

Methadone: the original research

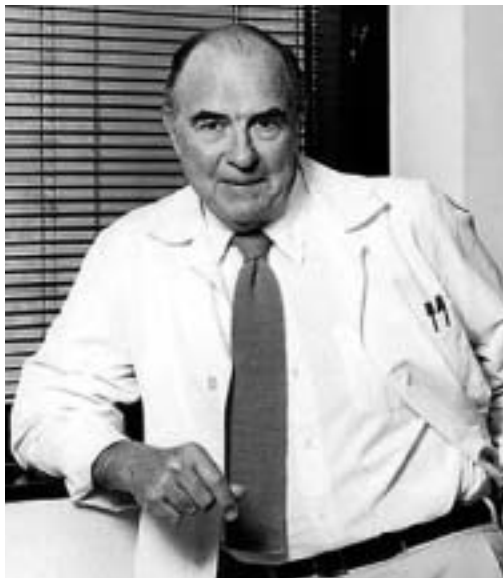
Mike Ashton continues his trawl through the back issues of *Drug and Alcohol Findings* for *DDN*, to remind us of the pioneers of methadone maintenance.

This August the pioneer of methadone maintenance, Dr Vincent Dole, passed away aged 93. Last year was the 40th anniversary of his and Dr Marie Nyswander's (later to become his wife) first research paper on the treatment, a milestone we commemorated in *Drug and Alcohol Findings* by reassessing its significance. From now until the end of October 2006 that assessment is available for free download from www.drugandalcoholfindings.org.uk. It argued that their paper was not just a historical milestone but remains of contemporary significance – a reminder of how methadone maintenance was first and arguably should still be done.

The 'maintenance' element was not the innovation; rather it was the technical advance represented by methadone. Maintenance we already had with morphine and similar drugs, but the roller-coaster cycles of these short-acting heroin substitutes meant patients were nearly always feeling the effects of the previous dose or anxiously awaiting the next, dominating their lives and impeding rehabilitation. The 'eureka' moment came when, a year before the first research was published, two of Dr Nyswander's patients were switched to methadone. They were among six admitted to New York's Rockefeller Institute's research ward in the search for a substitute drug which would prevent withdrawal from and craving for heroin and normalise physiological functioning. For convenience and to avoid perpetuating the risks entailed in injection, ideally it would be taken by mouth. Ideally, too, a single dose would hold patients over an entire day and the effects would come on and fade gently, avoiding heroin's multiple daily steep ascents into euphoria and descents into withdrawal.

Dr Nyswander and her colleague Mary Jeanne Kreek had both seen signs that methadone might fit the bill. It could be taken by mouth, prevented withdrawal, had been used for detoxification, and seemed longer lasting and more even-paced than the alternatives.

Early in 1964 it was tried on the first two patients. Their behaviour changed dramatically: 'They got up, got dressed, stopped obsessing about drugs and began going to night school', recalled Dr Nyswander. Still, she remained unconvinced that methadone could counter the temptations on the streets, waiting 'in total terror every night' for her charges to return to the ward. Temptations there had been in the form of people scoring drugs, but rather than join in, the pair 'went and got an ice



Left: Dr Vincent Dole, pictured in the early 1980s. Above: With Dr Marie Nyswander.

cream'. The remaining four patients were switched to methadone with similar results. Eventually all six found jobs while maintained on doses ranging from 100 to 180mg a day.

Dr Nyswander's trepidation was typical of her caring and dedicated attitude. While other therapists and clinicians dismissed the addicts' stories as the ramblings of disturbed minds, she insisted that much could be learned by carefully listening and encouraged the rest of her team to do the same.

By May of the following year, Dole's team had documented methadone's impact on the 22 patients who featured in the first research paper, establishing that for most it was indeed the substitute they had been looking for – a once-a-day oral drug which kept craving and withdrawals at bay and which (in high enough doses) neutralised normal doses of heroin, enabling patients to get on with their lives. In Britain and the USA, the mass expansion of methadone maintenance which followed the early research departed from the Rockefeller prototype, abandoning elements which British services are now being encouraged to revive. Professor Dole's team individualised dosing, titrating the amount they prescribed to eliminate each patient's need to supplement methadone with heroin and to render the patient's usual heroin dose ineffective. At around 80-120mg a day, their dose levels were way above those which became typical and which in Britain are now seen as having been sub-optimal.

The Rockefeller approach was also avowedly maintenance, analogous to long-term corrective (not curative) treatments for the metabolic diseases such as diabetes in which Professor Dole specialised. But the British clinics often emphasised eventual reduction and withdrawal, though often over an indeterminate time scale, a fudge which experts now want to see clarified.

Finally, the emphasis 40 years ago on intensive support and most of all on reintegration into work and education has been rediscovered by England's National Treatment Agency and is being emphasised in Scotland – with one important difference: Professor Dole's team saw their reintegrated patients as continuing on methadone, while in Britain today reintegration is seen as a way of ending treatment without unduly risking relapse.

Though it dates back 40 years, in these respects the Rockefeller prototype comes closer than many of today's programmes to what is now aspired to as good practice. Almost certainly this partly accounts for its startling success, but there may also have been other reasons not so readily replicated – not least dedicated, caring and well-trained staff such as Drs Dole and Nyswander.

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