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In the Service of Patients: The Legacy of Dr. Dole

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Summary

The underlying theme in Dr. Vincent P. Dole's work is the effect of metabolism on behavior. This led to ground breaking investigations at The Rockefeller University in electrophoresis, lipids, obesity, addiction, and the development of methadone maintenance in 1964 with his late wife, Dr. Marie E. Nyswander. Dr. Mary Jeanne Kreek, a research resident in his laboratory in 1964, is now continuing addiction research as a professor at Rockefeller. Dole developed methadone detoxification in the New York City jail system and office based methadone medical maintenance with Nyswander. His major concern was to resolve the stigma that methadone patients encounter.

Key Words: Development of methadone maintenance - Dr. Dole legacy

Introduction

With the death of Dr. Vincent P Dole in August of 2006 at the age of 93, the end of an era has come to pass in 20th century medicine-namely the initial unraveling of heroin addiction from what was thought to be compulsive immoral behavior to a legitimate medical disorder that could be treated with medication within clinics and private physicians' offices [4,5,8,41]. Although, known primarily for his work in developing methadone maintenance treatment for heroin addiction and the promulgation of the metabolic

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theory of addiction, his ground breaking accomplishments in this area can only be fully appreciated in the context of a distinguished career as a research scientist dating back to the 1940s. His work can be subdivided into two periods, the pre-addiction and the addiction period which started in the 1960s. However, upon examination it is really one continuous interconnected arc of metabolic research. His underlying major concern was the effect of metabolism on human behavior. The range of his work is unique as is the range of his scientific skills. He made original contributions to the understanding of electrophoresis, lipid chemistry, the treatment of hypertension and the metabolic foundations of obesity among other topics [3,4,31]. He showed that very obese people metabolize food differently than others, and that the craving for food was similar to the craving of a smoker for a cigarette and the craving of a narcotic addict for heroin although the metabolic pathways resulting in the various cravings differ [2,4,17,20].

His studies in obesity challenged popular belief that obese people lack will-power to control their food intake. He also noted the tendency for obese people to regain weight or relapse after dieting and that this relapse had a metabolic basis [2,4].

After finishing his studies in the metabolism of obesity, Dr. Dole embarked on the study of addiction and the development of methadone maintenance. His partner and wife in this historical research was Dr. Marie Nyswander, a psychiatrist who died in 1986. In addition to his scientific background, Dr. Nyswander brought to the development of methadone treatment a unique insight into the social and personal issues that heroin addicts and methadone patients face.

Prior to their collaboration, Dr. Nyswander had worked for almost two decades treating narcotic addicts in various venues including as a Lieutenant in the US Public Health Hospital in Lexington KY, the Musicians Clinic in NYC, in private psychiatric practice and with Dr. Beatrice Berle in a storefront in East Harlem that was part of the addiction program of the East Harlem Protestant Parish. She was a founder of Narcotic Anonymous (NA) based on the model of Alcoholics Anonymous (AA) [2,43,50].

Dr. Nyswander wrote several papers about her experiences treating addicts including the book, *The Drug Addict as a Patient* in 1956 which was the primary influence on Dole's understanding of addicts and addiction. For addicts to be considered patients was a revolutionary concept in the United States [43]. Addiction and heroin addicts were relegated to the criminal justice system or prison-like hospitals by a series of supreme court decisions, and national and local laws emanating from the Harrison Act of 1914 which, although only a tax and registration act, was interpreted by the Treasury Department to exclude physicians from treating addiction with maintenance medications [2]. However, from her experiences treating addicts as a psychiatrist, Dr. Nyswander concluded that many addicts need to be maintained on a narcotic to function since talking therapies of psychiatry and NA were unable to alleviate the craving which for many was the focal point leading to relapse [43].

It was the complementary knowledge and collaborative efforts of Dole and Nyswander that shaped both the research and the clinical development of methadone maintenance as a medical regimen: Dr. Dole was in charge of the laboratory research. Dr. Nyswander

recruited heroin addicts from the East Harlem for pilot at the Rockefeller University. From her years of experience she developed clinical protocols both at The Rockefeller University and at The Beth Israel Medical Center where the pilot moved into an expanded clinical research phase.

Although the pilot did not begin officially at The Rockefeller University until February of 1964, Dole and Nyswander were meeting during 1962/63 planning the research, the need for a maintenance medication and discussing the theories of addiction. Notwithstanding her psychiatric orientation, Nyswander accepted Dole's concept that, like extreme obesity, heroin addiction was a metabolic disease [8].

Dr. Mary Jeanne Kreek, a first year medical resident at New York Hospital –Cornell Medical Center in internal medicine and neuroendocrinology was recruited towards the end of 1963 to assist in the research pilot that began in February of 1964. Her duties included bone marrow biopsies and tests of narcotic tolerance. She worked with Dole and Nyswander on the seminal paper, *Narcotic Blockade* [7]. However, Kreek had to leave the project temporarily to finish her residency at Cornell. Upon returning to the Dole Laboratory she embarked on a landmark series of studies concerning the medical safety and side effects of methadone, how methadone functions in a stabilized patient, the biological basis of addictive disease: opiate, cocaine, and nicotine addiction and alcoholism [14,16,19,37]. She is now Professor and Head of the Laboratory of the Biology of Addictive Diseases at The Rockefeller University. A summary of the extent of her work and a list of her publications are available at the website of The Rockefeller University.

For the clinical phase at The Beth Israel Medical Center Dr. Nyswander recruited Dr. Joyce Lowinson in 1964, a second year psychiatric resident at New York Medical College who had shown an interest in the treatment of addicts on the detoxification ward at Metropolitan Hospital. Dr. Lowinson subsequently became a professor of psychiatry at the Albert Einstein College of Medicine (AECOM), developed the first methadone program associated with a medical school at AECOM and became the senior editor of *Substance Abuse: A comprehensive textbook*.

Dole also enlisted Dr. Norman Gordon, a psychologist to administer and analyze reaction time, coordination and related studies on methadone patients. Dr. Gordon's research demonstrated that stabilized patients were not impaired from methadone and could perform in all jobs for which they were trained or qualified [28].

Other researchers, administrators, and physicians who were affiliated with Dr. Dole during the program's development include Dr. Enoch Gordiss who subsequently became the head of NIAAA, Dr. Ann Ho who worked on various laboratory studies with Dr. Dole and then with Dr. Kreek, Dr. Jerome Jaffe who became head of President Nixon's drug programs in the Special Action Office of Drug Abuse Prevention and from 1971 to 1973 developed a network of methadone programs in the United States, Dr. Robert Newman who made the initial major expansion of methadone treatment in N.Y., Dr. Ray Trussell who transferred the original pilot to Beth Israel Medical Center, Dr. Harold Trigg who was the first medical director at Beth Israel; Dr. Melissa Freeman of Beth

Israel Medical Center who treated the first female methadone patients; Dr. Elizabeth Khuri and Dr. Robert Millman who developed the first adolescent methadone program; and this author who worked with Dr. Dole on topics related to the criminal justice system, the adjustments of patients during and after treatment, and the establishment of office based prescribing of methadone.

Modern Theory of Addiction

Possibly Dole and Nyswander's greatest achievement was to shift the paradigm of addictive behavior from a moral stigmatizing psychological failing to a chronic metabolic disease [8]. The metabolic theory evolved from a seminal paper published in 1966, *Heroin addiction: A metabolic disease*. Dole and Nyswander suggested the adaptation of a metabolic theory of addiction. Factors were introduced such a neurological susceptibility, an altered biological response to narcotics that results in continued use, a protracted abstinence syndrome and metabolic narcotic craving which precipitate relapse. According to Dole at the time the specific narcotic hunger leading to relapse was symptomatic of a metabolic alteration within the central nervous system irrespective of the addict's psychological profile, social class or emotional state [8].

In 1970 Dr. Dole published *The Biochemistry of Addiction.* In this article he predicted the existence of opiate receptors in the brain, their location, density and the technology needed to isolate them [9]. The complexity of the endogenous opioid receptor system was discovered, and is being currently mapped out and studied [16,48]. According to Dole, the metabolic alteration responsible for the specific narcotic craving described earlier in his work, appears now to be associated with as yet an undiscovered impairment or deficit in the function of the opioid receptor system [16].

In his paper written for the Lasker Award for Clinical Medical Research in 1988, Dole discussed methadone maintenance and its implications for theories of addiction and stressed the following [16]:

1) The high rate of relapse of addicts after withdrawal is due to a persistent disorder or defect within the endogenous opiate narcotic ligand system caused by long use of powerful narcotics such as heroin.
2) Methadone administered orally in daily adequate doses with blood levels in a range of 150ng/ml and 600ng/ml can compensate for this defect with continuous and stable occupancy of the narcotic receptors.
3) Methadone normalizes the neurological and endocrinologic processes in patients with this disorder.
4) The major purpose of long term research is to identify the derangement or defect within the endogenous opiate narcotic ligand system and correct it.
5) Methadone treatment is corrective not curative since most patients but not all relapse after withdrawal.
6) The return of specific narcotic craving after withdrawal is symptomatic of the defect within the endogenous opiate narcotic ligand system.

In 1994 Dole summarized the metabolic theory of addiction that has evolved over the past 40 years.

"A modern theory of narcotic addiction is that the compulsive and quite specific craving for narcotic drugs is a symptom of a deficiency in function of the natural opiate-like substances in the brain. To be sure, sociological and psychological forces enter into the making of an addict, but these factors determine exposure—whether or not addictive drugs are available in the environment and whether a person chooses to experiment with them. In any person with repeated exposure to a narcotic drug, the brain adapts and becomes pharmacologically dependent on a continuing input. In some susceptible persons —fortunately a minority of the population—the adaptation becomes fixed and with repeated use a regular input of narcotic becomes a necessity. The experimenter has become an addict. From this perspective methadone maintenance is replacement treatment, compensating for impairment in function of natural opiate-like substances"[21].

With this statement of the modern theory of addiction, social, psychological and biological components are incorporated, each with a defined and interrelated role. Eventually biological forces take over irrespective of the psychosocial elements that may be responsible for experimentation or initial use. The continued craving, relapse and tolerance associated with addiction have biological component, which are independent of will power and a person's psychological profile. The basic characteristics of a continued addiction are therefore biologically influenced. The resolution of personal problems does not mean that the majority of addicted individuals can subsequently resolve drug craving or other biological components of an addiction. A minority of addicted individuals can resolve their cravings but studies have shown that addiction in a majority of the persons can continue indefinitely irrespective of a person's emotional or intellectual characteristics [39]. Most important, methadone treatment is not a substitution of one addiction for another (methadone for heroin) but is compensation or replacement for the body's impaired natural opioids [7,8,14,16,17,20,36].

The Role of Adjunct Services in Methadone Maintenance Treatment

In reviewing the early papers produced by Dole, Nyswander and colleagues the reverberating theme is that although methadone is essential to relieve craving no one medication is able to address the many social, personal, and medical issues that patients present to methadone programs, and social services are essential for rehabilitation [6,43]. In 1988 when he received the Lasker Award for Clinical Medical Research, Dole reiterated the need for social services as follows:

"When somatic functioning has been normalized (by methadone), the ex-addict supported by counseling and social services can begin the long process of social rehabilitation"[16].

The issues of homeless and unemployment were recognized from the beginning of the program. In the 1960s these social ills were more readily addressed than today. Furnished rooms for the homeless and jobs requiring minimal skills were available. Although at program entry most of the patients were unemployed in need of housing

and estranged from families within a few months after entering the program most were productively engaged in employment, enrolled in school, housed, reunited with families and where applicable, functioning as homemakers. This dramatic turnaround within a period of 6 months to one year was a testimony to the efficacy of adequate doses of methadone, the resources in the community and the reality oriented counseling offered in the clinics which may have included legal help to address old warrants and court cases [17,23,32].

To assist in rehabilitation, Dole and Nyswander created a position in the clinics known as research or patient assistants. Successfully stabilized methadone patients were hired as a link to resolve issues between mistrustful patients and the professional clinic staffs [44]. Although the position no longer exists, eligible patients were hired and eventually absorbed into the clinics as counselors and administrators. McLellan et al showed that outcomes of methadone patients in a Veteran's Medical Center methadone program improved with enhanced on site services to patients which included a psychiatrist responsible for medical and psychiatric issues, a vocational counselor, and a family therapist over patients who received standard counseling in the study. Patients who only received methadone did less well than patients who received standard counseling. About 69% of the subjects who received only methadone had to be transferred to standard counseling since their adjustments were poor in regard to continuing use of opioids and cocaine [38]. However, these onsite services are expensive and may not be available to all programs unless they are located within large medical institutions such as the Veterans Administration which offer a panoply of medical, psychiatric and social services to veterans.

However, beginning in the 1970s a confluence of social changes and medical epidemics converged on the patient and addicted population. Economic downturns and the changing nature of work from manufacturing jobs to employment in the emerging information age which demanded a degree of computer skills and literacy adversely affected the employability of patients except for those with the skills and educations applicable in the new job market. Affordable housing for lower middle class and the poor began to disappear, and social benefits were reduced.

These social changes produced a new era of destitution, homeless and hunger affecting many cities and rural areas in the United States [49]. By the 1980s and 1990s improvised dwellings constructed from cartons and discarded materials were seen on the streets. Lack of affordable housing and chronic unemployment produced a modern form of destitution across the country and impacted negatively on the methadone patient population into the 21st century [49]. HIV and hepatitis C emerged within the population starting in the 1970s and possibly earlier for hepatitis C [30,42].

The methadone clinics were usually the patient's only point of contact with medical and social services. As conditions deteriorated for marginal populations, the needs of patients became more complex, diversified and more difficult to obtain and deliver. Clinics located in facilities without services would have to develop linkages with community agencies in order to address the issues that patients presented. This may entail

obtaining funds through grant applications.

Within the past two decades, services were developed in methadone programs to meet women's issues including partner violence [24]. In her evaluations of the methadone program in the mid 1960s thorough the early 1970s, Dr. Gearing noted decreasing retention rates over the course of time and in the 1970s, patients were entering treatment with life threatening medical conditions including pneumonias. She recommended that to obtain needed medical services, methadone treatment should be affiliated with medical centers [23]. Dole and Joseph also noted decreasing retention rates in treatment in cohorts that entered methadone treatment in the early 1970s. There existed a group of transient, chronically unemployed, ill patients who were cycling in and out of treatment and getting arrested on petty charges. There are no adequate services available to help stabilize these patients other than the methadone programs which had limited facilities to address their problems [13]. Problems related to social issues such as homelessness, chronic unemployment and polydrug abuse continue in methadone programs to the present day. While Dole advocated counseling, he was concerned about the philosophy of counseling with the primary goal of removing patients from methadone. Dole's premise was that the primary goal of counseling should be productive functioning in the community while the patient is enrolled in treatment. He believed that patients should be assisted in solving serious problems before attempting withdrawal, considering the serious risks that are involved such as high probabilities of relapse and death [39]. Also, Dole was against overly intrusive counseling that may threaten a patient's job or education because of the time that counseling was scheduled and the hours spent in counseling activities which may detract from employment and educational opportunities and family obligations.

Dole and the Criminal Justice System

In 1972 at the invitation of the New York City Department of Corrections Commissioner, Benjamin J. Malcolm, Dr. Dole, as a non-compensated volunteer, set up the first detoxification service in the New York City jails to withdraw arrested addicts from heroin using methadone. This was the first service of its kind in the United States. Dole was also responsible for enlisting the services of a major hospital, Montefiore Medical Center, to provide the ongoing detoxification services and primary medical care to prisoners in New York City Rikers Island Jail [10,11]. Dole established the jail medical services as a non-compensated volunteer. In 1972 he received a "Citation by the City of New York for Extraordinary Voluntary Service for Establishing the Methadone Detoxification Program- Volunteer of the Year".

In 1987, the service was developed into KEEP (Key Extended Entry Program) by the New York State Office of Alcoholism and Substance Abuse Services and the Department of Corrections. Heroin addicts were not only withdrawn from heroin but if they chose, they could be maintained on methadone and referred for treatment in the community upon their release. Arrested methadone patients could also be maintained on methadone in the jails and, when released, referred back to their programs for continued treatment. KEEP became a model worldwide for methadone treatment

in jails and prisons.

Adolescent Program

In 1968 Dole and Nyswander began research into the needs of addicted adolescents between the ages of 14 and 18 who were unable to enter methadone treatment because of their age. This was the first such research undertaken on an adolescent group. Linkages were made between a local high school located near The Rockefeller University, Dr. Dole's laboratory at the university and the Department of Public Health and Pediatrics Divisions of the New York /Cornell Medical Center now known as the Weill Cornell Medical Center [35].

In 1971 an ambulatory adolescent clinic to house the program was opened near the high school, the university, and the hospital. Applicants had to present a well documented history of heroin addiction of at least two years with at least one failure in treatment program. Parental consent was required and students had to be registered in the local high school. The students reported daily to the clinic and were eventually stabilized on average doses of 35 mg/dy with a maximum of 50/mg/dy. Emphasis was on rehabilitation although detoxification was available when the social situation warranted it. A panoply of supportive services were available: medical services either at the clinic or the hospital, counseling to continue education with tutoring if indicated, vocational referrals and job placements, legal services and recreational activities within NYC through an organization called Hospital Audiences. Over a three year period with 85 admissions there was an overall retention rate of 83%, 22 adolescents had been detoxified although two had to be restabilized because of relapses [35]. The physicians assigned to the program were Drs. Elizabeth Khuri, a pediatrician and Dr. Robert Millman, a psychiatrist. Both physicians had joint appointments at Cornell and in the Dole laboratory at The Rockefeller University.

Methadone Medical Maintenance

Methadone medical maintenance, the prescribing of methadone by a private physician in an office based practice was originally developed in 1983 at The Rockefeller University by Dole, Nyswander, Kreek and Joseph. The purpose of this program is to enable socially stable patients to be treated in the offices of private physicians or other venues of medical practice such as primary care centers instead of the traditional methadone clinics with rigid reporting regulations. The program gives patients the opportunity to further improve their social adjustments, job and educational opportunities. In this program patients report once month to their physicians who prescribe the methadone and receive a month's supply of methadone in a convenient tablet form in one or two vials rather than individual daily liquid formulations in vials which may spill and are difficult to store. Patients submit a urine sample at the time of their visit [41,46]. It was Dole's idea to transfer socially rehabilitated patients into the practices of physicians who had never worked in a methadone clinic to determine whether the doctors could treat the disease of addiction within their practices as they would treat other conditions. At the time of its initial expansion from The Rockefeller University, the

program was transferred to the office-based practices of internists Drs. David Novick, a hepatologist and Edwin A. Salsitz, a pulmonologist. While Dr. Novick did work with Dr. Kreek at The Rockefeller University on research projects, and Dr. Salsitz worked on the detoxification wards at Beth Israel, neither physician ever worked in a traditional clinic. Dr Salsitz harbored negative opinions about methadone as a maintenance medication since his only experience was on the detoxification wards with dysfunctional methadone patients who were poly drug abusers, alcoholics, chronically unemployed and some, destitute and homeless. He was unprepared, psychologically, for the first office patients in medical maintenance who were employed, well dressed, and well behaved. He advised this author that he never met or treated successful methadone patients. When he started to treat stable patients his attitudes changed, and he made "a 180 degree turn." Salsitz realized that his previous negative perceptions about the ineffectiveness of methadone treatment were really about the effects of poverty, chronic unemployment and destitution on human behavior and not about the success or failure of methadone treatment as a medical regimen.

Different models of medical maintenance have been developed in NY State by this author while employed at the N.Y. State Office of Alcoholism and Substance Abuse Services prior to 2003. They are still in existence and are being monitored by the agency.

During the past two years in Albany, NY methadone maintenance treatment for socially stable patients was added to an existing primary care center which has a pharmacy on the premises. At present 25 socially stable methadone patients have been integrated into medical care at the center with a physician who prescribes methadone. The patients receive their monthly methadone at the center pharmacy without observed ingestion. They are seen by the methadone prescribing physician and other specialists in the center, and if needed, the social service counseling staff. Patients are employed and most are married with families. This primary care center has proven to be successful for the delivery of multi-services without taxing the limited financing and space of a traditional methadone clinic. The use of primary care centers to offer methadone treatment is as yet an untapped resource for the expansion of the program and integration of methadone patients into mainstream medical practice.

The physician/commercial pharmacy model was developed at Weill Cornell Hospital with the medical director of the clinic assuming responsibility for care of 14 patients who receive their methadone in a neighborhood pharmacy upon presenting a photo ID card. The patients also receive psychiatric care if indicated, in this program since the medical director is a psychiatrist and will prescribe needed medications for anxiety and depression. The patients in this program are employed and report once per month. However, if there are any problems of a psycho-social nature, then the patients may see the psychiatrist more often.

The pharmacy and the primary care center had to be brought into compliance with the regulations of Federal Drug Enforcement Administration, the Federal Center for Substance Abuse Treatment, and the NY State Office of Alcoholism and Substance

Abuse Treatment as Narcotic Treatment programs with the installation of alarm systems and special safes to store the methadone.

Although the network of seven methadone medical maintenance programs in New York State has been successful according to records maintained at OASAS, the program has not been duplicated on a large scale in the United States. This may be due to the regulations for setting up programs and the expenses involved. Nevertheless, the successful implementation of a few medical maintenance projects in the United States did serve as a model for the introduction of buprenorphine treatment in office-based practices.

The Need for Evaluation

Inherent in Dr. Dole's work was his insistence on objective evaluation of the methadone program. When the pilot project of six patients moved to Beth Israel Medical Center in late 1964 a major evaluation was planned with the Columbia School of Public Health under the direction of Professor Frances Rowe Gearing. Patient retention in treatment, reasons for discharges, duration of treatment, employment status and patient demographics were among the variables studied. In addition a committee was formed to oversee the evaluation, make recommendations concerning the direction of the evaluation and the expansion of the program. No other treatment for addiction was subject to such a continuous investigation for a period of six years. The major findings were that the majority of the patients improved made favorable adjustments with reductions in or elimination of heroin abuse and crime, and increases in productive behavior such as employment, school and child care. However, because of the changes in social conditions patients were entering into treatment in the 1970s with life threatening major medical illnesses, chronic unemployment, and homelessness. It was recommended that methadone treatment be developed in conjunction with medical centers [23]. Also, in the 1970s the federal government introduced regulatory measures which Dole considered excessively intrusive into patient care. Paper work increased in the clinics and the perception of the program became one of control rather than treatment. Patients perceived a strong social stigma targeted to methadone and were ambivalent about entering and remaining in treatment [39,40].

In addition Dole and this author completed a major follow-up study of patients who were discharged from the program in good standing, against medical advice or death. Post treatment outcomes were studied including death rates both in treatment and during the post treatment period [13]. Taking the lead from the Gearing, Dole-Joseph studies, other investigators began to evaluate their programs including follow-up data. A mega analysis by Magura and Rosenblum showed a consistency of trends in all follow up studies: high relapse rates after leaving treatment, post- treatment death rates were at least twice the in-treatment rates with the excess of deaths in the post treatment period associated with heroin use. They recommended that care should be taken in recommending termination from treatment because of the high risks such as relapse rates and deaths [39].

However, evaluation was not confined to the overall clinical management of the

program but also to medical safety of methadone as studied by Kreek. Pregnancy and neonatal development were extensively studied in numerous investigations and methadone was found to be safe for use in pregnancy [22]. Most important are studies that showed methadone can stop the transmission of HIV if patients receive adequate doses [34].

Both this author and Dole indicated that claims about the success or failure of a program without evaluation was only propaganda irrespective of what a program is capable of achieving. Another factor about evaluation is the study not only of the successes but also of failures in treatment which will define the limits inherent in the program and/or the need for further services [32].

Interim Methadone Maintenance

Interim Methadone Maintenance although controversial, is a needed service in cities and countries where limited funding is available, and a heroin epidemic exists with the presence of HIV, hepatitis C, high mortality rates and drug related criminality among the addicted population. The concept has the support of Dr. Dole who wrote an editorial favoring this approach when there is limited access to comprehensive treatment [18]. Interim methadone maintenance provides patients with adequate doses of methadone to eliminate heroin use and counseling on an emergency basis. It is an alternative to traditional waiting lists where patients do not receive medication and continue to inject heroin. It is not an alternative for comprehensive treatment which must be developed. Evaluations of two interim clinic programs in New York City and Baltimore showed that: 1) heroin use and crime were reduced as compared to applicants on the traditional waiting lists, 2) an increase in the likelihood of patients in the interim program entering comprehensive treatment and 3) in New York City a higher rate of interim patients retained in treatment at 16 months than those on traditional waiting lists (72% vs. 56%) [47,51].

While an interim program is not a traditional clinical service, it is a service to the community by helping to reduce crime and to heroin addicts by reducing or possibly eliminating the transmission of HIV and hepatitis C until they enter a comprehensive program [18]. Notwithstanding favorable research the interim methadone maintenance concept has been rejected by the treatment community, the US Public Health Working Group on Methadone and state authorities such as the NY State Office of Alcoholism and Substance Abuse Services since the interim clinic is not a full service program with many of the social services that patients may require. It is now up to communities to evaluate the need for such a program which does have the ability to reduce heroin use, crime and the transmission of HIV and hepatitis until the patient enters a full service program. The National Alliance of Methadone Advocates supported the development of interim methadone maintenance to assist addicts on waiting lists until they entered regular treatment.

Awards

Dole received numerous distinguished awards throughout his career. Among these are the following:

- The Stouffer Award (1972) for his original work in isolating free fatty acids from plasma, demonstrating their origin in body fat stores and their interrelationships with insulin and carbohydrate metabolism.
- The Albert Lasker Award for Clinical Medical Research (1988) for hypothesizing the physiological basis of addiction and developing methadone maintenance treatment for heroin addiction.
- The Fourth annual New York City Mayor's Awards of Honor for Science and Technology (1988) for the development of methadone maintenance to treat heroin addiction.
- Prince Mahidol Award in Public Health (1996) for research into addiction and the development of methadone maintenance for heroin addiction

Stigma: the most destructive social force that methadone patients face.

The social stigma that methadone patients face appears to be pervasive throughout society although some progress is being made through education and advocacy. Patients are especially concerned about their treatment in the criminal justice system where they can be ordered to withdraw from methadone by probation and parole officers and judges irrespective of the adjustments they are making. It appears that physicians' judgments about the applicability of methadone treatment for a particular patient before the court is secondary to the judgments of non medically trained personnel in the court system. Also, methadone treatment for withdrawal or maintenance is not widespread in the jails and prisons. The New York City Rikers Island Jail addiction treatment programs have as yet not been widely accepted in the United States. There is now a campaign spearheaded by enlightened lawyers, judges and advocates to implement nationwide programs and changes in court practices. However, at the last AATOD meeting in 2005, Kathy Coughlin, the Assistant Commissioner of the New York City Department of Corrections reported that few if any referrals were made to methadone treatment in the Drug Courts of New York City.

Patients are also concerned about their treatment in hospitals if their enrollment in methadone maintenance is discovered by medical staff. They are concerned that they may not receive proper pain management or they may be withdrawn from their medication. Most of all they are concerned about the biased attitudes of physicians, nurses, and other health personnel.

The fear of social stigma pervades the patients' lives in the workforce if it is discovered that they are enrolled in methadone treatment. Patients may lose jobs or be placed under unusual surveillance. Furthermore if there should be a theft in an office, methadone patients feel that they would be the first to be suspected. Dr. Norman Gordon reported that in the workforce stable methadone patients are more stigmatized than alcoholics

who may have relapsed. He indicated that "methadone patients are very conscious of the fact that employers and potential employers frequently view their employment with a jaundiced eye"[29]. If a stable methadone patient is in the "closet" and never revealed on an application that he is in the program and urine tests are implemented in the firm, the patient faces indecision, panic about the tests and fear of possibly losing his job. A prime activity for patients therefore is to act consciously in a manner to avoid detection or bring attention to themselves especially at work. Patients therefore develop behaviors to conceal their enrollment in methadone treatment [26,27,40].

Dr. Dole was always at the service of patients and advocacy groups such as the National Alliance of Methadone Advocates to help resolve issues of stigma and misdirected policies that came to his attention. For him, his greatest legacy would be the elimination or reduction of the stigma that is directed to methadone patients, programs, and the medication itself. He communicated with patients through letters, email, phone contacts and personal interviews. Both Dole and Nyswander were concerned about the way methadone is perceived. In an article published on the tenth anniversary of methadone treatment they expressed their misgivings as follows:

"What was not anticipated at the onset was the nearly universal reaction against substituting one drug for another, even when the second drug enabled the addict to function normally. ..... The analogous long term use of other medications such as insulin and digitalis in medical practice has not been considered relevant"[12].

Kosten and George indicate in the following statements that Dole's metabolic theory can lessen the stigma associated with addiction and methadone treatment if patients understand their condition.

"Brain abnormalities resulting from chronic use of heroin, oxycodone and other morphine-derived drugs are underlying causes of opioid dependence (the need to keep taking drugs to avoid withdrawal syndrome) and addiction (intense drug craving and compulsive use)"[36].

"...patients who are informed about the brain origins of addiction can benefit from understanding that their illness has a biological basis and does not mean they are 'bad' people" [36].

Dr. Edwin A Salsitz who treats employed patients in his medical maintenance private office based practice at the Beth Israel Medical Center in New York City and this author found that stigma directed towards methadone treatment is the most destructive force that methadone patients face. They are concerned that revealing their status to family, employers and friends will lead to social alienation and possible job loss. Salsitz indicated that almost all of the patients and families have little or no conception of the nature of addiction and the role of methadone. Methadone is regarded as a heroin substitute, and therefore the patients are not considered cured since they do not have will power and are substituting one drug for another. The term opioid substitution therapy adds to the stigma. Salsitz advised that he must schedule sessions with patients and their families to explain that addiction is a metabolic disorder, and that methadone is a legitimate medication and not a heroin substitute. The conception of methadone maintenance as

a legitimate medical regimen is sometimes difficult to impart since the patients and their families harbor entrenched beliefs and misinformation received from the media, the general public and unfortunately from the medical profession itself [46].

In a speech to the 1997 AATOD conference Dr. Avram Goldstein, professor emeritus of pharmacology at Stanford University, stated that it is wrong to consider methadone a heroin substitute. He reported that the continuous occupancy of methadone on the mu receptor is the stabilizing factor that allows patients to stop the abuse of heroin and normalize their behavior.

"It is therefore not correct to think of methadone as a "substitute" for heroin; its totally different pharmacokinetic properties make it, in effect, a completely different drug. It is true that both heroin (morphine) and methadone can occupy the mu opioid receptors. But the steady, stable occupancy by methadone contrasts sharply with the repeated excessive "highs" followed by excessive "lows" with heroin"[25].

In a December 9, 1998 New York Times article "Report backs methadone for addicts", Dr. Alan Leshner, the then director of the National Institute on Drug Abuse, stated that "... probably the biggest disservice that has been done to getting effective treatment to heroin addicts is the inaccurate statement that methadone is a heroin substitute."

A major source of stigma and rejection for methadone patients comes from abstinence oriented therapeutic communities and 12 step programs based on the Alcoholics Anonymous model. What is not widely known is that Dr. Dole was on the board of AA and was a friend of its founder Bill Wilson. Wilson had a great deal of respect for Dole's development of methadone treatment for heroin addiction.

Wilson was not against the use of effective medications such as methadone to treat people with addiction. He realized that many alcoholics did not respond to AA, dropped out or did not enter the program only to disintegrate or die from the disease. He asked Dole to create a methadone for alcoholism. This encouraged Dole towards the end of his career to conduct alcoholism studies in his laboratory. However, he was unable to find an analogue of alcohol which could be used as a medication [19].

That the founder of AA, Bill Wilson, accepted methadone as a legitimate medication is in direct contrast to the philosophy of 12 step programs based on AA concepts such as therapeutic communities, Narcotics Anonymous, and local AA groups. Methadone patients have never been allowed to fully participate in 12 step programs or until recently to enter treatment in therapeutic communities since methadone is considered a mood altering drug akin to heroin. Methadone patients, therefore, formed their own MA groups (Methadone Awareness and Methadone Anonymous).

Patients are now beginning to organize and confront the media about biased presentations of methadone treatment. Recently a film maker who did not understand methadone produced a documentary, "Methadonia." By interviewing dysfunctional patients, some enrolled in methadone programs and some not, who were attending an abstinence-based group therapy program. It was a misguided effort. Methadone treatment was portrayed in a negative light adding to the stigmatization of patients. The title itself is stigmatizing derived from the term 'methadonians' which stable patients reject

as a subhuman description of themselves. This perception of the term, methadonians, by patients conforms to the observation of Goffman, the sociologist, that stigmatized individuals are regarded as "not quite human," and subjected to bias and discrimination which reduces their chances for life advancement [27,28].

Patients from the National Alliance of Methadone Advocates (NAMA) and the Committee of Methadone Program Administrators (COMPA) of New York State met with the producer. The representatives from NAMA were the first methadone patients he met who were not living in the streets, who were employed and socially stable. He was educated about methadone and agreed to add a 10 minute segment to the documentary by interviewing two patients: a married female lawyer with two children and a businessman who now devotees himself full time to advocacy work. A highly respected physician from a major medical school was enlisted to participate in the segment to explain methadone maintenance. Nevertheless, the damage was already done since the film was aired on nationwide television before patients were aware of it, and the segment was included in the documentary.

In the summer of 2005, NAMA posted an informal survey on its website with the following question: In Europe methadone treatment is called "Substitution Therapy." Do you think this term is positive, negative, not good for the US, or can't decide? Of the 389 respondents, only 26% thought the term was positive, 54% thought the term was negative, 11% thought that it was not a good term for use in the United States, and 8% could not decide. One patient indicated that when she hears the term substitution therapy all of the shame of heroin addiction returns. Gordis observed that the term substitution implies for the public and policy makers that there is little difference between heroin as used in addiction and methadone treatment [26]. Several patients were angered by the term since they felt it added to their stigmatization. The Center for Substance Abuse Treatment (CSAT) in the United States has now adopted the term Medical Assisted Treatment (MAT) to describe methadone and buprenorphine treatment.

Patients and applicants may incorporate the biases of society and enter methadone with great ambivalence including mythologies about methadone (e.g., it rots the teeth and bones) and self negation thereby potentially affecting their progress and the duration of treatment [39]. Education is needed if patients are to understand addiction, methadone treatment and confront the many aspects of stigma in their families, the media and the community.

Recently, NAMA and the methadone program of the Albert Einstein College of Medicine received a four year grant from CSAT to develop educational materials and new patient advocates to address addiction, treatment, stigma, the semantics of vocabulary, legal and medical issues. This is the first grant awarded to a methadone patient organization which will allow a systematic development of materials for patients and professionals to improve treatment, promote advocacy and to destroy myths and stigma by creating a scientific base of accessible knowledge for patients and others to disseminate. It is almost a throw back to the 1960s when Dole and Nyswander created the patient assistants in the original methadone clinics to educate the professional staffs

about addiction, methadone treatment and the patients.

Summary and Conclusion

Throughout his lifetime in research, Dr. Dole's insights transformed whatever topic he investigated. In a sense he planted the seeds and set the direction for further research and clinical development. However, Dr. Dole was always at the service of patients and advocacy groups such as NAMA to help resolve issues of stigma and misdirected policies that came to his attention. For him, his greatest legacy would be the elimination of stigma that is directed to methadone patients, programs, and the medication itself. He communicated with patients through letters, email, phone contacts and personal interviews. Dr. Dole always regarded methadone as a legitimate medication to normalize aberrant metabolism and thus behavior in the chronic disease of opioid addiction. Neither he nor Dr. Nyswander used the term "substitution therapy" in speech or in writing to describe methadone maintenance treatment. When one examines addiction research and the development of treatment today with all of its advances and set backs, the ideas of Dr. Dole seem to pervade those leading the good fight.

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