

METHADONE TREATMENT

Chapter 9

Review of the salient history

In 1966 two senior physicians and a first year resident in internal medicine training at Cornell Medical School's New York Hospital shifted a paradigm in the management of opioid dependence¹. Vincent Dole of the Rockefeller Institute (now Rockefeller University), a laboratory director investigating the metabolic substrate of obesity changed the trajectory of his career. Marie Nyswander, a physician psychoanalyst ran a walk-in storefront mental health clinic in Harlem. Her book, "*The Drug Addict as a Patient*" caught Dole's eye. The third of the triumvirate was Mary Jeanne Kreek, the first year resident.

At that time New York City was being assailed by yet another heroin epidemic. There were many heroin overdose deaths. Insidiously, it crept into every socio-economic, ethnic, and geographic niche of New York. Arrests for violating any aspect of the complicated drug offense laws was at an all time high. And most distressing, the age of the offenders and those who died was declining.

John Vliet Lindsey took office as mayor on New Years Day, 1966. Among his first promises to the City was to address the heroin epidemic now raging. His options were to increase enforcement personnel assigned to containing supply. This meant more

police on the street, more judges, and for those indicted and going to trial more years behind bars and more, much more alienation for an ever larger segment of the population.

The other approach was to reduce demand. This meant rethinking treatment options for heroin dependency and addiction. Since the 1920's and early 1930's the concept of maintenance therapy for the disease of opiate addiction was not a consideration². The body of law developed around the Harrison Narcotics Tax Act of December 1914 ruled out open-ended use of an opiate or opioid solely for the purposes of sustaining dependency. Under the fierce and combative leadership of Harry Anslinger the Federal Bureau of Narcotics closed clinics in the United States whose purpose was to use narcotics only for maintaining the dependency. Many of these physicians were taken into custody, indicted, tried and sentenced to long prison terms. This was the law when Mayor Lindsey the rethinking challenge was given to Vincent Dole. He and his colleagues Nyswander and Kreek created rigorously designed experiments to establish the effectiveness and the efficacy of opiate maintenance for *the disease* of opiate/opioid dependency. Given the chronic and relapsing nature of the disease all measures taken to detoxify, rehabilitate and then maintain recovery without medication assistance had a disappointingly low success profile.

Review of the Practical Pharmacology of Methadone

The success pharmacologically (and legally) turned on the selection of a pure mu agonist meeting specific goals. 1) It needed to be long-action. The pharmacokinetics (what the body does to the drug) must be such that a dosing schedule of once a day would be feasible. 2) It must have a safety profile established by its use as a pain-relieving agonist. It should have years of clinical use without untoward reports of a negative

impact on the kidneys, the heart, the liver, the lungs, skeletal system, central and the peripheral nervous systems, the blood, the immune capacity. 3) It should not be prohibitively expensive to scale up production.

In Vancouver, Canada as early as 1959 the physicians at the Narcotic Addiction Foundation were interested in methadone for short-term treatment. The position of precedence and proof of principle belong to this group for introducing long-term maintenance in 1963. It was at the prestigious Rockefeller Institute however where the definitive clinical investigations established open-ended treatment with methadone. Please note; the Dole protocol was tightly coupled to psychosocial interventions.³

The pharmacodynamics (what the drug does to the body) must be as specific as possible in order to substitute for diacetylmorphine (heroin) and, perhaps, be preferred to heroin. Methadone is almost a perfect fit. Mu (mu for morphine) receptor avidly binds methadone. When this occurs it is designated as having intrinsic activity at that receptor and the cascade of neuro-chemical events follow; 1) relief of withdrawal sickness, 2) provide a realistic feeling of wellbeing consistent with pursuing a crime-free style of living. 3) establish a blockade, to a degree, to the use of heroin. The latter is dose dependent.⁴

Methadone is legal and established in the pharmacopoeia. Its use for maintenance is not encumbered by threats of prosecution. Its oral route of administration has approximately one half the bioavailability as the parenteral route.