

# Forum

THE QUARTERLY NEWSLETTER FOR CLINICAL HEALTH CARE PROFESSIONALS ON ADDICTION TREATMENT

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## ***Methadone does not have harmful effects on immune system function in MMT patients***

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### **Clinical Concepts**

#### **Methadone & The Immune System**

The human immune system comprises a virtual army of specialized cells and substances poised to attack foreign chemicals, objects, and microorganisms.

Several types of white cells – B-cells, varieties of T-lymphocytes (e.g., CD4 cells), NK (natural killer) cells, and others – stand guard. Various antibodies, which are proteins that attack foreign substances and help mobilize white cells, circulate throughout the body.

Research has demonstrated that opioids, including methadone, interact with the immune system.

Is this harmful or helpful?

#### **Abnormalities Observed**

The immune system operates in delicate balance. A weakened, deficient immune response makes the person susceptible to infections or acceleration of existing disease, such as human immunodeficiency virus (HIV) infection. An overactive immune system may result in allergies or autoimmune diseases.[1]

Abnormalities have been observed in the immune responses of intravenous (IV) heroin abusers since the 1950s, long before the HIV epidemic. These included diseased lymph glands (once called “addict’s nodes”), elevated white cell counts, increased antibodies, and false-positive tests for syphilis, rheumatoid arthritis, and other illness.[2,3]

During ongoing methadone maintenance treatment (MMT) the abnormalities were moderated or eliminated; although, it could take a number of years.[2,4] Some researchers also noted that immune dysfunction was more last-

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### **Liver Disease in MMT: Treatment & Transplant**

#### **Part 3: MMT Clinics' Roles in HCV Therapy**

The second article in this series [1] expressed hopeful optimism for methadone maintenance treatment (MMT) patients with hepatitis C (HCV). Treatments continue to improve, offering better outcomes for those patients who receive and complete HCV-medication regimens.

Unfortunately, it appears that a proportion of patients do not become eligible for treatment, some are denied treatment, and others are unmotivated to pursue available therapy. Consequently, many are likely to develop chronic, life-threatening liver disease.[2]

What can MMT clinics do to help?

#### **Daunting Obstacles**

At Aegis Medical Systems, which serves 5,000 MMT patients throughout California, **Allan J. Cohen**, MA, MFT, Director of Research and Development, estimates that 85% of patients are at various stages of HCV infection, with a great many needing treatment.

Similarly, at the 14th Street Clinic in Oakland, CA, **Judith Martin**, MD, Medical Director, estimates that more than 90% of their 400 MMT patients are HCV-positive.

Martin says that at patient intake, and then during yearly followup exams, liver functions are assessed to detect any problems. The county does basic testing for HCV, which is on a voluntary and confidential basis.

However, the staging of infection, typing, and viral-load testing in those who are positive for HCV antibodies is difficult. Martin says that her clinic can-

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## Events to Note

For additional postings & information, see:  
[www.atforum.com](http://www.atforum.com)

### JULY 2002

#### NAADAC 26th Annual Conference on Addiction Treatment

July 3-6, 2002

Boston, Mass.

Contact: 800-548-0497 or 703-741-7686

#### 1st Ann. New England School for Treatment of Opioid Dependence

July 7-11, 2002

Newport, Rhode Island

Contact: Jessica Gogan, 207-621-2549;

[www.neias.org](http://www.neias.org)

#### ASAM Forensic Issues in Addiction

July 18, 2002

Washington, DC

Contact: 301-656-3920; [www.asam.org](http://www.asam.org)

#### ASAM Medical Review Officer Training Course

July 19-21, 2002

Washington, DC

Contact: 301-656-3920; [www.asam.org](http://www.asam.org)

#### 28th School of Alcohol & Other Drug Studies

July 21-26, 2002

Columbia, South Carolina

Contact: Joel Urdang, 803-896-5561;

[www.daodas.state.sc.us](http://www.daodas.state.sc.us)

### AUGUST 2002

#### 31st UCSD Summer Clinical Institute in Addiction Studies

August 19-22, 2002

San Diego, CA

Contact: Tracy Wilson, 858-551-3182;

[www.atfc.ucsd.edu](http://www.atfc.ucsd.edu)

#### Annual APA (Amer. Psychological Assn.) Convention

August 22-25, 2002

Chicago, IL

Contact: Candy Won, 202-336-6020;

[www.apa.org](http://www.apa.org)

### OCTOBER 2002

#### ASAM Review Course in Addiction Medicine

October 24-26, 2002

Chicago, Illinois

Contact: 301-656-3920; [www.asam.org](http://www.asam.org)

#### Psychiatric & Mental Health Congress

October 28-31, 2002

Las Vegas, Nevada

Contact: CME, Inc., 800-933-2632 or 949-

250-1008

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A.T.F.

## Straight Talk... from the Editor

### Methadone's Bench-To-Bedside Disconnect

Since its development in the 1940s, methadone probably has been studied more than any other drug in medicine. Yet, to this day, researchers continue to announce methadone effects in the laboratory that conflict with clinical experience.

That is, the way methadone appears to work on the laboratory bench – in test tubes or animals – often does not accurately predict its actions in methadone maintenance treatment (MMT) clinic patients; “at the bedside,” so to speak.

#### “Interesting” Results

It turns out that methadone, as well as other opioid agents, added in sufficient quantity to a great many types of cells or tissues may produce “interesting” results worthy of at least a conference abstract presentation or, these days, a press release. Unfortunately, findings of most interest to the news media are unfavorable toward methadone, serving to perpetuate the stigma and misunderstandings surrounding this medication.

While we cannot demand more responsible reporting from journalists, perhaps scientists should be held accountable for more prudent presentations of their research findings and conclusions in the first place.

#### Misleading Conclusions

During just this past year, there were assertions from researchers raising concerns separately about methadone's effects on heart rhythm and the immune system. The first allegation was discussed and set straight in *AT Forum* last fall (Vol. 10, No. 4) and in our special report, “Does MMT Affect Heart Health?” – both available at [www.atforum.com](http://www.atforum.com). The second topic, immune function, is explored and demystified in this current edition.

The experiments behind those assertions were typical of research conducted on isolated cells or tissues, sometimes taken from animals. They do not fully account for how methadone is metabolized and works in the human body, and particularly in patients receiving long-term, stable, methadone-maintenance doses.

After making statements about how the results of their laboratory experiments likely portend serious consequences for MMT patients, investigators sometimes follow with disclaimers like “...no compelling clinical evidence sup-

ports our conclusions.” This is usually followed by a call for further research on the subject.

#### Overlooked Disclaimers

Unfortunately, the disclaimers are often “overlooked” by news reporters and others. Had they looked at the research more carefully or more extensively examined the clinical literature on methadone, they would have realized that the preponderance of evidence, during many years of investigation, is often contrary to the latest revelations from the laboratory.

Basic laboratory science – bench work – can be invaluable for guiding intelligent clinical studies in humans; but the ultimate test is in patients at the bedside. This is true for any medication.

When it comes to methadone, it seems accurate to state: it can be harsh on cells and tissues in test tubes, and it's tough on rats and pigs, but it's safe and effective in people when used appropriately as part of an accredited MMT program.

#### Survey – HCV Support

As a survey follow-up to our article in this edition on how MMT clinics can support patients with HCV, please respond to the following questions:

1. What percentage of patients at your MMT clinic with HCV are receiving antiviral treatment for it? \_\_\_%
2. Does your MMT clinic have support programs for patients with HCV? \_\_\_ yes; \_\_\_ no; \_\_\_ don't know
3. Are there HCV-support groups in your community? \_\_\_ yes; \_\_\_ no; \_\_\_ don't know

*There are several ways to respond: A.* Provide your answers on the postage-free feedback card in this issue; *B.* Write or fax us [see info below]; or, *C.* Visit our Web site to respond online. As always, your *written comments* are important for helping us discuss the results in an upcoming issue.

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A.T.F.

# Practice Pointers: Dealing with “Situational Abstinence Syndrome”

Unexpectedly, a patient long stabilized on methadone maintenance treatment (MMT) for months or even years complains of insomnia, unusual sweating, joint aches and pains, or constant sniffing. The patient requests a methadone dose increase.

What’s happening here?

## Common Occurrence

This is a common occurrence, according to Edwin Salsitz, MD, Director of Methadone Medical Maintenance at Beth Israel Medical Center, New York. Unfortunately, asking for a dose increase is often viewed as a sign of instability in the person’s recovery.

A first question asked of the patient by clinic staff might be, “What did you take last night to bring this on?” But that would be a wrong reaction, Salsitz believes. There could be a number of reasons behind this, once a bout of flu or other disorder is ruled out.

Salsitz notes that these surprising withdrawal symptoms represent what might be called “Situational Abstinence Syndrome.” It is similar to “breakthrough” pain in someone on a previously adequate regimen of analgesics, or unexplained blood pressure elevation in a patient stable on antihypertensive medicine.

## Problematic Stress

A major culprit behind situational abstinence syndrome is stress. In this regard, it is absolutely critical that the symptoms are considered in the total context of the patient’s life.

Traumatic events, such as the tragedies of last September, death of a loved one, divorce, loss of a job, and many others can create added stress. Salsitz notes that, on a physiologic level, substance-addicted persons overreact to stress. Although, MMT generally stabilizes the stress-response system, methadone still may be metabolized faster during times of increased stress.

Also, since methadone fills opioid receptors in the brain and replaces the natural endogenous opioid system, the body may not produce sufficient endorphins to comfortably handle added stress. Hence, the patient may feel drug hunger or withdrawal symptoms that can be resolved by an increased methadone dose. [See also, “Addiction and the Duress of Stress” in *AT*

*Forum*, Summer 2000, Vol. 9, No. 3, pp. 3-4.]

Salsitz believes a dose increase in this circumstance should be viewed as more than just a temporary fix. For one thing, the effect is not immediate; it will take about five days to achieve a steady-state blood level at the new dose.

In some cases, a dose increase is all that is required for the patient. For others, additional counseling and support services might be appropriate. However, Salsitz stresses, a request for a dose increase does not necessarily indicate any behavioral instability and patients should not be penalized, such as being denied earned privileges or take home doses.

## Innate Senses

“I put myself in the patient’s position,” Salsitz says. “Most people have requested a new medication, or extra medicine, at some time in their lives to deal with unusual stress or physical symptoms. So, what’s wrong with an MMT patient requesting extra methadone?”

He believes that long-term patients develop an innate sense of when an increased methadone dose will help them continue to feel and function normally. For example, he had one patient whose sister committed suicide. “This was very traumatic for the patient,” Salsitz recalls. “She had been stable on 80 mg/day of methadone but immediately asked for an increase to 100 mg/day, which is where she comfortably stayed.”

## Flexible Options

Causes other than stress also need consideration. For various reasons – such as, changes in medication, lifestyle, or diet – a patient may start to metabolize methadone differently. The person may complain primarily of problems sleeping or awakening too early without feeling rested.

Increasing the methadone dose in response to these symptoms might not be the best solution. It could be better for the patient to take most of the dose in the morning as usual and the remainder in the evening just before retiring.

Salsitz also has observed that, in those persons who become fatigued during the afternoon, taking part of the methadone dose at that time perks them up. He acknowledges that this is counterintuitive, since one might expect that methadone

itself would be sedating. The unexpected refreshing effect might have something to do with substituting for an endorphin boost, much like the “second wind” that many people get late in the day by having a candy bar or cup of coffee.

The important thing to Salsitz is that patients should have the option, while remaining at the same total daily methadone dose, of experimenting with taking different proportions during the day. This is done with many other medications, to even-out drug actions or to minimize side effects.

Admittedly, this sort of dosing flexibility becomes challenging for those patients who must attend the MMT clinic daily to take their full methadone dose under observation. Yet, it is something clinic staff should keep in mind as a goal to help overcome unexplained situational abstinence syndrome.

*In terms of how methadone is metabolized and works in the body, there is no reason that once-daily dosing would be best or optimal for every patient.*

## Compassionate Attitudes

Salsitz concedes that his approach, based on his experiences in office-based methadone medical maintenance, applies to previously stable, treatment-compliant patients. These patients are viewed and treated as any other persons with chronic illness who have valid reasons behind their requests for additional medication. “Perhaps, extra methadone isn’t always the answer, but there is definitely something in these persons’ lives needing attention,” he says.

Regrettably, federal regulations in the past have not always fostered favorable doctor-patient relationships, he notes, especially when it comes to methadone prescribing. Even with the new, enlightened regulatory approach, there is still the question of whether MMT medical staff will take the time to be more understanding and flexible in their approaches.

Still, the average clinic can indeed gravitate toward more of a medical maintenance model, Salsitz believes. “This may not be appropriate for every patient, but a lot of it has to do with a compassionate attitude emphasizing individualized patient care.” It is totally in keeping with the spirit of the new federal regulations.

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ing in patients attending programs prescribing lower methadone doses.[3,5]

### Indirect Opioid Effects

The immunologic derangements seen in opioid injection-drug users (IDUs) were believed due to both direct and indirect effects.[4,6] See Table. Indirectly, many of the immune system alterations resulted from repeated injections of adulterated substances, using contaminated equipment (non-sterile needles), and frequent infectious complications.

The IDU lifestyle is usually characterized by stress, poor nutrition, altered sleep patterns, and use of multiple drugs of abuse.[4] Successful rehabilitation in MMT would eliminate injection-opioid use and improve lifestyle factors.

However, continued drug abuse during MMT can be problematic, as both cocaine and alcohol can significantly alter immune function.[6] Recent laboratory research also has found that cocaine increases HIV growth and might contribute to progression to AIDS.[7]

There also are indirect effects of opioids acting through the neuroendocrine system that controls the body's response to stress. The immune system responds negatively to stress and research has demonstrated that stress reactions become normalized during long-term MMT.[4,6,8]

### Direct Opioid Effects

Heroin, morphine, methadone, as well as endogenous (naturally occurring) opioids like endorphins, may act directly on immune system cells, and research has uncovered interesting qualities of cell function:

- White blood cells (lymphocytes) in heroin addicts have a reduced ability to fight invasive agents. During MMT, this trend typically reverses as lymphocyte response normalizes.[6]
- Certain immune cells, such as T-lymphocytes, have opioid receptors on their surface; hence, opioids would be expected to affect these cells.[3,9-11]
- T-lymphocytes also produce their own endogenous opioids – endorphins and enkephalins – as part of their self-regulatory function.[3] So, opioids are not necessarily foreign to these cells.
- Immune cell function is negatively affected more by acute phases of opioid withdrawal or loss of tolerance than by steady-state opioid dose conditions. IDUs periodically experiencing withdrawal states are thus at risk; whereas,

### Factors Contributing to Immune System Abnormalities in IDUs [4]

Unsterile needles and adulterants in injected drugs.

Infectious diseases of various types.

Lifestyle (stress, poor nutrition, altered sleep patterns).

Polydrug abuse (eg. cocaine, alcohol, benzodiazepines).

Altered stress response.

Direct effects of opioids on immune system cells.

the steady-state opioid tolerance in MMT patients would avoid such conditions. [3]

- New research suggests that certain immune cells express some of the same enzymes that metabolize methadone, but *not* heroin or morphine, and that these are genetically controlled. Thus, methadone may interact with immune cells quite differently than other opioids and there can be marked differences between individuals.[12]
- Recently, researchers discovered antibodies in some MMT patients that may neutralize methadone. Roughly 88% of HIV-positive MMT patients had such antibodies. This might be beneficial in preventing methadone from affecting immune cells, although reduced levels of active methadone could require upward dose adjustments.[13]

These points have several implications for MMT patients. Methadone's longer action, distinguishing it from short-acting opioids such as heroin, fosters stable plasma levels of the drug to keep opioid receptors on immune cells saturated and create less cellular stress. Furthermore, the human immune system may be capable of either directly metabolizing or neutralizing methadone as a self-protective mechanism.

### Opioids & HIV

With the emergence of HIV in the 1980s there was concern about whether methadone would affect susceptibility of these patients to HIV infection or alter the rate of progression to AIDS.[4]

A decade ago, the National Institute on Drug Abuse declared that, based on laboratory evidence, morphine, heroin, and cocaine, *but not methadone*, speed the growth of HIV. In fact, the agency noted that methadone may have a positive effect on immune functioning, allowing MMT patients to ward off HIV infection or slow progression of the disease.[14]

### Laboratory Controversies

Laboratory experiments over the

years have reported conflicting results. Some found that all opioid drugs negatively affected immune function.[1,9] Others observed that the performance of immune cells from MMT patients compared with healthy subjects were identical.[4,6]

Experiments involved dosing different types of isolated immune cells with heroin, morphine, or methadone to observe effects on cellular function.[1,9] Cells were taken from animals – eg, mice,[1] pigs and monkeys[3] – as well as humans.[4,9]

Often, healthy, opioid-naïve, immune cells were examined,[1,15] which might not accurately portray effects in HIV-infected individuals or in those with a history of opioid abuse.[10] Concentrations of opioid used in these test tube-based experiments frequently were many times greater than doses producing extreme toxicity in humans.[1,6,15]

Very recently, concerns were raised by researchers at the University of Pennsylvania who reported that methadone increased the ability of HIV to infect test tube-cultured cells. Also, when researchers added methadone to cells from HIV-infected patients in which the infection was dormant, the virus began to grow.[9]

It should be noted that the immune system cells examined were not from methadone-maintained patients, so valid conclusions cannot be drawn about HIV in MMT patients. Furthermore, prior research had noted the ability of sporadically administered opioids to activate dormant viruses; conversely, at steady-state serum levels, methadone was found to repress viral activity.[3]

Interestingly, the single doses of methadone used in the Pennsylvania study were vastly *less than* concentrations used in MMT.[9] Earlier research had demonstrated a similar inhibition of immune response with subtherapeutic methadone doses,[16] and such investigations might bring into question a potentially harmful effect of *inadequate* methadone doses on the immune system.

Kreek[6] and others[1] have noted that there are fundamental limitations of laboratory research, and results from such experiments must be interpreted cautiously. Mice are not humans, and isolated cells do not respond the same as people. Ultimately, the only valid measure is clinical studies in patients.

### Clinical Realities

Novick and colleagues studied immune cell activity in active heroin IDUs,

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# Current Comments: HIV in MMT

Elinore F. McCance-Katz, MD, PhD, observes that, with today's multidrug, highly-active antiretroviral therapies (called HAART), HIV-positive patients who are stabilized in MMT and take their medications do just as well as any other patients from the general population.

"The mere fact that a person is taking methadone does not appear to hinder their treatment or effect the progression of their HIV disease," she says.

McCance-Katz – Associate Professor, Departments of Psychiatry and Epidemiology, Albert Einstein College of Medicine, Bronx, NY – works with HIV-positive MMT patients and is an extensively published researcher in the field.

As for laboratory studies of methadone's effects on the immune system, she says, "It's very difficult to know how those experiments might relate to humans – if at all."

In clinical practice, there are many factors affecting the HIV-infected person's progress. "Many are quite ill before they are diagnosed and start receiving treatment. In MMT programs, these people receive much more in the way of care than just methadone," she notes.

For a recent pilot study,\* McCance-Katz and her team developed a simplified HAART regimen administered to patients in the MMT clinic along with methadone. After only 8 weeks, 4 of 5 patients had undetectable HIV viral loads, "which other HIV/AIDS specialists have told me is quite a positive response," she comments.

Also noteworthy, she observes that, due to a drug interaction between methadone and one of the antiretroviral medications used in the study, efavirenz, an average 52% increase in methadone dose was required in these patient who began experiencing symptoms of opiate withdrawal within 2 weeks of starting HAART.

"So, my view is that methadone certainly doesn't interfere with MMT patients' abilities to respond to antiviral therapy," she concludes. "However, patient adherence with the HAART regimen and the need to clinically monitor for drug interactions and provide adequate methadone dose must be addressed."

\*McCance-Katz EF, Gourevitch MN, Arnsten J, Sarlo J, Rainey P, Jatlow P. Modified directly observed therapy (MDOT) for injection drug users with HIV disease. *Am J Addict.* 2002; In press.

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long-term MMT patients, and healthy subjects who had never abused drugs.[4,17] All were HIV-negative. Tenure in MMT ranged from 11 to 21 years (median 16 years).

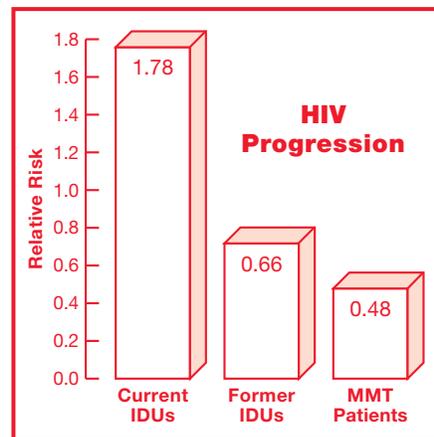
Whereas IDUs had deranged immune system activity, MMT patients were similar to healthy subjects. The authors concluded that immunologic abnormalities resulting from IV drug abuse can be normalized by effective MMT.

In another study, Kreek et al.[2] examined immune function in 48 younger MMT patients (ages 18-33) who had been in treatment from one month to 14 years. Patients with and without concurrent alcohol, cocaine, and other drug problems were included, but those with active AIDS disease were excluded.

Although some MMT patients with persistent drug abuse had abnormalities in immune cell function, the majority had normalized values. The researchers concluded that methadone did not appear to have any harmful direct or indirect effects on immune function.[2]

In a pivotal study,[18] Swiss researchers prospectively followed 297 current and former IDUs for several years to examine clinical progression of their HIV infection: 124 subjects continued injecting opioids, 80 were in an MMT program, and 93 remained free of illicit opioids without methadone. None of the subjects received antiretroviral therapy for HIV during the study.

The relative risk of HIV progression in MMT patients (48%) was significantly more than 3-fold *less* than that of continuing drug abusers (178%), and also was more favorable than in opioid-free subjects not in MMT (66%). **See Graph.**



During followup, fatal heroin overdoses occurred in 10 persistent IDUs (12%) and in 2 former IDUs who returned to drug abuse after a period of abstinence. There were no such deaths in MMT patients.

In fair balance, it should be noted that not all clinical investigations have demonstrated favorable effects of methadone regarding immune function and/or HIV parameters.[19-21] However, closer inspection of these studies reveals that the small samples of subjects usually included MMT patients who were relatively new to treatment and/or continued IV heroin or other drug abuse. Thus, there were multiple

limitations precluding an accurate interpretation of methadone benefits.[22]

Furthermore, a common parameter of HIV status in these reports was changes in CD4 T-cell counts.[20] Yet, recent opinion questions whether CD4 levels are the most useful marker of HIV disease progression, and the studies did not examine other markers, such as viral load, which better predict disease progression.[23,24]

## Methadone Safe, Beneficial

The preponderance of research indicates that methadone is not harmful to the immune system and, in fact, appears to normalize immune function and stress responses to help fight disease and infection. Furthermore, clinical researchers have concluded that methadone appears to be safe and beneficial for HIV-infected patients.

It may take a number of years in MMT and IV-drug abstinence before beneficial immune system effects fully emerge, and there can be differences between individuals. There also is a possibility that *inadequate* methadone doses *create* stress that may impede immune system function and cancel out such benefits. Effects of methadone dose on immune function represent an important opportunity for future research.

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not get reimbursement from Medi-Cal (California's version of Medicaid) for these expensive tests, and referrals to outside public or private treatment providers can present daunting obstacles.

Patients themselves may be hesitant. Martin notes that patients often fear knowing more about their disease, so they don't follow up on getting tested. Even with frequent reminders and encouragement, it can take several years before they become ready to proceed with treatment.

Cohen agrees, "Although most MMT patients are interested in taking better care of themselves, a certain percentage of patients simply decline testing and treatment. They seem to be in denial about what's going to happen to them or they don't care."

### Unjustified Prejudice

Another obstacle, Martin suggests, is the reluctance of liver specialists to even examine MMT patients. "For example, many hepatologists reject patients who are on methadone outright or insist on total drug abstinence for an entire year before they will do liver tests." This limits treatment to only about 10% of her patients, since many have a pattern of occasional drug or alcohol use.

This abstinence requirement is not based on any accepted clinical guidelines, she adds. Furthermore, research data show that occasional, but not continuous, substance use does not hinder outcomes of HCV-medication therapy, so there is no scientific basis for the requirement.

Cohen concurs: "This is not simply a matter of diagnosing a person with a treatable disease and then getting immediate, adequate treatment for that patient, as might be expected with other potentially chronic illness, such as asthma or diabetes. There are many biases and prejudices against patients in addiction treatment programs." He believes a requirement by liver specialists that MMT patients must first withdraw from methadone to receive HCV treatment is still pervasive, but is often not overtly stated.

### Fragmented System

A fragmented system of referrals and reimbursement for services poses yet another obstacle, according to Cohen. A patient's ability to pay for treatment, if they are self-paying, or the particular county's willingness to cover the expense are critical factors, since HCV therapy is costly.

## A most vital role of MMT clinics is in dealing with psychosocial issues.

In Bakersfield, where the Aegis corporate medical director resides, there is an arrangement with a local liver-treatment specialist who prescribes HCV medication, which is then administered to patients at the MMT clinic. However, that is not the typical arrangement.

At other clinics, liver specialists were turning away MMT patients until the clinics began arranging on their own for initial patient evaluations – e.g., lab tests, liver ultrasounds, and other tests besides biopsy. Then, referrals were accepted.

Still, at county medical facilities, patients usually have long waits for HCV treatment after referral. "This can be intimidating and these persons are not good at waiting," Cohen observes.

### Addressing Psychosocial Issues

A most vital role of MMT clinics is in dealing with a continuum of psychosocial issues. According to **Joan Zweben**, PhD – Executive Director of the 14th Street Clinic and East Bay Community Recovery Project, Oakland, CA, and Clinical Professor of Psychiatry at the University of California in San Francisco – it is up to the physicians to identify medically who can benefit from treatment. But, the MMT clinic staff can provide support in dealing with this chronic illness even if a medical regimen is not immediately available or necessary.

She says the MMT program's job is to make patients more treatment-ready, helping them overcome anything that might contribute to instability or undermine their ability to tolerate the demanding HCV-treatment regimen. For example, patients often need help with...

- shelter and a safe environment,
- a social support network,
- employment,
- treatment for other medical problems,
- psychosocial aspects of co-occurring disorders,
- transportation to medical appointments,
- staying motivated throughout treatment.

Zweben advises clinic staff to prioritize those areas needing most urgent attention. However, she says, "many of these

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## Liver Disease in MMT Continued from Page 6

are things that good clinics should be doing already.”

Addressing psychiatric comorbidity is critical. There are high levels of anxiety and mood disorders, including depression, in this patient population, Zweben notes, affecting perhaps 80% of patients. “These are important because if someone has distressing symptoms or emotional difficulties it effects everything you try to do to help them. Furthermore, HCV treatment causes depression in most patients, so this needs to be managed.”

Regrettably, in many parts of medicine there is a disconnect between the psychosocial component and the medical-treatment component, Zweben observes. Yet, it has been demonstrated that there is better compliance with HCV-treatment if psychosocial issues are addressed.

### Educating Patients

Patient support groups are an often overlooked component of even the best HCV treatment programs around the country, Zweben believes. Also, patients should be able to attend those groups at any stage of their HCV illness; it becomes an index of their readiness for treatment.

However, Zweben concedes that having such a program doesn’t automatically mean patients will come to it. “There is a need for persistence by clinic staff and repeated exposure to the support program.”

Martin observes that MMT clinics typically have many types of support groups and these should specifically address HCV. She also stresses that a major role of the clinic staff is to provide patients with education on HCV to overcome any fears.

“We need to show patients that we think this is an important illness and encourage them.” Martin says. Her counseling staff are specifically trained in encouraging patients to get evaluated and treated for HCV.

“It’s very important to emphasize with patients that the rigorous treatment for HCV is time-limited – a year or less,” Martin continues. “It doesn’t go on indefinitely, as with treatment for HIV. I also call attention to the many patients who have done well in tolerating HCV treatment and felt it was definitely worth it.”

### MMT Staff as Advocates

Adopting an active advocacy role in helping MMT patients overcome obstacles

**“MMT programs need to become more creative in helping their patients with HCV, including those who are not yet ready for treatment.”**

to treatment is a worthwhile goal, Cohen believes. Better communication with liver-treatment specialists could be an important first step.

In that regard, Martin proposes several ways clinics can interface between patients and outside liver-treatment specialists:

1. provide specialists with relevant data demonstrating that MMT patients are worth treating in terms of outcome success [see Part 2 in this series];
2. highlight patient strengths to the specialist in a letter or other communication;
3. provide support to specialists in managing patient compliance with treatment.

The last point involves MMT-clinic staff working closely with patients in a case-management role. This might entail having someone accompany the patient to hear the doctor’s instructions and making sure the patient follows through, or arranging transportation from the clinic to the specialist’s office. Martin acknowledges that most clinics do not have staff resources for this, but it is a worthy goal to work toward.

Cohen agrees that it could be useful to document the patient’s performance in MMT in terms that would be meaningful to outside providers, such as treatment compliance and keeping appointments – a “report card” of sorts. This could help overcome reluctance to treat the patient.

However, what happens if an MMT patient does not appear particularly promising for HCV treatment?

While treatment might not be appropriate for everyone, or successful, merely being on methadone and in an MMT program should not be a barrier, Cohen insists. Would a person with diabetes who has not been consistently compliant with insulin therapy or reliable in keeping doctor’s appointments automatically be denied HCV treatment?

Still, Martin cautions that, “it is important not to ‘burn out’ your referral base by

sending them poorly qualified patients.” Yet, some flexibility is necessary; “what many specialists consider as ‘stability’ in a patient is nearly impossible to achieve in a great many MMT patients,” she says.

### Partnering with Specialists

Partnering with liver specialists in the community can be enormously helpful, Cohen believes. For example, hepatologists may not want to assume full responsibility for the patient and a close collaboration with MMT clinic medical staff could help overcome any concerns.

Cohen suggests that MMT programs might themselves take a more active role in diagnosing and treating HCV, but this could engender liability problems. MMT clinics are typically licensed only to treat opioid addiction.

But, he believes that clinics might help administer medications prescribed by specialists and dispensed at local pharmacies. In such cases, MMT staff would need a backup network of specialists. For example, if modifications of treatment are necessary someone must assume responsibility.

In a practical sense, Martin is concerned that MMT clinics are not typically staffed to assume a role in supervising or administering anti-HCV medications. Also, there is usually no provision to reimburse clinics for the extra staff time that might be required. Added support from funding agencies would be crucial.

Despite the many obstacles, Martin stresses that, “MMT programs need to become more creative in helping their patients with HCV, including those who are not yet ready for treatment.” At present, results are better for patients doing well in MMT, living essentially middle-class lives, with ample support systems and financial resources. There is the ongoing challenge of helping HCV-positive patients new in MMT, with less stable lifestyles.

In sum, MMT programs can and should take more active roles in dealing with the HCV crisis. From a public health viewpoint it can be important in helping contain this widespread infection. From a patient welfare perspective, effective medications are available to help curtail HCV progression and prolong life if patients can gain access to treatment.

1. Hepatitis C – A “Giant Silent Killer.” Addiction Treatment Forum. Winter 2002;11(1):1. Available online at: [www.atforum.com](http://www.atforum.com).
2. Muir AJ, Provenza D, Killenberg PG. An evaluation of eligibility for therapy among veterans with hepatitis C. Hepatology. 1999;30(Suppl 1):190A.

## Survey Results - Liver Disease Fates

In the Fall 2001 edition of *AT Forum* (Vol. 10, No. 4) – along with the launch of the series on “Liver Disease in MMT: Treatment and Transplant” – readers were asked to comment on the fates of methadone patients seeking care for liver disease. Survey questions solicited “yes” or “no” responses to the following:

1. Do you know of patients who were denied treatment for hepatitis C (HCV) because they were on methadone?
2. Do you know of patients who were denied a liver transplant because they were on methadone?
3. Do you know of MMT patients who died because they could not get treatment or a transplant for their liver disease?

There were 150 survey responses via feedback cards and at the *AT Forum* web site ([www.atforum.com](http://www.atforum.com)). The **Graph** depicts a summary of those responding “yes” to each of the statements (bars with scale on left). Between 35% and 38% of readers said they knew of patients who were denied treatment or transplant for their liver disease because of their taking methadone, and/or died as a result of such refusal.

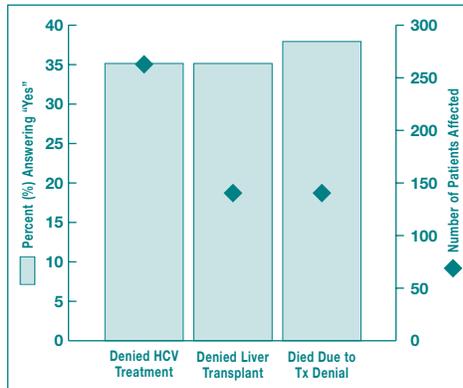
Persons responding affirmatively to any question also were asked how many patients they knew of who were affected. Total numbers of patients mentioned are depicted on the graph with diamonds (scale on right): 264 denied treatment for HCV; 133 denied liver transplant; 137 deaths.

### Tragedy Becoming Catastrophe

Even one patient being denied liver treatment or transplant simply because they are taking methadone as part of an MMT program would be a tragedy. That *many* patients are dying as a result of such neglect may make this a true catastrophe.

It should be noted that *AT Forum* surveys are based on informal responses, rather than systematic polls. In this case, however, it might be expected that responses grossly underestimate the actual extent of the problems.

The first article in the series observed that there is a very high prevalence of HCV among MMT patients, more than 90% in some clinics, and only about 12% receive antiviral treatment in the best of circumstances. A greater percentage of them would likely end up needing liver



transplants than among HCV-positive patients in the general public. Yet, since 1988, only an estimated 180 MMT patients have had liver transplants; less than a half-percent (0.5%) of the total procedures performed during that time.

### A Few Rays of Hope

As the first article in this series also described, certain MMT programs are becoming more proactive in helping their patients with hepatitis (also see the interviews in this edition). And, while nearly two-thirds of transplant centers prohibit methadone in one way or another, there are some enlightened programs around the country offering hope.

One patient responding to the survey – in MMT for 16 years and both HCV and HIV positive – wrote that he has always been treated fairly and supported by liver treatment specialists, even though they knew he was on methadone. About two years ago, he received a liver transplant at the University of Pittsburgh, which was paid for by private insurance and Medicare.

Hopefully, exceptional stories like this will become commonplace.

A.T.F.

ADDICTION TREATMENT

## Forum

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