ADDICTION TREATMENT

Forum

THE QUARTERLY NEWSLETTER FOR CLINICAL HEALTH CARE PROFESSIONALS ON ADDICTION TREATMENT

Vol. 16, #2 • Spring 2007

Opioid addiction is a complex disease process, often requiring multiple treatment episodes, employing different approches.

IN THIS ISSUE

MAT Cycle of Recovery	1
Events to Note	2
From Editor MMT Clinic Parity New Survey: Options in MMT?	2
TOTA Involving Patients in Treatment	7
Survey Results: Fighting Addiction Myths	8

AT Forum is made possible by an educational grant from Mallinckrodt Inc., St. Louis, MO, a manufacturer of methadone & naltrexone.

Clinical Concepts

MAT Cycle of Recovery from Opioid Addiction

Addiction to opioids is a complex disease process, often requiring multiple treatment episodes, employing different approaches. In an ideal world, those becoming addicted to opioids – whether prescribed or illicit – would be able to stop taking the drug, give up their unfortunate "habits," and become abstinent, or drug free for life.

This simplistic view neglects the well-established science of opioid addiction as a neurobiological disease with psychosocial consequences and, in many cases, influenced by genetics (CSAT 2005; Nature Neuroscience 2005). Different individuals may prefer and benefit from a menu of choices when it comes to addiction treatment.



For opioid addiction, the 3 approved pharmacotherapies comprising medication-assisted treatment, or MAT, provide scientifically-validated options. However, treatment providers must be able to assess the addiction severity, psychosocial needs, and other qualities of each patient for matching them with the best MAT approach at a particular time. Along with that, flexibility is required, allowing patients to cycle from one pharmacotherapy to the other as they progress in recovery.

Addiction Recovery A Journey

Definitions and desired goals of addiction *recovery* have been somewhat muddled by diverse opinions. This was discussed previously in *AT Forum*, noting that there are *many paths to recovery* for any individual (Leavitt 2005).

One of the most misleading myths is to view addiction as an acute condition, like a broken leg or infection, that can be "fixed" by a brief episode of clearly-defined treatment. Rather, recovery is a *process* involving "global health" goals, encompassing physical, emotional, spiritual, social, occupational, and lifestyle health objectives.

Additionally, there are different levels of addiction recovery; it is far from an allor-nothing accomplishment and, for most, it is a journey rather than a destination. Many patients cycle in and out of recovery, sometimes with repeated treatment episodes requiring different therapies, eventually leading to stable illicitdrug abstinence and achievement of vital global health goals.

A Cycle of Options

The addiction treatment field generally embraces either an abstinence/drug-free or medication-assisted approach to recovery (Davison et al. 2006). However, these occur in a variety of settings, incorporating a smorgasbord of philosophies and techniques, with each varying in its effectiveness and scientific support.

While many professionals shun the use of medications for treating opioid addiction – using drugs to solve drug problems is futile, they say – many decades of research and clinical experience suggest otherwise. In the U.S., there are 3 MAT pharmacotherapies approved by the FDA for opioid addiction (CSAT 2005): a) methadone maintenance treatment (MMT), b) buprenorphine maintenance, and c) naltrexone maintenance. (LAAM, a long-acting form of methadone, is still approved, but currently unavailable.)

Abstinence and MAT philosophies are not mutually exclusive, if it is accepted that many persons in addiction recovery may

Continued on page 3

Events to Note

For additional postings, including international meetings, see: www.atforum.com

July 2007

World Federation for the Treatment of Opioid Dependence (WFATOD) – Inaugural Meeting July 1-3, 2007

Ljubljana, Slovenia Contact: www.seea.net/

American Mental Health Counselors Association (AMHCA) 2007 Annual Conference

July 16-20, 2007 Williamsburg, Virginia Contact: www.AMHCA.org

August 2007

American Psychological Association 115th Annual Convention

August 17-20, 2007 San Francisco, California Contact: www.apa.org/

September 2007

NAADAC/MTAADAC Join Together Conference

September 5-8, 2007 Nashville, Tennessee Contact: www.naadac.org

EUROPAD 3 ITALIA – Heroin Addiction: The Clinical and Therapeutic aspects. (7th Italian National Conference)

September 27-29, 2007 Pietrasanta, (Lucca), Italy, EU Contact: www.europad.org

October 2007

Missouri Addiction Counselors Association October 5-7, 2007

Lake of the Ozarks, Missouri Contact: www.mattc.org/maca/

American Psychiatric Association Institutes on Psychiatric Services

October 11-14, 2007 New Orleans, Louisiana Contact: www.psych.org

20th ECNP Congress of the European College of Neuropsychopharmacology

October 13-17, 2007 Vienna, Austria Contact: www.ecnp.eu/emc.asp

AATOD (American Association for the Treatment of Opioid Dependence) Conference

October 20-24, 2007 San Diego, California Contact: www.aatod.org

[To post your event announcement in AT Forum and/or our website, fax the information to: 847-392-3937 or submit it via e-mail from www.atforum.com]

Straight Talk... from the Editor

MMT Clinics Need Treatment Options Parity

The feature article on the MAT Cycle of Recovery in this edition of *AT Forum* outlines benefits of offering a choice of pharmacotherapies – including methadone, buprenorphine, and naltrexone – in methadone maintenance treatment (MMT) clinics. As full-service opioid treatment programs, or OTPs, such clinics should be ideal settings for providing these options.

Inequities By Regulation

However, when it comes to buprenorphine therapy, MMT clinics are at a distinct disadvantage, compared with office-based practitioners who are qualified to prescribe the medication for addiction. Current CSAT regulations require that MMT clinics apply the *same* Federal treatment standards to buprenorphine as for methadone.

This imposes rigid rules for patients receiving buprenorphine at MMT clinics in terms of their monitoring, counseling, and take-home dose privileges. Office-based practitioners are not constrained by such regulations, and can offer much more liberal approaches to buprenorphine treatment for addiction.

This inequity makes buprenorphine maintenance, as delivered by private practitioners, more appealing to many patients; including the wrong patients – those who actually need more intensive treatment.

MMT Clinics Offer Advantages

MMT clinics offer a wide range of addiction and psychosocial therapy services, which private practitioners do not typically provide. Most patients, even those with the mildest addiction severity, could benefit by entering an MMT clinic – if they had a choice of treatment providers offering equally appealing options.

In some geographic locales, there are no easily accessible MMT clinics, so it is believed that private practitioners prescribing buprenorphine therapy help fill "treatment gaps." Still, the more logical solution might be to have more MMT clinics where necessary.

According to AATOD (American Association for the Treatment of Opioid Dependence), changes liberalizing CSAT regulations governing buprenorphine therapy in MMT clinics are expected this year. This would help achieve some parity among treatment providers, and it would be a very positive step.

Economic Barriers to Progress

However, another barrier is the relatively high cost of buprenorphine medication,

which is up to 10 or more times greater than methadone. And, buprenorphine maintenance delivered in MMT clinics is usually not covered by public funding or private insurance; so, many patients who might benefit from buprenorphine simply cannot afford it.

Given a choice, considering current restrictions, patients with the personal financial resources go to private practitioners. However, in most cases, they will not benefit there from the assessments and multifaceted rehabilitation services they might need. And, they will not have access to methadone maintenance if it turns out to be more appropriate for their needs.

Therefore, as of yet, a nationwide system has not been created whereby persons with opioid addiction have easy and affordable access to the most effective and engaging therapies for their particular severity of addiction and psychosocial problems. Until this is accomplished, we cannot expect great progress in treating the alarming rise of opioid addiction in the U.S. population.

Stewart B. Leavitt, MA, PhD, Editor Editor@ATForum.com

Addiction Treatment Forum
P.O. Box 685; Mundelein, IL 60060
Phone/Fax: 847-392-3937
Internet: http://www.atforum.com
E-mail: Feedback@atforum.com

NEW SURVEY: Options in MMT

As a followup to the MAT Cycle of Recovery article in this issue, *please respond to the following survey questions:*

- Do you think buprenorphine and naltrexone should be offered in MMT clinics? ☐ Yes; ☐ No; ☐ Don't Know.
- Does your MMT clinic also offer...
 □ Buprenorphine; □ Naltrexone;
 □ Neither.
- If there were public funding or insurance coverage for buprenorphine and/or naltrexone therapy in MMT clinics would it be more appealing?
 Yes; □ No; □ Don't Know.
- 4. Are you responding as □ an MMT patient, or □ MMT clinic staff member or other?

There are several ways to respond to AT Forum surveys: A. provide your answers on the postage-free feedback card in this issue; B. write, fax, or e-mail [info above]; or, C. visit our website to respond online. As always, your written comments are important.

MAT-Recovery... continued from page 1

indefinitely require ongoing medications to help them remain illicit-drug free. Others may not require MAT at all, and some may begin with MAT and transition to a medication-free state. Therefore, it is worthwhile to consider opioid-addiction treatment as a cycle of options with mutually-inclusive roles in recovery.

MAT-Recovery Model

A "MAT Cycle of Recovery Model" portrays each of the 3 approved pharmacotherapies for opioid addiction as a possible treatment-entry point, depending on the individual's addiction severity (see Figure). Assessment of severity could take into account a number of considerations, such as (CSAT 2005):

- Performance on standardized questionnaires, such as the Addiction Severity Index (ASI) or others;
- Quantity and type of opioid abused eg, heroin, long- vs short-acting opioid analgesics;
- Frequency and route of opioid administration IV, oral, snorted, smoked;
- Estimated opioid tolerance (based on opioid type, quantity, frequency, and route of administration);
- Signs/symptoms of opioid withdrawal, if present;
- Concurrent illicit-drug and/or alcohol involvement;
- Co-occurring psychiatric and physical disorders;
- Prior addiction treatment episodes.

At present, there are no formal guidelines incorporating all of those factors for clearly defining severe, moderate, and mild levels of opioid addiction. However, experienced and competent addiction treatment staff can almost always estimate the relative level of addiction severity with some accuracy, following a thorough history-taking, and medical and psychosocial assessment of the patient.

Methadone, buprenorphine, and naltrexone each has a role (discussed below) in helping patients with severe, moderate, and milder forms of opioid addiction, respectively. Following treatment entry incorporating an appropriate type of pharmacotherapy, based on addiction severity, the MAT-Recovery Model suggests that a patient may transition from one therapeutic agent to another as progress is made in recovery. For example, an individual might cycle from methadone to buprenorphine to naltrexone, and then to drug free (meaning MAT-free in this case).

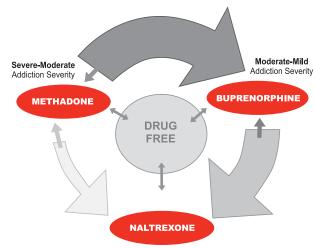
There also is the possibility that some patients may be able to transition directly from any MAT agent to a drug-free state, given sufficient time, motivation, and appropriate support. Or, they might remain on maintenance therapy with a particular agent for a lifetime of recovery.

A backward cycle also must be recognized. A person starting on buprenorphine may be unsuccessful and do better with MMT, or a person who "graduated" to naltrexone might relapse and benefit from a return to buprenorphine or MMT for a time.

This is a quite flexible approach – the opposite of a one-size-fits all model - and directed by individual patient needs. However, this MAT Cycle of Recovery Model may seem unrealistic, or at least idealistic, when considering how most addiction treatment programs function and are funded today.

Myth Of Detox As Treatment

Drug detoxification (detox) - or, medically supervised withdrawal in the case of prescribed medications - is often an entry requirement for abstinence-based addiction treatments. Detox often attracts opioid addicts who mistakenly believe that ridding their systems of the substances will allow them to remain drug free. For policy makers, funding agencies, and some treatment providers detox offers the enticing, though false, promise of a relatively quick and economical remedy.



Mild Addiction Severity & Special Populations (Prior opioid withdrawal or detox required)

Some clinicians have developed accelerated opioid detoxification methods using various degrees of sedation and the administration of drugs to provoke withdrawal. These rapid or ultra-rapid opioid detoxification procedures (called ROD or UROD, respectively) involve considerable risks and offer uncertain benefits, so they are not recommended (ASAM 2005).

Experts have repeatedly emphasized, and clinical evidence demonstrates, that detox alone incurs high rates of eventual relapse to opioid abuse. Most patients achieve little lasting benefit from the often arduous procedures (Davison et al. 2006).

In brief, detoxification is not addiction treatment (ASAM 2005), although agreement with this statement is not universal. Within the context of MAT for opioid addiction, medically supervised withdrawal of pharmacotherapy, at an appropriate time, could be a logical step within the scope of a long-term treatment and recovery process.

For example, a gradual tapering of daily methadone could set the stage for transitioning to buprenorphine maintenance, for which protocols have been described (Casadonte 2006). Then, tapering to full withdrawal of buprenorphine could be a prelude to naltrexone maintenance for a limited time.

Methadone "Gold Standard"

Based on its more than 40 years of success, methadone maintenance treatment (MMT) is accepted as the "gold standard" for opioid addiction treatment. Many articles in AT Forum through the years have discussed this in considerable detail (for example, see Leavitt 2004).

MMT could be effective for any level of opioid addiction, and it is essential for severe cases. As a pure opioid agonist, methadone can be gradually increased to whatever dose is most adequate for achieving desired therapeutic outcomes (such as, alleviating opioid withdrawal and stemming drug craving). And, its psychotherapeutic benefits for patients with depression and/or anxiety could be of vital importance (see "New Understandings of Methadone Benefitting Mood" in this edition of *AT Forum*).

However, methadone, like all other pharmacotherapies, is neither a cure for addiction nor guaranteed to reduce all substance abuse in all patients. According to some authorities, up to a quarter or more of MMT patients may not respond favorably during a single treatment episode (Gossop 2006); which is not to say that some other treatment modality could be more effective, or that a future MMT experience would not be successful.

The ultimate goal of MMT is rehabilitating persons with a complex mix of psychological, social, medical, and other problems. So, treatment programs must provide a range of support services

MAT-Recovery... continued from page 3

tailored to the unique needs of each individual.

A drawback of MMT for some patients is the highly regulated climate in which services are delivered. New patients are closely monitored

and must report for dosing on a daily basis, and attend weekly or more frequent counseling. Patients with opioid addiction of less severity and shorter duration may find this off-putting; for them, buprenorphine or naltrexone might be viable options.

Buprenorphine An Intermediate Solution

Like methadone, buprenorphine is an opioid analgesic. It was FDA-approved in 2002 (with and without naloxone as an added component) for treating opioid addiction.

Buprenorphine is unique in that it has a "ceiling" – above certain doses it ceases to have opioids effects. This can be helpful in preventing accidental overdose, and the addition of naloxone expectedly makes the medication less subject to abuse via IV injection. These safety factors led to buprenorphine's approval for prescribing by community-based physicians (CSAT 2005).

The federal government allows any specially-qualified physician, including those in MMT clinics, to treat up to 100 patients with buprenorphine for addiction. Up to a month's supply of the medication can be prescribed for each patient, including those new to treatment; although, when buprenorphine is prescribed in MMT clinics the same rules apply as for methadone maintenance (see editorial in this edition of *AT Forum*).

Patient entry criteria for buprenorphine therapy have not been fully specified. However, research evidence has demonstrated that buprenorphine is most applicable for patients with mild to moderate opioid addiction severity. In those who would require more than 60 mg/day of methadone for stabilization, MMT is favored over buprenorphine in terms of both treatment retention and illicit-opioid abstinence (Leavitt 2003, p. 12; Leavitt 2004).

As an addiction treatment modality, buprenorphine maintenance should be accompanied by nonpharmacologic support. This might include: group or individual counseling, compliance monitoring (eg, urine testing), contingency contracting, psychiatric assessments and treatment of comorbid disorders, and attention to physical health (Gossop 2006). Without such supports, as often occurs in private medical practices, the long-term benefits of buprenorphine for many patients must be questioned (Leavitt 2004).

Naitrexone Underrated, Underused

Naltrexone was developed in the mid-1960s as an opioid antagonist; that is, it blocks opioids from activating their receptors and having any effect. It helps eliminate opioid craving and drug-seeking behaviors, and was approved for that purpose by the U.S. FDA in 1984 (Leavitt 2002). An important benefit of naltrexone is in preventing relapse in patients who have achieved opioid abstinence.

Naltrexone is administered orally once daily, or less often in higher doses, and newer extended-release formulations last up to 28 days. It is generally safe, non-addicting, and can be prescribed by any physician, in any quantity, for distribution by local pharmacies. Patients must be completely withdrawn from opioids before naltrexone is started.

Research evidence shows that the success of naltrexone as an opioid addiction therapy depends on having a motivated and compliant patient. Consequently, it has been particularly effective in special populations – eg, airline pilots, healthcare professionals, lawyers, etc. – who are under pressure from licensing boards or other agencies to remain opioid free. Ongoing participation in

No single approach to MAT should be considered effective for everyone with an opioid addiction.

multifaceted programs of drug rehabilitation, with naltrexone as but one component, can be essential for long-term success (Davison et al. 2006; Leavitt 2002).

Naltrexone for opioid addiction has been largely underrated and

underused by addiction treatment programs. And, while it is possible, patients rarely transition successfully from MMT to naltrexone as a next step toward recovery (CSAT 2005). Cycling from buprenorphine to naltrexone could be more logical, but this does not appear to have been formally investigated as an option.

MMT Clinics As "One-Stop Shops"

No single approach to MAT should be considered effective for everyone with an opioid addiction. Improved clinical outcomes are rarely achieved simply by ingesting a daily dose of any medication (Gossop 2006), and effective MAT involves a combination of therapies.

In fulfilling their roles as opioid treatment programs (OTPs, CSAT 2005), MMT clinics could be ideal settings for achieving the MAT-Recovery Model, serving as "one-stop shops" in providing access to the 3 approved pharmacotherapies. Unfortunately, MMT programs face more constraining regulations than other providers.

In most cases, MMT clinics cannot lower the quality or quantity of services to offer more economical treatment with buprenorphine or naltrexone (Connock et al. 2007; Rosenheck and Kosten 2001). More support services for patients receiving buprenorphine or naltrexone could be ultimately beneficial for some patients, but requiring this only of MMT programs places them at a competitive disadvantage in most parts of the U.S. (also see editorial in this edition of *AT Forum*).

Consequently, at present, most MMT programs appear to be disinterested in actively or extensively providing other pharmacotherapies for opioid addiction. Hopefully, this trend may change in the future, benefitting both patients and their communities.

ASAM (American Society of Addiction Medicine). Public Policy Statement on Rapid and Ultra Rapid Opioid Detoxification. Updated December 2005.

Casadonte PP. Transfer from methadone to buprenorphine. PCSS, 2006. Available at: http://www.pcssmentor.org/pcss/documents2/PCSS_MethadoneBuprenorphineTransfer.pdf. Accessed 5/1/07.

Connock M, Juarez-Garcia A, Jowett S, et al. Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation. Health Tech Assess. 2007;11(9). Available at: http://www.hta.ac.uk/execsumm/summ1109.htm. Accessed 5/1/07.

CSAT (Center for Substance Abuse Treatment). Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2005. Available at: http://www.atforum.com/SiteRoot/pages/addiction_resources/MAT-TIP_43-MMT_Guidelines2005.pdf. Accessed 5/1/07.

Davison JW, Sweeney ML, Bush KR. Outpatient treatment engagement and abstinence rates following inpatient opioid detoxification. J Addict Dis. 2006;25(4):27-35.

Gossop M. Methadone: Is it enough? Heroin Addict Relat Clin Probl. 2006;8(4):53-64. Available at: http://www.atforum.com/pdf/europad/HeroinAdd8-4.pdf. Accessed 5/1/07.

Leavitt SB. A Community-Centered Solution for Opioid Addiction: Methadone Maintenance Treatment (MMT). AT Forum [special report]. 2004. Available at: http://www.atforum.com/SiteRoot/pages/addiction_resources/com_ctrd_mmt.pdf. Accessed 5/1/07.

Leavitt SB. Addiction recovery: New understandings of an old concept. AT Forum. 2005(Fall);14(4). Available at: http://www.atforum.com/SiteRoot/pages/current_pastissues/fall2005.html#addictionrecovery. Accessed 5/2/07.

Leavitt SB. EBAM (Evidence-Based Addiction Medicine) for Practitioners. AT Forum [special report]. 2003. Available at: http://www.atforum.com/SiteRoot/pages/addiction_resources/ EBAM_16_Pager.pdf. Accessed 5/1/07.

Leavitt SB. Naltrexone in the Prevention of Opioid Relapse. AT Forum [special report]. 2002. Available at: http://www.atforum.com/SiteRoot/pages/addiction_resources/NTX-Opioid.pdf. Accessed 5/1/07.

Nature Neuroscience (multiple authors). Focus on Neurobiology of Addiction [special issue]. Nature Neuroscience. 2005(Nov);8(11). Available at: http://www.nature.com/neuro/journal/v8/n11/index.html. Accessed 5/1/07.

Rosenheck R, Kosten T. Buprenorphine for opiate addiction: potential economic impact. Drug Alcohol Depend. 2001;63:253-262.

Practice Pointers

New Understandings Of Methadone Benefitting Mood

Co-occurring opioid addiction and mental disorders are common in patients entering methadone maintenance treatment (MMT). Reports have varied, but, overall, nearly three-quarters of MMT patients may have experienced a mental illness of some sort during their lives, with more than half suffering from a mood disorder, such as depression or anxiety, when entering addiction treatment.

In the Winter 2004 edition of *AT Forum* (Vol 8, #1), an article titled "Methadone & Mood" described research demonstrating a stabilizing effect on mood of *adequate* methadone dosing. Furthermore, evidence was presented suggesting that methadone has pharmacologic qualities of antidepressant and anxiety-reducing (anxiolytic) medications,

which could be of benefit for many patients.

Taking this a major step forward, Peter L. Tenore, MD – a practitioner with the Albert Einstein College of Medicine, Division of Substance Abuse, Department of Psychiatry, Bronx, NY – has thoroughly examined available research evidence to create the most comprehensive and convincing review to date demonstrating methadone's potential benefits in diminishing mood disorders among MMT patients. His paper, "Psychotherapeutic Benefits of Opioid Agonist Therapy," is in review for publication in a major addiction treatment journal. Some highlights and conclusions of that paper, made available in advance exclusively to *AT Forum*, are presented here.

Endorphin Supplementation Therapy

Tenore found that opioids have been widely used for various disorders, dating back to 3400 BC. In addition to their pain-relieving qualities, for centuries opioid mixtures also served to treat a variety of psychiatric disorders. However, with the development of newer antidepressant and anxiolytic medications in the early 1950s, so-called "Opium Cures" were abandoned.

Still, research on the antidepressive and anxiolytic qualities of opioids has continued extensively. The story begins with endorphins, naturally-occurring neurochemicals that attach to opioid receptors and have been described as the "brain's own morphine." In the depressed brain, a relative deficiency of endorphins indirectly influences a decrease in another brain chemical, dopamine.

Dopamine is a key messenger, or neurotransmitter, in the brain's pleasure-reward centers. Among other things, diminished dopamine results in a loss of pleasure or joy in life (called, decreased hedonic tone), which is characteristic of depression.

In the classic "Opium Cure," an opioid supplement overcomes the brain's deficiency of endorphin, which in turn releases more dopamine, restores neurochemical balance, and alleviates depression. Tenore discovered convincing clinical research evidence of this beneficial opioid effect; surprisingly, with depressive symptoms often relieved much more rapidly by opioids than antidepressant medications, such as fluoxetine or amitriptyline.

A number of controlled clinical trials of buprenorphine in depressed patients, who were either nonaddicted or addicted to other opioids, found potent beneficial effects in relieving depression. And, an equivalent or greater antidepressant effect was found for methadone.

Further research demonstrated that combining antidepressant-



specific medications with methadone conferred no added benefit attributed to those drugs alone. Methadone was a potent antidepressant in and of itself. And, significantly, the positive effects on mood were irrespective of reductions in illicit drug use during therapy.

Finally, according to past research, methadone can also lower excessive serum cortisol levels. Cortisol, a glucocorticoid hormone, is released by the adrenal glands in response to stress. Endorphins play a role here by regulating the release of cortisol, thus helping to calm down the stress response when it gets out of control.

When there is insufficient endorphin, the stress response can run amok, which can result in

anxiety and, later, depression possibly brought on by mental exhaustion. Clinical investigators demonstrated that relatively small amounts of methadone, as a surrogate for the lacking endorphin, could rapidly decrease elevated blood cortisol and relieve symptoms of anxiety and depression.

Based on these considerable research findings, Tenore concludes that, in the treatment of anxiety or depression, methadone, buprenorphine, and other opioids might be viewed at least in part as "endorphin supplementation therapy."

Methadone Boosts Mood-Stabilizing Serotonin

Looking beyond endorphin supplementation, research has demonstrated that opioid medications alter a number of other brain chemicals and systems affecting mood regulation. Among these are serotonin, catecholamines (epinephrine/norepinephrine), and the glutamate-NMDA system – all of which play a role in mood disorders and are targets of psychiatric medications.

For example, tricyclic antidepressants (TCAs, such as, amitriptyline or imipramine) alleviate depression (and anxiety) by increasing the availability of catecholamines, dopamine, and serotonin in the brain. Similarly, methadone has been shown to activate typical sites for TCAs and increase catecholamines, according to Tenore's review.

Along with that, methadone was found to have SSRI (selective serotonin reuptake inhibitor) capabilities in raising brain serotonin levels, thereby restoring deficiencies of this neurochemical. Serotonin – or, 5HT as is it sometimes known – is vital for regulating mood, anger, aggression, sleep, and appetite. The SSRI medications, and certain opioids like methadone, act to block the reabsorption of naturally-occurring serotonin, so the brain chemical can work longer and more effectively.

Tenore notes that when methadone is combined with certain SSRIs – such as fluoxetine, paroxetine, and sertraline – there can be a drug interaction resulting in up to a 26% increase in serum methadone levels. This may serve to further enhance methadone exposure and increase its beneficial psychiatric effects in making serotonin more available.

However, if methadone is administered with certain other sero-tonin-enhancing medications (eg, monoamine oxidase, or MAO, inhibitors), excessively high, potentially toxic serotonin levels might result.

MAO is a brain chemical that breaks down serotonin; so, by inhibiting MAO, more serotonin can be made available. It is

believed from the research that methadone, itself, can beneficially inhibit MAO; but, combining methadone with a MAO-inhibitor medication can result in too much of a good thing (too much serotonin), so the combination should be avoided.

Turning Down the Neuro-Excitatory Volume

Considerable research has demonstrated that methadone, as well as buprenorphine, also counteracts serotonin-diminishing effects exerted by the glutamate-NMDA receptor system. NMDA (N-Methyl d-Aspartate) receptors, located throughout the brain, help regulate pain perception and mood, among other functions.

When NMDA receptors are activated by the neurochemical glutamate, the production of new serotonin is squelched and existing serotonin is broken down faster. As noted above, abnormally decreased serotonin levels strongly influence symptoms of depression and anxiety.

Additionally, excessive effects of glutamate can increase the stressful excitation of neurons, the primary functional cells in the brain. This harmful action of glutamate can contribute to anxiety, seizures, and obsessive-compulsive disorders.

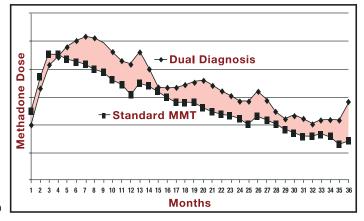
Many opioids function both to reduce glutamate effects and as NMDA antagonists, according to the research evidence. Opioids do this by blocking (antagonizing) glutamate from activating the NMDA receptors, and thereby diminish the serotonin-reducing and other harmful effects. In this regard, methadone was found to be up to 16 times more potent than morphine, exerting significant antidepressive and anxiolytic effects as an NMDA antagonist; whereas, buprenorphine effects were about equal to morphine.

Higher Stabilizing Methadone Doses Needed

In examining the research literature on dual-diagnosed patients in MMT – those with opioid addiction and mood disorder – Tenore found that the common myth about psychiatric comorbidity increasing treatment resistance was not confirmed. In fact, patients with mental disorders can and do respond well to methadone-maintenance therapy, as evidenced by longer treatment-retention and reductions in substance abuse.

However, Tenore points out that MMT patients with psychiatric disorders have been repeatedly shown in clinical studies to require *higher doses of methadone for stabilization*. For example, during a 36-month period Maremmani and colleagues in Italy compared the methadone requirements in patients with dual-diagnoses to those of patients with only opioid addiction who received "standard MMT" (see *Graph*).

Beyond an initial induction period, patients with dual disorders required 40% higher methadone doses for stabilization; a significant difference that continued throughout the 3 years, even though it was possible to gradually lower doses over time. Furthermore, it took 4 months longer for the dual-diagnosed patients to reach stabilized dosing levels (7 mo. vs 3 mo.) before doses



Dual-diagnosed patients should be educated on the psychiatric benefits of methadone, and not be fearful of increasing doses or remaining in treatment for prolonged periods.

could be tapered back to any degree.

The higher doses in dual-diagnosed MMT patients, which have been extensively documented and are often much greater than in patients with only addiction, probably reflect the need for methadone's beneficial effects on multiple neurobiological systems affecting mood.

Dual-diagnosed patients receiving effective MMT have been shown to reduce psychiatric-disturbance scores to levels of patients having only opioid addiction; to improve treatment retention to exceed that of single-diagnosis patients; and, to improve their addiction severity index scores compared with baseline in every domain.

Furthermore, these benefits of methadone appear to be independent of continued substance abuse. However, Tenore emphasizes, dual-diagnosed patients receiving adequately *high* methadone doses do decrease illicit drug use to the same extent as any other MMT patients who are provided adequate methadone doses.

The many neurobiological benefits of methadone also help explain why many patients prefer not to completely withdraw from the medication. Tenore describes the case of a patient maintained on 60 mg/day of methadone, with no prior anxiety disorder, who tapered down to 12.5 mg/day. At that point, severe anxiety emerged. When the methadone dose was raised to 25 mg/day, anxiety symptoms were relieved within 2 days.

Methadone may have vital beneficial effects even at the lowest doses. Patients with underlying psychiatric vulnerabilities could find it practically impossible to *completely* discontinue methadone (or buprenorphine) without substitute mood-stabilizing medications and/or intensive psychosocial support.

Minimizing Human Suffering

In summarizing for *AT Forum* the findings expressed in his review paper, Tenore observes, "The extensive research that I examined collectively and convincingly demonstrates that MMT patients can benefit from the effects of many different, potent psychiatric medications within a single agent – methadone; provided it is administered in adequately higher doses."

"In fact, in our experience, certain patients who repeatedly request increases in methadone doses may actually have psychiatric diagnoses that were undetected by clinic staff."

"It is clear that methadone – as well as buprenorphine and other opioids to some extent – supply depressed and anxious brains with the serotonin, dopamine, and catecholamines that they are lacking," he continues. "At the same time, these opioids help control the stress response and block mood-disrupting glutamate-NMDA and/or cortisol effects."

He concludes, "Dual-diagnosed patients should be made aware of the multiple psychiatric benefits of methadone, and not be fearful of increasing doses or remaining in treatment for prolonged periods. Methadone doses in these individuals should be titrated upward in an aggressive, but not reckless, manner to prevent early treatment drop-outs, to relieve psychiatric symptoms, to decrease illicit opioid use, and to minimize human suffering."

[NOTE: Tenore's paper contains nearly 90 citations of research resources, which may be consulted once it is published. Meanwhile, inquiries may be sent to him at: ptenore@dosa.aecom.yu.edu.]

Current Comments

TOTA: Texas Opioid Treatment Alliance Involving MMT Patients in Their Treatment & Recovery

Patients at TOTA-member

clinics are empowered

to take more personal

responsibility for their

treatment and ongoing

recovery from addiction.

It seems to make good sense that individuals entering methadone maintenance treatment (MMT) programs should be engaged as active participants, with a say in their treatment and goals for recovery. Yet, in many MMT clinics throughout the United States that is not the case; treatment is something done to patients who have very little empowerment.

To counter that, TOTA – the Texas Opioid Treatment Alliance - was started in 2000 by Tom Payte, MD, Steve Tapscott, MA, and Kim Comstock, MEd, LPC. Founded as a private, nonprofit corporation, TOTA's primary goal is to increase the availability, affordability, and quality of MMT care in Texas. In relatively few years, the group has established a significant

MMT-provider network, making treatment available to indigent persons and helping member clinics establish Patient Advocacy Groups, or PAGs, according to Kirk Broaddus, LCSW.

He is Chairman of the TOTA 8-person Board of Directors, which includes MMT providers and, uniquely, a majority of Board members are MMT patients. Broaddus is both an MMT patient and an addiction counselor at MARS (Maintenance and Recovery Services) clinics in Austin, Texas. The Board oversees a \$750,000 annual grant coming from the Texas Department of State Health Services, which is earmarked primarily for indigent patients who otherwise would be unable to afford treatment. Headquarters for the Alliance is in Houston, where a full-time staff helps manage grant funds and other administrative matters.

Patient-Provider Parity is a Key Objective

An important objective in founding TOTA is achieving patientprovider parity, both on the Alliance Board and within member clinics, notes Comstock, who is Director of the MARS clinics. "A primary way of achieving this parity is by establishing a PAG at each member clinic," she says. These groups involve patients in many aspects of the clinic, empowering them to take more personal responsibility for their treatment and for their ongoing recovery from opioid addiction.

She concedes, however, that this is a shift in philosophy for some MMT clinic operators, who are used to exerting full control. Having patients involved in determining their individualized treatment and in advocating for better treatment can require a more open-minded approach and willingness to change.

PAGs Benefit Patients

According to Broaddus, PAGs help provide financial assistance to needy patients through their own fundraising efforts. For example, he says that raffles are popular fundraising events, with the winner receiving a week's free treatment and the balance of funds going to support indigent patients.

Each TOTA-member clinic may also participate. For every dollar raised by PAG fundraising efforts, the provider is encouraged to contribute a matching amount.

Although this places some financial responsibility with providers, Broaddus observes it is a win-win situation. By PAGs providing financial assistance to patients, with matching support from providers, it helps MMT clinics retain those patients in ongoing addiction treatment until they can pay their own way.

PAGs also help organize Methadone Anonymous groups and special patienteducation programs. In some cases, Broaddus notes, PAGs have been active in getting methadone doses raised to

more adequate levels, in part by pro-

viding research evidence to clinic staff. Much of that educational material came from Addiction Treatment Forum articles.

As a program operator, Comstock agrees that well-run PAGs help bring new ideas to the attention of clinic staff. "At one time we were using serum methadone levels to guide dosing, which was not very helpful. Today, we use close observation of dose effects and patient feedback to arrive at adequate dosing."

TOTA Benefits MMT Programs

TOTA presently has as members about 28% of the 72 MMT programs in Texas. Comstock says their goal is to enroll half of all programs in the state, at which point TOTA can affiliate with AATOD (the nationwide American Association for the Treatment of Opioid Dependence).

This year, during their membership drive, there is no cost to join TOTA, Broaddus adds. Newly-joining MMT programs are provided training in creating PAG groups that are structured to meet the individual needs of each participating MMT clinic.

In some cases, new TOTA members are provided seed money to help them jump-start the PAG fund for needy patients. The major purpose of the yearly grant that TOTA receives from the state is to help provide free treatment slots at member clinics for patients needing financial assistance.

Comstock explains, "A patient coming to a TOTA-affiliated clinic, and meeting appropriate entry criteria, can fill one of those funded slots. This approach provides patients some choice in where they go for MMT and it encourages excellence in our members' clinic operations to attract those patients."

Another goal of the funding grant TOTA receives is to increase MMT availability throughout the state, particularly by expanding treatment availability to underserved rural areas, she continues. So, along with enrolling more members, TOTA's also hopes to increase the territory it serves throughout Texas.

In the past, TOTA also has sponsored state-wide conferences for member programs, providing educational opportunities for clinical staff, as well as PAGs and all other patients. Along with their educational outreach programs, TOTA has advocated for more harm reduction efforts in Texas, such as needle exchanges.

As Comstock observes, "Not all patients immediately stop using illicit drugs, and we need to help keep them safe and free from needle-borne diseases like HCV and HIV. This will eventually make for healthier patients in addiction recovery."

Lastly, both Comstock and Broaddus emphasize that TOTA is not a restrictive alliance. An MMT program can belong to TOTA as well as other organizations of interest to them. The program's willingness to follow TOTA philosophies of involving patients in their recovery by establishing and supporting PAGs, and by striving for excellence in the delivery of opioid-addiction treatment services to all who need it is most important.

As a followup, readers were surveyed on how they go about fighting against such myths, if at all. There were 203 responses to the survey; two-thirds from methadone maintenance treatment (MMT) clinic staff and a third from patients.

What Should Be Done?

Asked what MMT staff or patients should do to counteract addiction myths in the media, 67% of respondents said complaint letters should be written to publishers and news editors; 11% said news media spreading myths should be boycotted; 29% suggested protesting to political leaders; 3% suggested doing nothing; and, 43% had other suggestions. Multiple responses were allowed, so the total is more than 100%.

The most common "other" suggestions included becoming involved in patient advocacy and education projects.

Was Action Taken?

Respondents also were asked if they had ever personally taken action on what they thought should be done. Most – about 6 out of 10 – indicated that they had done so, with clinic staff and patients almost equal in this regard (see *Graph*).

It might be expected that persons feeling strongly about how addiction treatment is negatively portrayed in the media would be more likely to respond. So, it is surprising that 40% said they took no action.

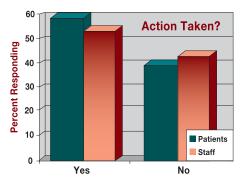
What Was Done?

Those responding that they had taken some action were asked what they did. About one third of those providing information on this question said that they wrote letters to media editors or political leaders. A few said that they spoke directly with those opinion leaders and decision-makers.

By far, the most common theme in the responses was "education." Whether one-on-one, or in groups, a number of persons indicated that they had tried to educate others about the nature of addiction and benefits of MMT.

However, as one patient pointed out, "Unfortunately, my efforts were largely ignored. There would be more impact if addiction treatment professionals become actively involved."

A staff member observed, "Before social and political change can come about, doc-



tors themselves must start viewing addiction as a medical disorder. Education on this needs to be started during their medical training."

And, a patient acknowledged, "The news media have promoted misinformation, scare tactics, and negative sensationalism for so long that they are reluctant to change. Addicts running wild stories sell more newspaper than tales of recovery."

Education Resources Available

One staff member said she works with community groups to educate them and overcome stigma attached to MMT. To help her and others in such efforts, at the ATForum.com website there are two papers available.

A Community-Centered Solution for Opioid Addiction – Methadone Maintenance Treatment (MMT) provides evidence on the benefits of MMT. It is available at: http://www.atforum.com/SiteRoot/pages/addiction_resources/com_ctrd_ mmt.pdf

Methadone Maintenance Treatment in the Criminal Justice System focuses on scientific evidence demonstrating the benefits of MMT within court, jail, and prison settings. It is available at: http://www.atforum.com/SiteRoot/pages/addiction_resources/MMTCJS204-06-06Revision2.pdf

ADDICTION TREATMENT

Forum

is published quarterly by:

Clinco Communications, Inc.

P.O. Box 685 Mundelein, IL 60060

Phone/Fax: 847-392-3937

Editor: Stewart B. Leavitt, PhD

Publisher: Sue Emerson

© 2007 Stewart B. Leavitt, PhD

Addiction Treatment Forum is made possible by an educational grant from Mallinckrodt Inc., a manufacturer of methodone and naltrexone. All facts and opinions are those of the sources cited. The publishers are not responsible for reporting errors, omissions or comments of those interviewed.

RETURN SERVICE REQUESTED

P.O. Box 685 Mundelein, IL 60060 FORUM

U.S. POSTAGE

PAID

PALATINE, IL

PERMIT # 7117