

# NEW TREATMENTS FOR OPIATE DEPENDENCE

*Oral methadone orthodoxy  
may be blinding us to  
effective alternative  
treatments for the opiate  
addict.*

For some opiate addicts the usual oral methadone regimes are inappropriate or ineffective. Alternative regimes are available. Injectable methadone ampoules can now be labelled to help prevent diversion. Long-acting substitutes for methadone and drugs that block the effects of opiates can improve treatment compliance and prevent relapse. New combinations of drugs can achieve safe opiate withdrawal in 4-5 days.

**Colin Brewer**

*The author is a psychiatrist and the Medical Director of the Stapleford Centre, a private addiction treatment clinic offering outpatient and inpatient services.*

CONVENTIONAL WISDOM in Britain is that the medical treatment of opiate addiction is largely limited to the amelioration of withdrawal symptoms and the prescribing of methadone. Conventional wisdom is wrong, mainly because it appears to ignore a lot of recent medical research.

Even in the use of methadone there have been developments, while in the field of rapid and comfortable opiate withdrawal, that overworked cliché 'breakthrough' is for once appropriate. This paper will summarise the main developments of the past decade in opiate addiction treatment.

Before doing so, it is important to realise that many drug users improve once they recognise they have a problem and symbolise that by seeking help. The placebo effect of any intervention is much stronger than most people realise and all of us in the healing and helping business are walking placebos, whatever else we may be.

Economy and respect for the patient dictate that, before giving help, we ask ourselves: how do I know that this patient/client wouldn't do just as well without my proposed intervention? Only objective, controlled trials can enable us to be reasonably confident that what we do is of real rather than symbolic value. Unless otherwise stated, the studies referenced in this paper concern controlled clinical trials.

## **New ways with methadone**

Oral methadone is the commonest — often, the only — medical response to opiate dependence, but anxiety about diversion to the black market means doses are often inadequate and sometimes derisory. This anxiety is understandable but largely unnecessary. More treatment units could dispense methadone daily to be taken under supervision at the clinic, especially at the start of treatment. Alternatively, the prescription can include a request to the pharmacist to witness the patient swallowing the methadone on the premises. Many pharmacists are willing to do this.

Long-term US follow-up studies sug-

gest methadone is very effective in reducing heroin use and stabilising lifestyles but, as with all drugs, adequate dosage is essential. Generous methadone programmes give better results than miserly ones.<sup>1</sup>

Too many people fail to make the crucial distinction between methadone as an aid to withdrawal, and methadone maintenance. The former is time-limited and for those aiming to become opiate free in weeks or months; the latter is indefinite and for those who have tried and failed to withdraw from opiates many times.

However, oral methadone programmes are of little help for those to whom the act of injection is as addictive as the substance injected. The recent AIDS reports from the Advisory Council on the Misuse of Drugs recognised the case for including at least short-term prescribing of injectable opiates among the range of treatment options.

Several drug dependency units prescribe injectable opiates for some of their patients, sometimes for many years, and a few prescribe them relatively freely. Understandably, most of these units tend not to publicise the fact. In the age of AIDS, there is a case for more openness about this important issue, though consensus is no more likely than with other controversial medical issues, such as abortion. The Advisory Council's suggestion that injectable prescribing should be "exceptional" does not reflect prescribing practices at some major drug dependency units; it was almost certainly a compromise to avoid a split in the committee.

As with oral methadone, the initial aim of prescribing injectables is to encourage and enable patients to lead a healthier, more stable and less criminal lifestyle. One then tries to wean them on to oral or opiate-free programmes.

The recent introduction of larger 35mg/3.5ml and 50mg/5ml methadone ampoules on a named patient basis will considerably reduce the cost of injectable methadone (to about £1.50-£3 per day on a private prescription). Being able to prescribe a larger dose in a single ampoule will reduce

the number of ampoules dispensed, permitting them to be individually labelled to make their source easily traceable. This should help minimise the increased risk of diversion on to the illicit market which is an important disadvantage of injectable programmes.

### Long-acting 'methadone'

Laevo alpha acetyl methadole (LAAM) is a long-acting analogue of methadone used in some US and Dutch methadone maintenance and withdrawal programmes for over 10 years. It has not yet been used in Britain, though interested researchers could probably obtain it from US or Dutch sources. Its main advantage is that it only needs to be taken every two or three days. It also avoids the withdrawal symptoms experienced with daily methadone doses by some people who rapidly metabolise the drug.

At least 50 per cent of methadone patients find LAAM as good as or better than methadone, but the correct medical procedures for initiating it must be carefully followed to minimise the risk of overdose. It takes up to three days for the drug to reach blood levels sufficient to prevent withdrawal. During this time, daily monitoring is essential and additional opiates may be required on a rapidly diminishing schedule.

### Dealing with alcohol

Many opiate abusers drink little or no alcohol but some drink excessively. Alcohol taken in excess is highly toxic, while smoking or even injecting 'clean' opiates is virtually never fatal to addicts. Alcohol and opiates in combination can be lethal, while

alcohol abuse can make it difficult to stabilise methadone dosage.

If counselling and exhortation fail, the alcohol problem can easily be solved in most cases by making the continued prescribing of methadone conditional on patients agreeing to take Antabuse (disulfiram) under supervision two or three times a week.<sup>3</sup> Since most methadone patients value their methadone more than their alcohol, they will usually agree to this stipulation. Supervised Antabuse has been shown in several controlled trials to improve considerably the effectiveness of conventional alcoholism treatment.<sup>4,5</sup>

Antabuse causes an unpleasant, incapacitating and occasionally dangerous reaction if alcohol is consumed — but it is very much less dangerous than persistent alcohol abuse and has no significant interactions with methadone or other opiates or with other commonly abused drugs.

### Narcotic antagonists

Drugs known as 'narcotic antagonists' counter the effects of heroin and other opiates. People taking the antagonist naltrexone, which has been available in Britain since 1985, can take several grams of heroin without feeling any effect. This chemical blockade protects those who have withdrawn from heroin from the many temptations to resume its use, especially on impulse. Naltrexone aids the development of drug-free behaviour patterns and makes it more likely that they will persist for long enough to become established.<sup>6</sup>

As with Antabuse, supervision of the medication by a third party is crucial, and the tablets should be dissolved in water and drunk to minimise the opportunities for evasion. Family members are often the most appropriate 'supervisors'; since they should generally be involved in treatment anyway, this demands little extra effort. Probation officers, friends, counsellors and workmates can also be involved in the supervisory process.

In the USA, naltrexone has given good results in a group normally thought of as having a poor prognosis — addicted prisoners on work-release schemes.<sup>7</sup> I believe it should also be offered to those in residential programmes who continue to use opiates — naltrexone is more constructive and humane than expulsion.

Experience with Antabuse indicates that the process of supervision tends to strengthen the therapeutic relationship and that less counselling is required, mainly because the relapse rate is reduced.<sup>8</sup> A long-acting depot injection of naltrexone is being developed which will obviously improve compliance with treatment. However, even the currently available oral naltrexone need only be given every two or three days.

Naltrexone is unlikely to help those who are socially isolated and/or rootless. Neither will it find much application among true polydrug abusers, as opposed to those

who sometimes use and abuse other drugs but are primarily opiate abusers.

### Clonidine detoxification

Clonidine relieves, but does not abolish, opiate withdrawal symptoms. Instead of or in combination with methadone, it has a place, but does not really cut the withdrawal period. Many addicts relapse during withdrawal because they get fed up with feeling below par for days or weeks on end. With clonidine alone, dropout rates tend to be higher than with methadone.

Clonidine's advantages include the fact that it has no abuse potential and its use is not followed by withdrawal symptoms. Clonidine can lower blood pressure, but most drug abusers are young with healthy cardiovascular systems and tolerate low blood pressure without danger.

If clonidine is stopped abruptly, people with already significantly raised blood pressure may suffer further increases as a 'rebound' effect. Apart from such cases, in my view clonidine can safely be used in outpatient withdrawal.

Combining clonidine with naltrexone and benzodiazepines is a major advance in withdrawal techniques.<sup>9</sup> Given on its own, naltrexone precipitates withdrawal symptoms in opiate addicts within five minutes of swallowing it. This is unpleasant, but not

---

### *In rapid withdrawal, that overworked cliché 'breakthrough' is for once appropriate*

---

dangerous. However, if clonidine and benzodiazepines are given beforehand, this withdrawal is usually adequately controlled; if the benzodiazepine doses are generous, most patients have no recollection of the worst of the symptoms.<sup>10</sup> For those with jobs, return to work within four or five days is the rule. Using this method, withdrawal from methadone takes no longer than from heroin.

A high-tech variant is to use the short-acting (and rather expensive) narcotic antagonist naloxone by intravenous drip while the patient is given a brief general anaesthetic.<sup>11</sup> These techniques appear to be safe as well as humane.

MANY ABUSERS neither want nor need medical treatments, but nobody should be denied access to a range of treatments including medical ones, especially if the non-medical kind are proving inadequate. Patients have a right to objective evidence about the effectiveness (and, in the private sector at least, the cost-effectiveness) of the various treatment options. Health professionals have a duty to provide it, which means they must be familiar with the scientific literature, though there is nothing to prevent others in the treatment industry familiarising themselves with it too. ■

1. Anglin M.D. et al. "Outcome of narcotic addict treatment in California." In: Tims F.M. et al. eds. *Drug abuse treatment evaluation: strategies, progress and prospects*. Rockville, Md: NIDA, 1984, p.106-128.

2. Tennant F.S. et al. "Clinical experiences with 959 opioid-dependent patients treated with LAAM." *J. Substance Abuse Treatment*: 1986, 3(3), p.195-202.

3. Liebson I. et al. "Alcoholism among methadone patients: a specific treatment method." *American Journal of Psychiatry*: 1973, 130(4), p.483-5.

4. Azrin N.H. et al. "Alcoholism treatment by disulfiram and community reinforcement therapy." *Journal of Behaviour Therapy and Experimental Psychiatry*: 1982, 13, p.105-112.

5. Heather N. "Antabuse treatment for alcohol problems: is it effective and, if so, why?" In: Brewer C, ed. *Effective treatment options in addiction. Proceedings of the First Stapleford Symposium*. In press. Royal College of Psychiatrists.

6. Rawson R.A. et al. "Five-year follow-up of opiate addicts with naltrexone and behaviour therapy." In: Harris L.S. ed. *Problems of Drug Dependence*. NIDA Research Monograph 49. USGPO, 1984.

7. Brahen L.S. et al. "Naltrexone treatment in a jail work-release program." *Journal of Clinical Psychiatry*: 1984, 45(9), p.49-52.

8. Azrin N.H. "Improvements in the community reinforcement approach to alcoholism." *Behaviour Research and Therapy*: 1976, 14, p.339-48.

9. Charney D.S. et al. "The combined use of clonidine and naltrexone as a rapid, safe and effective treatment of abrupt withdrawal from methadone." *American Journal of Psychiatry*: 1986, 143(7), p.831-7.

10. Brewer C. et al. "Opioid withdrawal and naltrexone induction in 48-72 hours with minimal drop-out using a modification of the naltrexone-clonidine technique." *British Journal of Psychiatry*: 1988, 153, p.340-3.

11. Loimer N. et al. "Naloxone treatment for opiate withdrawal syndrome." *British Journal of Psychiatry*: 1988, 153, p.851-2.