

# Release

## Drugs, The Law & Human Rights

### Methadone

#### Introduction

Methadone is a synthetic *opioid* (a family that includes drugs like opium and morphine, derived from the opium poppy, as well as synthetics); it is a strong painkiller often used in the treatment of heroin addiction. This form of treatment, often known as Opioid Substitution Therapy (or OST) emerged from research carried out in the 1960s by US scientists Dole, Nyswinder and Kreek. It is now very widely practiced.

Methadone has a long-lasting effect and a smooth action; it prevents heroin withdrawal symptoms without producing some of the pleasurable effects of heroin. It is, nonetheless, an addictive drug in its own right, producing tolerance and its own withdrawal syndrome. It is available on the street, and usually comes in the form of a sticky green liquid; the liquid mixture is made in other colours however, and also in tablet form. Both the liquid and tablet forms are made for oral use, but are occasionally injected; ampoules for injection are produced but are prescribed to relatively few heroin users.

Known colloquially as ‘juice’, ‘meth’ or ‘green’, the drug’s effects are similar to those of heroin but the onset is more gradual and the effect more long-lasting, (from 24 to 30 hours). Overdose can be fatal.

#### Chemistry

Methadone is a full mu-opioid agonist. Methadone also binds to the glutamatergic NMDA (N-methyl-D-aspartate) receptor, and thus acts as a receptor antagonist against glutamate. Glutamate is the primary excitatory neurotransmitter in the CNS. NMDA receptors have a very important role in modulating long term excitation and memory formation. Acting as an NMDA antagonist may be one mechanism by which methadone decreases craving for opioids and tolerance, and has been proposed as a possible mechanism for its distinguished efficacy regarding the treatment of neuropathic pain.

Methadone has a slow metabolism and very high fat solubility, making it longer lasting than morphine-based drugs. Methadone has a typical elimination half-life of 15 to 60 hours with a mean of around 22. However, metabolism rates vary greatly between individuals, up to a factor of 100, ranging from as few as 4 hours to as many as 130 hours, or even 190 hours. This variability is apparently due to genetic variability in the production of the

associated enzymes CYP3A4, CYP2B6 and CYP2D6. A longer half life frequently allows for administration only once a day in heroin detoxification and maintenance programs. Patients who metabolize methadone rapidly, on the other hand, may require twice daily dosing to obtain sufficient symptom alleviation while avoiding excessive peaks and troughs in their blood concentrations and associated effects. This can also allow lower total doses in some such patients.

The toxic effects of an overdose can be treated with naloxone.

### History

There are some curious ‘urban myths’ in circulation regarding the origins of methadone; they centre on its discovery by the Nazis and naming after Adolf Hitler (in reference to the name *dolophine*, a prior brand name.) It is true that the chemical was first synthesized in the Third Reich by chemists working within the Nazi state at I.G. Farbenindustrie, and was originally referred to simply as *va 10820*. The regime was attempting to achieve self-sufficiency in terms of analgesic supplies (and more or less everything else). The name dolophine was in fact coined by the US pharmaceutical company Eli Lilly; at the end of the war, the US had taken over numerous promising research projects and materials from the defeated Nazi state, including what was to be called (by the American Medical Association in 1947) Methadone. That same year, Eli Lilly marketed the drug as dolophine, probably deriving from the French term for pain. The name *Adolfine*, which pushes the supposed Hitler connection even further, was in fact a product of US street slang; it was never used at all in Germany.

Methadone was initially used in the US as a short-term method for heroin withdrawal, alleviating withdrawal symptoms of those incarcerated at the ‘Narcotics Farm’ at Lexington, Kentucky. It was only later that its far greater utility was recognised by Vincent Dole, Marie Nyswander and Mary Jeanne Kreek, who initiated Methadone Maintenance Therapy in New York in the 1960s. These researchers theorised addiction as a metabolic disease - essentially, some people do not produce sufficient endogenous opioids (naturally occurring morphine-like chemicals in the brain) to keep them going through life’s rich tapestry of pain and disappointment; they are driven by a compulsion to self-medicate this condition, or to make up for this lack of ‘inner analgesics’ by adding to the supply from external sources. In our society, this means the illicit market. The many health and social problems clustered around addiction to an illegal drug like heroin, can be effectively alleviated by supplying a legal, clean and secure source of an alternative drug that has the same function, namely methadone. Methadone has the additional advantage, from this point of view, in that its action is slow and smooth, and lasts 24 hours or more, permitting a single daily dose. This disease theory of addiction and the availability of the therapeutic tool to make it practical was quite revolutionary in the US, which had consistently viewed addiction in criminal and moral terms.

The context in the UK was rather different; the 'British System' of treating addiction involved doctors supplying heroin to those who were addicted to it. However, the increase and the demographic shift in the heroin using population in the 1960s, combined with the symbolic linkage of drugs and the counter-culture and rapid social change, led the government to move over to a new approach to managing addiction: the setting up of clinics at large psychiatric hospitals which quickly forced people off their previous heroin prescriptions and onto methadone, which many of them did not want. In the intervening years, methadone was widely prescribed in the UK, but not along the lines proposed by Dr Dole and his colleagues; instead, doses were too low and people were 'reduced' very rapidly to zero in an attempt to coerce them to come off drugs. This approach was, on the whole, a lamentable failure.

The New Labour government elected in 1997 had a policy of expansion of methadone prescribing and addiction treatment; the improvements in prescribing practice have been rather patchy, but the guidelines that doctors are supposed to employ do at least recognise that higher doses (18 to 120 mls) and a maintenance orientation are appropriate for those users who cannot or do not wish to give up using drugs. Despite the pronouncements of certain ideologically driven abstentionist doctors working in this field, the proportion of users who do not wish to give up all drugs is high.

### Use and culture

Most of the methadone used in contemporary Britain is prescribed to people addicted to heroin; it can only be given on prescription. (Methadone is also used as an analgesic for treating those in severe pain, such as cancer patients.) Many of those receiving methadone are required to agree to 'supervised consumption'; this means that they are required to drink their daily dose in a pharmacy or drug clinic, and are not allowed to take the drug away. The rationale behind this is that it prevents leakage of the drug onto the black market and allows healthcare professionals to monitor their patients' condition. The unfortunate consequence of the practice is that it exposes methadone patients to public hostility and denies any right to privacy. While some patients may need the condition imposed, many do not, and a flexible and individually tailored prescribing regime is called for in all circumstances.

Methadone is nonetheless available on the black market, usually coming in the form of a sweet and sticky green liquid. It produces similar effects to other opiates - tranquility, drowsiness, relaxation, but their onset is much smoother and lacking the peaks and troughs familiar to heroin users.

### Health

The drug is highly addictive, though it takes some time to become dependent (no figures

can be given because this varies between individuals). Withdrawal from methadone is generally agreed by opiate users to be considerably worse than withdrawal from heroin, and is best done gradually (by reducing doses) and with medical support.

The effects of methadone have been extensively researched. Again, there are various myths in circulation: that it 'gets into your bones', damages the bones, rots the teeth and so on. These are quite unfounded. The main side-effects are sweating, reduced libido, constipation, itching skin, irregular or ceased periods and inability to achieve orgasm. All of these effects vary according to individual and dose. There has been recent concern that certain heart irregularities are linked to methadone, particularly in 'high doses' (100 mls plus); specifically, a lengthening of the *QT- interval*, a part of the heart cycle. This is present in some cases and can lead to potentially dangerous heart disturbances. However, reduction in dose usually solves this problem, as does the (much less often used) alternative measure of transferring the patient onto an alternative opiate such as heroin or morphine, neither of which produces these QT interval abnormalities.

In general methadone is a very safe and effective medication, and is certainly responsible for keeping large numbers of people alive who would otherwise not be.