadian Politicians Declare MMT Programs Cost Effective

Globe and Mail (Canada) Update; July 27, 2004 -- New Brunswick politicians have proposed that the province invest in more methadone programs for addicts, saying that a cost-benefit analysis shows it would be more than worthwhile.

For every dollar invested in a methadone program, there is a yield of about $16 ($12.25 in US Dollars) for the same year. This analysis was conducted by the research unit for the opposition Liberal party and used information from the Fredericton Community Health Clinic, which operates a methadone program for addicts. The community center currently has 60 clients and a large waiting list.

"The survey covered democratic, social, and economic data from the perspective of an addicted lifestyle on the street [before the program] and changes to lifestyle [after the program]," a press release on the cost-benefit analysis said. It found that the methadone-treatment program cost approximately $3,000 (Canadian dollars) a year per client, while the health care and justice system costs were found to be $43,769 (Canadian) a year, according to the study.

MMT Rarely Available to Prison Inmates

Join Together Online; July 20, 2004 (Annie Turner) -- Recognizing a huge opiate-addiction problem among inmates, New Mexico is extending methadone maintenance treatment (MMT) to local prisons. Across the country, however, few prisons provide MMT to patients.

In February, Bernalillo County, NM, announced the opening of the nation's first public-health office inside a county jail, and said the program would pilot an MMT initiative as part of its patient services. One month later, the New Mexico Medical Society became the only statewide medical society to endorse prison and jail-based opioid-replacement treatment, passing a resolution calling for "legislation to require the initiation of voluntary opioid replacement treatment ... in jails and prisons in New Mexico."

Methadone would be offered to all inmates *already enrolled in MMT* at the time of their arrest. The clinic also will provide preventive services to inmates, such as immunizations, screening and treatment for STDs, and HIV testing, counseling, and consultation.

However, the New Mexico program may not go far enough. Despite compelling evidence of the efficacy and necessity of opioid-replacement treatment in prisons and jails, the Key Extended Entry Program (KEEP) at Rikers Island remains the only *unrestricted* methadone-treatment program for incarcerated inmates in the US. Since 1987, unlike the handful of prisons nationally that provide methadone to inmates who were in MMT prior to their incarceration, Rikers allows inmates to participate in KEEP *regardless of treatment history*, and refers them to designated slots in community-based treatment programs upon release. Research shows that 78% of KEEP patients report to their assigned treatment programs upon release.

The World Health Organization supports the use of MMT for inmates to prevent the spread of HIV and AIDS among intravenous-drug users, noting in a 2004 policy brief, "Prisoners on methadone maintenance prior to imprisonment should be able to continue this treatment while in prison. In countries in which methadone maintenance is available to opiate-dependent individuals in the community, this treatment should also be available in prisons."

Opiate addiction is not the only substance-use disorder being undertreated in correctional facilities. Drug treatment on the whole lacks adequate funding and support to meet inmates' needs, experts say. On average, 30% of inmates were under the influence of illicit drugs at the time of their offense, and half of them used drugs within a month of their offense, according to the Office of National Drug Control Policy. However, according to a 2002 SAMHSA report, only 56% of state prisons and 33% of jails provide on-site addiction treatment of any sort.

Tobacco During MMT Worsens Abstinence Syndrome in Newborns

Drug and Alcohol Dependence; September 6, 2004 (projected release date) -- Few studies have examined the role tobacco has on the opiate neonatal abstinence syndrome (NAS). This study examined the effect of prenatal tobacco exposure on NAS for infants born to mothers maintained on methadone during gestation.

Twenty-nine pregnant women and their newborn infants participated. Tobacco exposure was based on maternal self-report with 16 women reporting cigarette consumption of 10 or less per day and 13 reporting smoking 20 cigarettes or more a day. The onset, peak, and duration of NAS were examined.

Results showed that, compared with light smokers (10 or less cigarettes/day), infants born to mothers who reported smoking 20 or more cigarettes per day had significantly higher NAS peak scores of 9.8 versus 4.8, and took longer to peak (113.0 hr versus 37.8 hr). The authors concluded that tobacco use in conjunction with methadone plays an important role in the timing and severity of NAS in prenatally exposed infants.

See: Choo RE, Huestis MA, Schroeder JR, et al. Neonatal abstinence syndrome in methadone-exposed infants is altered by level of prenatal tobacco exposure. *Drug Alcohol Dep*. 2004(Sept);75(3):253-260.

Study Examines Buprenorphine vs Methadone Deaths

Addiction; August 2004 -- An investigation assessed trends in the number, mortality, and the nature of deaths involving buprenorphine versus methadone in Paris from June 1997 to June 2002.

Researchers reviewed pre-mortem data, autopsy reports, police reports, hospital data, and post-mortem toxicological analyses. There were 34 cases of buprenorphine and 35 cases of methadone detected among 1,600 investigations performed at the Laboratory of Toxicology in the Medical Examiner's Office in Paris. Buprenorphine was determined as being directly implicated in 4 of 34 death cases (12%) and methadone in 3 of 35 death cases (9%). Their role in the lethal process was strongly plausible in 8 buprenorphine and 11 methadone deaths.

The authors concluded that analysis of causes of death reveals the difficulties in determining the role of either buprenorphine or methadone in the death process, as many other factors may be involved, including: circumstances surrounding death, past history, differential selection of subjects into either addiction treatment modality, and concomitant intake of other drugs (especially benzodiazepines and neuroleptics). The potential for synergistic or additive actions by other drugs of abuse -- particularly opioids, benzodiazepines, other psychotropic agents, and alcohol -- must also be considered.

See: Pirnay S, Borron SW, Giudicelli CP, et al. A critical review of the causes of death among post-mortem toxicological investigations: analysis of 34 buprenorphine-associated and 35 methadone-associated deaths. *Addiction*. 2004(August);99(8):978-988.

Report Shows Link Between Addiction, Mental Illness

Substance Abuse and Mental Health Services Administration (SAMHSA) News Release; July 29, 2004 -- A new report, "Serious Mental Illness and Its Co-Occurrence with Substance Use Disorders," illustrates the association between mental illness and addiction among adults aged 18 or older.

According to the report, 33.2 million American adults had a serious mental illness and/or addiction in 2002. The rate of serious mental illness was about 19% among those with alcohol dependence or misuse, 29% among those with illegal drug dependence or misuse, and 30% among adults who had both drug and alcohol dependence.

The report further indicated that less than half (48%) of adults with both serious mental illness and an addiction received some type of treatment. However, only 12% of these patients received both mental health and addiction treatment services.

"The time has come to ensure that all Americans who experience co-occurring mental and substance use disorders have an opportunity for treatment and recovery," SAMHSA Administrator Charles Curie said. "Clearly our systems of services must continue to evolve to reflect the growing evidence base that promotes integrated treatment and supportive services. Both disorders must be addressed as primary illnesses and treated as such."

For the report, see: http://www.oas.samhsa.gov.

Independent Mood & Anxiety Disorders Common in Drug Addicts

Archives of General Psychiatry; August 2004 -- An extensive survey presents nationally representative data on the prevalence and comorbidity of DSM-IV alcohol and drug use disorders and independent mood and anxiety disorders.

Researchers found the prevalences of DSM-IV independent mood and anxiety disorders in the US population were approximately 9% and 11% respectively. The rate of substance use disorders was 9.35%. Overall, about 1 in 5 people with an addictive disorder also has a co-occurring mental disorder, Only a few individuals with mood or anxiety disorders were classified as having solely substance-induced disorders.

Independent mood and anxiety disorders exclude transient cases of these disorders that result from alcohol and/or drug withdrawal or intoxication, conditions that usually improve rapidly without treatment once substance use ceases. The distinction is important because the diagnosis of current mood and anxiety disorders among active substance abusers is complicated by the fact that many symptoms of intoxication and withdrawal from alcohol and other substances resemble the symptoms of mood and anxiety disorders and thus, the additional psychiatric disorder may be overlooked.

"It would be incorrect for healthcare professionals to assume that the majority of mood and anxiety disorders are due to substance intoxication or withdrawal, and will remit when the patients stop drinking," says NIAAA Director Ting-Kai Li. "These findings suggest that treatment professionals should be prepared to treat or refer patients in stable remission from substance use for comorbid mood and anxiety disorders. Earlier research has demonstrated that, left untreated, such disorders may lead to substance-use relapse and other negative outcomes."

***See*:** Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders. Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2004(August);61:807-816.

U.S. EDs Report: Abuse of Anti-Anxiety Drugs Up

SAMHSAnews@health.org; August 13, 2004 -- The number of drug-abuse related visits to hospital emergency departments (EDs) involving benzodiazepine medications exceeded 100,000 in 2002, a 41% increase since 1995, according to the Substance Abuse and Mental Health Administration's Drug Abuse Warning Network (DAWN). Nearly half of the visits involving benzodiazepines -- which include such psychotherapeutic sedatives as Valium, Xanax, Klonopin, and Ativan -- were connected with suicidal ideation, gestures, or attempts.

The new DAWN report, "Demographic Characteristics of Benzodiazepine-Involved ED Visits," shows that in 2002 the highest rates of benzodiazepine-involved visits to emergency rooms were among adults age 26-44. Men are now as likely as women to go to emergency departments because of drug abuse involving benzodiazepines.

The report is available online at:
http://www.oas.SAMHSA.gov.

Patients Taking Antidepressants Should Not Stop Cold Turkey

PRNewswire; August 2, 2004 -- Nearly 12 million Americans are affected by depression each year. The effects of depression can be managed through prescribed medications; however, some patients follow their doctor's advice initially and then stop taking their prescriptions before the treatment is finished. This decision can have consequences, including the development of a "discontinuation syndrome."

"A discontinuation syndrome is a cluster of symptoms that appear after an antidepressant has been abruptly discontinued," says Laura A. Mandos, PharmD, associate professor of clinical pharmacy at University of the Sciences in Philadelphia. "Discontinuation syndromes have been reported with selective serotonin reuptake inhibitors… and some of the tricyclic antidepressants. Common symptoms include nausea, dizziness, insomnia, vivid dreams, vertigo, mood swings, malaise, and headaches."

Why do patients decide to quit cold turkey? Sexual factors may be an influence, as a loss of libido and ejaculatory disturbances can result. Some individuals are afraid of becoming addicted to the drugs or the potential dangers they may pose.

Suicide is also a concern. The U.S. Food and Drug Administration issued a public health advisory asking makers of 10 antidepressant drugs to add or strengthen suicide-related warnings on their labels.

Discontinuation syndrome should not be confused with drug dependency or addiction because there "is no psychological craving for the medication," according to Mandos. The symptoms of discontinuation syndrome may last anywhere from 3 days to 3 weeks. "In general, it is prudent to always taper off an antidepressant to lessen the risk of experiencing a discontinuation syndrome," she says. "It is very important for patients not to stop taking their antidepressant medications abruptly."

New Drug Combo Helps HCV-HIV Co-Infected Patients

Reuters News; July 28, 2004 -- A new drug combination that includes a chemically modified form of interferon known as peginterferon is much more effective in treating hepatitis C (HCV) in patients co-infected with HIV than the standard hepatitis C treatment, according to two studies published in the *New England Journal of Medicine*.

Approximately 300,000 HIV-positive people in the United States also have HCV [and this dual infection is relatively common in present and former injection drug users]. The standard treatment for HCV is ribavirin and interferon, which is a synthetic version of a naturally occurring immune system protein. The new studies examined the use of peginterferon, which stays active in the body for a longer period of time than interferon.

The first study, found that the HCV virus was suppressed in 27% of the 66 patients co-infected with HIV who were treated with peginterferon and ribavirin for 48 weeks, compared with 12% of the 67 HIV-positive patients who received interferon and ribavirin for the same period of time.

The second study compared the efficacy and safety of peginterferon plus either ribavirin or placebo with interferon plus ribavirin. The overall rate of sustained virologic response was significantly higher among the recipients of peginterferon plus ribavirin than among those assigned to interferon plus ribavirin (40% vs 12%), or peginterferon plus placebo (40% vs 20%).

Based on these studies it appears that, among HCV-HIV co-infected patients, the combination of peginterferon alfa-2a plus ribavirin is significantly more effective than either interferon alfa-2a plus ribavirin or peginterferon alfa-2a by itself.

See: Chung RT, et al. Peginterferon alfa-2a plus ribavirin versus interferon alfa-2a plus ribavirin for chronic hepatitis C in HIV-coinfected persons. *NEJM*. 2004(Jul);351(5):451-459. Torriani FJ, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. *NEJM*. 2004(Jul);351(5):438-450.

Treatment Admissions Rise for Narcotic Pain Med Abuse

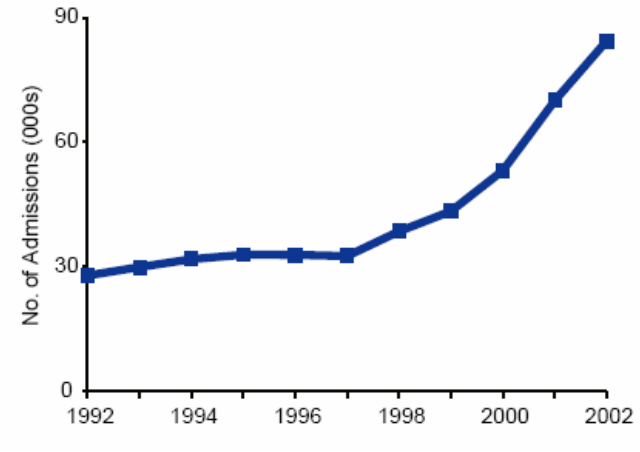
SAMHSA Press Release; July 23, 2004 -- In the 10 years between 1992 and 2002 treatment admission rates for abuse of narcotic pain medications more than doubled, the Substance Abuse and Mental Health Services Administration (SAMHSA) said in a new report.

Titled "Treatment Admissions Involving Narcotic Painkillers 2002 Update," the report shows that these admissions increased for all ages, but especially among people aged 20 to 30. Furthermore, between 1997 and 2002, the proportion of new users -- those entering treatment within 3 years of beginning use -- increased from 26% in 1997 to 39% in 2002. The median duration of use before

first seeking treatment decreased from 9 years of use in 1992 to 4 years of use in 2002.

In 2002, there were about 84,000 admissions to treatment where the primary, secondary or tertiary substance of abuse was a narcotic pain medication. Narcotic pain medications were the primary substance of abuse in about half of these admissions. In the other half, abuse of narcotic pain medications was secondary to abuse of another substance, generally alcohol or heroin. In 2002, Maine had the highest rate in the nation: 207 admissions per 100,000 population.

In overall context, admissions to addiction treatment involving the abuse of narcotic painkillers made up a small proportion -- about 4% -- of the 1.9 million admissions reported to SAMHSA's Treatment Episode Data Set (TEDS) in 2002. However, these treatment admissions have increased in publicly funded substance abuse treatment facilities across the nation during the last few years.



The number of treatment admissions in which narcotic painkillers were involved was relatively stable between 1992 and 1997, but increased dramatically between 1997 and 2002 (***see graph***). In 1992, the treatment admission rate for narcotic painkiller abuse in the United States was 14 admissions per 100,000 persons aged 12 or older. By 2002, it had increased to 35 admissions per 100,000, more than doubling the rate since 1992.

A separate report from SAMHSA's Drug Abuse Warning Network (DAWN) showed that drug-abuse-related emergency department (ED) visits involving opioid pain relievers have been increasing since 1994. Two pain relievers, oxycodone and hydrocodone, account for the largest proportion of the increase.

■ In 2002, opioid analgesics accounted for more than 119,000 ED mentions, or 10% of all the drug mentions in drug-abuse-related ED visits. More than half (54%) of opioid cases involved multiple drugs.

■ Oxycodone and hydrocodone were the most frequently named pain relievers, accounting for 40% (47,594 mentions) of the opioid pain relievers involved in the ED visits.

■ The most frequent substances found in combination with oxycodone and hydrocodone were alcohol, benzodiazepines, other opioid pain relievers, and cocaine.

■ Methadone accounted for only about 10% (11,709) of ED mentions during 2002.

See: http://www.samhsa.org.

Rural Areas Lead in Pain Med Addiction Treatment

SAMHSA News Release; August 6, 2004 -- Rural areas outpaced urban areas in substance abuse treatment rates for abuse of narcotic painkillers in 2002. This is the conclusion of a new report, "Treatment Admissions in Urban and Rural Areas Involving Abuse of Narcotic Painkillers: 2002 Update," released by the Substance Abuse and Mental Health Services Administration.

The report found that nationwide admissions for abuse of narcotic painkillers increased from 1992 to 2002 by 269% for non-metropolitan areas without a major city, compared with a 155% increase for the nation as a whole. Large central metropolitan areas had the smallest increase, 58%.

"Abuse of narcotic painkillers is accelerating in rural areas, and with it the need for effective substance abuse treatment and recovery support services," SAMHSA Administrator Charles Curie said. "Increasing substance abuse treatment capacity is a top priority for SAMHSA.

The report is based on SAMHSA's Treatment Episode Data Set (TEDS) for 2002. TEDS provides information on the demographic and substance abuse characteristics of the 1.9 million admissions to treatment for abuse of alcohol and drugs from reporting facilities.

This report is located on the Internet at:
http://www.oas.samhsa.gov.

NIH Study Leads to Review of Alcohol Guidelines

Associated Press; July 28, 2004 -- With some studies showing that drinking too much alcohol could cause problems, and others showing moderate drinking brings health benefits, the National Institutes of Health (NIH) has conducted a new analysis of the extensive research on alcohol's effects.

The review, which aimed to alleviate confusion about positive and negative alcohol effects, looked at how many

drinks provide health benefits without the harm, and whether people at risk, such as those with diabetes, should abstain from drinking.

The NIH analysis determined that the health benefits of alcohol are dependent on a person's age, gender, and overall medical history. For the general population, consuming 2 drinks a day for men and 1 a day for women is linked to lower mortality and is unlikely to cause harm. A drink is defined as 5 ounces of wine, 12 ounces of beer, or 1.5 ounces of distilled spirits.

The study was published in the June 2004 journal *Alcoholism: Clinical & Experimental Research*.

New Drug May Curb Alcohol Cravings for Some

Reuters News; July 30, 2004 -- The U.S. Food and Drug Administration has approved a drug that may reduce alcohol cravings in some problem drinkers who have quit.

The FDA approved Campral (acamprosate) after studies showed that more subjects who were given the drug stayed away from alcohol, compared with those who were given a placebo. The drug has been used in Europe for 15 years.

"While its mechanism of action is not fully understood, Campral is thought to act on the brain pathways related to alcohol abuse," the FDA wrote. However, the FDA said that Campral might not be effective for people who are currently drinking when they start taking the drug, or for those who are misusing other substances. It is expected that the drug could be on the market by the end of this year.

[Acamprosate is only the third drug FDA-approved specifically for treating alcoholism, coming after naltrexone and disulfiram. -- Ed.]

Study: Drug Use Varies Widely by State

SAMHSA News Release; August 6, 2004 -- Drug use in the District of Colombia (DC) is twice that in Iowa and some other states, the Substance Abuse and Mental Health Services Administration (SAMHSA) reported in a new state-by-state study called "2002 State Estimates of Substance Abuse."

DC also had the nation's highest rate of monthly use of marijuana, 10.8%, while Alabama had the lowest rate, 4.4%, among people aged 12 or older. For past-month use of illicit drugs other than marijuana, Alaska, Arizona, DC, Louisiana, Nevada, North Carolina, Oklahoma, Oregon, Rhode Island, and Washington had the highest rates.

This report available at: http://www.oas.samhsa.gov.

Management of SAMHSA Programs Faulted

Alcoholism & Drug Abuse Weekly; July 12, 2004 -- A General Accounting Office (GAO) report faults the Substance Abuse and Mental Health Services Administration (SAMHSA) for incomplete program planning efforts and for operating with a strategic plan that dates back to October 2002.

With the federal block-grant program soon changing to a performance partnership grant program, the report concluded that SAMHSA hasn't completed the necessary hiring and training to ensure that it has the proper staff to administer and evaluate the grants.

The GAO report recommended that SAMHSA develop a detailed succession strategy; train the agency's staff so they can implement the performance partnership grants with states; create a procedure that enables applicants to correct administrative errors in applications and resubmit them; and expedite a strategy plan for the performing partnership grants and submit it to Congress.

AATOD Launches New Web Site

American Association for the Treatment of Opioid Dependence (AATOD), Press Release; August 2004 -- This association has launched a revamped web site (http://www.aatod.org) with expanded features providing a much greater degree of navigability. New features include a search engine, site map, and drop-down boxes.

Content has been greatly expanded and divided into 8 categories. In effect, the new site doubles the former content along with adding a number of reference documents. Also at the site is the most current information about the approaching AATOD national conference, which will convene in Orlando, Florida between October 16-20, 2004.

#95 – September-October 2004

HARRT Plus Methadone Effective for HIV

AIDS Weekly; July 19, 2004 -- In a clinical study, researchers prospectively assessed the safety and efficacy of once- and twice-daily directly observed therapy (DOT) in 54 methadone maintenance treatment (MMT) patients co-infected with HIV and hepatitis C.

"Methadone and highly active antiretroviral therapy (HAART) were dispensed daily as DOT, with patients in the twice-daily HAART group self-administering the second dose," wrote B. Conway of the University of British Columbia and colleagues. "Clinical and laboratory end points were monitored, along with the impact of ongoing cocaine use."

Virus loads decreased significantly in a majority of patients, and these lower levels were attained regardless of ongoing cocaine use. Methadone dosing was adjusted for 32 patients without modification of HAART. Hepatic toxicity limiting treatment was rare.

The researchers concluded, "A DOT program of co-administered methadone and HAART can be implemented with good results even for patients who continue to use cocaine." The full study, "Directly Observed Therapy for the Management of HIV-Infected Patients in a Methadone Program," was published in the journal *Clinical Infectious Diseases* (2004;38(supplement 5):S402-S408).

Does Methadone Spoil?

Addiction Treatment Forum; Summer Edition -- With up to a month's supply of take-home methadone permitted by federal regulations, there has been concern about the shelf-life of the medication. Independent research and commentary confirms that methadone itself is a relatively stable drug, and any spoilage or contamination is due more to what is used to dilute the medication at the time of dispensing.

Based on a review of existing literature and a consensus of opinion among consulted pharmacists, the American Association for the Treatment of Opioid Dependence (AATOD) issued several recommendations in June 2004:

A. Methadone hydrochloride products that are diluted should be dispensed using distilled water only.

B. New, clean, air tight, light resistant containers should be used for dispensing.

C. Take-home containers should be securely refrigerated as soon as possible, and remain refrigerated until used.

AATOD specified that, if these procedures are followed, liquid methadone should remain stable for up to 30 days from the date of MMT clinic dispensing.

However, is dilution at the time of clinic dispensing required or necessary? Typically, product labeling specifies, "to be diluted with water or other liquid to 30 mL (1 fl. oz.) or more before oral administration." This could be interpreted as meaning dilution "just before the dose is taken," in which case the patient might be the one to add liquid for dilution. Tap water or any other fluid could be used, since storage is not a concern.

For the complete article, see:
http://www.atforum.com/SiteRoot/pages/current_pastissues/summer2004a.shtml#anchor6

HCV Treatment Should Be Offered to Methadone Patients

Addiction; September 2004 -- Approximately 170 million people world-wide are chronically infected with the hepatitis C virus (HCV). While the seroprevalence in the general population ranges between 0.2 and 2%, 50-90% of injection drug users are chronically HCV-infected. However, many patients who are in methadone maintenance treatment are still excluded from therapy for HCV infection.

The authors of this review article examined clinical trials published between 1987 and 2003 that focus on the treatment of chronic HCV in patients with drug addiction. They found only seven clinical trials investigating HCV treatment among current or former drug abusers. Thus far, no trials using the newer pegylated IFN-α have been conducted.

Data about sustained response and adherence in HCV-infected methadone patients were either comparable to control groups or to representative clinically-controlled trials using the same treatment regimen (IFN-α monotherapy or combined with ribavirin). Psychiatric comorbidity did not negatively influence adherence or treatment outcome; however, patients with persistent drug abuse seemed more likely to discontinue treatment early. The authors concluded that there is no clinical evidence suggesting that HCV treatment with IFN-α should be withheld from methadone patients.

See: Schaefer M, et al. Treatment of chronic hepatitis C in patients with drug dependence: time to change the rules? *Addiction*. 2004;99(9):1167-1175.

Interim Methadone An Important Intervention

CPDD (College on Problems of Drug Dependence); June 2004 -- Interim methadone maintenance was developed to address the problem of long wait lists for entry into methadone maintenance treatment (MMT) programs. It consists of methadone maintenance with only emergency

counseling for up to 4 months for individuals awaiting admission to full-service treatment.

A randomized clinical trial examined whether individuals on the wait list for a mobile MTT program who received interim maintenance had superior outcomes in terms of MTT entry and reductions in drug use, HIV risk behaviors, and criminal activity as compared with individuals assigned to the wait list without interim treatment. Adult heroin dependent individuals (n=319) who met criteria for MTT entry and for whom no treatment slots were available were randomly assigned to either interim maintenance or a wait list.

Preliminary results indicated that interim MMT participants had significantly greater decreases from baseline to 4 month follow-up in heroin, cocaine, and alcohol use, and days of illegal activities. Although both groups reported similar levels of baseline heroin and cocaine use, interim participants were significantly less likely than the usual wait list group to test heroin positive at follow-up, while the groups did not differ with regard to cocaine test results. Importantly, 84% of the interim group entered treatment within the 4-month follow-up period, compared with only a quarter of the usual wait-list group.

Source: Schwartz RP, et al. Interim methadone maintenance: Preliminary findings. Paper presented at: CPDD (College on Problems of Drug Dependence) 65th Annual Meeting; June 2004; San Juan, Puerto Rico.

Length of Stay in MMT a Critical Success Factor

CPDD (College on Problems of Drug Dependence); June 2004 -- The strategy for treating narcotic abusers in MMT programs is based on the goal of reducing illicit drug use. When evaluated separately, length of stay (LOS) and methadone dosage have been found to correlate with negative opiate toxicology results. Surprisingly, however, there is a dearth of literature that looks at the interrelationships between these two variables. Therefore, this study compared LOS and methadone dosage with opiate toxicology results during a three-month period for 2,959 adults enrolled in seven MMT programs. Age was also evaluated.

Consistent with previous studies, it was found that longer LOS and higher methadone dose were significantly correlated with reduced opioid toxicology results. However, LOS was found to have a greater effect than methadone dosage or patient age. According to the researchers, methadone should be viewed as a tool to enhance other aspects of treatment in order to promote longer LOS, ultimately yielding a higher percentage of negative opioid toxicology results.

Source: Brown LS, et al. The interrelationships between length of stay, methadone dosage, and age at an urban opioid treatment program. Paper presented at: CPDD (College on Problems of Drug Dependence) 65th Annual Meeting; June 2004; San Juan, Puerto Rico.

Methadone Dose Impacts MMT Retention

CPDD (College on Problems of Drug Dependence); June 2004 -- To study factors serving as long-term MMT-retention predictors researchers investigated all patients (n=470) who were admitted to the Adelson Clinic (Israel) between July 1993 - December 2002 and followed up until July 2003. The sample was 72% male with an average age of about 37 years.

Patients with methadone doses of 100 mg/day or more (n=298) had significantly longer retention (mean=6.1 years), as compared with patients having less then 100 mg/d methadone (n=119). Additional significant variables fostering treatment retention included: patients with negative urine tests for opioids and benzodiazepines, older admission age (> 30 years), and having children. Overall, then, higher methadone dose, no opioid abuse, and having children, were significantly associated with longer retention in treatment.

Source: Peles E, Adelson M. Factors that predict retention: Ten years follow-up in methadone maintenance treatment clinic in Israel. Paper presented at: CPDD (College on Problems of Drug Dependence) 65th Annual Meeting; June 2004; San Juan, Puerto Rico.

Higher Methadone Doses Necessary to Suppress Heroin Abuse

CPDD (College on Problems of Drug Dependence); June 2004 -- Clinical research has shown that “high” methadone doses (e.g., 80-100 mg) are more effective at suppressing heroin use than moderate doses (e.g., 40-50 mg). This increased efficacy may result from greater cross-tolerance to heroin, as recent laboratory research has shown that subjective and physiological effects of heroin persist during maintenance on 30-60 mg methadone, but are minimal when participants are maintained on 120 mg methadone.

The purpose of this present study by researchers at the Johns Hopkins School of Medicine, Baltimore, was to examine the relationship between methadone dose and the reinforcing

effects of heroin as measured by the choice to take heroin in a laboratory setting. Seven participants completed a 5-month double-blind, within-subject, study conducted in an inpatient laboratory while being maintained on methadone at 50, 100, or 150 mg/day.

It was found that only maintenance on 150 mg/d of methadone produced near complete suppression of heroin self-administration. The researchers concluded that these results add to a growing literature suggesting that methadone's therapeutic efficacy may be enhanced by the use of higher maintenance doses that produce more effective opioid cross-tolerance.

Source: Donny EC, Brasser SM, Stitzer ML, Bigelow GE, Walsh SL. Relatively high doses of methadone are necessary to suppress heroin self-administration in the human laboratory Paper presented at: CPDD (College on Problems of Drug Dependence) 65th Annual Meeting; June 2004; San Juan, Puerto Rico.

Bone Health in MMT Patients Examined

CPDD (College on Problems of Drug Dependence); June 2004 -- Bone pain complaints among MMT patients have raised concerns. Consequently, researchers assessed the prevalence of bone pain, vitamin D insufficiency, and osteoporosis in persons receiving methadone maintenance. Subjects (n=88) recruited from an urban MMT program during 2003 had a median age of 42 years and were 61% female, of whom 34% were post-menopausal.

The survey found that a majority of patients (64%) reported bone pain. Furthermore, 43% of the patients were somewhat or very worried that methadone affects bone health; 20% delayed initiation of MMT due to this worry; 33% felt this worry would influence their MMT duration; and 8% had declined a recommended increase in methadone dose due to concerns about bone health.

Results indicated that almost half of the MMT subjects overall believed that methadone adversely affects bone health. The prevalence of vitamin D insufficiency was substantial and a high prevalence of osteoporosis also was demonstrated, especially among male subjects. Methadone was not attributed as a cause of these conditions; however, since these bone diseases are treatable the researchers recommended that further study is warranted to address the abnormal bone health of patients in MMT.

Source: Kim TW, et al. Bone health in methadone maintenance treatment. Paper presented at: CPDD (College on Problems of Drug Dependence) 65th Annual Meeting; June 2004; San Juan, Puerto Rico.

MMT Helps Normalizes Menstrual Cycles

CPDD (College on Problems of Drug Dependence); June 2004 -- While menstrual disruption by heroin has been demonstrated, there is little published data showing any effect of methadone maintenance treatment. Therefore, researchers retrospectively examined data from 191 polydrug-using women enrolled in MMT as part of two clinical trials, lasting 25 to 29 weeks. Participants had been maintained on 70 to 100 mg of methadone per day.

As expected, women in this study had a high prevalence of menstrual cycle-length irregularities. The 133 eligible participants were categorized as: regular 28%; irregular 47%; transient amenorrhea 5%; persistent amenorrhea 8%; or cycle restarters 12%. Each additional week in MMT was associated with a decreased risk of both abnormally long and short cycles. Of the 27 women who had amenorrhea secondary to heroin abuse before entering the study, 59% began to have periods again. Urine positivity for opioids or cocaine was not significantly associated with either short or long cycles.

These findings indicate that menstrual cycle length begins to normalize as time in methadone maintenance increases. For some patients with secondary amenorrhea likely due to opiate dependence and its associated morbidity, there may be a resumption of menses during MMT.

Source: Schmittner J, et al. Menstrual function during methadone maintenance. Paper presented at: CPDD (College on Problems of Drug Dependence) 65th Annual Meeting; June 2004; San Juan, Puerto Rico.

Woman Jailed for Recovery in MMT

The Roanoke Times; August 21, 2004 (Laurence Hammack); and, *Richland News Press*; August 31, 2004 (editorial) -- A Virginia woman, Kimberly Bucklin, was prescribed methadone maintenance treatment (MMT) to help her break an OxyContin addiction; yet, a judge had prohibited her from taking the methadone when he put her on probation. Consequently, Bucklin was sentenced to three years in prison for violating her probation.

According to Bucklin's attorney, Tom Scott, this case presents a conflict between law enforcement's fight against drug abuse and the medical needs of recovering addicts. "It

really is a medical decision and not a legal decision," he said of her need for methadone.

Last year, Bucklin was charged with child abuse and possession of OxyContin. Following her arrest, she became a patient at a methadone clinic. However, she was ordered in June 2003 to discontinue all use of methadone within six months as a condition of her probation and a six-year suspended prison sentence.

Against the medical advice of the clinic physician, the 29-year-old began to gradually reduce her daily dose of methadone. But after she suffered cravings and withdrawal symptoms, the clinic restored her to a higher dose and continued her treatment past the six-month deadline. In February, Bucklin was charged with violating her probation and has been in the county jail ever since -- except for a brief hospital stay shortly after she was locked up, when she was treated for severe methadone withdrawal.

According to a brief filed by Scott and ACLU attorneys, the danger with a judge ordering someone off methadone is that it often prompts the addict to return to the original drug at a time when he or she has a low tolerance because of treatment, creating a danger of a fatal overdose. Furthermore, by setting and enforcing a time limit on Bucklen's participation in methadone treatment, the court may have stepped outside the field of judicial discretion and started to make medical decisions -- which is a dangerous legal precedent.

#96 – November-December 2004

Methadone, Buprenorphine Exhibit Similar Safety Profiles

CPDD (College on Problems of Drug Dependence); June 2004 — Although there has been concern about potential adverse effects of buprenorphine on liver function, there has been little controlled research evaluating its safety and side effects.

Researchers randomized 164 subjects to buprenorphine (n=84) or methadone (n=80) for a 16-week trial using a flexible dosing schedule. There were no differences between groups in percent of abnormal vital signs or liver function tests. Medical staff reports of adverse events were infrequent and showed no pattern suggesting a specific medication-related effect. The researchers concluded that buprenorphine and methadone produce similar profiles on these measures of safety and side effects.

From: Lofwall MR, Strain EC, Stitzer ML, Bigelow GE. Comparative safety and side-effect profiles of buprenorphine vs. methadone in the outpatient treatment of opioid dependence. Paper presented at: CPDD (College on Problems of Drug Dependence) 65th Annual Meeting; June 2004; San Juan, Puerto Rico.

Methadone Doses >100 mg/d Required in up to 60% of MMT Patients

Europad Conference; Paris; November 2004 — This review of published studies examined the benefits, safety, and some possible metabolic reasons behind the need for methadone doses exceeding 100 mg/day (and, rarely, ranging up to 1000 mg/d). The author concluded that, in a large population of opioid dependent patients, great individual variability is seen in the range of doses required to achieve abstinence from opioid and cocaine abuse in more than 90% of patients. Higher average doses correlate with less substance abuse and better retention. Interindividual differences in dose requirement are based in part on acquired and genetic differences in metabolism. Requiring a higher dose does not correspondingly result in greater inability of the patient to withdraw from methadone-supported treatment.

A number of points were emphasized regarding the distribution of methadone doses necessary to achieve stabilization in a typical clinic population:

1. 40-60% of patients may entirely cease illicit opioid abuse at methadone doses of 100 mg/day or less;
2. 20-30% will require doses from 101 to 200 mg/d;
3. 8-15% may require between 201 to 300 mg/d;
4. 6-15% percent may require doses greater than 300 mg/d and 0.2%, > 900 mg/d.

Thus, as many as 60% of patients in an MMT clinic may require more than 100 mg/d for methadone stabilization. Furthermore, cocaine abuse decreases may be expected at doses greater than 100 mg/d.

See: Shinderman MS. When enough is not enough. Research and practice supporting prescription of clinically effective doses in excess of 100 mg in methadone maintenance treatment. From: Program and abstracts of the 6th European Europad Conference; November 1-3, 2004; Paris, France.

Systematic Data Confirm Effectiveness of MMT

Europad Conference; Paris; November 2004 — Researchers summarized the findings of 5 systematic literature reviews on the efficacy of maintenance treatments for opioid dependence published in the Cochrane Library. The analysis covered 52 studies encompassing more than 12,000 participants.

Results indicated that methadone maintenance treatment (MMT) is more effective in retaining patients in addiction treatment than opioid detoxification using methadone, buprenorphine maintenance treatment, LAAM maintenance, heroin given together with methadone, or no treatment. Higher doses of methadone were more effective than medium and low doses. As for the influence of different modalities on death rates or criminal activity, there were no statistically significant differences in the studies reporting these results. The authors concluded that data from systematic reviews demonstrate that MMT at appropriate doses is most effective in retaining patients in treatment and suppressing heroin use.

Source: L. Amato, M. Davoli and C. A. Perucci. Effectiveness of opiate maintenance therapy, an overview of systematic reviews. From: Program and abstracts of the 6th European Europad Conference; November 1-3, 2004; Paris, France.

MMT Patient Health Merits Close Monitoring

Drug & Alcohol Review; September 2004 — This study investigated the health status of a representative sample of patients (n=107) receiving methadone maintenance treatment (MMT) in New Zealand. The publication of New Zealand norms in 1999 enabled comparisons of the health of the MMT program study participants, using a standardized health survey, with that of the general population.

Although more than half of participants rated their health as good, very good, or excellent, 44% rated their health as fair or poor. Compared with population norms, the health of the MMT-study participants *overall* was significantly poorer. Results highlight the impact of a chronic disorder and co-existing health-related problems on the health and well-being and day-to-day functioning of this patient group.

Higher frequency of benzodiazepine abuse was associated with poorer social functioning, mental health, and role functioning. A higher frequency of cannabis use was associated with poorer role functioning due to emotional problems. Findings support routine monitoring of health status in patients receiving MMT as a guide to preventative and treatment interventions and health maintenance strategies.

See: Deering D, Frampton C, Horn J, Sellman D, Adamson S, Potiki T. Health status of clients receiving methadone maintenance treatment using the SF-36 health survey questionnaire. *Drug Alcohol Rev*. 2004;23(3):273-280.

Grant to Fund Interim Methadone in Baltimore

Alcoholism & Drug Abuse Weekly; October 11, 2004 — Baltimore officials announced that a $1 million grant from the U.S. Department of Health and Human Services (HHS) will allow them to fund interim methadone treatment for hundreds of people who are on waiting lists for treatment.

HHS awarded the grant to Baltimore Substance Abuse System Inc, a group that oversees Baltimore's drug treatment efforts. It will fund interim methadone treatment for about 1,200 opioid-addicted individuals during the next year, making Baltimore's interim methadone treatment program the largest in the nation.

Addicted individuals will be able to participate in the interim program for up to 4 months — the limit under federal law — and will be encouraged to enroll in an extended treatment program to continue their recovery. A study conducted by the Friends Research Institute of Baltimore found that 80% of patients who participate in interim methadone treatment seek long-term treatment.

Methadone Medical Maintenance: Physician-Pharmacy Model

CPDD (College on Problems of Drug Dependence); June 2004 — In June of 2001, the Adult Services Clinic (ASC, an MMT program at Weill Cornell Medical College) in cooperation with a local pharmacy opened the Physician-Commercial Pharmacy model of methadone medical maintenance (MMM). Methadone patients who were enrolled for at least 4 years in the ASC and who demonstrated social stability for the last 3 continuous years of treatment (e.g., no criminality, or substance abuse, cooperative behavior in clinic, employment or school) were considered eligible for this program.

Patients reported monthly to a private physician. The physician collects urine samples and can request patients to bring in medication for counts for quality assurance. The pharmacy, on physician's orders, dispenses a month's supply of methadone in dry tablet form. Patients must have

income or insurance to pay for physician visits and methadone. There is no observed ingestion of methadone.

Fifteen patients entered the program. Four voluntarily returned to the ASC for health reasons, loss of employment, or a preference for continued treatment in the ASC. The 11 patients remaining in MMM preferred the services of the physician and the pharmacy over the ASC and improved the quality of their lives. In this pilot, both MMM and the MMT program complement each other and should be available to meet the long-term needs of rehabilitated patients.

Source: Beeder A, Wells A, Curet E, et al. Methadone medical maintenance: Physician-pharmacy model. Paper presented at: CPDD (College on Problems of Drug Dependence) 65th Annual Meeting; June 2004; San Juan, Puerto Rico.

New Online Resources: Methadone – HIV-Drug Interactions

As part of its "Criteria for the Medical Care of Adults with HIV Infection" series, the New York State Department of Health AIDS Institute has updated its monograph on "HIV Drug-Drug Interactions." In addition to providing helpful information on the nature of drug interactions in general, a series of tables describe interactions of drugs used to treat HIV/AIDS with other medications, including methadone. The monograph is available at: http://www.hivguidelines.org/public_html/a-drug/a-drug.htm

Another guidebook — "Pain Management/Addiction Management Medications and HIV Antiretrovirals: A Guide to Interactions for Clinicians" – is available from the New York/New Jersey AIDS Education and Training Center. Released in fall 2004, this monograph describes potential interactions of HIV/AIDS medications with opioid analgesics and medications used in the treatment of opioid dependence: methadone, buprenorphine, naltrexone, etc. It can be accessed and downloaded online at: http://www.nynjaetc.org/clinPop4.htm

Also see the special the *AT Forum* White Paper report, "Methadone-Drug Interactions," for convenient reference tables. Available for viewing and download at: http://www.atforum.com/SiteRoot/pages/rxmethadone/methadonedruginteractions.shtml

Access to the above web sites was verified in December 2004.

Few Jails Support Arrested Persons on Methadone

Journal of Urban Health; November 2004 — Anecdotal evidence suggests that many jails fail to adequately detoxify arrestees/inmates who are enrolled in methadone programs. The objective of this study was to assess how jails manage arrestees/inmates enrolled in methadone programs.

A national survey of 500 jails in the United States was conducted. The jails were specifically asked about management of opiate dependency among arrestees/inmates enrolled in methadone programs. Among the 245 (49%) jails that responded, only about 1 in 4 (27%) reported they contacted the respective methadone programs regarding dose, and only 1 in 8 (12%) continued methadone during the incarceration.

Very few jails (2%) used methadone or other opiates for detoxification. Most used clonidine. However, half (48%) of jails failed to use either clonidine, methadone, or other opiates to detoxify inmates from methadone. Moderately large jails and those located in the South and Midwest were significantly more likely to continue methadone. Very large jails, those with an estimated prevalence of opiate dependence of 6% to 10% among arrestees/inmates, and those located in the Northeast were significantly more likely to use recommended detoxification protocols.

In sum: very few jails provide continuous treatment to arrested persons on methadone, and half failed to detoxify arrestees/inmates using recommended protocols. These practices jeopardize the health and well-being of persons enrolled in methadone programs and underscore the need for uniform national policies within jails.

See: Fiscella K, Moore A, Engerman J, Meldrum S. Jail management of arrestees/inmates enrolled in community methadone maintenance programs. *J Urban Health*. 2004;81(4):645-654.

Methadone Taper Effective for Opioid Withdrawal, But Relapse Common

Cochrane Review; October 2004 — Despite widespread use in many countries of tapered methadone for detoxification from opioid dependence, evidence of the efficacy of this practice to prevent relapse and promote lifestyle change has not been systematically evaluated.

To determine whether tapered methadone is effective in managing opioid withdrawal, the authors did an extensive literature search to identify randomized, controlled trials focusing on tapered methadone (maximum 30 days of

treatment) versus all other pharmacological detoxification treatments, placebo, or different modalities using methadone for the treatment of opiate withdrawal.

The results indicate that tapered methadone and other medications used in the included studies are effective in the treatment of the heroin withdrawal syndrome, although symptoms experienced by subjects differed according to the medication used. Greater improvements were achieved when other services such as counseling and other supportive services were offered along with detoxification.

The studies included in this review confirm that slow tapering with temporary substitution of long-acting opioids, such as methadone, accompanied by medical supervision and ancillary medications can reduce withdrawal severity. Nevertheless the majority of patients relapsed to heroin use.

Source: Amato L, Davoli M, Ferri M, Ali R. Methadone at tapered doses for the management of opioid withdrawal. Cochrane Database Syst Rev. 2004;18(4):CD003409.

Voucher Rewards Promote Cocaine Abstinence in MMT Patients

Journal of Consulting & Clinical Psychology; October 2004 — This study determined whether long-term abstinence reinforcement could maintain cocaine abstinence throughout a yearlong period. Patients who injected drugs and used cocaine during methadone treatment (n = 78) were randomly assigned to 1 of 2 abstinence-reinforcement groups or to a usual care control group.

Participants in the 2 abstinence-reinforcement groups could earn take-home methadone doses for providing opiate- and cocaine-free urine samples; participants in 1 of those groups also could earn up to $5,800 in vouchers for providing cocaine-free urine samples during 52 weeks.

Both abstinence-reinforcement interventions increased cocaine abstinence, but the addition of the voucher intervention resulted in the largest and most sustained abstinence. Therefore, voucher-based reinforcement of cocaine abstinence in methadone patients can be a highly effective maintenance intervention.

Reference: Silverman K, Robles E, Mudric T, Bigelow GE, Stitzer ML. A randomized trial of long-term reinforcement of cocaine abstinence in methadone-maintained patients who inject drugs. *J Consult Clin Psychol*. 2004;72(5):839-854.

Higher Methadone Doses Correlate with SMLs, Less Opioid Abuse

Europad Conference; Paris; November 2004 — This study evaluated the relationship between high methadone doses and methadone blood levels in former heroin addicts in methadone maintenance treatment (MMT).

Assessments of serum methadone level (SML) and drugs in urine were performed on 114 MMT patients (71% male) from the Adelson Clinic (Israel) who were on steady maintenance doses of methadone for at least 14 days, and had ingested their dose in the clinic for at least 3 days before being evaluated. The average daily methadone dose was 172 mg (range 40-290 mg), and the mean SML was 674 ng/ml (range 110 – 1,660 ng/ml), with no differences between genders. *[Timing of SML measurement – trough, peak, or averaging – was not specified. – Ed.]*

Methadone dose was significantly correlated with SML. Patients with positive urine for opioids (N=35) had significantly lower daily methadone doses (mean 157 mg/day) as compared with patients having negative urine for illicit opioids (mean 178 mg/day). The authors concluded that high methadone dose significantly correlates with methadone blood levels and with reductions in opioid abuse.

Source: Peles E, Bodner G, Adelson M. Correlation between high methadone dose and methadone blood level. From: Program and abstracts of the 6th European Europad Conference; November 1-3, 2004; Paris, France.

[Prior investigations have not found a strong association between higher methadone doses and corresponding trough or peak SML values; although, higher doses have indeed been associated with less continuing opioid abuse. See: Leavitt SB. Methadone Dosing & Safety. Addiction Treatment Forum *Special Report. Available at: http://www.atforum.com/SiteRoot/pages/rxmethadone/dosingandsafety.shtml]*

Does Take-Home Methadone Regimen Influence SMLs?

Europad Conference; Paris; November 2004 — Patients had been stabilized in a methadone maintenance program for about 12 months at the beginning of this study. At the time of the first measurement of serum methadone levels (SML), patients were divided into two groups according to their different regimens of take-homes: Group L (n = 33) with "less" – 1 or 2 days – and Group M (n = 31) with "more" – 3 consecutive days – take-homes per week. Afterward, 2 weeks of supervised daily methadone administration without

any take-homes was ordered for all patients for purposes of the second SML measurement.

During the first SML measurement, there was a significant correlation of methadone dose and SML in Group L but not in Group M. At the second testing there were similar and significant correlations of dose and SML in both groups. The results suggest that the regimen of take-homes should be taken into account when considering serum methadone levels for clinical purposes.

From: Okruhlica L, Klempova D, Hrabovsky M, et al. The use of methadone plasma concentration is assessing compliance with treatment. From: Program and abstracts of the 6th European Europad Conference; November 1-3, 2004; Paris, France.

Daily Methadone Boosts Retention, Compared with Buprenorphine

Europad Conference; Paris; November 2004 — While methadone maintenance is a highly effective treatment for heroin addiction, daily attendance is often difficult for many patients. Consequently, there is great interest in the possibility of replacing methadone with longer-acting opioid agonists, such as buprenorphine which, like LAAM, can be administered three-times a week.

While the current Cochrane and other reviews of comparative trials of methadone and buprenorphine are flawed, an independent meta-analysis was completed showing that methadone-treated subjects were 34% more likely to be retained in treatment than buprenorphine subjects. Viewed another way: it is necessary to treat only 6 heroin addicts with methadone for 19 weeks to prevent one premature loss that would have occurred with buprenorphine.

However, since the trials examined were double-blind, subjects receiving buprenorphine came as often to the clinic as those taking methadone. It is possible that retention may be better in buprenorphine maintenance for addicts who find it difficult to attend for daily dispensing. Buprenorphine may also be preferable in cases where there is a high risk of combined drug toxicity early in maintenance. However, the author concluded that methadone is the maintenance drug of first choice unless daily dispensing is very inconvenient or there is a high risk of combined drug toxicity early in maintenance.

Reference: Caplehorn J. Which maintenance regime is the best for retention: methadone, LAAM, or Buprenorphine. From: Program and abstracts of the 6th European Europad Conference; November 1-3, 2004; Paris, France.

Sex Dysfunction During MMT Related to Decreased Testosterone

Europad Conference; Paris; November 2004 —Therapists have long underestimate sexual difficulties among patients in methadone treatment. This is most likely because these patients express few complaints about sexual issues; being embarrassed, ashamed, or because they compensate with chemical pleasures afforded by alcohol, cannabis, benzodiazepines, cocaine, or other drugs. The author of this study and his team questioned 370 patients in methadone treatment in Geneva, Switzerland, to obtain more precise data about sexual dysfunctions. Along with this, hormonal functioning was assessed in 150 of the patients.

The results showed decreases in the level of pituitary hormones – LH and FSH –in certain patients and a consequent decrease of testosterone. These observations were correlated with the reported sexual dysfunctions and with the intake of alcohol, tobacco, cannabis, and/or cocaine. Abnormally low levels of testosterone can provoke premature andropause *[male menopause]*. In addition to sexual dysfunctions – e.g., decreased libido, and erection and ejaculation troubles – such patients may experience fatigue, loss of strength and vitality, irritability, depressive tendencies, sleep disorders, impaired concentration and memory, osteoporosis, and lipid imbalances with an accumulation of fat mostly around the waist. When this clinical situation is misinterpreted, antidepressants may be wrongly prescribed, which further aggravates the sexual dysfunctions due to medication side effects. Following discussions with consulting endocrinologists, the author prescribed testosterone for patients with the lowest levels of testosterone. Clinical results were very encouraging and a high level of patient satisfaction was achieved.

Source: Deglon JJ. Sexual dysfunctions and opioids. From: Program and abstracts of the 6th European Europad Conference; November 1-3, 2004; Paris, France.

Attitudes of Patients *and* Their Doctors Make a Difference in MMT

Europad Conference; Paris; November 2004 — In persons with opioid dependence, their respective stages of change, as described by Prochaska and DiClemente, can be important for acceptance of and adherence to methadone treatment regimens. Patients in low stages of readiness to change (Pre-

contemplation and Contemplation stages) are likely to face the prescription of methadone with an attitude of denial or strong ambivalence. Conversely, as readiness increases, reaching the stages of Determination and Action, the patient is more and more motivated to pursue the treatment and a general improvement in adherence appears.

In contrast to this awareness of patients' changes in attitude toward treatment, there is little recognition that the behaviors of *doctors* treating these patients are similarly affected by attitudes coming from their own stage of change regarding the prescription of methadone. In low stages of readiness to change – i.e., in Pre-contemplation – the doctor is likely to deny the effectiveness of substitution treatment, and in Contemplation he/she tends to be ambivalent toward it, resulting in inappropriate methadone prescription and management of treatment (e.g., duration, dosage, quality of counseling, etc). In both cases, negative consequences will be likely to develop, which will affect therapeutic relationships and patients' adherence to treatment.

Doctors in advanced stages of change – i.e., Determination and Action – are more likely to prescribe methadone according to accepted guidelines. This will work well with patients who are themselves in upper-level stages of change; however, problems may arise with patients in lower stages of change. Differences between attitudes of patients and doctors, relating to their respective stages of readiness to change, can give rise to a variety of consequences that must be taken into account and there are implications for the improvement of doctors' attitudes toward methadone-maintenance treatment.

Reference: Guelfi GP, Spiller V. Prescription of methadone: how do stages of change of patients and doctors interact. From: Program and abstracts of the 6th European Europad Conference; November 1-3, 2004; Paris, France.

Assessing Suicide Risk in MMT Patients

American Journal on Addictions; October 2004 – Methadone maintenance treatment (MMT) patients with both depression and drug dependence are at an elevated risk for suicide, yet suicide remains difficult to predict. Therefore, this study examined clinical features and patient characteristics associated with suicide risk among depressed opioid-dependent patients.

A history of suicide attempts was more associated with female gender, violent behavior in the past 30 days and lifetime, and less education. Family conflict and depression severity were associated with current suicidal ideation. Therefore, when evaluating MMT patients with depressive disorders, these features should be considered in efforts to identify those at heightened risk for suicide and to plan interventions.

See: Phillips J, Carpenter K, Nunes E. Suicide risk in depressed methadone-maintained patients: Associations with clinical and demographic characteristics. *Am J Addict.* 2004;13(4):327-332.

Caution for MMT Patients: Some Vitamins Harmful in Excess

Annals of Internal Medicine; January 2005 (early publication) – There is great interest among methadone maintenance treatment (MMT) programs and patients in the benefits of better nutrition as an aid to addiction recovery. *[See also, the Fall 2004 edition of* AT Forum *at: http://www.atforum.com/SiteRoot/pages/current_pastissues/fall2004.html.]*

A new report from researchers at Johns Hopkins University highlights potential dangers in taking excessive amounts of certain vitamins unless the particular patient has a diagnosed deficiency of such nutrients. Researchers examined deaths reported in 19 randomized trials, including approximately 136,000 adults, which compared vitamin E with either a dummy pill (placebo) or no treatment. Amounts of vitamin E tested in the trials ranged from 16.5 International Units (IU) daily to 2000 IU daily. *[A typical once-a-day multivitamin/ multimineral pill contains about 30 IU of vitamin E.]* Compared with placebo or no treatment, intake of vitamin E in amounts of 400 IU or more daily for longer than 1 year significantly increased the risk for death. The review did not find the exact lowest amount of vitamin E that was associated with this increased risk.

Findings from these trials may not apply as strongly to young, healthy adults. However, some patients in MMT may have preexisting risk factors that could be worsened by excessive vitamin E intake.

While medical experts have recommended that people of all ages could improve their health by adding daily vitamins and minerals to their diets, excessively high doses of these same otherwise beneficial substances can result in health risks. For example:

- Vitamin A in excess of 15,000 micrograms (mcg) per day can influence bone fractures, joint pain, headaches, nausea and vomiting, fatigue, and diarrhea.

- Vitamin B3, or niacin, in excess (more than 16 mg/day) may cause dilation of blood vessels and potentially painful tingling called a "niacin flush." High doses may contribute to diarrhea, nausea and vomiting, and liver damage in the long term.
- Vitamin C excess (more than 1,000 mg/day) can cause diarrhea and kidney stones.
- Vitamin D from supplements (greater than 50 mcg/day) can result in kidney damage, weakened bones and muscles, and possibly death.

Source: Miller ER, et al. Meta-analysis: High-dosage vitamin E supplementation may increase all-cause mortality. *Ann Internal Med*. 2005 (early publication); 142:E-53-62. Supplemental information from: *canada.com News* (Kirkey S. Vitamin E alarm sounded. November 11, 2004) and Harvard Medical School Consumer Health Information at http://www.intelihealth.com.

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Pain During MMT Influences Higher Methadone Dosing

Tel Aviv, Israel; February 2005 – The aim of this study was to characterize patients with chronic pain in methadone maintenance treatment (MMT). Between September and December, 2003, 170 consecutive patients from an MMT clinic participated in a questionnaire survey on pain (duration and severity). Chronic pain was defined as current pain lasting for 6 months or longer. The patients' maintenance methadone dosage during the month before and month of the survey were recorded.

Of the 170 patients studied, 94 (55.3%) experienced chronic pain. As might be expected, they had a significantly higher proportion of chronic illness (74.5%) compared with non-pain patients (44.7%; $p < 0.0005$). Pain duration significantly correlated with pain severity and also was significantly associated with methadone daily dosage: patients with pain duration of 10 years or more (n=26) were receiving the highest methadone doses (182 ± 59 mg/day), those with pain duration from 1 to 10 years (n=59) 161 ± 56 mg/day, and those with pain duration of <1 year (n=9) 134 ± 73 mg/day. In comparison, patients in the non-pain group (n=76) were receiving 147 ± 53 mg/day of methadone (p=0.03).

The authors conclude that pain duration and severity are significantly correlated. Although methadone was not prescribed for the treatment of pain but rather for opioid addiction, patients in the MMT clinic with prolonged pain were prescribed significantly higher methadone doses compared with those having short pain duration or no pain.

Source: Peles E, Schreiber S, Gordon J, Adelson M. Significantly higher methadone dose for methadone maintenance treatment (MMT) patients with chronic pain. *Pain*. 2005;113(3):340-346.

*[**See also**, an article on this subject in* AT Forum, *Winter 2004, at: http://www.atforum.com/SiteRoot/pages/current_pastissues/winter2004.shtml#anchor1. Pain is a common complaint among MMT patients, which may influence a need for much higher methadone doses than clinicians commonly realize. – Ed.]*

MMT Patients' Experiences With Chronic Pain

Bronx, New York; Albert Einstein College of Medicine; December 2004 – Recent studies indicate that severe chronic pain is common among patients in methadone maintenance treatment (MMT). This study used qualitative methods to explore the experiences of MMT patients with chronic pain.

Twelve patients screening positive for chronic severe pain on the Brief Pain Inventory were interviewed for the study. Results suggest that chronic severe pain has major consequences in the lives of methadone-maintenance patients and may be linked to illegal drug use, social isolation, and role failure.

A variety of barriers limited their access to effective treatment. A common complaint about the care patients received was providers' lack of concern or inability to "listen." Patients who were satisfied with treatment focused on the psychosocial dimensions of care they received. These preliminary results suggest that treatment approaches should emphasize emotional support and an emphasis on the psychosocial effects of pain.

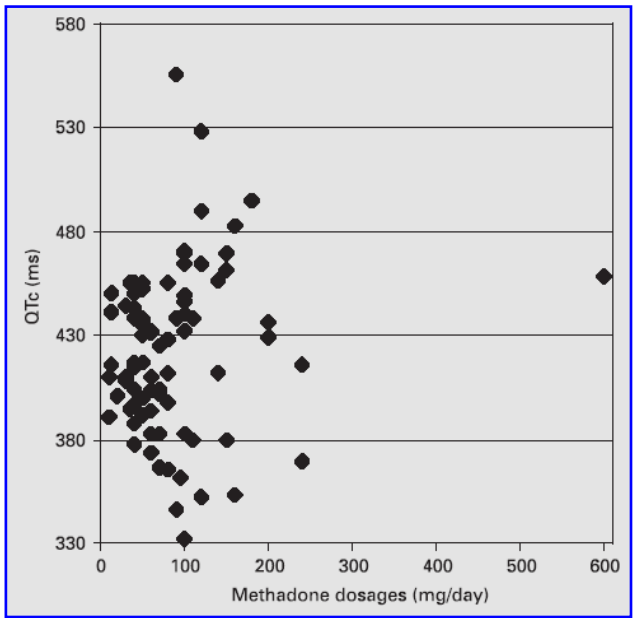
See: Karasz A, Zallman L, Berg K, Gourevitch M, Selwyn P, Arnsten J. The experience of chronic severe pain in patients undergoing methadone maintenance treatment. *J Pain Symptom Manage*. 2004;28(5):517-525.

QTc Prolongation Not Correlated With Methadone Dose

Pisa, Italy; PISA-SIA (Study and Intervention on Addictions) Group; January 2005 – This study assessed the incidence of abnormal QTc-interval values in a population

of long-term MMT patients receiving methadone doses ranging between 10 and 600 mg/daily (mean ± SD = 87 ± 76 mg/d). Baseline ECG recordings were performed in 83 former heroin addicts in MMT for at least 6 months while no other known QT-prolonging agent was being administered.

In these patients, 83% had a more prolonged QT interval than reference values for persons of the same sex and age, although these values were within an acceptable range and no patients exhibited cardiac symptoms. Only 2 patients displayed a QTc interval of >500 ms. Of importance, ***no correlation emerged*** between QTc values and methadone dosages (see ***graph***).



At equivalent methadone dose levels, QTc intervals vary widely. Higher methadone doses do not appear to elevate

The authors concluded that patients on long-term methadone maintenance treatment commonly show longer than expected QTc interval values. This data supports the recommendation that patients entering methadone treatment should be screened for cardiac risk factors. ECGs might be considered in ongoing patients, especially before starting QT-prolonging medications.

Source: Maremmani I, Pacini M, Cesaroni C, Lovrecic M, Perugi G, Tagliamonte A. QTc Interval Prolongation in Patients on Long-Term Methadone Maintenance Therapy. *Eur Addict Res*. 2005;11(1):44-49.

For a discussion of cardiac risks and recommendations during MMT, see: Leavitt SB, Krantz M. Cardiac Considerations During MMT, *AT Forum* Special Report, available at:
http://www.atforum.com/SiteRoot/pages/rxmethadone/cardiacmmt.shtml

Routine ECG Not Recommended During MMT

Norway; Senter for medikamentassistert rehabilitering; November 2004 – The Norwegian Medicines Agency recently reported dose-dependent QT prolongation and occurrences of torsades des pointes in patients treated with methadone. Therefore, the agency recommended that an ECG is performed before induction to methadone.

The authors of this paper performed a literature search in Medline and Embase, and found that QT prolongation during methadone therapy is dose-dependent and primarily seen with doses higher than those usually used in maintenance therapy and/or in cases with known risk factors. They recommend that a routine ECG should ***not be*** recommended, but before starting therapy the physician should secure an adequate case history including information on any family history of cardiac disease and other risk factors.

Source: Krook AL, Waal H, Hansteen V. Routine ECG in methadone-assisted rehabilitation is wrong prioritization [Article in Norwegian, English abstract]. *Tidsskr Nor Laegeforen*. 2004;124(22):2940-2941.

[This article lists only 7 references obtained via literature search; a more extensive literature examination plus the most recent research (see above) does not demonstrate a strong correlation of methadone dose and QTc interval prolongation. ***Also see the AT Forum White Paper report:*** *Cardiac Considerations During MMT, available at: http://www.atforum.com/SiteRoot/pages/rxmethadone/cardiacmmt.shtml. –Ed.]*

Methadone Studied in Pregnant Patients

Zurich, Switzerland; February 2005 – The aim of this study was to analyze polydrug abuse, pregnancy outcome, and fetal-maternal complications among pregnant women in a major Swiss methadone-maintenance program.

This was a prospective study of data collected from all pregnant opiate addicts and their neonates during 1996 to 2001. The average methadone dose at delivery in the 89 pregnancies was 40.9 ± 32.7 mg/day (range 0-150). Maternal complications occurred in 73% and fetal complications in 34% of the pregnancies. Sixty-four percent of the women continued abuse of cocaine and/or heroin.

Birthweight was lower in polydrug abusers than in those consuming only methadone ($p = 0.001$).

The authors concluded that the high rate of maternal complications demonstrates a need for further improvement in antenatal management of opiate addiction in pregnancy. Methadone maintenance was inefficient in preventing pregnancy exposure to additional illicit-drug consumption. Additional illicit heroin and/or cocaine abuse does not seem to increase the incidence of fetal-maternal complications during pregnancy, but reverses the positive impact of methadone on birthweight.

Source: Kashiwagi M, Arlettaz R, Lauper U, Zimmermann R, Hebisch G. Methadone maintenance program in a Swiss perinatal center. Management and outcome of 89 pregnancies. *Acta Obstet Gynecol Scand*. 2005;84(2):140-144.

[The average methadone dose of about 50 mg/d, with most women receiving no more than approximately 70 mg/d, may have been inadequate to stem concurrent substance abuse. Other studies have demonstrated a need for higher adequate dosing in pregnant patients, particularly during the 3rd trimester. –Ed.]

Methadone-Related Deaths Examined in New Mexico

Santa Fe, New Mexico; February 2005 – The objectives of this study were to determine death rates from methadone over time, to characterize methadone-related deaths, and to discuss public health surveillance of methadone-related deaths.

The researchers analyzed medical examiner data for all unintentional drug overdose deaths in New Mexico between 1998 and 2002. Of 1,120 drug overdose deaths during this period, there were 143 (12.8%) methadone-related deaths; although, the death rate decreased during the time period. Of those 143 deaths, 22.4% were due to methadone alone, 23.8% were due to methadone plus prescription drugs (no illicit drugs), 50.3% were due to methadone plus illicit drugs, and 3.5% were due to methadone plus alcohol. Of 79 decedents (55.2%) with a *known* source of methadone, most (68 or 86%) obtained methadone via physician prescription — 31 for methadone maintenance treatment (MMT), 27 for managing pain, and 10 had unknown reason for prescription.

The authors concluded that it is important for surveillance of methadone-related deaths to assess multiple-drug causes. Also, methadone for pain management must be examined alongside MMT and, when possible, the alleged contribution of methadone to the death should be described in the context of other drugs possibly causing death.

Source: Shah N, Lathrop SL, Landen MG. Unintentional methadone-related overdose death in New Mexico (USA) and implications for surveillance, 1998-2002. *Addiction*. 2005;100(2):176-188.

Factors Influencing Retention in MMT

Portland, OR; RMC Research Corporation; February 2005 – This study examined individual and system characteristics associated with retention in methadone maintenance treatment (MMT) among Medicaid-eligible adults in Oregon and Washington.

Older patients, patients with a history of MMT, and persons with stable Medicaid eligibility had higher rates of retention than did patients with disabilities, polysubstance users, and those with an arrest record. In Oregon, which delivers methadone maintenance treatment through managed care, retention rose sharply from 28% to 51% between 1994 and 1998 and then leveled off. During the same time period, retention in Washington State grew from 28% to only 34%.

The higher rates of retention in Oregon, in part, can be explained by differences in service delivery influenced by financing. Faced with long waiting lists, Washington providers were more than twice as likely to administratively discharge patients for rule violations as their Oregon counterparts. Given the importance of retention, policies and practices that influence retention should be carefully considered. Because Medicaid eligibility has a dramatic impact on retention, policies that help extend eligibility or stabilize eligibility among individuals actively engaged in treatment should be carefully considered.

Source: Deck D, Carlson MJ. Retention in Publicly Funded Methadone Maintenance Treatment in Two Western States. *J Behav Health Serv Res*. 2005;32(1):43-60.

Increased MMT Caseloads May Degrade Treatment

London, UK; December 2004 – Changes in caseload and in the provision of counseling and comprehensive services were examined among 27 outpatient methadone programs across England between 1995 and 1999. The number of patients treated at the programs doubled during this time and average waiting times increased.

More patients presented for treatment with alcohol and stimulant problems, dual diagnosis, and involvement in the Criminal Justice System. Provision of individual counseling

and comprehensive services was high at both time points, although services for family/relationship problems were reduced at followup.

Changes were reported in disciplinary procedures. Drug-positive urine tests were more likely to result in loss of patient privileges, and there was a significant increase in discharges for breaking program rules, missing appointments, and consuming alcohol. The study allows only tentative conclusions to be drawn, but these changes may be indicative of increased pressures placed on the programs and their staff.

See: Stewart D, Gossop M, Marsden J. Increased caseloads in methadone treatment programs: Implications for the delivery of services and retention in treatment. *Subst Use Misuse*. 2004;39(13-14):2239-2260.

Approach Helps MMT Patients Gain Employment

New York; Institute for Treatment and Services Research; December 2004 – Traditionally, methadone-maintained patients have made only limited progress in vocational rehabilitation programs, largely because they encounter multiple individual barriers to their employment. The Customized Employment Supports (CES) model is designed to help patients overcome these employment barriers and attain paid work as soon as possible.

To facilitate this transition, the model assigns CES counselors small caseloads so that, using intensive interventions, they can engage patients in a working alliance and enhance patients' self-efficacy. Methods used to help patients increase their self-efficacy are derived from social psychological literature and include role modeling, persuasion, and minimizing emotional arousal. Because the transition to competitive work is a major change, many patients initially take smaller steps such as entering training programs and accepting informal employment. The CES model is being further evaluated in a randomized clinical trial.

Source: Blankertz L, Magura S, Staines GL, et al. A new work placement model for unemployed methadone maintenance patients. *Eur Psychiatry*. 2004;19(8):510-513.

Antidepressant Effects of Methadone Vs. Buprenorphine Studied

Australia; December 2004 – Research suggests that buprenorphine, as well as methadone, may possess antidepressant activity. The Beck Depression Inventory (BDI) was completed at baseline and at 3 months by 54 heroin-dependent subjects receiving either buprenorphine or methadone maintenance as part of a larger, pre-existing, double blind trial conducted by NDARC (Australia).

Depressive symptoms improved in all subjects, with no statistically significant difference between methadone and buprenorphine groups: methadone patients experienced a mean reduction of 48% in their severity while for buprenorphine it dropped by 46%.

Source: Dean AJ, Bell J, Christie MJ, Mattick RP. Depressive symptoms during buprenorphine vs. methadone maintenance: findings from a randomised, controlled trial in opioid dependence. *European Psychiatry*. 2004 Dec;19(8):510-3

[The reported mean doses at month 3 were methadone 48 mg/day (± 20) and buprenorphine 9 mg/day (± 4). These dose ranges for both agents would probably be considered lower than optimal and other research has suggested that achieving antidepressive effects of methadone require much higher adequate dosing levels. –Ed.]

Methadone, Buprenorphine Comparable for Opioid Detox

Germany; November 2004 – This study compared buprenorphine with methadone to determine which medication is better for the detoxification of young opioid addicts.

Subjects included 93 consecutive opioid-dependent patients from an in-patient detoxification unit for adolescents, of whom 42 chose buprenorphine and 51 chose methadone for detoxification. Both groups were equivalent with regard to sociodemographic and addiction-specific variables such as age, gender, initiation of drug consumption, and duration of opioid intake.

Buprenorphine appeared to be more effective in this age group, but the differences between the two medications were not statistically significant: 23.5% of the methadone patients and 38.1% of the buprenorphine patients finished detoxification successfully, and the buprenorphine patients finished detoxification 1.62 days earlier. The authors concluded that buprenorphine seems to be at least as effective as methadone for opioid withdrawal in young addicts.

Ebner R, Schreiber W, Zierer C. Buprenorphine or methadone for detoxification of young opioid addicts?

[Article in German]. *Psychiatr Prax.* 2004;31 Suppl 1:S108-S110.

Norwegian Clinical Trial Favors Methadone Over Buprenorphine

Norway; January 2005 –Methadone-assisted treatment was approved in Norway in 1998 and buprenorphine in 2000. This study compared the efficacy of methadone (n = 25) and buprenorphine (n = 25) maintenance treatment in a group of long-term (>10 years) opioid-addicted persons.

After randomization patients received either 16 mg sublingual buprenorphine or individually adjusted methadone (mean 106 mg, range 80 - 160) for 26 weeks, with a rehabilitation program run in parallel. After 180 days, patient retention was highest in the methadone group (85% vs. 36%, $p < 0.0005$). Days in treatment were 167 vs. 114 ($p < 0.001$) favoring methadone. Positive urine-test rates for opiates (20% vs 24%, $p < 0.01$) and cannabis (33% vs 45%, $p < 0.001$) were lower in the methadone group, which also had lower self-reported risk behavior and psychological distress.

The authors concluded that, for older, long-term opioid addicts with significant co-morbidity and unsuccessful medication-free treatment, methadone maintenance appears to be the treatment of choice. However, in cases where methadone is poorly tolerated, buprenorphine therapy may be a good alternative.

Source: Kristensen O, Espegren O, Asland R, et al. A randomised clinical trial of methadone vs. buprenorphine to opioid dependants [in Norwegian, English abstract]. *Tidsskr Nor Laegeforen*. 2005;125(2):148-151.

[An important feature of this study was that doses of both methadone and buprenorphine were probably more clinically adequate than have been used in other trials, which have focused on much lower dosing. –Ed.]

In Cocaine + Opioid Addiction MMT Is Best

American Journal of Psychiatry; February 2005 – This study compared effects of buprenorphine versus methadone and evaluated the efficacy of combining contingency management with maintenance treatment for patients with co-occurring cocaine and opioid dependence.

Subjects with cocaine + opioid dependence (N=162) were provided manual-guided counseling and randomly assigned in a double-blind design to receive daily sublingual buprenorphine (12–16 mg) or methadone (65–85 mg), and to contingency management or performance feedback. Contingency management subjects received monetary vouchers for opioid- and cocaine-negative urine tests, which were conducted three times a week. Voucher value escalated during the first 12 weeks for consecutive drug-free tests and was reduced to a nominal value in weeks 13–24. Performance feedback subjects received slips of paper indicating the urine test results.

Methadone-treated subjects remained in treatment significantly longer and achieved significantly longer periods of sustained abstinence and a greater proportion of drug-free tests, compared with subjects who received buprenorphine. Subjects receiving contingency management achieved significantly longer periods of abstinence and a greater proportion drug-free tests during the period of escalating voucher value, compared with those who only received performance feedback. However, there were no significant differences between groups in these variables during the entire 24-week study.

The authors concluded that methadone may be superior to buprenorphine for maintenance treatment of patients with co-occurring cocaine and opioid dependence. It appears that combining methadone or buprenorphine with contingency management may improve treatment outcomes, at least on a short-term basis.

Source: Schottenfeld RS, Chawarski MC, Pakes JR, et al. Methadone versus buprenorphine with contingency management or performance feedback for cocaine and opioid dependence. *Am J Psychiatry*. 2005;162:340-349.

Cocaine Abstinence During MMT Influenced by Rewards

Baltimore, MD; November 2004 – Researchers at Johns Hopkins University School of Medicine determined whether abstinence engendered by intermittent reinforcement might generalize to non-reinforced periods and enhance overall rates of cocaine abstinence among methadone maintenance patients.

Participants were randomized to 1 of 3 groups. The ***quantitative*** group (n = 14) earned incentives for a 50% decrease in urine benzoylecgonine (cocaine metabolite) concentrations; the ***qualitative*** group (n = 13) earned incentives for providing urine specimens with cocaine metabolite concentrations <300 ng/mL. Both reinforced groups received 12 random opportunities to earn $100 in vouchers for abstinence. A ***control*** group (n = 15) was

encouraged to abstain on 12 occasions under the same schedule.

Incentive participants achieved significantly more cocaine abstinence on earning than on non-earning days, with no difference between quantitative and qualitative groups. The authors state that this study supports the efficacy of incentives for motivating brief abstinence but it did not find that unpredictable opportunities to earn incentives generalized to non-reinforced days. In other words, when patients were not actually rewarded for abstinence they continued to use cocaine.

Source: Sigmon SC, Correia CJ, Stitzer ML. Cocaine abstinence during methadone maintenance: effects of repeated brief exposure to voucher-based reinforcement. *Exp Clin Psychopharmacol*. 2004;12(4):269-275.

Also see *a report in* AT Forum *Nov-Dec 2004 News Update:* Silverman K, Robles E, Mudric T, Bigelow GE, Stitzer ML. A randomized trial of long-term reinforcement of cocaine abstinence in methadone-maintained patients who inject drugs. *J Consult Clin Psychol*. 2004;72(5):839-854.

Six-Fold Growth of MMT in Australia

New South Wales (NSW), Australia; November 2004 – According to the New South Wales Chief Health Officer, methadone maintenance is an effective treatment for opioid dependence. It is the major treatment used in Australia and the risk of overdose death is substantially reduced in opiate-dependent people who are enrolled in methadone treatment.

In 2004, 10,008 males were on the NSW methadone program, representing 64% of all clients on a program. In 2004, 71% of methadone clients were in treatment in urban areas, with 18% in rural areas and 10% in the correctional system. Since 1986, the number of patients on the methadone program has increased almost six-fold.

Buprenorphine became available in August 2001 as an additional treatment for opioid dependence. It has been shown to be effective as a maintenance treatment, and in the short term as an appropriate drug for an opioid withdrawal program.

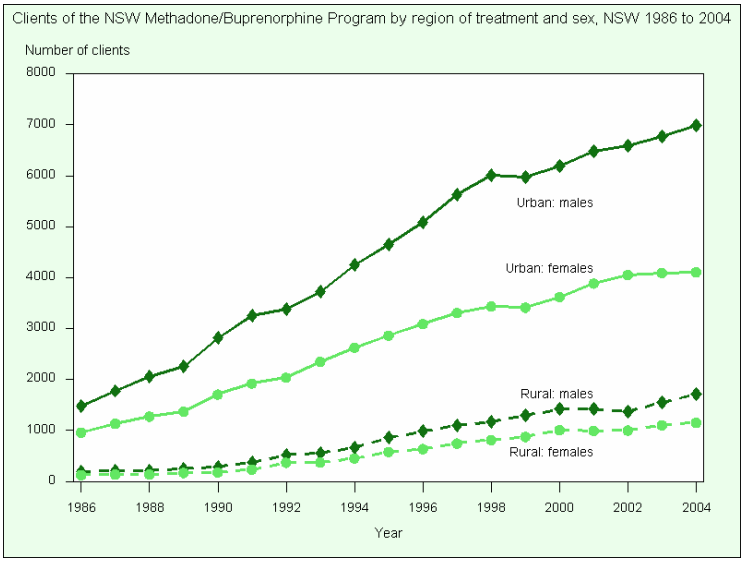
Source: "Report of the New South Wales Chief Health Officer: Health-Related Behaviors; Methadone/buprenorphine Program Use". Available at: http://www.health.nsw.gov.au/public-health/chorep/beh/beh_illimethadoneloc.htm

[As of November 2004, in NSW, Australia, about 13,500 patients were receiving methadone and 2,340 were being administered buprenorphine for opioid addiction (personal communication, Alex Wodak, MD, December 14, 2004). – Ed.]

UK Methadone Budget Hits $430 Million

The Observer (UK); December 12, 2004 (J. Doward, W. Lee) – More than half the government's $950 Million (£500) budget in the UK to combat drug addiction is now being spent on methadone. The heavy reliance on methadone, which many ex-users end up taking for years, has raised concerns that former addicts could end up using methadone into their fifties.

It is the first time a figure has been put on the government's methadone budget, which is expected to rise in years to come as more resources are put into tackling drug addiction. Experts are now calling for the government's drugs policy-makers to examine alternatives to methadone in the war on heroin addiction.



They argue that, although methadone is highly effective as a heroin substitute and is vital in helping the vast majority of users escape a life of crime, it does carry risks. Studies show that some methadone users can remain on the drug for anything between five and 10 years. As a result, "Addaction," the drug and alcohol treatment charity, warns that users may still be taking it when they are middle aged.

SAMHSA Releases TIP on Co-Occurring Disorders

Rockville Maryland; Substance Abuse and Mental Health Services Administration (SAMHSA); January 31, 2005 – Co-occurring substance abuse and mental

disorders are more common than most treatment counselors, medical personnel, or the general public realize. A new Treatment Improvement Protocol (TIP) released by SAMHSA estimates that 50-75% of patients in substance abuse treatment programs have co-occurring mental illness. Most people with co-occurring disorders do not receive treatment for both mental disorders and substance abuse, and many receive no treatment of any kind.

Substance Abuse Treatment for Persons with Co-Occurring Disorders, TIP 42, provides principles, assessment instruments, strategies, settings, and models for treating patients wherever they show for treatment, whether it be in substance abuse treatment facilities, mental health facilities, or medical offices or clinics.

TIP 42, inventory number BKD515, can be ordered for free through SAMHSA's National Clearinghouse for Alcohol and Drug Information (NCADI), P.O. Box 2345, Rockville, MD 20847-2345, by calling 1-800-729-6686, or via http://ncadi.samhsa.gov; ***see also:*** http://store.health.org/catalog/productDetails.aspx?ProductID=16979

State Standards for Addiction Programs, Counselors Available

Rockville, Maryland; Substance Abuse and Mental Health Services Administration (SAMHSA); January 26, 2005 -- SAMHSA announced the availability of *A National Review of State Alcohol and Drug Treatment Programs and Certification Standards for Substance Abuse Counselors and Prevention Professionals*. The publication contains a national overview of state-by-state information on licensing, certification, and credentialing standards for alcohol and drug treatment facilities, programs, counselors, and prevention professionals.

Copies of this item, number BKD517, can be obtained, free of charge, from the National Clearinghouse for Alcohol and Drug Information (NCADI) by calling 1-800-729-6686 or via http://ncadi.samhsa.gov; ***see also:*** http://store.health.org/catalog/productDetails.aspx?ProductID=17024

New AIDS Threat Hits US

Observer (UK); February 13, 2005 (Robin McKie) – A strain of HIV that is highly resistant to almost all antiretroviral drugs and which leads to the rapid onset of AIDS has been detected in New York. Doctors and hospitals across the city have been placed on alert and told to test all new HIV cases for evidence of the strain.

The strain has so far [as of Februrary 13, 2005] been reported in only one person, a New York man in his mid-forties, but it is still causing considerable worry among health officials. The man is believed to have had unprotected sex with hundreds of partners. He complained of feeling ill in November, was found to be HIV positive in December and had contracted full-blown AIDS by January.

Most experts warned of the need for vigilance. Although it is premature to say a new killer that is drug resistant is going around, there is cause for concern and caution.

#98 – March-April 2005

Methadone Clinic Dispels Community Fears

Seattle *Herald*; January 31, 2005 – A methadone maintenance treatment (MMT) clinic in Everett, Washington, has not had any of the adverse effects feared by residents and city officials, but has instead proven to be a success.

For 7 years, concerns within the local community delayed the opening of the MMT clinic. Residents feared it would draw drugs and crime; city officials worried that it would stifle revitalization efforts in the downtown area. It has been 1 year since the Seattle-based non-profit agency, Therapeutic Health Services, opened the clinic in January 2004. Since then, the facility has retained 76 of its original 96 patients. Overall, the clinic serves 212 patients, and urine tests indicate that 86% of them remain drug-free.

"After all these years it's really pleasant to go back to the City Council and county and say this is not what you feared," reflects Norm Johnson, the director of Therapeutic Health Services. "None of the things people worried would happen have happened. None."

Future plans include providing mental health counseling and alcohol treatment, in addition to the vocational training already offered on site. "It really is saving lives," says Susan Romero, 34, a methadone patient since 1999. "It's not what people think. It's just regular people getting help."

Incentive Rewards Foster Cocaine Abstinence During MMT

Farmington, CT; April 2005 – In this study, the researchers evaluated a low-cost contingency management (CM)

procedure for reducing cocaine use and enhancing group therapy attendance in 77 cocaine-dependent methadone patients.

Patients were randomly assigned to 12 weeks of standard treatment or standard treatment with CM, in which patients earned the opportunity to win prizes ranging from $1 to $100 for submitting cocaine-negative urine samples and attending therapy. Patients in the CM condition submitted more cocaine-negative samples and attended more group sessions than patients in standard treatment. The best predictor of cocaine abstinence at follow-up was duration of abstinence during treatment.

On average, patients in the CM condition earned $117 in prizes. Data from this study suggest that some aspects of reinforcement can be practical for implementation by community-based methadone treatment clinics.

Source: Petry NM, Martin B, Simcic F Jr. Prize reinforcement contingency management for cocaine dependence: integration with group therapy in a methadone clinic. *J Consult Clin Psychol*. 2005;73(2):354-359.

See also, a feature article and an interview with the lead author of this study, Nancy Petry, PhD, in the upcoming Spring 2005 edition of *AT Forum*.

Impact of MMT on QTc Interval Studied

West Haven, CT; April 1, 2005 – In this followup to an earlier research report, investigators prospectively assessed the effect of oral methadone on the corrected QT interval (QTc) among 160 patients in methadone maintenance treatment (MMT) who were free of structural heart disease. They also measured serum methadone levels (SMLs) and simultaneous QTc intervals in a subset of 44 participants. (The QTc is a measure of heart rhythm and large increases in this interval as measured on the ECG strip can signify potential problems.)

Six months after starting MMT, the average QTc interval increased by 12.4 ms (milliseconds), and by 10.7 ms at 12 months. The QTc changes from baseline to 12 months correlated with the trough and peak SMLs ($r = 0.37$ and 0.32, $p = 0.008$ and 0.03, respectively). The authors recommended that ECG assessments should be considered in MMT patients known to be at risk of heart arrhythmias from other causes or taking medications known to prolong the QTc interval.

(Although the small increases in QTc were statistically significant, there were no methadone-associated heart problems in the patients and the clinical importance, if any, of the measured increases is uncertain. Also, the correlations of QTc changes with SMLs were quite modest, albeit statistically significant, so it is still undetermined whether higher SMLs may affect heart rhythm. Furthermore, other research has demonstrated that the SML typically does not correlate well with methadone dose; thus, this study does not establish a relationship between methadone dose and QTc changes. –Ed.)

Source: Martell BA, Arnsten JH, Krantz MJ, Gourevitch MN. Impact of methadone treatment on cardiac repolarization and conduction in opioid users. *Am J Cardiol.* 2005;95(7):915-918.

For additional information, see: Leavitt SB, Krantz MJ. Cardiac Considerations During MMT. AT Forum (special report). October 2003. Available at: http://www.atforum.com/SiteRoot/pages/addiction_resources/CardiacPaper.pdf.

Relationship of Drug Abuse & Intimate Partner Violence Among Female MMT Patients

New York, NY; March 2005 – Researchers examined whether frequent drug use increases the likelihood of subsequent sexual or physical intimate partner violence (IPV) and whether IPV increases the likelihood of subsequent frequent drug use.

A random sample of 416 women on methadone maintenance was assessed at baseline, at 6 months, and 12 months following the initial assessment. Women who reported frequent crack cocaine or marijuana use at 6 months were significantly more likely than non-drug using women to report IPV at 12 months. In addition, women who reported IPV at 6 months were more likely than women who did not report IPV to indicate frequent heroin use at 12 months.

The authors conclude that the relationship between frequent drug use and IPV goes both ways (is bidirectional) and varies by type of drug.

Source: El-Bassel N, Gilbert L, Wu E, Go H, Hill J. Relationship between drug abuse and intimate partner violence: a longitudinal study among women receiving methadone. *Am J Public Health*. 2005;95(3):465-470.

A Model For Integrating HCV-Treatment Services With MMT

Bronx, NY; April 15, 2005 – Despite the high prevalence of hepatitis C virus (HCV) infection among drug users enrolled

in methadone maintenance treatment (MMT) programs, few drug users are being treated with combination therapy. The most significant barrier to treatment is lack of access to comprehensive HCV-related care.

The authors describe a pilot program to integrate care for HCV infection with substance abuse treatment in a setting of maintenance treatment with methadone. This on-site, multidisciplinary model of care includes: comprehensive screening and treatment for HCV infection; assessment of eligibility; counseling with regard to substance abuse; psychiatric services; HCV support groups; directly observed medication therapy; and enhanced linkages to a tertiary care system for diagnostic procedures. This approach has led to high levels of treatment adherence, with liver biopsy and substantial rates of initiation of antiviral therapy.

See: Litwin AH, Soloway I, Gourevitch MN. Integrating services for injection drug users infected with hepatitis C virus with methadone maintenance treatment: challenges and opportunities. *Clin Infect Dis*. 2005;40(Suppl 5):S339-S345.

MMT Programs Have Important Role in HCV Education

San Francisco, CA; March 2005 – This study describes knowledge about hepatitis C virus (HCV) infection and interest in treatment for the infection among 110 opioid dependent patients from an MMT program in San Francisco. None had been treated for HCV and only 30% had been evaluated for HCV treatment.

While only 34% knew about HCV treatment, 54% of the sample became "definitely interested" in HCV treatment after hearing the risks and benefits. Men were approximately 5 times more likely than women to be familiar with HCV treatments. Whites were 7 times and Latinos were about 6 times more likely than African-Americans to know about HCV treatment. The findings suggest that methadone programs can play an important role in increasing access to HCV treatment through educating patients about treatment options.

See: Walley AY, White MC, Kushel MB, Tulsky JP. Knowledge of and interest in hepatitis C treatment at a methadone clinic. *J Subst Abuse Treat*. 2005;28(2):181-187.

Peginterferon For HCV Does Not Alter Methadone During MMT

Baltimore, MD; March 2005 – Researchers studied the possible interaction of methadone and peginterferon alfa-2a (40 kd) in patients with chronic hepatitis C undergoing methadone maintenance therapy (MMT). (Peginterferon is a newer, more potent, and longer-lasting form of traditional interferon used to treat HCV.)

Twenty-four adults with chronic HCV who had been receiving a consistent methadone maintenance regimen for at least 3 months were enrolled in this open-label, multicenter, nonrandomized drug-interaction study. All patients received 180 micrograms subcutaneous peginterferon alfa-2a once weekly for 4 weeks and continued their methadone regimen. Serial blood samples were collected at baseline and immediately before and for up to 1 week after study drug administration for the purposes of quantifying methadone and peginterferon alfa-2a serum concentrations.

Methadone concentrations were increased after 4 doses of peginterferon alfa-2a by only 10% to 15% when compared with baseline. The authors concluded that peginterferon alfa-2a does not appreciably alter methadone concentrations in MMT patients.

Reference: Sulkowski M, Wright T, Rossi S, et al. Peginterferon alfa-2a does not alter the pharmacokinetics of methadone in patients with chronic hepatitis C undergoing methadone maintenance therapy. *Clin Pharmacol Ther*. 2005;77(3):214-224.

MMT-Patient Deaths in Texas Analyzed

Austin, TX; April 4, 2005 – Investigators at the University of Texas, Austin, analyzed causes of death in 766 patients who died while in methadone treatment in Texas between 1994 and 2002.

Compared with deaths in the general population of Texas, deaths of MMT patients were approximately 4.5 times more likely to be from a drug overdose, 3 times more likely to be from liver disease, 2 times more likely to be from a respiratory disease, 1.5 times more likely to be from a homicide, and 1.5 times more likely to be from AIDS, but less likely to be from suicide, motor vehicle accidents, cardiovascular diseases, or cancer.

Among MMT patients, 20% died of liver disease, 18% of cardiovascular disease, and 14% of drug overdose. An older cohort had been in treatment longer, had more take-home doses, were on higher doses, and tended to die of chronic diseases. A younger cohort tended to die from traumas, including drug overdose. Average time in MMT was 43 months and mean daily methadone dose was 77 mg.

Given these rates, the authors recommend that the scope of MMT services should include on-site treatment for other medical conditions. Also, staff should be educated about and then counsel patients about the risk of death for new MMT patients.

Reference: Maxwell JC, Pullum TW, Tannert K. Deaths of clients in methadone treatment in Texas: 1994–2002. *Drug Alcohol Depend*. 2005;78(1):73-81.

[It is of interest that MMT patients were less likely than the general population to have died of cardiovascular disease. This appears to support other research suggesting that long-term methadone exposure may lessen coronary artery disease severity and its often fatal consequences. ***See:*** *Marmor M, Penn A, Widmer K, Levin RI, Maslansky R. Coronary artery disease and opioid use.* Am J Cardiol. *2004;93:1295-1297. – Ed.]*

Immune System Effects of Methadone, Buprenorphine Compared

Catania, Italy, April 2, 2005 – Buprenorphine may be a useful alternative to methadone in carefully selected patients; however, it has been proposed that opioids can produce changes in the immune system. This study compared such effects with sublingual buprenorphine and methadone.

Researchers followed for 12 months 62 patients randomized to either: A) methadone (average dose 100 mg/day), or B) sublingual buprenorphine (average 32 mg/day). Urine toxicological screening and plasma levels of key markers of immune systems function were assessed.

Urine screening was negative for opioids in 17.6% of group A and in 10.7% of group B. The effects of buprenorphine and methadone on the immune system were similar, with elevated cytokine levels suggesting that the two drugs stimulate immunologic hyperactivity in immune systems that were formerly inhibited by heroin.

See: Neri S, Bruno CM, Pulvirenti D, et al. Randomized clinical trial to compare the effects of methadone and buprenorphine on the immune system in drug abusers. *Psychopharmacology* (Berl). 2005, April 2 [Epub ahead of print].

Transitioning Pregnant Women to Buprenorphine or Methadone

Baltimore, MD; April 2005 – Researchers at the Johns Hopkins University School of Medicine compared the safety and withdrawal discomfort associated with transitioning pregnant opioid-dependent women from short-acting morphine onto buprenorphine or methadone.

Participants (n = 18) were patients in a comprehensive treatment setting. Methadone was first given to all patients within 24 hours of treatment admission and was discontinued and Immediate Release Morphine (IRM) was initiated. The initial total daily dose of IRM was six times the last daily methadone dose. After that, randomized induction onto methadone or buprenorphine was accomplished over 3 days. Total withdrawal scores during this transition period were judged mild and not statistically different for both methadone (mean dose 53.5 mg/d) and buprenorphine (mean dose 10.9 mg/d). Furthermore, no significant differences between medication groups were observed when individual withdrawal items were examined.

No differences were observed between treatment groups in safety measures, including: fetal movement or maternal body temperature, heart rate, and blood pressure. The researchers concluded that transitioning opioid-dependent pregnant women from IRM to methadone or buprenorphine during the second trimester of pregnancy can be conducted with similar comfort and safety.

Source: Jones HE, Johnson RE, Jasinski DR, Milio L. Randomized controlled study transitioning opioid-dependent pregnant women from short-acting morphine to buprenorphine or methadone. *Drug Alcohol Depend.* 2005;78(1)33-38.

Primary Care Delivery of Methadone vs Buprenorphine

Leuven, Belgium; February 2005 – The authors of this study conducted a systematic review of the evidence on the effectiveness of community maintenance programs with methadone or buprenorphine in treating opioid dependence.

Randomized controlled trials spanning 1990-2002 were reviewed. The studies selected were set in a range of countries, employed a variety of comparators, and suffered from a number of biases. The evidence indicated that higher doses of methadone and buprenorphine are associated with better treatment outcomes. Low-dose methadone (20 mg per day) is less effective than buprenorphine (2-8 mg per day); however, higher doses of methadone (>50-65 mg per day) are more effective than buprenorphine (2-8 mg per day). There was some evidence that primary care settings could be an effective venue for providing this treatment, but such evidence was sparse.

The investigators concluded that the literature supports the effectiveness of methadone or buprenorphine in treating opioid dependence. Evidence is also emerging that the provision of methadone or buprenorphine by primary care physicians is feasible and may be effective.

See: Simoens S, Matheson C, Bond C, Inkster K, Ludbrook A. The effectiveness of community maintenance with methadone or buprenorphine for treating opiate dependence. *Br J Gen Pract*. 2005;55(511):139-146.

Multiple Factors Slow Buprenorphine Acceptance

Wired Magazine; April 1, 2005 – Physician ambivalence, slipshod regulation, and poor marketing efforts have thus far prevented buprenorphine from fulfilling its promise as an effective tool to fight opioid addiction, according to a well-researched article in this publication.

Buprenorphine has been praised by opioid addicts who have failed to overcome their addiction using methadone. However, after more than two years on the market, relatively few patients are using buprenorphine. Reckitt Benckiser, manufacturer of the medication, says 5,000 doctors are prescribing it, but other experts say the number is half that or less.

In New York City, home to 200,000 heroin addicts, records show that 34,000 people were on methadone in 2004, while just 1,000 filled a buprenorphine prescription. "It's depressingly few," said Lloyd Sederer, New York City's deputy executive commissioner for health and mental hygiene.

Addiction experts had hoped that general practitioners would feel comfortable prescribing buprenorphine, but that has not happened so far. Another problem is that lawmakers drafted poor regulations for the drug, according to the article in *Wired Magazine*, including a 30-patient limit on group practices. Methadone clinics are banned from prescribing multiple-day doses to a patient, a restriction that doesn't apply to other providers.

Critics add that Reckitt, better known for consumer products like Lysol, has been very conservative in marketing the drug. Advocates like Sederer are promoting the drug to health workers and patients at needle-exchange programs, methadone clinics, treatment centers, and other places where heroin addicts congregate. In New York, the goal is to get 60,000 addicts on buprenorphine by 2010.

Herbert Kleber, MD, medical director for the Center on Addiction and Substance Abuse (CASA) at Columbia University, said a poorly designed physician-education curriculum has also hindered acceptance of buprenorphine. "The courses are a disaster," said Kleber, who has been hired by the federal government to redesign the curriculum. Kleber said the courses reinforce stereotypes about addicts as untrustworthy and fails to allow doctors to interact with actual patients.

For the complete article, see:
http://wired-vig.wired.com/wired/archive/13.04/bupe.html?pg=1

#99 – May-June 2005

MMT Effects on Menstrual Cycle Studied

Addiction; June 2005 – While the menstrual disruption of heroin has been demonstrated in the past, there are few published data concerning methadone maintenance and menstrual function.

This study was conducted to evaluate whether cycle length was more regular during methadone maintenance treatment (MMT). Participants included a total of 191 heroin and cocaine-using women from two clinical trials lasting 25-29 weeks at an outpatient research treatment program in Baltimore, MD. Each woman was maintained on 70 to 100 mg/day of methadone.

In the 133 women for whom data was available, menstrual cycle-length patterns were determined to be: irregular in 47%; regular - 28%; cycle restart - 12%; persistent amenorrhea (absent menstruation) - 8%; and transient amenorrhea - 5%. Each additional week of MMT was associated with a significantly decreased risk of overly long (> 40 days) or short (< 20 days) menstrual cycles. Of 27 women with secondary amenorrhea before entering MMT, nearly 60% restarted menses. Positivity for illicit opioids or cocaine was not significantly associated with short or long cycles.

The authors concluded that menstrual cycle length begins to normalize during MMT and menses resumption may occur in some women.

See: Schmittner J, Schroeder JR, Epstein DH, Preston KL. Menstrual cycle length during methadone maintenance. *Addiction*. 2005;100(6):829-836.

MMT Under-Used in US State and Federal Prisons

Providence, RI; May 25, 2005 – In the United States, vigorous enforcement of drug laws and stricter sentencing guidelines during the past 20 years have contributed to an expanded incarcerated population with a high rate of drug use. One in five state prisoners reports a history of injection drug use, and many are opioid dependent.

In June 2003, investigators from the Miriam Hospital/Brown Medical School, Providence, Rhode Island conducted a survey of the medical directors of all 50 US states and the federal prison system to describe their attitudes and practices regarding methadone. Of the 40 respondents, having jurisdiction over 88% (n =1,266,759) of US prisoners, 48% use methadone, predominately for pregnant inmates or for short-term detoxification. Only 8% of respondents refer opioid-dependent inmates to methadone maintenance programs upon release.

The results highlight the need to de-stigmatize the use of methadone in the incarcerated setting, expand access to methadone during incarceration, and to improve linkages to methadone treatment for opioid-dependent offenders who return to the community.

Source: Rich JD, Boutwell AE, Shield DC, Key RG, McKenzie M, Clarke JG, Friedmann PD. Attitudes and Practices Regarding the Use of Methadone in US State and Federal Prisons. *J Urban Health*. May 2005 [Epub ahead of print].

[The theme of the next AATOD (American Assoc. for the Treatment of Opioid Dependence) Conference — "Treating People with Dignity: Working with Criminal Justice and Health Care Systems" — will focus on this topic. It will be held April 22-26, 2006 at the Hyatt Regency, Atlanta, Georgia. For more information visit http://www.aatod.org or call 856-423-3091. – Ed.]

Prison-Based MMT Vital for Individual & Public Health

Addiction; June 2005 – This study in Australia examined the long-term impact of methadone maintenance treatment (MMT) on mortality, re-incarceration and hepatitis C seroconversion in imprisoned male heroin users.

Study participants comprised 382 imprisoned male heroin users who had been in a randomized controlled trial of prison-based MMT in 1997-98. Subjects were followed-up between 1998 and 2002 either in the general community or in prison. There were no deaths recorded while subjects were enrolled in MMT; however, 17 died while out of MMT. Re-incarceration risk was lowest in those who had MMT of 8 months or longer, while MMT periods 2 months or less were associated with greatest risk of re-incarceration. Increased risk of hepatitis C seroconversion was significantly associated with prison sentences of less than 2 months and MMT episodes of less than 5 months. Subjects were at greatest risk of MMT dropout during short prison sentences of 1 month or less. HIV incidence was low in those receiving MMT.

The authors concluded that retention in MMT was associated with reduced mortality, re-incarceration rates, and hepatitis C infection. Prison-based MMT programs are integral to the continuity of treatment needed to ensure optimal outcomes for individual and public health.

Source: Dolan KA, Shearer J, White B, Zhou J, Kaldor J, Wodak AD. Four-year follow-up of imprisoned male heroin users and methadone treatment: mortality, re-incarceration and hepatitis C infection. *Addiction*. 2005;100(6):820-828.

MMT in Primary Care Setting Successful

Washington, DC; June 1, 2005 – Providing methadone maintenance treatment (MMT) in a primary care setting is feasible and can result in healthy outcomes for patients addicted to heroin who are stable on methadone, according to the findings of the first study conducted outside a research setting.

Appearing in the May issue of the *Journal of General Internal Medicine* [soon to be released], the study by Joseph Merrill, MD, MPH, of the University of Washington and Seattle's Harborview Medical Center, finds that primary care facilities can acheive successful results in helping patients recover from heroin addiction, while providing treatment for other health problems and improving physician attitudes about addiction.

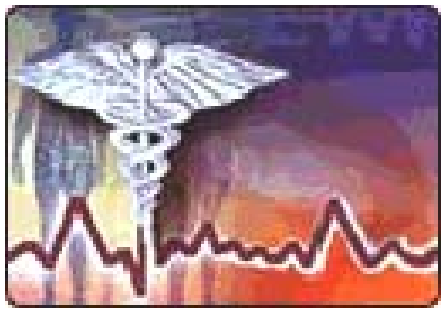
"Getting the necessary regulatory approvals to provide methadone in a primary care setting can be a complex task, but it can result in better medical care for patients who are in stable recovery from heroin addiction and are already in a treatment program," Merrill observed.

Harborview Medical Center and Evergreen Treatment Services, a community opioid treatment program (OTP), were granted approvals to provide MMT from the multiple federal, state, and local regulatory authorities that oversee methadone treatment. The program was the first to receive such approvals through a formal regulatory process rather than through a research exemption.

The program had 30 stable patients at the beginning and was able to retain 28 of them after one year. Initially they received methadone take-home doses no more than 3 times per week and eventually became eligible to receive it once per month. Patients were recalled for random urine and other tests.

Merrill's study, funded by the Robert Wood Johnson Foundation's Substance Abuse Policy Research Program and the Washington State Division of Alcohol and Substance Abuse, also found that some patients needed treatment for the hepatitis C virus, high blood pressure, tobacco use, and psychiatric disorders, but had not accessed such medical care while being treated at other MMT programs.

Reports to FDA of Long QT and TdP with Methadone Analyzed



Tucson, AZ, University of Arizona Health Sciences Center; May 2005 – Some anecdotal case series have associated methadone, with QT prolongation and the serious torsades de pointes (TdP) ventricular arrhythmia. The purpose of this study was to review and analyze such adverse events reported to the Food and Drug Administration (FDA) to determine the patient characteristics, dosages of methadone, and outcomes of methadone-treated patients.

The authors retrieved and retrospectively analyzed reports of adverse events associated with methadone voluntarily reported to the FDA MedWatch program from 1969 to October 2002. In a total of 5,503 reports of adverse events associated with methadone for various reasons, 43 (0.78%) noted the occurrence of TdP and 16 (0.29%) QT prolongation. All but 3 cases were reported from year 2000 onward, and it appears that most cases involved methadone used in pain management.

Doses were reported in 42/59 (71%) of cases and widely varied: mean dose was 410 +/- 349 mg/day (median 345, range 29-1680). The dosages for 10 of the 42 cases (29%) were within a range often used for methadone maintenance treatment, 60-100 mg/day.

Female gender, interacting medications, hypokalemia, hypomagnesemia, and structural heart disease – risk factors previously identified with other drugs known to cause TdP – were found in three quarters of cases. Only 5 cases (0.09%) were fatal; 2 involved very high amounts of medically administered intravenous methadone and 1 involved concurrent administration of cisapride *[both of which are known hazards that are commonly avoided in practice today. Also see note below. – Ed]*.

The authors concluded that their analysis of these cases provides evidence that prolonged QT and TdP can occur over a wide range of methadone dosages, including those often recommended for addiction treatment.

Source: Pearson EC, Woosley RL. QT prolongation and torsades de pointes among methadone users: reports to the FDA spontaneous reporting system. *Pharmacoepidemiol Drug Saf*. June 2005 [Epub ahead of print].

*[**NOTE:** Data such as these, while important and worthy of attention, should be considered in proper perspective. The authors concede that, "Conclusions sought from data in the FDA adverse event reporting system must be tempered with the knowledge of the limitations inherent in a voluntary reporting system," although an underreporting of such cases also is assumed. They further acknowledge that, "…it is impossible, without additional information, to be absolutely certain if methadone caused or contributed to the prolonged QT and TdP."*

In fair balance, they state, "Methadone treatment programs are generally considered to be a life-saving intervention for many patients addicted to heroin. The risk of TdP is likely to be small and should not deter caregivers or patients from methadone treatment." And, they go on to recommend: "We believe it is premature to suggest routine requirements for ECGs before or during methadone treatment. However, it would be advisable for caregivers to take a careful medical history screening for known risk factors for TdP (history of syncope, family history of sudden death, electrolyte imbalance, bradycardia). It would be prudent not to co-prescribe methadone with other drugs known to prolong the QT interval because of the potential for additive effects."

These same recommendations have been addressed in the AT Forum *special report, "Cardiac Considerations During MMT," which is available at: http://www.atforum.com/SiteRoot/pages/addiction_resources/CardiacPaper.pdf – Ed.]*

Cocaine May Cause Fatal Coronary Aneurysms

New York Times; May 10, 2005 – Cocaine use can cause coronary aneurysms, which in turn can lead to fatal heart attacks.

A study published in the May 2005 issue of the journal *Circulation* found that aneurysms occurred in about 30% of cocaine users in their mid-40s, compared with nearly 8% of nonusers in the general population. Researchers noted that the ballooning of coronary arteries could cause heart attacks years after the end of cocaine use. For example, the study cited the case of a 38-year-old man who had multiple aneurysms and no history of atherosclerosis, but had used cocaine for two years while in his 20s.

The authors did not estimate how much cocaine use was related to aneurysm development, but said that frequency of use was a factor. "The risk was definitely more common in people who used cocaine at least once a week," said study co-author Timothy D. Henry, research director at the Minneapolis Heart Institute Foundation. Researchers speculated that cocaine use weakens artery walls by causing surge in blood pressure and damaging cells.

Retention in MMT Decreases with Repeated Episodes

Toronto, Ontario, Canada; June 2005 – Investigators examined factors predicting 2-year retention in methadone maintenance treatment (MMT) and the impact of repeated treatment episodes on retention.

Data included 9,555 treatment episodes. The odds of remaining in treatment for 730 days (2 years) or more increased with age and varied by region and provider type, but decreased with an increasing number of methadone-treatment episodes. In comparison with other studies, these analyses show much higher rates of retention in MMT but suggest that repeat episodes may not be as beneficial as existing research suggests.

Source: Strike CJ, Gnam W, Urbanoski K, Fischer B, Marsh DC, Millson M. Factors predicting 2-year retention in methadone maintenance treatment for opioid dependence. *Addict Behav*. 2005;30(5):1025-1028.

MMT Promotes Treatment for HIV Among IDUs

Vancouver, BC, Canada; May 20, 2005 – Researchers examined the impact of methadone maintenance therapy (MMT) on subsequent antiretroviral therapy (ART) use in a prospective group of injection drug users (IDUs).

At 24 months after enrollment, the rate of ART use was significantly greater among those who were in MMT at baseline than among those not in MMT (70% vs 44%). When other factors also were considered, participation in MMT alone was independently associated with an elevated rate of ART use. Thus, MMT appears to significantly facilitate the receipt of treatment for HIV by injection drug users.

See: Wood E, Hogg RS, Kerr T, Palepu A, Zhang R, Montaner JS. Impact of accessing methadone on the time to initiating HIV treatment among antiretroviral-naive HIV-infected injection drug users. *AIDS*. 2005;19(8):837-839.

Depression Prevalent in Entrants to Opiate Addiction Treatment

Drug and Alcohol Dependence; June 1, 2005 – This study determined the rate of current major depressive disorder (MDD) among entrants to treatment for heroin dependence in three treatment modalities and a non-treatment comparison group in Sydney, Australia.

Participants included 615 current heroin users: 201 entering methadone/buprenorphine maintenance, 201 entering detoxification, 133 entering drug free residential rehabilitation, and 80 not in treatment. Overall, current major depressive episode was reported by 25% of the heroin users; ranging from 26% or greater in the treatment groups to 16% of those not in treatment.

Females were nearly twice as likely to have current major depressive episode. Factors most associated with depression in the treatment groups were post traumatic stress disorder (PTSD), attempted suicide in the last 12 months, and severe physical disability. Among the non-treatment group those with depression were also more likely to have PTSD. Women entering treatment were three times more likely to meet criteria for current major depression than women not in treatment. Among men, however, the rates were not significantly different.

The authors concluded that depression is a significant concern among entrants to treatment for heroin dependence. An essential component of treatment should be a consideration of depression, with the provision of appropriate treatment where required.

Source: Teessona M, Havarda A, Fairbaima S, et al. Depression among entrants to treatment for heroin dependence in the Australian Treatment Outcome Study (ATOS): prevalence, correlates and treatment seeking. *Drug Alcohol Depend*. 2005;78(3):309-315.

'Pleasure Gene' for Heroin Addiction Discovered

The Guardian (UK); June 2, 2005 – Researchers have identified a critical gene that appears to control craving and relapse behavior in heroin addicts.

By examining the neurons of heroin-hooked rats, Ivan Diamond at CV Therapeutics in California and colleagues found that the AGS3 gene can increase the output of pleasure and addiction signals from a region of the brain known as the nucleus accumbens. This region was already known to be important for pleasure and reward, and central to heroin addiction.

Diamond and colleagues believe that AGS3 regulates addiction pathways and that the findings could eventually be used to help control craving and prevent relapse in heroin addicts. "The hope is that we can design a drug that will stimulate or inhibit receptors in the brain and manipulate the pathway that causes drug craving," said Diamond.

The research was published in *Proceedings of the National Academy of Sciences*.

Does Buprenorphine Treatment Attract New Patients?

Drug and Alcohol Dependence; July 1, 2005 (early release) – Office-based buprenorphine will expectedly bring into treatment patients who have never received pharmacotherapy for addiction. In a cross-sectional and longitudinal analysis, researchers from Yale University School of Medicine compared patients entering a clinical trial of buprenorphine in a Primary Care Clinic (PCC) and those entering a local Methadone Maintenance Treatment Program (MMT), and also compared the clinical characteristics and treatment outcomes of PCC patients with no history of methadone treatment (new-to-treatment) to those with prior methadone treatment.

PCC subjects (N = 96) were enrolled in a 26-week clinical trial of office-based buprenorphine/naloxone provided in a PCC, and MMT subjects (N = 94) were enrolled in methadone maintenance during the same time period. PCC subjects compared with MMT subjects were significantly more likely to be male, full-time employed, have no history of methadone treatment, have fewer years of opioid dependence, and lower rates of injection drug use (IDU). For patients specifically new-to-treatment, PCC subjects were significantly younger, more likely to be white, had fewer years of opioid dependence, were less likely to have a history of IDU, and had lower rates of hepatitis C than subjects with prior MMT experience.

Of particular interest, abstinence and treatment retention were comparable in both groups. The results suggest that office-based treatment of opioid dependence is associated with new types of patients entering into treatment; however, treatment outcomes with buprenorphine in a PCC do not vary based solely on history of prior MMT.

Source: Sullivan LE, Chawarski M, O'Connor PG, Schottenfeld RS, Fiellin DA. The practice of office-based buprenorphine treatment of opioid dependence: is it associated with new patients entering into treatment? *Drug Alcohol Depend*. 2005;79(1):113-116.

[This study is of special interest because is characterizes the demographic profile and addiction history of persons most likely to be attracted to buprenorphine treatment for opioid addiction. It is also important to note, however, that the treatment modalities were comparable in terms of retention and drug abstinence outcomes. – Ed.]

NAS Outcomes Comparable Between Buprenorphine & Methadone?

Drug and Alcohol Dependence; July 1, 2005 (early release) – Researchers, primarily from Johns Hopkins University School of Medicine, compared the neonatal abstinence syndrome (NAS) in neonates of methadone and buprenorphine maintained pregnant opioid-dependent women and provided preliminary safety and efficacy data.

This randomized, double-blind, flexible dosing, parallel-group controlled trial was conducted in a comprehensive drug-treatment facility that included residential and ambulatory care. Participants were opioid-dependent pregnant women and their neonates. Treatment involved daily administration of either sublingual buprenorphine (4-24 mg/d) or oral methadone (20-100 mg/d) using flexible dosing. Primary outcome measures were: (1) number of neonates treated for NAS; (2) amount of opioid agonist medication used to treat NAS; (3) length of neonatal hospitalization; and (4) peak NAS score.

Two of 10 (20%) buprenorphine-exposed and 5 of 11 (45.5%) methadone-exposed neonates were treated for NAS. Although differences between groups on outcome measures were not statistically significant, the total amount of opioid-agonist medication administered to treat NAS in methadone-exposed neonates was three times greater than for buprenorphine-exposed neonates and length of hospitalization was shorter for buprenorphine-exposed than for methadone-exposed neonates. Peak NAS total scores were comparable in the two groups.

The authors concluded that the results suggest that buprenorphine is not inferior to methadone on outcome measures assessing NAS and maternal and neonatal safety when administered starting in the second trimester of pregnancy.

See: Jones HE, Johnson RE, Jasinski DR, et al. Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on the neonatal abstinence syndrome. *Drug Alcohol Depend*. 2005;79(1):1-10.

[It is difficult to draw valid conclusions from this small study in only 21 patients, which also may account for the lack of statistical differences in outcomes. Therefore, the appropriateness and safety of buprenorphine during pregnancy appears to require further study that will expectedly be provided by a planned multicenter trial. – Ed.]

Abstracts & Highlights from the ASAM 36th Annual Conference; April 14-17, 2005; Dallas, TX

Sleep Disorders Common in MMT; Complicated by Benzo Abuse and Pain

Researchers at the Adelson Clinic in Tel-Aviv, Israel, examined the sleep patterns and potentially interacting factors in 101 MMT patients during a one-year period. According to assessments of sleep quality, three-quarters (75.2%) were "poor" sleepers and about 25% were "good" sleepers. Average methadone dose was 157 ± 53 mg/day. Sleep problems were significantly associated with higher methadone dose, benzodiazepine abuse, chronic pain, and psychiatric disorder (approximately 48% had a psychiatric disorder and 49% had chronic pain). The authors noted that there is a need during MMT to curtail benzodiazepine abuse, replacing it with proper treatment for sleep disorders, as well as the need for specific pain treatments for many patients.

Source: Peles E, Schreiber S, Adelson M. Variables associated with sleep disorders in methadone maintenance treatment (MMT) patients. Abstract 8A.

Take-Home Methadone Not Always Welcomed by Patients

Investigators at the University of Pittsburgh Medical Center methadone maintenance treatment clinic examined the beneficial effects of methadone take home privileges. The clinic made 3-day a week privileges for unemployed patients available for the first time and extended weekend take-homes available to those in MMT for only 3 months.

Surprisingly, a significant minority of patients were reluctant to accept the take-home privileges, and larger numbers experienced drug relapse shortly after gaining them. Part of the reason attributed to this was a psychoanalytic theory of patients being fearful of leaving the clinic, which is experienced as a strict but loving "parent."

Source: Zisowitz C. Ambivalent response to extended take-homes at a methadone clinic. Abstract 35A.

Speaker Highlights

Herbert Kleber, MD speaking on "Marijuana: No Longer a Harmless Giggle" noted that current adult prevalence of marijuana use is 4%, although most users quit in their 20s. The prevalence among black and Hispanic populations has sharply risen. Marijuana potency has continued to rise and can exceed 15% to 20% in some strains; half-life is 7 days, and THC often can be detected in urine up to 2 weeks after the last use. Decreased motivation and memory deficits in marijuana users can cause significant learning disabilities that hinder treatment attempts.

H. Westley Clark, MD, David Felin, MD, and Nora Volkow, MD speaking during Symposium #4 observed that the 2003 National Survey on Drug Abuse and Health reported that 6.3 million Americans aged 12 and older were users of prescription drugs for nonmedical purposes. An estimated 4.7 million abused pain relievers, 2.1 million misused tranquilizers or sedatives, and 1.2 million abused stimulants. OxyContin and Ritalin misuse have increased significantly in the recent past.

The adolescent population is over-represented when it comes to prescription opioid abuse, and depression and somatic complaints are often associated with such misuse. Because pain and opioid abuse or dependence often go together, there is a need for pain management specialists and addiction medicine specialists to become familiar with each other's approaches and methods. Closer cooperation is needed because of the frequent cross-over involved in treating pain and addiction, which often coexist in the same patient. There are increasing opportunities for some treatment services to be provided in primary care settings, including the use of buprenorphine for detoxification or maintenance treatment for opioid dependence. To date, a total of 7,200 US physicians have been trained in using buprenorphine for opioid addiction and 4,700 have received the necessary waiver to prescribe it.

Source: Comments abstracted from Haynes TL. *Medscape Psychiatry & Mental Health*. 2005;9(1). http://www.medscape.com.

Outcome Measures Available Online from SAMHSA

SAMHSA News Release; June 3, 2005 – The Substance Abuse and Mental Health Services Administration (SAMHSA) announced the online availability of SAMHSA's National Outcome Measures (NOMS) – a data resource to help federal and state substance abuse and mental health managers facilitate evidence-based decision making and ultimately improve services in the communities they serve.

Using maps and charts, the database describes states' substance abuse and mental health prevalence, treatment, and funding data. It also provides substance abuse prevention data. As new data are collected, the website will also present cross-year data to help users examine program changes over time.

In collaboration with states, SAMHSA has identified National Outcome Measures for a number of domains, such as: abstinence from drug and alcohol abuse; decreasing symptoms of mental illness and improved functioning; increased access to services for both mental health and substance abuse; retention in services for substance abuse or decreased inpatient hospitalizations for mental health treatment, and others.

To access NOMS go to http://www.nationaloutcomemeasures.samhsa.gov/

Drug-Death Data in 32 Cities, 6 States Released by SAMHSA

SAMHSA News Release; June 7, 2005 – The Substance Abuse and Mental Health Services Administration unveiled findings on drug-related mortality from the 2003 Drug Abuse Warning Network (DAWN) that provide a picture of deaths involving recent drug use in 6 states and 32 metropolitan areas.

Among the metropolitan areas, Baltimore and Albuquerque had the highest rates of drug misuse deaths, exceeding 200 deaths per one million population. In 6 states providing mortality data – Maine, Maryland, New Hampshire, New Mexico, Utah, and Vermont – fatality rates for drug misuse ranged from 88 to 162 deaths per one million population.

This is the first time there has been any state information from DAWN. These data show substantial variations in drug-related deaths across jurisdictions within the states, with the highest rates not always found in urban centers.

The study, "Drug Abuse Warning Network, 2003: Area Profiles of Drug-Related Mortality" is a new version of DAWN that is the result of a major redesign, so these data cannot be compared with data from prior years. In one key change, DAWN now captures any death related to recent drug use. Findings are presented for deaths involving drug misuse and abuse, as well as drug-related suicides.

Of particular interest, the DAWN mortality data indicate that the typical drug misuse death involves multiple drugs, an average of 2.7 drugs per case. Opioids, which include prescription pain relievers and heroin, were found more often than any other type of drug in 29 of the 32 metropolitan areas and all of the 6 states. Cocaine was the most frequently reported drug in 3 metropolitan areas and was in the top 5 drugs in 28 metropolitan areas and all 6 states. Alcohol was one of the 5 most common drugs in 30 of the 32 metropolitan areas and 5 of 6 states.

The report indicates that stimulants – reported as either methamphetamine or amphetamines – appeared in the top 5 drugs in 5 metropolitan areas: Minneapolis-St. Paul; Ogden-Clearfield, Utah; Phoenix; San Diego; and, San Francisco.

Drug-related suicide deaths were much less frequent than deaths involving drug misuse. On average, less than 20% of drug-related suicides involved an illicit drug. Alcohol was among the 5 most common drugs in drug-related suicides in all but one of the 32 metropolitan areas and 5 of the 6 states.

Source: Office of Applied Studies, SAMHSA, Drug Abuse Warning Network, 2003, available online at http://dawninfo.samhsa.gov.

SAMHSA Directory of Drug, Alcohol Treatment Programs Updated

SAMHSA News Release; May 2005 – The guide, *National Directory of Drug and Alcohol Abuse Treatment Programs 2005*, provides information on thousands of alcohol and drug treatment programs located in all 50 states, the District of Columbia, Puerto Rico, and four US territories. It includes more than 11,000 public and private facilities that are licensed, certified, or otherwise approved by substance abuse agencies in each of the states.

This updated printed directory complements SAMHSA's Internet-based Substance Abuse Treatment Facility Locator, which is updated continuously and provides road maps to the nearest treatment facilities, as well as addresses, phone

numbers, and information on services available. The URL is: http://findtreatment.samhsa.gov

To obtain a free copy of the *National Directory of Drug and Alcohol Abuse Treatment Programs 2005*, contact SAMHSA's Clearinghouse or call (800) 729-6686.

#100 – July - August 2005

AT Forum "News & Updates" Reaches 100 Mark

From the Editor…

Every 1 to 2 months we produce and post brief summaries of news stories, research reports, and other items of interest that come from our continuous scan of news and literature in the addiction field. As of this edition, 100 monthly or bimonthly *News & Updates* installments have been posted at this website, spanning July 1996 through July-August 2005 and containing more than 2,000 entries. These serve as a vital history of happenings and developments during the past 9 years in the addiction field, with a special emphasis on methadone maintenance treatment (MMT).

To examine past items, all News & Updates have been assembled into archive "Web Volumes" (WEBVOLs), each containing 10 monthly or bimonthly installments. These may be accessed under the "Addiction Resources" tab at ATForum.com (see: http://www.atforum.com/SiteRoot/pages/addiction_resources/addiction_resources.shtml) and can be downloaded in Microsoft Word® format. Items of particular interest can be located by using the search engine at the website (see top right corner of web page) and/or the "find" function in the MS Word document (press Ctrl + F and then insert the search term of interest).

Optimal Methadone During MMT Demonstrated

Redfern, NSW, Australia; July 15, 2005 – Researchers assessed 24-hour trough serum methadone levels (SMLs) in 94 methadone maintenance treatment (MMT) patients classified as 'responders' or 'non-responders,' based on urine toxicology evidence of recent illicit-opiate use.

Compared with treatment responders, non-responders (n = 37) had a significantly lower average methadone dose (73 mg/day versus 147 mg/day; $p<0.001$), and lower mean trough SML (266 ng/mL versus 409 ng/mL *[racemic, R+S methadone]*; $p = 0.001$). Statistical analyses revealed that methadone dose and duration of treatment were significantly associated with treatment response. Each year of MMT increased the odds of abstinence from illicit opioid use by 34%, and each added 20 mg/day of methadone increased the odds of abstinence by 36%.

The methadone dose-to-body-weight ratio and trough SML were no better predictors of treatment response than daily dose. Optimal therapeutic thresholds that may help guide dose titration for patients continuing to use illicit opiates were: daily dose between 100 and 140 mg/day, and trough SML between 400 and 500 ng/mL.

Source: Hallinan R, Ray J, Byrne A, Agho K, Attia J. Therapeutic thresholds in methadone maintenance treatment: A receiver operating characteristic analysis. *Drug Alcohol Depend*. 2005 (July); [Epub ahead of print].

[This well-designed observational study reinforces findings of earlier research, as presented in the AT Forum *report,* Methadone Dosing & Safety in the Treatment of Opioid Addiction*. This is available for viewing and download at: http://www.atforum.com/SiteRoot/pages/rxmethadone/dosingandsafety.shtml. – Ed.]*

Recruiting Others to Help Support MMT Patients Improves Success

Baltimore, MD; July 2005 – This article reports on a behavioral intervention designed to encourage opioid-dependent patients receiving methadone to include drug-free family members or friends in treatment and to use these individuals to facilitate development of a supportive, non-drug-using social network.

The report uses data from 59 opioid-dependent outpatients who identified a drug-free significant other to participate in their treatment. Fifty-five (93.2%) brought a significant other (most often the patient's mother, 29%) to both the initial evaluation session and at least one joint session. Social support activities were related to family (33%), church (28%), and self-help groups (30%). Approximately 78% of patients who participated in the social support intervention achieved at least 4 consecutive weeks of abstinence. Women responded better than men. The authors conclude that methadone-maintained patients can and will include non-drug-using family members and friends in treatment, and these individuals can be mobilized to help patients improve their recovery.

Source: Kidorf M, King VL, Neufeld K, et al. Involving significant others in the care of opioid-dependent patients receiving methadone. *J Subst Abuse Treat*. 2005;29(1):19-27.

Methadone, Buprenorphine On New WHO Essential Drugs List

AIDSmap News; July 4, 2005 -- Methadone and the opiate substitute buprenorphine have been added to the World Health Organization's Essential Drugs list, it was announced at the end of June 2005. This followed nearly 2 years of lobbying by treatment advocates for inclusion of the drugs on the list, which indicates that international experts consider the availability of the drugs to be essential for delivering health care, and national governments are expected to take note of the recommendation when making policy. Methadone and buprenorphine are the only 2 agents listed in the category "Medicines Used in Substance Dependence Programs."

For more information see the WHO Essential Medicines Library at: http://mednet3.who.int/EMLib/

Predictors of Heroin Relapse Among MMT Patients

Amsterdam, The Netherlands; August 1, 2005 – The risk of relapse to frequent heroin use was studied among 732 participants in the Amsterdam Cohort Study (ACS) on HIV/AIDS among drug users. These patients previously experienced successful periods of abstinence from or only occasional use of heroin.

The majority of subjects (86%) experienced relapse episodes within 5 years. Factors incurring high risk for relapse included: less education, intense use of heroin prior to the period of heroin abstinence or well-controlled use, intense use of cocaine during the heroin-abstinence period, and having a drug-using partner or having no partner. Relapse also was significantly associated with the daily dose of methadone: patients receiving less than 60 mg/day of methadone were at significantly greater (approximately 50% greater) risk of relapse than those receiving more than 100 mg/day. There was beneficial influence of methadone dosage or program attendance on the risk of relapse into cocaine.

The authors concluded that higher doses of methadone in a harm-reduction setting extend the duration of no or only occasional use of heroin. Other factors, such as no use of cocaine and having a non-drug-using partner seem to be equally important.

Source: Termorshuizena F, Krola A, Prinsa M, et al. Prediction of relapse to frequent heroin use and the role of methadone prescription: An analysis of the Amsterdam Cohort Study among drug users. *Drug and Alcohol Dependence*. 2005;79(2):231-240.

Cardiac QTc Changes During MMT Found Clinically Insignificant

Tel Aviv, Israel and New York, NY; June 2005 – Researchers evaluated the relationship between serum methadone level (SML) and QT-corrected interval (QTc) in 138 former heroin-addicts who attended the Adelson methadone maintenance treatment (MMT) clinic in Israel for from 3 months to more than 10 years. Patients were on a steady dose of methadone for at least 14 days and had ingested their dose in the clinic for at least 3 days prior to being evaluated.

The average QTc was 418 ms, mean methadone dose was 171 mg/day, (range 40-290 mg/day), and mean SML was 700 ng/ml (range 99-2350 ng/ml). The QTc was modestly but significantly correlated with methadone dose ($r = 0.18$, $p = 0.04$) and with duration in treatment ($r = 0.23$, $p = 0.007$); however, QTc correlated with SML only in males ($r = 0.21$, $p = 0.04$). Mean QTc was significantly shorter in 97 patients with any drug abuse during MMT (413 ms), compared with 41 non-drug-abuse patients (431 ms).

The authors emphasized that, "we found the prolongation to be minimal and safe within the normal range in a noteworthy sample of 138 patients who were treated for up to 10.7 years and with doses up to 290 mg/day methadone."

From: Peles E, Bodner G, Kreek MJ, Adelson M. Clinically insignificant changes in QT intervals in Methadone Maintenance Treatment patients. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

Also see: Does Methadone Harm Heart Health? *Addiction Treatment Forum*. 2005 (fall);14(3):6. Available at: www.ATForum.com.

Vitamin D Deficiency: A Potential Cause of Bone Pain During MMT?

From AT Forum *Editor*; August 2005 – An earlier report in these News & Updates (#95; September-October 2004) noted that a majority of MMT patients complain of bone pain. Researchers examining MMT patients have found a substantial prevalence of vitamin D insufficiency and a high rate of osteoporosis, especially among male subjects. Methadone was not attributed as a cause of these conditions; however, since they are treatable disorders the researchers recommended that further study is warranted to address the potentially abnormal bone health of patients in MMT.

A recent letter in the British Medical Journal; July 9, 2005 appears to support the hypothesis that vitamin D deficiency may be related to musculoskeletal complaints; therefore, its detection and correction might be a worthwhile therapy in MMT patients. The letter author notes that many studies have shown a high prevalence of vitamin D deficiency in various populations complaining of musculoskeletal pain. In many instances, treatment with vitamin D supplements produced clinical improvement in symptoms. Thus, "All patients with persistent, musculoskeletal pain are at high risk of the consequences of unrecognized and untreated vitamin D deficiency." The management of otherwise undetermined musculoskeletal pain should include assessment of vitamin D status (by measuring serum 25-hydroxyvitamin D concentrations), together with appropriate vitamin D supplementation in those found to be deficient.

Source: Lewis PJ. Vitamin D deficiency may have role in chronic low back pain [letter]. *BMJ*. 2005;331:109.

New Program Addresses Needs of Pregnant MMT Patients

Warwick, RI; July 14, 2005 – Kent Hospital will soon introduce a unique program for expectant mothers in recovery from opiate addiction. The concept is endorsed by the National Association of Methadone Advocates (NAMA), an organization composed of methadone patients and health care professionals that are supporters of quality opiate agonist treatment.

As Rhode Island's second largest provider of obstetrical services, Kent Hospital also operates a neonatal special care nursery in collaboration with its Care New England partner, Women & Infants Hospital of Rhode Island. This new program is designed to provide educational and psychosocial support for expectant mothers who are receiving methadone for treatment of opioid dependence, according to Sharon Dembinski, MS, PNP, CMA, a pediatric nurse practitioner in the neonatal special care nursery, who worked with her colleagues at the hospital to develop the model.

Dembinski noted that expectant mothers who qualify for participation will receive one-on-one counseling on the specific medical concerns connected with pregnancy during methadone treatment. Patients will also receive no-cost childbirth education and infant care classes as well as support from the hospital's department of social services to link into additional community-based resources. A special focus will be placed on mother and newborn needs during and after childbirth.

Alcohol Use Impairs MMT Outcomes in Pregnant Patients

Baltimore, MD; June 2005 – The harmful effects of alcohol and drug use in pregnancy are well-established; however, the impact of comorbid alcohol use on the treatment outcomes for methadone stabilized pregnant women requires further study.

These investigators examined 163 methadone stabilized patients admitted to the Center for Addiction and Pregnancy (CAP) who were categorized based on self-reported drinking of alcohol to intoxication (AI) or not drinking alcohol (non-alcohol intoxication; NAI) in the thirty days prior to treatment enrollment.

The AI group had more months of regular lifetime drinking (85 vs. 19 months) and were more likely to have been treated for alcohol problems (lifetime) compared to the NAI group. The AI group also reported more current and lifetime cocaine use, and had more extensive histories of cigarette smoking than the NAI group. On treatment outcome measures, heroin use was similar between groups; however, the AI group was more likely to test positive for cocaine during treatment. The AI group also spent significantly fewer days in treatment compared to the NAI group.

Assessing for any alcohol use to intoxication (past thirty days) among pregnant drug dependent women may help providers to identify patients at risk for early treatment dropout and cocaine relapse. Programs should routinely monitor patients for alcohol use and reinforce abstinence from both drugs and alcohol. For women who also use cocaine, providers should address the patient specific pattern of alcohol and cocaine use, as well as relapse prevention strategies.

From: Tuten M, Jones HE. Alcohol use to intoxication predicts poorer treatment outcomes in methadone-stabilized pregnant women. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

Methadone vs Buprenorphine Effects in Pregnancy Compared

Adelaide, Australia; June 2005 – A prospective study assessed the efficacy and safety of buprenorphine maintenance (BM) regarding pregnancy progression and the incidence and severity of Neonatal Abstinence Syndrome (NAS) compared with methadone maintenance (MM) and non-opioid exposed control pregnancies. Preliminary results from a sample size of 20-24 pregnancies in each group of

women show that there is no difference in the abuse of additional substances between mothers on either BM or MM programs. There were more adverse events for BM and MM pregnancies than control-group pregnancies throughout the antenatal period, labour, and delivery, and the first 4 weeks of the postnatal period. Buprenorphine appears to produce NAS of intermediate severity between methadone exposed and control infants, and more total morphine is needed to control NAS in methadone exposed infants than buprenorphine exposed infants during the 4-week postnatal follow up period.

Source: Gordon AL, Stacey H, Pearson V, et al. Buprenorphine and methadone in pregnancy: Effects on the mother, fetus and neonate. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

Higher Methadone Reduces Maternal Opioid Abuse; Increases NAS

San Francisco, CA; June 2005 – Research has indicated the clinical effectiveness of providing methadone to pregnant, opioid-dependent women, but the proper dosage remains controversial. Ideal dosing of methadone in pregnancy would minimize both illicit opioid use and the severity of neonatal abstinence syndrome (NAS). Clinical research into the relationship between maternal methadone dose and NAS has produced equivocal results and is becoming outdated due to increases in maternal methadone doses. The authors of this study examined the relationship of maternal methadone dose with maternal opioid use and NAS severity.

This study included 142 consecutive neonates born to methadone maintained mothers at San Francisco General Hospital from 1995-2004. The primary predictor was maternal methadone dose (low = 10-55 mg/day, medium = 60-110, and high = 120+); outcome measures included maternal illicit opioid use and length (days) of neonate treatment with dilute tincture of opium for NAS symptoms. Results indicated that illicit opioid use was significantly less frequent with increasing methadone dose (low dose = 38%, medium = 20%, high = 9%), but length of neonatal treatment was significantly longer (low dose = 13 days, medium = 26 days, high = 28 days. The researchers concluded that higher maternal methadone doses are more effective at controlling illicit opioid use by the mother, but they may be associated with increased severity of NAS.

Source: Shapiro B, Martinez A, Pletcher M, Haug N, Sniderman S. Retrospective examination of the relationship between maternal methadone dose and neonatal abstinence syndrome. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

[The risk/benefit balances evident in this study must be considered. More adequate higher-dose methadone, which is appropriate for many pregnant women in MMT, can achieve a 29% reduction in continued opioid abuse with its risks of infection and/or other severely harmful effects on the fetus. At the same time, the newborn may require longer treatment for NAS; however, this can be achieved via standard medical protocols without long-lasting negative effects. – Ed.]

Opiates Better Than Sedatives for Treating NAS

Medical News Today; July 27, 2005 – Sedatives have been the gold standard for treating newborns suffering from neonatal abstinence syndrome (NAS); however, new research suggests that opiates are superior to sedatives for treating infants born to women who used heroin or were treated with methadone while pregnant.

Opiates appear to better "ameliorate the withdrawal, facilitate feeding, and potentially reduce the likelihood of seizures," according to new systematic reviews done by David Osborn, a neonatologist at the Royal Prince Alfred Hospital in Sydney, Australia, and colleagues. The researchers also found that infants treated with opiates regained birth weight more quickly than those who only received supportive care and the duration of necessary care was shortened by an average of 4 days. Also, when compared with diazepam, opiates reduce the incidence of treatment failure.

In the examined research studies, newborns suffering from NAS were treated with opiates (morphine, methadone, paregoric, or tincture of opium), sedatives (phenobarbitone, diazepam, or chlorpromazine), or supportive care only. None of the studies compared opiate treatment with placebo.

"The interesting information," Osborn says, "suggests that these infants can be treated without admission to the special care nursery unless withdrawal is complicated and that this is facilitated by the use of morphine instead of phenobarbitone. This helps keep mothers and babies together, helps in educating the mothers in mothercraft skills and to recognize signs of infant withdrawal, and helps in assessment of the quality of the mother-infant interaction in a supervised environment."

See: Osborn DA, Jeffery HE, Cole M. Opiate treatment for opiate withdrawal in newborn infants. The Cochrane Database of Systematic Reviews 2005, Issue 3.

For online information, visit: http://www.cochrane.org.

Substances of Abuse May Worsen Opioid Withdrawal

Mannheim, Germany; June 2005 – Opioid withdrawal, stress, or cues associated with opioid consumption can induce opioid craving. If opioids are not available, opioid-dependent patients usually search for alternative substances of abuse and these investigators surveyed 89 opioid-dependent patients participating in an out-patient opioid maintenance program to estimate the potential of several non-opioid drugs in being able to alleviate opioid withdrawal.

Overall, the study demonstrated a low efficacy of non-opioid drugs in stemming opioid withdrawal symptoms. Of the patients surveyed, 26% to 62% even reported a worsening of opioid withdrawal for cannabis, alcohol, cocaine, and amphetamine. Only benzodiazepines and tricyclic antidepressants were reported to have a moderately positive effect on opioid withdrawal.

Source: Hermann D, Klages E, Welzel H, Mann K, Croissant B. Low efficacy of non-opioid drugs in opioid withdrawal symptoms. *Addiction Biology*. 2005;10(2):165-169.

Spirituality Influences on MMT Outcomes

Baltimore, MD; June 2005 – Although spirituality is an integral component of some of the most popular approaches to substance-abuse treatment (such as 12-step programs), there is little empirical evidence for a predictive relationship between spirituality and outcomes in methadone maintenance treatment (MMT).

In the present study, 169 opiate- or cocaine-abusing treatment seekers completed a survey that assesses spirituality independent of religiosity. Religious affiliation was 56% Protestant, 24% Catholic, 8% other (e.g., Buddhist, Jewish), and 12% none. A higher spirituality score was associated with greater cocaine-negative urinalyses but not with any other indices of treatment outcome. Time spent on religious activities showed a small correlation with retention in treatment and with numbers of cocaine- and heroin-negative urinalyses. Women were more likely than men to report spiritual beliefs or experiences, and African Americans had higher spirituality scores than other groups and were more likely to report spiritual experiences. In general, religious/spiritual beliefs were common in this sample of substance abusers seeking MMT and were associated with treatment outcomes, but differed by gender and race. The results of this study support previous reports that spiritually plays a role in substance-abuse recovery and suggest that demographic characteristics should be considered in the design of spiritually-oriented behavioral interventions for the treatment of addictions.

From: Heinz AJ, Epstein DH, Preston KL. Spiritual activities and previous spiritual experience as predictors of treatment outcome among patients in an inner city methadone maintenance program. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

Incentives for Cocaine-Abstinence During MMT Examined

Baltimore, MD; June 2005 – Researchers examined 6-month follow-up outcomes for cocaine-abusing methadone maintenance patients who received usual care with (n = 198) or without (n = 190) abstinence incentives during a 3-month intervention conducted at 6 regionally diverse methadone clinics. Stimulant-negative urinalysis rates were significantly different between incentive and control groups at 1 month (50% versus 31% negative) but not at 3 (46% versus 38%) or 6 months (38 vs. 35%). Irrespective of treatment group, the longest duration of stimulant abstinence during treatment predicted 6-month follow-up outcomes. The authors concluded that, although abstinence incentive effects were not sufficiently robust to produce post-treatment group differences, these interventions may improve long-term outcomes by increasing the prevalence and duration of abstinence during treatment.

See: Stitzer ML, Peirce J, Wong C, Roll J. Motivational incentives in methadone-maintained stimulant abusers: 6-month follow-up results. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

Interim Methadone Maintenance Studied

Baltimore, MD (Friends Research Institute); June 2005 – Interim methadone maintenance provides an alternative for individuals on waiting lists for comprehensive methadone treatment programs (MTP). It consists of methadone

maintenance with only emergency counseling, for no more than 120 days, for individuals awaiting admission to comprehensive treatment. A randomized clinical trial examined whether individuals on the wait list for a mobile MTP who received interim maintenance (n = 199) had greater reductions in drug use and criminal activity as reported on the Addiction Severity Index (ASI) compared with individuals assigned to a wait list without interim treatment (n = 120).

Results indicated both short- and longer-term (10 month) superiority of interim treatment in all instances. At follow-up, interim participants were still less likely than wait list participants to test heroin positive, while the groups did not differ with regard to cocaine test results. It appears that meaningful improvements in drug use and crime indices are associated with interim methadone maintenance as compared with waiting list controls, and these improvements persist for up to 10 months.

Source: Schwartz RP, Highfield DA, Battjes RJ, et al. Interim methadone maintenance: 10 month follow-up. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

Major Depression Affects Response During MMT

Toronto, Canada; June 2005 – There is a high rate of comorbid major depressive disorder (MDD) among patients in methadone maintenance treatment (MMT), and patients with MDD may have an altered response to opioids, including methadone. This study examined a small group of stabilized MMT patients with (n=5) and without (n=8) MMD to compare methadone concentrations and mood changes during a typical dosing period. Average methadone dose was about 98 mg/d.

Preliminary results confirmed that depressed subjects had lower positive mood scores, significantly greater changes in mood, and higher total mood disturbance. Furthermore, depressed subjects experienced more subjective opioid withdrawal. The authors conclude that MMT patients with comorbid MDD may be more sensitive to negative opioid effects, including the experience of opioid withdrawal.

See: Elkader AK, Sproule BA, Selby P, Brands B. Influence of major depressive disorder on the pharmacokinetic-pharmacodynamic relationships of methadone. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

Warning: Suicidality in Adults Taking Antidepressants

Washington, DC; FDA Notice; July 1, 2005 -- In response to recent scientific publications that report the possibility of increased risk of suicidal behavior in adults treated with antidepressants, the U.S. Food and Drug Administration (FDA) has issued a Public Health Advisory (PHA) to update patients and healthcare providers with the latest information on this subject.

The FDA advises health care providers and patients to be aware of the following:

- Adults being treated with antidepressant medicines, particularly those being treated for depression, should be watched closely for worsening of depression and for increased suicidal thinking or behavior.
- Close observation of adults may be especially important when antidepressant medications are started for the first time or when doses for the specific drugs prescribed have been changed.
- Adults whose symptoms worsen while being treated with antidepressants, including an increase in suicidal thinking or behavior, should be evaluated by their health care professional.

These recommendations are consistent with warnings already present in approved labeling for antidepressants used by adults. The FDA will provide updated information as it becomes available; meanwhile, the following documents may be of interest:

FDA Talk Paper (6/1/05), see:
http://www.fda.gov/bbs/topics/ANSWERS/2005/ANS01362.html

FDA Public Health Advisory (6/30/05), see:
http://www.fda.gov/cder/drug/advisory/SSRI200507.htm

FDA Drug Information Page (6/30/05), see:
http://www.fda.gov/cder/drug/antidepressants/default.htm

Tapering from Opioid Agonist Therapy Difficult

Seattle, Washington; June 2005 – Controversy has existed regarding whether opioid agonist treatment, such as with methadone, should be indefinite or whether patients should taper off the medication after a period of stabilization. Longitudinal studies have indicated most patients are not able to taper off MMT successfully, and the majority of those who do so relapse to opiate abuse within one year. Little is known, however, about patient tapering efforts

within a treatment environment that is supportive of both indefinite methadone treatment and medication tapering in the rehabilitated patient who desires it.

In this study, all records of patients since 1997 receiving MMT at a Veterans' Administration facility (n = 216) were reviewed. Patients (n = 30, 13.9% [all male]) who had 1) received at least 6 months of methadone maintenance treatment and 2) started a slow methadone taper scheduled to last a minimum of 120 days were included in the study. It was found that *no* patient successfully completed tapering during the study period, although one patient completed a detoxification after his approved taper was stopped due to recent drug use. This patient was re-addicted and readmitted within one year.

Three (10%) patients were continuing on their taper at study's end. Four patients (13.3%) successfully switched to buprenorphine, which had become an interim goal, and none of these have tapered off buprenorphine. One patient transferred to another program, one was administratively discharged for fighting, and one had his taper stopped for mishandling of take home doses. The remaining 20 (66.7%) patients stopped their tapers for the following reasons: feeling unstable/withdrawal symptoms (n = 4, 13.3%), drug use-positive urinalyses (n = 12, 40%), psychiatric instability (n = 3, 10%), pain management (n = 1, 3.3%).

Conclusion: Tapering off opioid agonist treatment is very difficult. Patients attempting tapers should be informed about the difficulty and monitored closely for signs of instability.

Source: Calsyn DA, Malcy JA, Saxon AJ. Natural history of slow taper attempts from methadone maintenance treatment. Meeting program & abstracts: CPDD (College on Problems of Drug Dependence) 67th Annual Meeting; June 18-23, 2005; Orlando, Florida.

New Sleep Medication Expectedly Safe for Long-Term Use

Medical News Today; July 26, 2005 – Takeda Pharmaceutical Company Limited has received approval from the U.S. Food and Drug Administration for ramelteon (Rozerem®), 8 mg tablets for the treatment of insomnia. Ramelteon is the first and only prescription sleep medication not designated as a controlled substance by the U.S. Drug Enforcement Administration.

Ramelteon has a unique therapeutic mechanism of action, compared with existing insomnia treatments, because it selectively targets two receptors in the brain's suprachiasmatic nucleus (SCN). The SCN is known as the body's "master clock" because it regulates 24-hour or "circadian" rhythms, including the sleep-wake cycle. In clinical studies with more than 4,200 patients ramelteon was shown to decrease the time to sleep onset and also to carry minimal risks of rebound insomnia and dependency.

For more information, see:
http://www.rozerem.com/index.aspx.

[Since insomnia is a major concern among MMT patients, the above information is provided as a public service and does not imply an endorsement by AT Forum*. – Ed]*

Lofexidine Aids Transfer from Methadone to Buprenorphine

Addiction Biology; June 2005 – According to the authors of a study conducted in the UK, current clinical practice allows patients with low levels of physiological dependence on opioids (equivalent to methadone doses of 30 mg/d or less) to be transferred to buprenorphine. They investigated the response of opioid-dependent patients receiving doses of methadone between 30 and 70 mg/day when transferred to buprenorphine at doses between 12–16 mg/day.

Twenty-three patients receiving inpatient opioid detoxification agreed to take part in a trial of facilitated transfer to buprenorphine (which was substituted in doses increasing from 4 mg to a maximum of 16 mg) plus adjunctive lofexidine (maximum of 2.4 mg/d). All except 2 patients successfully completed transfer to buprenorphine.

The subjects were split into intermediate methadone dose (ID; 30–49 mg/d; n = 10) and high methadone dose (HD; 50–70 mg/d; n = 11) groups. Average stabilization dose of buprenorphine for the entire sample who completed transfer was 14.0 mg/d and average daily lofexidine dose during transfer was 0.57 mg. The HD group experienced increased opioid withdrawal symptoms and used significantly more lofexidine to complete transfer compared with the ID group.

This study suggests that transfer to buprenorphine is feasible from daily methadone doses of 30 to 70 mg/d in an inpatient setting and may be facilitated by the use of lofexidine.

Source: Glasper A, et al. Induction of patients with moderately severe methadone dependence onto buprenorphine. *Addiction Biology.* 2005;10(2):149-155.

Survey: Buprenorphine May Cause Physical Dependency

Beverly Hills, CA; June 29, 2005 – The Waismann Method organization, released findings of its Buprenorphine Dependency Survey, which showed that almost three-quarters (70%) of respondents taking buprenorphine in order to cease their narcotic dependency found themselves dependent on the drug and needing assistance to stop taking it.

Clifford Bernstein, MD, medical director for the Waismann Method and board certified by the American Society of Addiction Medicine to dispense buprenorphine as a treatment for opiate dependency, says he has seen a recent increase in patients seeking treatment for buprenorphine, a drug that was originally prescribed to help them. "Although [buprenorphine] doesn't carry the negative stigma associated with visiting a methadone clinic, the Waismann Method survey shows that people who take buprenorphine run the risk of developing a physical dependency. Patients need to be educated that it's a replacement therapy which is half opiate in composition."

Results from the survey also indicated that 53% of those dependent on the drug were told by their doctors that buprenorphine would cure their opiate dependency. In addition, 50% of respondents were never told they could develop a physical dependency.

[In fair balance, it should be noted that the Waismann Method organization, headquartered in Beverly Hills, CA, specializes in providing rapid opiate detoxification under anesthesia as a treatment for opioid addiction. – Ed.]

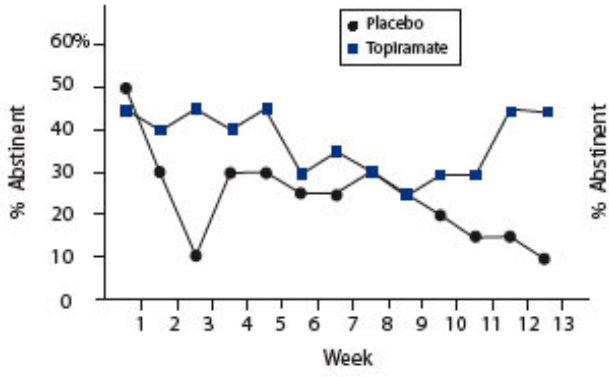
Topiramate Shows Promise for Cocaine Addiction

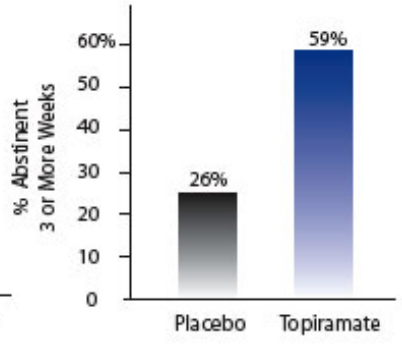
NIDA Notes; May 2005 (Vol. 19, No. 6; writer Lori Whitten) – In a small pilot study, topiramate – a medication currently used to treat seizure disorders – has helped cocaine-addicted outpatients stay off the drug continuously for 3 weeks or more. Previous research has shown that outpatients who avoid relapse for 3 to 4 weeks during treatment with behavioral therapy and medication have a good chance of achieving long-term cessation.

Kyle M. Kampman and colleagues at the University of Pennsylvania School of Medicine and the Veteran Affairs Medical Center in Philadelphia treated 40 crack-cocaine-smoking outpatients, mostly African American males, for 13 weeks at the University of Pennsylvania Treatment Research Center (TRC). Because topiramate exacerbates cocaine withdrawal symptoms, the investigators selected patients who were able to attain at least 3 days of self-reported abstinence immediately before starting the trial and who, based on their level of addiction, were not likely to enter severe withdrawal.

After a 1-week baseline period, Kampman's team gave topiramate to 20 study participants, and placebo to the other 20. To avoid potential topiramate side effects, including sedation and slurred speech, they initiated treatment with 25 mg/d and increased it by 25 mg/d every week to 200 mg/d. They maintained this maximum dose during weeks 8 through 12, then tapered to zero during week 13. The patients also received cognitive behavioral coping skills therapy twice weekly throughout the study. The researchers verified cocaine abstinence two times a week with urine tests.

See Graphs: In almost every week of the study, more patients were abstinent in the topiramate group than in the placebo group. Of the 40 participants in the study, by the end of the 13th week almost 60% of those taking topiramate attained 3 or more weeks of continuous abstinence from cocaine compared with 26% of those taking placebo. All 40 patients showed improvement from week 1 to week 13, as reflected by lower Addiction Severity Index (ASI) scores; however, patients taking the medication improved more, with average ASI scores in the topiramate group falling by 69% compared with 50% in the placebo group.





Source: Kampman KM, et al. A pilot trial of topiramate for the treatment of cocaine dependence. *Drug and Alcohol Dependence*. 2004;75(3):233-240.

[Other research also has demonstrated topiramate's efficacy in treating alcoholism and as a migraine preventive. There does not appear to be anything in its mechanism of action or metabolism that would preclude its use with methadone in MMT patients, although specific research in this population is lacking. – Ed.]

Who Joins Alcoholics Anonymous?

New York, NY; July 2005 – Alcoholics Anonymous (AA), the prototype 12-Step Program founded in 1935, claims to have more than 2-million members and there always have been questions regarding the composition of that membership – that is, who is the typical AA member? Outsiders have been hindered in their survey attempts by the anonymity of members and independence of individual AA groups; yet, the organization itself conducts membership surveys every 3 years. Here are some facts from the most recently released survey based on 7,500 responses:

- More than half (56%) are ages 41 through 60. About a quarter are 21 through 40 years of age.
- A majority are men (65%) and white (89%). More than a third (38%) of all members are married. *[However, it should be noted that within any community there may be individual groups whose members are more substantially female, minority, unmarried, etc. –Ed.]*
- The average sobriety of members is 8 years; although, a quarter (26%) at any given time have less than 1-year sobriety. Of interest, 36% have been sober for more than 10 years.
- Members come from all occupations, but the 5 top-ranked groups include: retired (14%), self-employed (11%), manager/administrator (10%), professional/technical (10%), skilled trade (9%).
- AA members attend an average of 2 meetings per week, and most of them (86%) have a group they attend on a regular basis ("home group").

Source: Data from the AA General Service Office, New York and featured in the *AA Grapevine* (magazine), July 2005.

The 7th International Conference on Pain & Chemical Dependency

The next International Conference on Pain & Chemical Dependency is scheduled to take place January 11-14, 2006 at the New York Marriott at the Brooklyn Bridge. This will be the seventh in a series of conferences designed to show the interface between pain management and chemical dependency and how this relationship often plays a role in the undertreatment of pain, both acute and chronic. Since undertreatment of pain is a universal phenomenon, there will be an emphasis on international issues with presentations by world-renowned practitioners and speakers in the fields of pain management and addiction medicine.

For information about the preliminary program, registration, and housing, visit http://www.Painandchemicaldependency.org or call ***404-233-6446.***