

A secret history?

The truth behind methadone

WHILE RESEARCHING for *The Methadone Briefing* – a new book for practitioners – it has become apparent that the widely believed, and much repeated, story that methadone was discovered as part of a desperate German war effort is not true.

In fact the process that resulted in the discovery of methadone began with the discovery of pethedine in 1937. Pethedine was first synthesised by two scientists, Eisleb and Schaumann, who worked for the German chemicals conglomerate I.G Farbenindustrie at Hoechst-Am-Main in Germany. It was given the serial number Hoechst 8909 and given its original name: Dolantin.¹

There were early hopes that this would be a non-addictive analgesic. But as with diamorphine before it, and buprenorphine since, these hopes were not realised – and so the search continued.

Close colleagues Max Bockmühl and Gustav Ehrhart began working on compounds based on the structure of Dolantin in the hope of finding drugs that would either be:

- water soluble hypnotics
- non-addictive analgesics structurally dissimilar to morphine (thus getting round strict regulations on opioids)²
- or substances which could slow down the processes in the gastrointestinal tract (making surgery easier).³

In total this research ended up yielding 300 new compounds.⁴

In 1938 they created the compound now known as methadone. It was given the serial number *Hoechst 10820* and named Polamidon.

The scientists conducted cursory trials on *10820* (which revealed that it was an analgesic), applied for a patent on September 25th 1941⁵ and handed the drug over to the military for further testing under the code name Amidon.

Perhaps the military used doses that were too high resulting in the discounting of *10820*'s analgesic properties;⁶ perhaps the war simply put a stop to further development.⁷ Either way, no attempt was made to bring *Hoechst 10820*

Named after Hitler, the drug we now know as methadone has a shady past, developed by the Nazis in a wartime panic. Or was it?

into commercial production during the war and work continued on further pethedine-based compounds.

In contrast, commercial production of pethedine began in 1939. Construction of a new production plant was started,⁸ and by 1944 production had risen to 1600 kilograms per annum.⁹

After the war all German patents and trade names were requisitioned by the allies. The Hoechst factory fell in the American sector so it was they who took over control of production and investigated the wartime work of the plant.

The US Government sent a team of four men – Kleiderer, Rice, Conquest and Williams – to investigate what had been happening at Hoechst. That year, The Kleiderer Report was published by the US Department of Commerce.¹⁰

The fact that this was the first time that methadone's effects were recorded in print has been used to support the idea that the German scientists did not know what they had invented.¹¹ However, while they may not have fully appreciated the potential of the drug, the origins of the research and subsequent accounts of the work at Hoechst demonstrate that they certainly knew that *10820* had analgesic properties.

The formulae for methadone and all the other Hoechst products were distributed freely around the world and put into commercial production by many companies. This effectively curtailed the profitable production at Hoechst of all the drugs that had been patented under the Nazis. The pethedine plant, only half finished in 1945, was dedicated instead to penicillin production.

The companies which got hold of the formula were free to choose their own trade names.

It was the American pharmaceutical giant Eli-Lilly – and not the Germans – which gave *10820* the trade name Dolophine.¹² Far from being a derivation of Adolf it was probably derived from a combination of the French words dolor (pain) and fin (end).

In 1947, a group of researchers led by Isbell published a review of their experimental and

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SUMMARY

In 1938, two German scientists discovered what is now known as methadone. They passed it on to the military authorities but little was done about the drug and it lay unexploited until the end of the war, when commercial production began in America. It would be nearly twenty years, however, before the value of methadone as a substitute for heroin was recognised.

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The Methadone Briefing by Andrew Preston is a reference guide for anyone who prescribes methadone or works with clients who take the drug. It is available from ISDD at £3.00 plus £0.30 p&p (discounts for bulk orders).

clinical work with the drug. They gave volunteers unbelievable doses of up to 200mg four times a day and unsurprisingly found "rapidly developing tolerance and euphoria". They soon found that they had to reduce the levels for people on such high doses because of, among other things, "... signs of toxicity

American pharmaceutical giant Eli-Lilly gave 10820 the trade name Dolophine, not the Nazis

... inflammation of the skin [at injection sites] ... deep narcosis and ... a general clinical appearance of illness." They also found that "morphine addicts responded very positively".¹³

They concluded that methadone had high potential for addiction: "We believe that unless the manufacture and use of methadon [as it was then called] are controlled, addiction to it will become a serious health problem."

Among the many studies in the late 1940s which found methadone to be an effective analgesic came the original research findings of the men who first synthesised the drug, Bockmühl and Ehrhart, published at last in 1949.¹⁴

This initial flurry of reports showed that although methadone was a powerful analgesic, it had few advantages over other analgesics and all the disadvantages – nausea, respiratory depression and a potential for dependence. Consequently it remained just another, relatively unused drug in the analgesic repertoire until 1964, when Vincent Dole and Marie Nyswander rediscovered it. They had been looking for an oral opioid which needed to be resistant to tolerance, as it would be used in the treatment of heroin addicts. Following their initial trials, they gave methadone – or *Hoechst 10820*, Polamidon, Amidon or Dolphine – a new lease of life. ○

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