Cannabis in Western Medicine: An Abbreviated History†

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The medicinal uses of cannabis historically appear to have two different lineages: 1) the therapeutic use for physical and mental conditions; and 2) the study of alterations of consciousness. In the therapeutic context, alteration of consciousness was regarded as a troublesome side-effect of overdose or oversensitivity. In the study of altered states of consciousness, on the other hand, psychoactive effects were the focus of study.

This latter lineage began with Dr. J.J. Moreau in Paris in 1843 with his use of the drug both as an experimental psychotomimetic and a psychotherapeutic agent in major mental illness (Moreau 1845), which was also used concurrently socially in his hashish club, later chronicled by Gautier in 1846. This popular account and tales of the Land of the Saracens by travelers such as Bayard Taylor (1855) inspired other writers like Fitzhugh Ludlow (1857) to popularize upper-class social use in the later 19th century. Dr. Victor Robinson, eminent medical historian at Temple University School of Medicine from 1929 to 1947 carried on this tradition in his *Essay on Hashish* in 1912, which lent further depth to his later writings in 1946. The more pedestrian therapeutic applications originated virtually at the same time on the other side of the world in India.

It remained for William Brooke O'Shaughnessey, M.D., a brilliant thirty-year-old Irish physician serving with the British East India Company, to introduce the drug to Western medicine (1842). O'Shaughnessey, who as a medical student invented intravenous fluid therapy, saving lives during a cholera epidemic (Moon 1967), wrote a 49-page monograph describing his classic study of cannabis containing the elements of literature review, botanical and physical description, animal experiments, normal human studies and clinical trials with different diseases (O'Shaughnessey 1838). He noted the drug to have numerous useful properties. Cannabis was low in toxicity:

> The reader will remember that this infant [who with the aid of cannabis survived febrile convulsions] was but sixty days old when 130 drops were given in one day, of the same preparation of which ten drops has intoxicated the student Dinonath Dhur who took the drug for experiment. One hundred thirty drops are equal again to 15 grains of the resin, one grain of which occasioned profound trance [or catalepsy] in two men suffering under rheumatism (p. 29).

As an analgesic and stimulator of the appetite:

> In several cases of acute and chronic rheumatism admitted about this time, half-grain doses of the resin were given, with closely analogous effects;... alleviation of pain in most ... remarkable increase of appetite in

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> all . . . unequivocal aphrodisia, and great mental cheerfulness. In no one case did these effects proceed to delirium, or was there any tendency to quarrelling. The disposition developed was uniform in all, and in one was the headache or sickness of stomach a sequela of the excitement (p. 20).

Concerning tetanus:

> The preceding facts are offered to the professional reader with unfeigned diffidence, and to the inferences I feel disposed to derive from the consideration. To me they seem unequivocally to shew, that when given *boldly*, and in large doses, the resin of Hemp is capable of arresting effectually the progress of this formidable disease, and in a large proportion of cases of effecting a perfect cure (p. 26).

On rabies:

> I am not however rash enough to indulge the hope which involuntarily forces itself upon me, that we will ever from this narcotic derive an effectual remedy, for even a solitary case of this disease – but next to cure, the physician will perhaps esteem the means which enable him "to strew the path to the tomb with flower," and to divest of its *specific* terrors the most dreadful malady to which mankind is exposed (p. 22).

On convulsions:

> The preceding cases constitute an abstract of my experience on this subject, and which has led me to the belief that in Hemp the profession has gained an anti-convulsive remedy of the greatest value (p. 29).

On cholera:

> It is but fair to state, however, that the character of the epidemic was not at the time malignant. I admit the cases to be inconclusive, but I conceive them to be promising, and that they deserve the close attention of the practitioner (p. 23).

The use of cannabis as a treatment for diverse maladies involving nervous system spasm or irritability spread rapidly through Western medicine. The Report of the Ohio State Medical Committee on *Cannabis Indica* in 1860 from the State Society's annual meeting, reports clinical impressions of 19 practitioners. The committee report reviewed 20 years experience with the drug crediting O'Shaughnessey with introducing the drug and inspiring his professors back at the University of Edinburg who corroborated its efficacy as a calmative and hypnotic (McMeens 1860). As early as 1847, cannabis was prescribed in Tiffin, Ohio by Dr. E. Dresbach, who described it as being effective as an anticonvulsant. Dr. Fronmeuller of Fuerth summarized his experience:

> I have used hemp many hundred times to relieve local pains of an inflammatory as well as neuralgic nature, and judging from these experiments, I have to assign to the Indian hemp a place among the so-called hypnotic medicines next to opium; its effects are less intense, and the secretions are not so much suppressed by it. Digestion is not disturbed; the appetite rather increased; sickness of the stomach seldom induced; congestion never. Hemp may consequently be employed in inflammatory conditions. It disturbs the expectoration far less than opium; the nervous system is also not so much affected. The whole effect of hemp being less violent, and producing a more natural sleep, without interfering with the actions of the internal organs, it is certainly often preferable to opium, although it is not equal to that drug in strength and reliability. An alternating course of opium and Indian hemp seems particularly adapted to those cases where opium alone fails in producing the desired effect. The best form is small pills, made from the spirituous extract, with a little of the powdered leaves. The smallest dose may be set down at eight grains; a rapid increase is frequently required (McMeens 1860: 124).

Dr. W.P. Kincaid of Neville described three years of clinical trials for diverse illnesses and concluded:

> In conclusion, I would remark, that I regard the hemp as an excellent nervous stimulant, applicable in all diseases of a *purely* nervous character (McMeens 1860: 140).

From 1860 to its removal from availability to physicians in 1937 at least 12 separate therapeutic uses for cannabis were described:

1. Analgesic-hypnotic
2. Appetite stimulant
3. Anticpileptic-antispasmodic
4. Prophylactic and treatment of the neuralgias, including migraine and tic douloreux
5. Antidepressant-tranquilizer
6. Antiasthmatic
7. Oxytocic
8. Antitussive
9. Topical anesthetic
10. Withdrawal agent for opiate and alcohol addiction

11. Childbirth analgesic
12. Antibiotic

After its removal:

1. Intraocular hypotensive
2. Hypothermogenic (Mikuriya 1975: xxiv).

As the pharmaceutical industry grew it developed increasingly sophisticated means of microscopic examination, assay and standardization of crude botanical drugs:

> A sample is taken for examination to the laboratory, the sample being representative of the lot being taken from every container if the shipment is from a new source or consists of only a few bags. In the case of 52 carload lots the number of containers sampled averages about 10 percent.
>
> The representative sample is taken to the Botanical Laboratory where it is examined for that particular drug. Examination of a drug that contains no alkaloids or active substances usually consists of the physical examiniation and determining the ash and the acid insoluable ash.
>
> Drugs that contain alkaloids, volatile oil, or active substances are given the physical examination, usually the ash and acid insoluble ash determination and if these meet the specifications, are sent for assay or physiological tests. The volatile oil assay and moisture determination are done in the Botanical Department.
>
> The drugs such as Ergot, Digitalis and Strophanthus for which there are now no chemical assays are tested on animals as specified in the U.S.P. or the National Formulary.
>
> . . . If the tests show the drug to be inferior or does not meet the standards we have set up . . . the lot is held in the warehouse until the Purchasing Department has notified the shipper that the drug is unsatisfactory and is being returned to them.
>
> We have a few instances of rejections, usually from new sources of supply. Before a lot is rejected a second sample is withdrawn and a complete re-examination is made to confirm the first results.
>
> Crude drugs are purchased unground because it is more difficult to add foreign substances to them . . . It would be very difficult to determine this adulterant if the drug were ground.
>
> The U.S.P. or National Formulary tests are usually followed. We work with the revision committee of both the U.S.P. and N.F. to improve assay methods (*Lilly's Bulletin* 1891: 1-2; Seybert 1968).

Lacking direct chemical analytic methods, the industry developed standardized bioassay:

1. Select medium-sized, short haired dogs weighing less than 15 kilos, of fair degree of intelligence, preferably fox terriers. Do not feed for 12 hours prior to the test.
2. Determine susceptibility of the dogs by administration of minimum dose of standard preparation. The standard preparation is obtained from the Food and Drug Control Laboratory at Washington.
3. The dose of sample to be tested is determined by multiplication of the weight of the dog by the standard dose per unit weight.
4. Dose is administered in capsule.
5. The results of administration are apparent in about one hour. Muscular incoordination and drowsiness indicate activity.
6. The activity of the sample is dependent upon the degree of reaction and susceptibility of the dog. Do not use the dog oftener than once every three days.
7. The standard dose for various preparations is as follows:

Drug (as fluid extract)	0.1g/kg
Fluid extract	0.1cc/kg
Tincture	1.0cc/kg
Solid extract	4.0mg/kilo
Powdered extract	40.0mg/kilo

8. Retest the sample following adjustment on the basis of the first assay (Wheeler 1968).

As chemical technology advanced, pharmaceutical preparations became more purified with the development of derivative salts, with cannabin, cannabindon, cannabine and cannabinon being marketed by Merck in 1896. Cannabis was also combined with different drugs in proprietary preparations. For example, Squibb around the turn of the century included cannabis in "Chlorodyne," a gastrointestinal antispasmodic employing morphine as its main ingredient (Squibb 1899). Shortly before removal from availability in 1937, 28 different preparations containing cannabis were on the market (Sasman 1938).

Because of the fluctuation of prices of Indian cannabis due to taxation policies of the British colonial government there were continuing efforts to develop

American medicinal strains. From 1918 to 1937, Parke Davis and Eli Lilly ran a joint research project at Parkedale, a botanical experimental facility near Rochester, Michigan in an effort to produce a viable American strain (Wheeler 1968). As a result, in 1913 Parke Davis scientists claimed that American-grown cannabis had the same effects as Indian but at about one-tenth of the strength (Wheeler 1968).

The main drawback of cannabis clinically was variability of strength from batch to batch or even within the bottle. The fragrant resin with the physical consistency of pine pitch might age and lose its potency or settle to the bottom and cause overdose. Nineteenth century medicinal cannabis literature has numerous accounts describing the mental side-effects of unwitting overdose as an untoward side-effect of therapy for diverse conditons or the result of self-experimentation. Another drawback was its long latency from administration to onset of effects due to the insolubility of cannabis resin in water-based preparations. As the synthetic water-soluble analgesics and sedatives made their appearance at the end of the 19th century, their swifter and more certain action upstaged hemp drugs in popularity and use declined.

In unsuccessful opposition to the 1937 Marijuana Tax Act that he correctly feared would deprive medicine of cannabis, Dr. William C. Woodward, legislative counsel, articulated the offical stance of the American Medical Association:

> . . . there is positively no evidence to indicate the abuse of cannabis as a medicinal agent or to show that its medicinal use is leading to the development of cannabis addiction. Cannabis at the present time is slightly used for medicinal purposes, but it would seem worthwhile to maintain its status as a medicinal agent for such purposes as it now has. There is a possibility that a re-study of the drug by modern means may show other advantages to be derived from its medicinal use (Report of the Committee on Legislative Activities 1937).

With the removal of cannabis preparations, most of medicine and science forgot about the therapeutic properties of cannabis and began studying marijuana, "killer weed." The 1944 LaGuardia Commission, Frances Ames in 1958, Weil, Zinberg and Nelsen in 1968 all studied the medical hazards of acute marijuana use.

Cannabis as a therapeutic agent went underground. In the 1949 *Federation Proceedings of the American Society of Experimental Biology*, Davis and Ramsey described antiepileptic effects of a THC congener administered to five institutionalized epileptic children. In 1950, W.S. Loewe, Ph.D. from the University of Utah, published in *Archiv fur Experimental Pathologie und Pharmakologie* a brilliant study of 11 different THC homologs structure-activity relationships for potency, analgesia, anticonvulsant activity and hypnotic qualities.

From 1954 to 1959 these homologs were studied secretly for their potential incapacitating effects by the Army at the Edgewood Arsenal in Maryland (Berger 1971). In 1967, when I was a research psychiatrist at the National Institute of Mental Health charged with the mission of setting up the "first" research budget for the federal government I learned of these activities from Van M. Sim, M.D., who in a phone conversation informed me that the results were classified. The results were quietly declassified in 1971 revealing that Arthur D. Little and Co., co-contracting with the University of Michigan, had discovered that THC homologs are potent hypothermogenic agents and reconfirming THC anticonvulsant activity first reported by O'Shaughnessey (Little & Co. 1971).

I must admit to occasional encouragement of alcoholic patients to attempt cannabis substitution. One case I described as making the switch in 1968 has continued the treatment successfully to date using less than three marijuana cigarettes per week. Generalizing on my experience with less than a dozen cases, it is my observation that the substitution can be successful if there is immediate social support but fails if this is not available.

Soon after, Hepler and Frank reported lowering of intraocular pressure in a fortuitous discovery (1971). Frederick Blanton, an ophthalmologist from Brevard County, Florida, circumventing government red tape, made his own marijuana brownies for use with his glaucoma patients. He reported success to his colleagues at Johns Hopkins which was well received but when he reported his findings to his local colleagues he was suspended from the local medical society, expelled from the two hospitals where he had operating privileges and investigated by the state board of medical examiners (Berger 1973). No doubt controlled studies will be funded — eventually by the federal government — a far cry from when the Department of Agriculture used to supply a cannabis reference standard to the pharmaceutical industry and the AMA supported retention of cannabis for medicinal use.

In light of overwhelming historical evidence that cannabis is a safe and efficacious remedy, immediate restoration to prescription status is warranted. Despite the advent of technololgy, these intelligent observations articulately described in the past must not be forgotten. Failure to heed previous insights results in superfluous

repetition, stupidity through ignorance and resultant failure.

Because of arrogance of the present and taint of "killer weed" in public opinion, abetted by an ignorant scientific and medical establishment that forgot what it once knew, the current prognosis is at best guarded. Society's loss is not just the added harm and suffering of patients who could benefit – but the diminution in stature of the medical and scientific communities in their flight from reason and whose inability to counsel governmental agencies results in their continuing inability to formulate efficacious rational social policy.

Although Harry Anslinger is dead and gone and the ludicrous "killer weed" stereotype fading, opposition to putting cannabis back in the pharmacy is retained by non-clinician bureaucrats whose academic perspectives dismiss the large body of historical clinical therapeutic data as being "folk medicine" (Petersen 1977). My profession shall someday be grateful to the efforts of Robert Randall, courageous young glaucoma sufferer (successfully treated by smoked cannabis) and the humanistic court that rightfully decided that the treatment of disease of a citizen was more important than the irrational federal prohibitory laws concerning cannabis. The National Organization for the Reform of Marijuana Laws (NORML) will, in the not too distant future, be appreciated for their efforts to restore cannabis derivatives to the physicians' armamentarium of drugs.

While all this will eventually be successful, it is a shame that this initiative could not have come from within the medical and scientific communities, that because of their intimidation by public opinion, prevented therapeutic applications and study of a most unique chemical. Cannabinoids are the only natural complex non-nitrogenous, water-insoluble psychoactive molecule yet discovered that also have a dose-range safety factor immeasurably greater than most psychoactive drugs.

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