

Medical Writers' Circle

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a series of articles written by medical professionals about the management and treatment of hepatitis C

Liver Transplantation and Methadone

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Methadone is a highly effective treatment for opioid dependence. Unfortunately, methadone maintenance therapy (MMT) continues to be a barrier to standard medical care. Although there is no evidence-based medicine that would indicate that MMT patients have worse outcomes than non-MMT patients receiving liver transplants (LT), transplant programs continue to preclude patients undergoing MMT from transplantation.^{1,2} In a recent nationwide survey, just over half of respond-

ing transplant centers stated that they would consider active MMT patients for transplant waiting lists; however, one third of these centers still required patients to stop their methadone therapy prior to listing.³

At UC Davis Medical Center (UCDMC), MMT patients are evaluated for liver transplantation in the same manner as any other patient. All transplant candidates must undergo certain standard medical, surgical, psychosocial, and financial evaluations (*see table 1*). For

example, when evaluating a patient's psychosocial criteria, our team would consider living arrangements, communication, transportation, social support as well as the patient's understanding and expectations of the transplant process. Additionally, patients with a history of substance abuse are required to sign an abstinence agreement, undergo random toxicology screenings, attend treatment programs (Narcotics Anonymous, Alcoholics Anonymous, MMT), and work with an addiction specialist as necessary. Toxicology screenings include barbiturates, benzodiazapenes, cocaine metabolites, opiates, cannabinoids, and ethanol. Chronic hepatitis C Virus (HCV) leading to cirrhosis is the number one cause for liver transplant. Intravenous-drug use (IVDU) is the greatest risk factor for hepatitis C.¹ It is well

Table 1: Psychosocial criteria for liver transplant candidacy

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|--|
| Stable Mental Health |
| Appropriate Housing |
| Social Support Network |
| Adequate Income or Sufficient Medical Insurance Coverage |
| Basic Nutrition |
| Reliable Transportation |

* As established on individual patient by the local liver transplant selection committee.



Table 2: Methadone maintenance therapy (MMT) and Hepatitis C Virus (HCV)

| Author | Year | Organ | N= | Comments |
|------------------------------------|------|-------|-----|--|
| Sylvestre D et al. ⁵ | 2004 | NA | 76 | MMT patients can be successfully treated for HCV. 28% of 76 ex-heroin addicts had sustained virological response |
| McCarthy JJ & Flynn N ⁴ | 2001 | NA | 460 | MMT should not preclude patients from HCV treatment. 87% of the MMT patient population is HCV positive |

known that hepatitis C is highly prevalent in MMT patients.⁴ In fact, approximately 80-90% of this population test positive for HCV.^{2,4} Since HCV is the most common cause for LT and the majority of MMT patients have hepatitis C, the need for an LT in the MMT population is greater than in most patient populations (*see table 2*). Unfortunately, MMT patients are grossly under-represented as transplant recipients (*see figure 1*). Figure 1 depicts the LT disparity between the HCV positive population and the MMT population: in other words, only a few MMT patients with HCV and

End-Stage Liver Disease have the opportunity to be evaluated for LT.

Stigma regarding MMT continues to be a barrier to patients receiving liver transplant. Although methadone is a widely-accepted, highly effective treatment for opiate addiction, MMT patients continue to be discriminated against. The primary reason for this bias was investigated in a 2001 survey which showed that a majority of transplant centers required MMT cessation prior to LT. The general conclusion was that there was a significant misunderstanding between heroin abuse and

methadone maintenance therapy as treatment.³

More specifically, methadone is often seen as an abused drug, not as a treatment for opiate addiction. Thus, MMT patients may still be perceived as not fully “recovered”; they are treated as if they are “addicted” to a drug (i.e., methadone) and are not “worthy or ready” for standard medical care, such as treatment of HCV and LT. The practice of requiring MMT discontinuation in order to receive a liver transplant may be considered unethical if not harmful; however, there is an emerging opinion supporting the cautious

inclusion of MMT patients in liver transplantation (*see table 3*).⁶

The NIH 2002 Consensus Statement on HCV management clearly supports methadone treatment for opiate addiction. The document states that methadone helps reduce risky behaviors and should not be used as a reason to exclude a patient from HCV treatment. In addition to standard combination therapy, one must consider LT as common treatment for HCV.

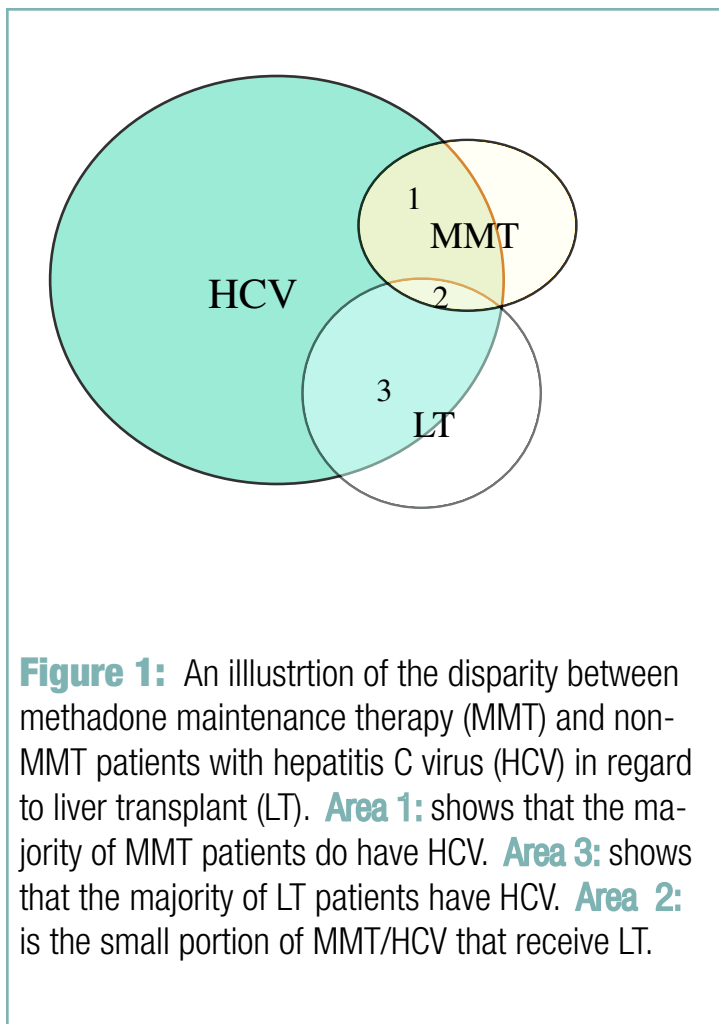
A substantial portion of MMT patients have a proven track record of medical follow up appoint-

Table 3: Collection of literature about methadone maintenance therapy (MMT) and liver transplants

| Author | Year | Organ | No. | Comments |
|--|------|-------|-----|--|
| Liu L et al. ² | 2003 | Liver | 36 | Graft survival rates in liver transplant recipients were comparable between MMT and non-MMT patients |
| Di Martini A & Weinrieb R (Editorial) ⁶ | 2003 | Liver | NA | MMT patients should be eligible for transplant |

ments, repeated laboratory studies, and adherence to taking their methadone. MMT patients with a history of drug and alcohol addiction can be successful in HCV treatment and they are expected to adhere to the LT immunosuppressive drug regimen. Some even suggest that compliant MMT patients are the best candidates for HCV therapy among IVDUs.⁸ At UCDCMC, we recommend that patients on MMT needing a liver transplant should not be required to stop taking methadone. We believe

that each patient should be evaluated independently and equally with respect to history and compliance behavior. Finally, MMT should not exclude patients from receiving LT.



References:

1. Kanchana TP, Kaul V, Manzarbeitia C, Reich DJ, Hails KC, Munoz SJ, Rothstein KD. Liver transplantation for patients on methadone maintenance. *Liver Transpl* 2002 Sep;8(9):778-782.
2. Liu LU, Schiano TD, Lau N, O'Rourke M, Min AD, Sigal SH, et al. Survival and risk of recidivism in methadone-dependent patients undergoing liver transplantation. *Am J Transplant*. 2003 Oct;3(10):1273-1277.
3. Koch M, Banys P. Liver transplantation and opioid dependence. *JAMA* 2001 Feb 28; 285(8): 1056-1058.
4. McCarthy JJ, Flynn N. Hepatitis C in methadone maintenance patients: prevalence and public policy implications. *J Addict Dis*. 2001;20(1):19-31.
5. Sylvestre DL, Litwin AH, Clements BJ, Gourevitch MN. The impact of barriers to hepatitis C virus treatment in recovering heroin users maintained on methadone. *J Subst Abuse Treat* 2005;29:159-165.
6. DiMartini A, Weinreb R. Liver transplantation for methadone-maintained opiate dependents: making the case for cautious optimism. *Am J Transplant* 2003; 10:1183-1184.
7. NIH Consensus Statement on Management of Hepatitis C: 2002. *NIH Consens State Sci Statements*. 2002 Jun 10-12;19(3):1-46.
8. Davis GL, Rodrigue JR. Treatment of chronic hepatitis C in active drug users. *N Engl J Med* 2001 Jul;345(3):215-216.



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