

- U.S. Food and Drug Administration, 2003. Product Discontinuation Notice: ORLAAM. www.fda.gov/cder/drug/shortages/orlaam.htm, August 23.
- Varescon, I., et al., 2002. Buprenorphine abuse: High dose intravenous administration of buprenorphine [French]. *L'Encephale* 28(5 Pt. 1):397-402.
- Vastag, B., 2003. In-office opiate treatment "not a panacea": Physicians slow to embrace therapeutic option. *Journal of the American Medical Association* 290(6):731-735.
- Walsh, S.L., et al., 1994. Clinical pharmacology of buprenorphine: Ceiling effects at high doses. *Clinical Pharmacology and Therapeutics* 55(5):569-580.
- Walsh, S.L., et al., 1995. Effects of buprenorphine and methadone in methadone-maintained subjects. *Psychopharmacology* (Berlin) 119(3):268-276.
- Wang, E.C., 1999. Methadone treatment during pregnancy. *Journal of Obstetric, Gynecologic, and Neonatal Nursing* 28(6):615-622.
- White, J.M., and Irvine, R.J., 1999. Mechanisms of fatal opioid overdose. *Addiction* 94(7):961-972.
- Woody, G.E., 2003. Buprenorphine/Naloxone-Facilitated Rehabilitation for Opioid-Dependent Adolescents/Young Adults. CTN protocol NIDA-CTN-0010. www.drugabuse.gov/CTN/clinician_info.html, October 31, 2003.



RESPONSE: INTEGRATING BUPRENORPHINE THERAPY INTO CLINICAL PRACTICE

Martin C. Doot, M.D., J. Thomas Payte, M.D., and Arthur Van Zee, M.D.

We're looking at buprenorphine as a means to incorporate more flexibility into our abstinence-based treatment model.

Arthur Van Zee: Dr. Jones's paper is very informative. I found much that was new to me even after 7 months' experience with buprenorphine. I wish I had it when we were starting out.

Martin Doot: The information in this article is consistent with other reviews of buprenorphine therapy I've seen. I wish it had more on the psychosocial aspects of drug treatment, though.

J. Thomas Payte: If I had only one source, this article is the one I would want to have. When it is published, I want all the physicians in our programs to have it as background reading. I particularly liked the explanations of how partial agonists work and how they differ from full agonists and antagonists.

Programs and strategies

Van Zee: We are looking to buprenorphine as a possible solution to a very difficult situation. Our clinic is in the heart of Appalachia, in the southwestern corner of Virginia. Until about 3 years ago we had no large-scale opioid addiction, but the OxyContin epidemic changed that. There are now tens of thousands of new opioid addicts in our region. Methadone treatment programs may be 2 hours away by car. Try to imagine a 23-year-old single mother getting her daughter up at 4:30 every morning to drive to Tennessee to get a methadone dose. Because of these difficulties, prior to buprenorphine, I would just detox patients and set them up with our local counseling team. Now,

I can offer them comprehensive treatment with an effective medication.

We've had some wonderful success stories already—people who started induction 7 months ago and who have come very far, not just in terms of abstinence, but also in terms of real personal growth. We've also had many lapses. I think I've initiated 46 patients on buprenorphine; 23 are still in the program, and about 15 to 17 are doing well.

Doot: I work in a multispecialty, office-based group practice affiliated with a large teaching hospital near Chicago. We're looking at buprenorphine as a means to incorporate more flexibility into our abstinence-based treatment model. We intend to offer it for maintenance as well as to improve outcomes with abstinence-based treatment.

Our group participated in the buprenorphine clinical trials because our State agency wanted an abstinence-based perspective on the medication. Patients chose buprenorphine or traditional abstinence-based therapy. Our counselors found that after a while they had a group of patients they were encouraging to use 12-step facilitation and relapse prevention techniques, who were well past detox but still using buprenorphine. What came out of this was a new model, in which we meet patients where they are, accept some of the goals they set for themselves, and then move them along the continuum of change.

Our counselors are comfortable with this model. I've had some say to me, 'I really think this patient

would do better on maintenance.’ That never happened before.

Payte: I have been in addiction medicine full-time since the 1960s and was involved in one of the last clinical trials of buprenorphine. Now I work for Colonial Management Group, which operates 43 methadone treatment programs in 14 States. The physicians in our organization have shown intense interest in buprenorphine, and we are now gearing up to use it. For me, buprenorphine is particularly promising because of its safety and flexibility. It’s not as strong as methadone, and has long-lasting action, so you don’t see significant problems if a patient misses one or two doses, as you do with methadone.

Which patients?

Doot: The new medication will be particularly useful for patients who cannot achieve recovery through traditional abstinence-based programs. Some people drop out of these programs because the biological dimension of their addiction is so powerful they can’t get past it to begin to address the other tasks of treatment—healing their family, healing the way they think, entering a spiritual recovery program. Buprenorphine is going to play a tremendous role in keeping these individuals in therapy.

A patient who abuses multiple drugs is likely to have a difficult time sticking with buprenorphine. With these patients, you’re likely to get into 12-step, abstinence-oriented kinds of interventions anyway, because we don’t have medications for cocaine and those for alcohol don’t work terribly well. You ask yourself, ‘Should this be a patient we gradually taper off the buprenorphine as they learn how to use the 12-step recovery program?’ I think there is going to be a role for the gradual buprenorphine taper.

My partners and I are particularly interested in using buprenorphine to help impaired health care professionals. At present, however, I don’t consider buprenorphine a first-line option for most of these patients. First, opioid-dependent physicians generally do well in abstinence-based programs, which are more acceptable in the eyes of society. Second, the article makes an excellent point: We need more research on whether buprenorphine impairs cognitive functioning and psychomotor performance. I suspect it doesn’t, but until I know, I can’t go before a licensing board and say, ‘This doctor can continue to do surgery while taking this medication.’

Payte: If it weren’t for its relatively high cost, I would see buprenorphine as a trial entry drug for virtually every new patient coming to our methadone clinics. But if I were asked to choose among patients, I would be tempted to give a preferential nod to the younger patients with shorter abuse histories and less severity, in consideration of the safety factor. Actually, I would be prone to refer adolescents for treatment in a physician’s office rather than expose them to the atmosphere of a methadone clinic.

Some established methadone patients also can gain advantages from switching to buprenorphine, particularly greater safety. Some want to get away from the ‘M’ word—the stigma associated with methadone. Our long-term, stabilized patients now have once-monthly attendance at many of our clinics, so the attraction of buprenorphine’s less frequent clinic visits is somewhat attenuated.

Generally, patients will let you know if they are not doing well on buprenorphine. If their drug craving persists on what should be an adequate dose—24 to 32 mg, you may have to switch to the stronger agonist. But it’s easier to go from buprenorphine to methadone than the other way around.

Van Zee: I’ve found that I can’t predict very well who’s going to do well and who isn’t. I’ve seen people do well who I thought wouldn’t have much of a chance. And I’ve been disappointed with people who had much more social and emotional support but didn’t succeed. I would probably exclude the individual who is obviously psychiatrically unstable and anyone with impending legal problems—that is, anyone facing a stay in prison in the near future. Most often, though not always, it’s impractical to induce buprenorphine and maintain a patient on it in jail.

What I like to see happen is that an individual is seen by the counselors, starts 12-step meetings, and then comes to me. I also believe that putting a patient on buprenorphine should be a decision made by the entire treatment team.

Doot: Ideally, you’d like the candidate for buprenorphine to have psychosocial stability, be willing to sign a contract, have adequate resources to follow through, and have family support. However, we have adjunct treatments that can overcome many of the problems that would disqualify patients. If you can supply the proper psychosocial support—get a patient into a

If it weren’t for its relatively high cost, I would see buprenorphine as a trial entry drug for virtually every new patient coming to our methadone clinics.

halfway house, for example—you have a much better chance of success.

It's important to keep asking, 'What are we missing?' Often there are other treatable conditions that are standing in the way of recovery from addiction.

Dosing schedules and diversion

Doot: Some of the early guidelines for buprenorphine recommended Subutex [buprenorphine alone] for initiating therapy. In the clinical trial I participated in, we used Suboxone [buprenorphine combined with naloxone] for induction, with no problems. I haven't seen a need for Subutex in the clinic, and I was pleased that Dr. Jones clarified that in her paper.

In most situations, I think daily dosing is best. My patients remember easier to take something once in the morning than to try to recall if it's Monday, Tuesday, or Wednesday. Missing doses could potentially raise the risk for relapse by reducing protection against craving.

Payte: I agree wholeheartedly. In my brief experience with buprenorphine, patients have sometimes forgotten to take their tablets for a day or two before finally remembering. Even at that point, they were fairly comfortable. Buprenorphine just doesn't give as strong a reminder as methadone. Also, because of blood level fluctuations over the dosing intervals, I expect we will obtain the smoothest and best medication effect by not going to every-other-day dosing. The rationale for wider dosing intervals would come into play in clinics whose patients aren't allowed take-home doses but who can't attend every day.

Doot: Some patients actually need the structure of clinic dispensing. The patients who come to me for office-based treatment tell me they don't want to come every day, but some don't do well coming in only once a week.

Van Zee: That's been our experience. In midsummer, before we tightened up our program, a lot of our buprenorphine was getting out on the street. Now we have a minority of patients who don't get take-home medication, but instead come to the clinic every day or every 2 or 3 days. For some, this has been a real help in getting to clean urines, faithful attendance at meetings, and so on.

I do feel good about the fact that when buprenor-

phine is diverted onto the street, its downside in terms of inadvertent overdose is small compared to methadone.

Payte: Methadone diversion is something I've been living with for years. I participated on an Institute of Medicine panel that tried to determine its impact. We concluded that the negative effects were difficult to pinpoint and probably overemphasized as a reason to deter take-homes. Buprenorphine particularly reduces the risk even more.

Doot: I have found that patients on higher buprenorphine doses often split their doses. Rather than taking the full 24 mg in the morning, they will come back and say, 'Well, Doc, I took one in the morning and two at night.' As long as they take the total daily dose, those who split it seem to benefit just as well as those who didn't.

Van Zee: A small minority of my patients had nausea if they took the whole dose at once. They did better splitting the dose.

To save our people money, we only prescribe the 8-mg tablet, not the 2 mg. If someone is on 12 mg a day, it's about half as costly to take one-and-a-half 8-mg tablets as it is to take an 8 and two 2s. Also, the bigger the quantity purchased at one time, the lower the price. We have patients buy a whole month's supply. If we don't think a patient should have that much on hand, we have them buy a month's supply and store it at the clinic for dispensing 8 or 10 days at a time.

The learning curve

Van Zee: I've learned some things the hard way; in fact, my program is probably being salvaged by the nurses and counselors who are making it work in spite of my mistakes. We have learned two basic lessons: One, it is a mistake to overstate the value of medication in recovery; and two, you need a tight structure to have a successful program.

We assumed early on that if the medication took away the craving and the patients didn't wake up every morning sick and thinking about where to get pills, and their urines were clean, they should do all right. We underestimated the psychosocial adjustments needed for recovery, and so set ourselves up for disappointment when people who seemed to be doing well would relapse after 3 or 4 months. And we

It's about half as costly to take one-and-a-half 8-mg tablets as it is to take an 8 and two 2s.

were forced to add structure. Now each patient signs a contract upon entering the program, promising to attend 12-step meetings 3 times a week and meet with a counselor once a week. In addition, we do random pill counts and urine testing. We have found that people do better when the requirements are clear.

Doot: I expect it will continue to be difficult to motivate primary care physicians to ‘hang out their

shingle’ and announce that they intend to take care of the addicts among their patients. This has been the disappointment with all the medications developed so far to treat substance use disorders. Physicians have tended not to diagnose the problem, perhaps because they do not have much hope of helping. Buprenorphine may change that situation. &