



# **History of Methadone**

# New York City

- ◆ Heroin use had increased to epidemic proportions
- ◆ Number 1 cause of death rates for men and women 15-35 was related to drug use
- ◆ Legal profession was calling for change fearful of riots occurring in The Tombs
- ◆ Community organizations (i.e. Urban League) were also calling for a response to the situation

# Dr. Dole

- ◆ Dr. Vincent P. Dole was a metabolic researcher at Rockefeller University who became interested in addiction from his work in obesity. He was asked to try to solve the problem in New York.
- ◆ His work in obesity with that of Dr. Jean Meyer of Harvard University has led us to understand that obesity has a metabolic origin.
- ◆ He was struck that his obese patients seemed to be addicted to food and was thinking about applying what he knew about obesity to study addiction when he was offered a \$10,000 grant to solve the addiction problem.

# Dr. Marie Nyswander

- ◆ Marie Nyswander had joined the Public Health Corp during the war and was assigned to the Public Health Hospital in Lexington, KY that was the only place that treated addiction in the US.
- ◆ In 1956 she wrote “The Drug Addict as Patient” which for its time was decades ahead of the current belief.

However nothing seemed to work and most of the addicts she treated relapsed. She was beginning to think of risking her license and prescribing morphine because they would at least be better off getting a legal source.

# The First Study

- ◆ 2 Addicts – both males with a history of >8 yrs addiction
- ◆ Given morphine and like the obesity study before allowed to have as much as they wanted – which they did
- ◆ The result was they sat in front of the TV all day waiting for their next shot
- ◆ Dole and Nyswander were not looking for a medication to treat addiction. As in the obese studies they were simply following the metabolic pathways of morphine
- ◆ Certainly morphine was not a good maintenance drug which was also one of the reasons for the study. So thinking they had failed they switched their patients to methadone the standard to withdraw addicts in preparation for release from the hospital.

# A Change in the Study

- ◆ Methadone was known to be a synthetic and different from morphine so thought the researchers perhaps we can run the same tests with methadone that we did with morphine and have a comparative drug.
- ◆ So the subjects instead of decreasing their methadone dose began to have it increased.
- ◆ The subjects were delighted of course...and then something happened.

# Surprising Changes Occur

- ◆ After several weeks of methadone their subjects began to behave different: one began to paint and the other insisted they allow him to finish high school.
- ◆ So it was decided that the two could leave the hospital grounds to pursue other endeavors and return at night.
- ◆ Both were freed of their drug craving and began to become whatever they potentially are.
- ◆ 4 more patients were admitted and the same results achieved.

# First 22 Patients

Maintenance Therapy of Ex-Addicts With Methadone Hydrochloride, Summary of First 15 Months (February 1964 to May 1965)

No.	Ethnic*	Age		Status Before Admission to Program							Status Since Admission					
		FD	A	Previous Treatments				Arrest	Education	Best Job §	Army □	Mth Rx Dose †	P #	HS**	Present Activity	
		F	S	M	P											
1	E	16	22		3	3		6	8th grade	Truck driver		15	150	1a	Cert	Preparing for college (Sept 1965)
2	E	18	31	3	3	2		8	1 year h/s	Odd jobs (few m)		15	180	1a	Cert	Horticulture school
3	P	21	33	2		4		14	2 years h/s	Office clerk		10	100	1a	Cert	Employed (rehabilitation work)
4	E	20	30	1	2	3	1	1	Graduated h/s	Store manager	A3	10	180	1a		Employed usher/cashier theater
5	E	17	22			6		4	2 years h/s	Shipping clerk		11	100	3		Employed (parking lot foreman)
6	E	21	25				12	1	2 years college	Musician		10	100	3		Employed intermittent (musician)
7	E	18	25			2		6	Graduated h/s	Radio operator military N4		3	100	2		Employed (office work)
8	N	17	32	1		2		9	2 years h/s	Clothes presser		1½	100	1	NS	Seeking employment
9	N	22	37		1	1		3	2 years h/s	Truck driver	A4	1½	80	1	NS	Seeking employment
10	P	15	23					1	2 years h/s	Head usher	A3	1½	90	2	CtArmy	Working as waiter
11	N	16	27	1		4		1	3 years h/s	Stock clerk	A5	1½	130	1	NS	
12	E	18	22	3		3	2	4	1 year college	Mason		1	100	1		Seeking employment
13	P	25	35	1		2		3	1 year h/s	Paint sprayer		½	110	1		Employed
14	P	20	32	1		4		9	2 years h/s	Supervisor of shipping		1	100	1	NS	Employed
15	N	18	30	2				6	3 years h/s	Shipping clerk	AF4	¼	70	1	NS	Seeking employment
16	E	18	24			10		0	8th grade	Installing windows		3	115	2	NS	Employed
17	P	14	30					2	2 years h/s	Office clerk	M3	3	70	2	NS	Welfare (seeking employment)
18	P	19	25			16		10	2 years h/s	Office clerk	AF 2½	3	110	2	NS	Employed (hospital record room)
19	E	17	19			1	1	0	Graduated h/s	None		3	120	2		Vocational school (barber)
20	P	13	20				1	2	3 years h/s	Stock boy		3	50	2	NS	Employed (hospital laundry)
21	E	19	26			2		8	2 years h/s	Construction labourer		1½	100	2	NS	Seeking employment
22	N	14	30					2	8th grade	Shipping clerk	AF 4	1½	10	2	Cert	Leather goods co. interpreter

FD=age of first heroin use, A=age starting treatment, P=phase of treatment, A=army, M=marines, N=navy, NS=night school

# Initial Program at Rockefeller

- ◆ Had to be able to stay in the hospital for 6 months to stabilize.
- ◆ No take home medication given.
- ◆ No other drug problems.
- ◆ No mental health problems.
- ◆ No women.

# At Rockefeller



Marie Nyswander, 1919–1986

Vincent Dole, 1912-2006

# Expanding the Program

- ◆ When Drs. Dole and Nyswander found that methadone worked the same for a second group of patients he went to Dr. Ray Trussell the Health Commission of New York City to ask for some beds.

# Methadone Gets a Godfather

- ◆ Dr. Trussell would become a Godfather to the early methadone program.
- ◆ He found 6 beds at Manhattan General (Bernstein Inst.) to expand the Rockefeller Program.
- ◆ And he found money to expand the program.

# Further Expansion

- ◆ From the initial 6 patients the program quickly grew to several hundred... and then 1000.
- ◆ By 1970 the program grew to nearly 4,000 patients attending 46 programs overseen by Dole and Nyswander.
- ◆ Management of the program depended on patients as many of the first patients were hired as Research Assistants.

# The Gearing Evaluation

- ◆ Dr. Dole asked for an independent evaluation which was set up at Columbia University School of Public Health under Dr. Frances Rowe Gearing.
- ◆ Dr. Gearing reported on the Dole-Nyswander patients at three methadone maintenance conferences held in New York in 1968, 1969, and 1970.

# **New York City Program**

- ◆ In 1970 there were 4,000 patients.
- ◆ New York City under the direction of Dr. Robert Newman oversaw an 18 months expansion to around 23,000 patients.
- ◆ The numbers entering treatment were unprecedented with every New York City hospital having at least 1 program some had 2 and some specialized as the Bellevue MMTP that treated pulmonary diseases and opiate addiction.

# Decreases in Drug Arrests, Property Crimes and Serum Hepatitis New York City 1971 – 1973\*

## Decrease in Cases

Category	Number	(%)	Decrease per 1000 Admissions
Drug Arrests	24,900	(45)	1251
Property Crimes	77,000	(22)	3869
Drug Dependent Deaths	324	(37)	16
Serum Hepatitis	1,500	(68)	75

# Prison Detox

- ◆ Another first was setting up a detox program in The Tombs.
- ◆ The Commissioner of Prisons was concerned that riots would break out because of the conditions and asked Dr. Dole to do something.
- ◆ Set up over the weekend and started the following Monday.

# **Very First Study To Find Opiate Receptors**

- ◆ **Ingolia, N.A. and Dole, V.P. 1970.  
Localization of d and l-methadone after  
intraventricular injection into rat brains.  
Journal of Pharmacology and Experimental  
Therapeutics 175: 84-87.**

# The Dole Test

- ◆ This was the first narcotic addiction program in which "success" was evaluated with the help of effective urine tests.
- ◆ Still called "The Dole Test" in some criminal justice settings.

# Final List of Firsts

1. **First methadone maintenance clinic.**
2. **First detox program.**
3. **First hospital set up for addictive disorders (Bernstein).**
4. **First prison detox program.**
5. **First addiction program to have rigorous scientific evaluation to validate it.**
6. **First urine test.**

# **Dole and Nyswander's Contribution**

**In spite of all these firsts the significant contribution that Dole and Nyswander made was to change the paradigm from approaching opiate addiction as a criminal justice/behavior disorder to a medical condition (metabolic disorder).**

# 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.”

- ◆ Dole and Nyswander use the word replacement in a metabolic sense they do not mean that methadone replaces heroin or that methadone is a substitute for heroin.