On Cannabis, Chloral Hydrate, and Career Cycles of Psychotropic Drugs in Medicine

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SUMMARY: This article compares the careers of two psychotropic drugs in Western psychiatry, with a focus on the nineteenth century: Cannabis indica and chloral hydrate. They were used by doctors for similar indications, such as mania, delirium tremens, and what we would now call drug dependence. The two show similar career paths consisting of three phases: initial enthusiasm and therapeutic optimism; subsequent negative appraisal; and finally, limited use. These cycles, which we term "Seige cycles," are generally typical of the careers of psychotropic drugs in modern medicine. However, differences in the careers of both drugs are also established. The phases of chloral show relatively higher peaks and lower valleys than those of cannabis. Chloral is the first typically "modern" psychotropic drug; a synthetic, it was introduced in 1869 at a time of growing asylum populations, pharmaceutical interests, and high cultural expectations of scientific medicine. Cannabis indica, introduced in the 1840s, is typically a "premodern" drug steeped in the climate of cultural Romanticism. We conclude that the analytical concept of the Seige cycle is a useful tool for future research into drug careers in medicine.

KEYWORDS: psychotropic drugs, cannabis, chloral hydrate, addiction, pharmaceutical industry, Merck, Jacques-Joseph Moreau de Tours, Oscar Liebreich

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Introduction

In their conception, production, marketing, and use, therapeutic drugs are more than just medical commodities: they also reflect dynamics of development and transformation in the science and art of healing as a cultural process. However scientific and modern in nature, medicine and its therapies are bound up with dynamic mixtures of opinions, practices, and rituals that shape the landscape of health care. Given increasing visibility by the marketing practices of the pharmaceutical industry, and used in contexts that have grown more and more subjected to media attention, psychotropic drugs have become important focal points of cultural mediation and imagination in public domains. These sociocultural dynamics associated with psychotropic drugs have not only been paramount in defining public images and policies, they have also influenced the production of medical and scientific knowledge. In the past decade historical and sociological research has drawn attention to the interplay between public, medical, and scientific spheres in shaping the careers of drugs such as LSD and the minor tranquilizers, which were developed after the Second World War.¹

The careers of psychotropic drugs in modern medicine, despite all their differences, have three characteristics in common. First, these careers do not follow linear paths, but run in cycles. Second, they are the product of complex interactions between science, medicine, industry, and the public sphere (including drug-using subcultures). Third, they are closely intertwined with the careers of other drugs, and should be studied in a comparative perspective.

The first of these observations, the idea of a cyclical dynamic of the careers of psychotropic drugs, is not a new concept. As early as 1912 the German psychiatrist Max Seige formulated the idea when describing the “flood” of sedatives and hypnotics that had overwhelmed the pharmaceutical market since 1900:

The first reports sounded in every respect extremely favorable; but before long it became clear that [these drugs] did not satisfy the traditional conditions of

Cito, tuto et jucunde [quickly, safely, and pleasantly]—at least, that even in small doses they caused all kinds of unpleasant or detrimental side effects. Finally most of them found a small, limited, special territory within which the conscientious physician uses them.2

By the middle of the century similar observations were being expressed in the medical literature. For instance, in 1954 Ernest Jawetz showed that medical approval of pharmaceutical drugs followed a pattern: “At first, the use of a new remedy rises quickly in a period of optimism; then some untoward side effect is noted, and the approval wanes rapidly to a low level based on mistrust and fear; finally, use stabilizes at a moderate level.”3

Drug career cycles generally encompass three phases: first, an expanding use of the drugs, accompanied by high expectations; then, rising criticism and disappointment; and finally, contracting use and limited application. These phases need not be sequential: they often overlap. The cycle sometimes ends with the disappearance of the psychotropic drug from the medical market and its replacement by newer drugs (which often follow similar career paths). But a drug can also reappear and start a new career cycle—for instance, when it is used for a new diagnostic category, as in the case of ADHD and methylphenidate (Ritalin) in the 1990s.4 Because it was Max Seige who first pointed out the cyclical nature of the careers of psychotropic drugs, we have named this general dynamic a “Seige cycle.”5

The Seige cycle is not a “universal” law. Instead, its relevance is as an analytical tool that enables a comparative perspective on drug careers. These dynamics point to significant changes in the ways Western societies have used and regarded drugs. In the nineteenth century, drug careers often began with very broad indications for their use; but by the end of the

twentieth century, antidepressants such as Prozac would start their career with narrow and specific indications for use in order to gain a niche in the pharmaceutical market. The Seige cycle is a general abstraction of many drug career paths that show us significant similarities as well as changes.

Furthermore, the career of a drug has to be understood within the contexts of existing and changing armories of available drugs, both trademarked and in the public domain. The administration of psychotropic substances has been an underlying constant in mental health care, regardless of changes in therapeutic fashion. Psychiatrists have prescribed drug treatment since the nineteenth century, and there has been a steady demand for psychotropic drugs—whether as patent medicines, prescription medicines, natural remedies, or recreational agents. These categories of drugs are therefore, in a sense, in continuous competition with each other.

These characteristics have been especially prominent since the mid-nineteenth century. The introduction of chloral hydrate in 1869 as the first synthetic compound used in mental health care marks the start of modern psychopharmacology. Chloral hydrate was intimately connected to the rise of scientific laboratory medicine and to the scientific, therapeutic, and cultural expectations of a new era of medicine. Since 1869 these cultural hopes and expectations have increasingly combined with the growing field of psychiatry and institutionalized mental health care, on the one hand, and with the expanding pharmaceutical industry on the other hand. These historical actors played directing roles in the careers of psychotropic drugs.

We will explore here the significance of sociocultural factors in shaping the career cycles of Cannabis indica and chloral hydrate. By comparing the career paths of these drugs we aim to contribute to a better understanding of the dynamics of therapeutic drug development and use in the medical and public spheres.

Cannabis in Transition

The cannabis introduced into medicine in the first half of the nineteenth century was received as a new drug by both the medical profession and the general public. Of course, there was the species Cannabis sativa, classified

by Linnaeus in 1753, indigenous to Europe and used in medicine since antiquity: Dioscorides mentions its use in the preparation of ear drops and in abortus provocatus. There is ample evidence from Dutch pharmacopoeias of its continued use as a medicine; in the seventeenth century, cannabis extracts were primarily used in Dutch medicine as analgesics. But the “new drug” introduced into nineteenth-century medicine was a form of cannabis with notable psychoactive properties: Cannabis indica, first classified by Lamarck in 1783. As has often been described, interest in the effects of this plant was kindled during the British colonization of India and the French conquest of Egypt, but it was not until the 1840s that it became well known in medical and public spheres, as various extracts of Cannabis indica became available, produced by pharmacists in London (Squire’s), Edinburgh (Smith’s), Paris (De Courtive’s and Personne’s), and Cairo (Gartinel’s).

One of the most influential early medical writers on cannabis, Jacques-Joseph Moreau (de Tours), published his first article on the subject in 1841; his important monograph followed in 1845. Moreau organized the drug sessions of the Club des Hachischins in Paris in 1845 that became famous (and notorious) because of the writings of Théophile Gautier and, in the following decade, Charles Baudelaire, including the latter’s Les paradis artificiels. The work of Moreau was pivotal in transferring cannabis from the medical to the public domain. Although a satisfactory


9. There has been some debate as to whether there is actually more than one species of cannabis plant. A categorization into three species—C. sativa, C. indica, and C. ruderalis—based on differences in seeds, stalks, growth habits, and resin content, is accepted by most authorities. See Peter Stafford, Psychodelics Encyclopedia, 3rd ed. (Berkeley: Ronin Press, 1992), pp. 157–59. A nineteenth-century researcher, Ernst Freiherr von Bibra, saw as the only differences between C. sativa and C. indica that the latter grew to greater heights and had much more psychoactive content: Die narkotischen Genussmittel und der Mensch (Nuremberg: Schmid, 1855), pp. 265–66.


biography of this pioneering psychiatrist is still lacking, his life has often been described.\textsuperscript{12}

In *Du hachisch et de l’aliénation mentale*, published in 1845, Moreau studied the effects of cannabis on the human mind, its use as a research tool in exploring the field of psychopathology, and its clinical use in the treatment of mental disorders. *Du hachisch* has been of major influence on subsequent research. Moreau started a systematic study of the psychologi- cal action of psychotropic drugs, which became a model for later research in experimental psychopharmacology and psychopathology.\textsuperscript{13} His initial interest in the drug, he wrote, was solely curiosity about its effects on himself. This led him to questions of the exploration of psychopathology and its boundary with both ordinary states of consciousness and dream states.\textsuperscript{14} Here, self-experimentation as a basic research method in psychopharmacology did not limit itself to exploring the psychological and somatic effects of drugs, but was also used to explore non–drug-induced psychopathology. The method’s results were held to be valid for the understanding of “natural” mental disorders. Moreau defined an essential underlying assumption of psychoactive drug research, later described as the “psychotomimetic” view of the effects of psychoactive drugs: namely, the identity of the psychological nature of the delirium in both insanity and drug intoxication.\textsuperscript{15} This “experimental psychopathology” was accompanied by the use of cannabis as a psychotropic drug treatment. What were the specific characteristics of the introduction and subsequent clinical use of the drug?

Moreau explored the psychotherapeutic opportunities of psychoactive drugs in the clinics of Bicêtre and Salpêtrière, as secondary to his


primary interest in the subjective experiences of psychopathology. He experimented with the therapeutic use of cannabis prepared as in the Orient in the form of a kind of candy, *dawamesc*. He hypothesized that the manic excitement accompanied by the gaiety and happiness provoked by cannabis use could be effective against the idea fixation present in melancholia. Cannabis could give a supple intelligence to the mentally retarded (*aliénés stupides*) and increased energy to the demented, but only in the case of melancholia did he actually notice temporary improvements after the administration of cannabis. More promising results were found in the use of the drug to maintain patients in a state of “acute mania” in order to prevent their progression into a state of “chronic mania.” He presented evidence of seven cases of this, but also recognized that more experiments were needed.\(^{16}\)

In following cannabis’s career path through nineteenth-century psychiatry we are much indebted to the pioneering study in the Anglo-American literature by the American psychiatrist E. T. Carlson, published forty years ago in the *American Journal of Psychiatry*.\(^{17}\) Following the work of Moreau, cannabis entered the first phase of its Seige cycle. The drug was used in nineteenth-century psychiatry for a number of indications: as a sedative and hypnotic in cases of insomnia and delirium tremens; for withdrawal symptoms in drug addiction (narcomania); and in the treatment of mania, melancholia, and neurasthenia (the “new” mental disorder “discovered” in 1869 by George Beard). The knowledge of the therapeutic use of cannabis was quickly taken up in other countries. *Du haschisch* was reviewed, hardly a year after its publication, in the *American Journal of Insanity*. The reviewer—the journal’s founder, Amariah Brigham—had studied in Paris and was a devotee of French science and literature; he might therefore have first learned of cannabis by reading Gautier. Brigham began to experiment with the drug on his own patients at the lunatic asylum in Utica. He recommended cannabis as “a very energetic remedy, and well worthy of further trial with the insane.”\(^{18}\)

However, there was a condition that limited the expansion of the use of cannabis. Pharmaceutical companies drew their marketing strength from


their guarantee of standardized preparations, and although companies such as Merck started to produce their own cannabis drugs, these were not valued highly in terms of market potential because the chemists could not isolate the psychoactive component. The Austrian pharmacologist Carl Ritter von Schroff recognized that the effects of cannabis were extremely variable across individuals, confirming the conclusions of Moreau and the Hachischins. The American psychiatrist George M. Beard wrote in 1880: “Cannabis indica . . . has the reputation of untrustworthiness and unreliability, both of preparation and of action.” His hope that cannabis would lose this reputation was unfulfilled. Only in the 1940s was its specific psychoactive component, tetrahydrocannabinol (THC), isolated.

This unreliability of effect was one reason why cannabis entered almost immediately into the second phase of its Seige cycle, which for a long time remained coexistent with the first phase. In addition to the questioned efficacy of cannabis, there were also unsolicited side effects of the drug; by 1890 these included primarily mental excitement and confusion, and secondarily, headaches and dizziness. Further, there were cultural and social “side effects,” including addiction problems, subcultural use, and the questioning of medical authority. Much was made by 1890 of the findings that chronic cannabis users in India and Egypt showed symptoms of mental alienation. In 1894 cannabinomaniac made its appearance in British physician Norman Kerr’s volume on narcomania, alongside chloralism and morphinism (for which the administration of cannabis was also indicated as a medical treatment). Cannabis by that time was the most popular drug in high- and middle-class literary, occultist, and “decadent” users’ circles, surpassing even opium and peyote. The Indian Hemp Commission Report to the House of Commons in 1894 concluded, however, that

23. E.g., in Lewin, Nebenwirkungen (n. 22), pp. 151–53.
on the whole, if moderation and excess in the use of drugs are distinguished . . . the weight of evidence is that the moderate use of hemp drugs is not injurious. . . . The popular impression that hemp drugs are a fruitful source of insanity is very strong, but nothing can be more remarkable than the complete break-down of the evidence on which it is based.  

The pharmacologist Walter Ernest Dixon concurred with the conclusions of the report in regarding cannabis as a harmless stimulant and food supplement.  

Cannabis as a therapeutic drug entered the third phase of its Seige cycle around 1900—not so much because a consensus had been reached about its acceptable uses, or that final criteria for these uses were now generally accepted, but because there was no consensus about its undesirability as a medication. The drug was still mentioned in pharmacopeias (for instance, as a hypnotic in a Dutch pharmaceutical vademecum of 1917). But it was hardly, if ever, used, and had disappeared from the spotlight as a medical drug. At the same time, it still had an extensive nonmedical use and surfaced in public spheres as a dangerous narcotic, especially in the United States. California was the first state to opt for prohibition in 1915, and in the 1930s the drug became the focus of an intensive federal campaign.  

Romantic Traits versus Scientific Appeal  

How can we evaluate cannabis's Seige career cycle? Why did cannabis fail to "make it" as a psychotropic drug treatment in the nineteenth century, when it showed some promise and was less dangerous than other drugs? The "drug scare" at the close of the century provides one significant explanation from a medical science standpoint. Another, often-mentioned explanation is the failure to produce a standardized compound with predictable variations in individual reactions, which discouraged medical science from further experimentation.  

To us, this latter explanation is too facile. Other drugs (and one might as well argue, all psychotropic drugs) show more or less extreme variations in individual responses to administration. The volume on the side  

26. Quoted in Stafford, Psychedelics Encyclopedia (n. 9), p. 170. See also Abel, Marihuana (n. 8), pp. 126–32.  
effects of drugs compiled by Louis Lewin at the end of the nineteenth century is eloquent enough on this fact. More important is that the lack of standardization also implies that physicians did not have access to a regular supply of cannabis, as they did to chloral or morphine. Of course, if the demand had been high enough, pharmaceutical companies could have produced more cannabis extract, with or without standardization. Furthermore, there is some counterinformation that leads us to question that cannabis was in such a short supply: during the American Centennial Exposition of 1876 in Philadelphia, some pharmacists carried stocks of ten pounds or more of cannabis.

We therefore suggest another hypothesis to explain the differences between the career paths of cannabis and chloral. In our view, interest in cannabis was not high because the drug did not belong to the new “scientific” era of modern psychopharmacology starting in 1869. Cannabis did not look forward to the hopes of final conquest of physiological and mental diseases by modern medicine; on the contrary, it looked backward to an ancient, obsolete medical tradition, which became regarded as the “unscientific” era of mesmerist and Romantic speculations. The combination of these cultural connotations with rising drug scares, along with the failure to produce standardized compounds and to control variations in response, accounts for the Seige career cycle of cannabis.

At first sight this might seem questionable. Moreau was a pupil of the leading French psychiatrist Jean-Étienne Dominique Esquirol, and a member of importance in the circles of “the Paris school of medicine.” This put him on the frontline of the development of a scientific medicine based on a sensationalist physiology. Did not the physiological organism and its functions receive pride of place in Paris medicine, displacing the “shadowy” vital forces that permeated body and mind and could be manipulated by the hypnotizing techniques of mesmerist healers?

However, the historical position of the psychiatrists associated with Paris medicine was not as clear-cut as this. Moreau’s mentor Esquirol had a deep interest in what medical science now would analytically distinguish as biological and psychological phenomena. The same holds for Moreau; his volume on cannabis mostly concerns itself with qualitative descriptions and interpretations of cannabis intoxication and other forms of inebriety. We have already seen how he came to his experiments through curiosity about the effects of cannabis on himself; his starting point was the exploration of phenomena of psychopathology and their boundary with ordinary

31. Lewin, Nebewirungen (n. 22).
32. Abel, Marihuana (n. 8), p. 181.
states of consciousness, and not their cure. In this, and in the material on
which he bases his observations, he was much influenced by the cultural
tradition of Romantic exoticism. In the works of the French Romantic
artists of Moreau’s time, the Orient functioned as the Other, showing ter-
ritories of the human mind not explored in Western bourgeois society.
Whether covert in the poems of Charles Baudelaire’s Fleurs du Mal, in the
stories of Gérard de Nerval, or more openly in the best-selling serial The
Count of Monte Christo by Alexandre Dumas, cannabis was explicitly linked
to an orientalized dreamworld in which man encounters his desires and
fears. This is exactly what Moreau (who had traveled for three years in
the Orient) did in a more “scientific” vein by analyzing the similarities
between states of intoxication, dreaming, and the mental world of the
insane. His observations are far from scientific in the sense of our age of
so-called evidence-based medicine (and they may therefore provide in-
sights in ways that our modern methods cannot). One example from the
methodology of Du hachisch et de l’aliénation mentale may suffice: Moreau
bases his exploration of the merging of the waking and dream worlds on
stories of travels in Dalmatia by the writer Charles Nodier, who told about
real existing vampires.33

It was not merely in its name that Cannabis indica, from its introduc-
tion into Western medicine, was associated with Oriental exoticism. This
Romantic trait lived on in the tradition of experimental psychopathology,
but was relegated to a secondary position in the scientific medicine of the
later nineteenth and the twentieth century (although we can continue to
trace its influence “under the surface”). Cannabis indica was further asso-
ciated with other medical approaches: It had been used in homeopathic
medicine from at least 1839.34 More important, mesmerists used the drug
as an auxiliary method in their healing and visionary sessions. An alterna-
tive cannabis model was elaborated in 1848 by the mesmerist Dr. Louis-
Alphonse Cahagnet, the developer of the “celestial telegraph.” He used
a methodology of qualitative observations similar to that of Moreau, but
he gave far higher doses (up to ten times) to the participants in his ses-
sions. Differences in dosage, psychological preparation and expectations
of the participants, and setting resulted in communication with spirits
and in out-of-body experiences. In Cahagnet’s view, cannabis produced
an ecstasy in which reality was better understood. To him madness and
hallucinations were simply different forms of reality, and these value-laden

34. Abel, Marihuana (n. 8), pp. 181–82. This is probably a continuation of the earlier
use of Cannabis sativa.
terms should be replaced in scientific language with the term “internal life” (as opposed to the normal, “external life”). This, of course, was not of general importance or interest to most of the “scientific” physicians of the later nineteenth century. In 1891 one could read in the *St. Louis Medical Journal* that young men rarely prescribe cannabis. “With a wish for speedy effect, it is so easy to use that modern mischief maker, hypodermic morphia.”

Furthermore, as James Mills has shown in his book *Cannabis Britannica*, cannabis in British India became associated with criminal behavior and mental alienation, due to the attempts of Indian smugglers to evade British tax laws. Cannabis received continued enthusiasm in the deviant subcultures of its regular users in the twentieth century. A cultural history of cannabis would discover new Seige cycles in its career. For instance, new hopes that cannabis would have an effect on social revolutionaries emerged in the 1960s, and these hopes led to its relative acceptance in the Netherlands as a recreational drug that helped people to relax in an increasingly regimented corporate world. This new cycle was begun without a conclusive medical and scientific consensus on its use.

In the last decade cannabis users, with support from allies within the medical profession, have succeeded in reintroducing cannabis into medicine—not primarily as a psychotropic drug, but in the treatment of multiple sclerosis, AIDS, and neuropathic pains, and in palliative care. Apart from the justification and efficacy of this use, our analysis of cannabis’s earlier cycle leads us to doubt whether the drug will ever be able to meet the regulatory requirements of modern health care. Many will still criticize it as today’s “most abused drug,” despite its relative harmlessness when

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compared to even legal drugs such as alcohol and benzodiazepines. Cannabis as a medical drug, whatever its possible beneficial effects, has lost its innocence to the Romantics of the 1840s. Its career will therefore remain constricted by its historical connotations unless, as our theory suggests, its marked comeback can somehow be sustained by evidence produced in the laboratory and by medicine’s increased hope for the treatment of new diseases that are feared by the public. The recent experience of the medical marijuana movement in obtaining public support for its claims of success in the treatment of AIDS and MS provides a cogent example of the undulating nature of drug career paths. The theory of Seige cycles indicates that drugs once introduced into society never really die, but rather fade in and out of history in a process of hope, fear, and renewal.

The Modern Morpheus

A comparison of the Seige career cycle of cannabis with that of the first “modern” drug, chloral hydrate, proves enlightening. Research on the therapeutic use of chloral hydrate started in the 1860s, although the chemical had been synthesized by Justus von Liebig as far back as 1832. This synthesis served as an illustration of the opportunities presented to an incipient medical science by a new laboratory chemistry that succeeded in producing new chemicals “on the bench.” In the short term, von Liebig’s research led to the introduction of chloroform, a conversion of chloral with alkali, introduced as an anesthetic in medicine in 1847; but it took more than thirty years before this laboratory chemistry solidified its connection to a new “scientific” medicine. Until then, the impact of chloral hydrate remained limited to references in the chemistry literature. Its pharmacological effect had to await the discovery by Rudolph Buchheim and Adolph Trachtenberg at the University of Dorpat (Russia) in 1861. It would take another eight years before chloral took its place in medical practice.

It is tempting to associate the new interest in chloral hydrate in the 1860s with the increase of the asylum population in Germany, France, Britain, and the United States that started in the same decade. In Germany, for instance, the ratio of psychiatric patients to the total population rose


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from 1 in 5,300 in 1852, to 1 in 500 in 1911. Alternatively, the French historian Roselyne Rey argued that the introduction and massive application of the anesthetics ether and chloroform played a seminal role in creating a new mass market for painkilling and sedative drugs such as chloral hydrate. However, neither dimension of causality can be given primacy. A study of the Seige cycle of chloral hydrate brings to light mutually reinforcing factors functioning within the context of the new scientific medicine: product innovation in the pharmaceutical industry, therapeutic experiments by psychiatrists, and changing cultural evaluations of therapeutic opportunities.

Chloral hydrate’s movement through the system of mental health care started, as with cannabis, in academic life. The new drug was tried first on psychiatric patients, just as psychiatrists Moreau and Brigham had tested cannabis on their patients. Chloral became famous because of the experiments of Oscar Liebreich on the inmates of the Charité asylum in Berlin, and on the patients of the medical faculty ward of his teacher Rudolf Virchow. But the assumptions of the research were very different: Moreau had started with his own explorations of the subjective and qualitative effects of cannabis. Liebreich, however, developed his research from a postulated physiological mechanism: blood chloroform was formed out of chloral, and this process explained the pharmacological response. His experimental results could therefore be replicated and theoretically generalized in the accumulated evidence of animal and patient experiments.

Whereas the first investigators of cannabis had remained cautious in their praise of the drug, with chloral hydrate, in contrast, we see in the first phase of its Seige cycle a speedy and enthusiastic acclaim of the drug in different countries. Its use was not only accompanied by much more enthusiasm, but also went beyond qualitative evidence, taking on greater quantitative dimensions. In this first phase, chloral was heralded as the new “wonder drug.” In Germany the influential Allgemeine Zeitschrift für Psychiatrie immediately published a whole range of clinical

47. Liebreich, Chlormalhydrat (n. 45).
studies. Dutch journals followed suit with a series of reports on the new drug “that produced a complete sedation without any detrimental side effects.” Liebreich claimed that chloral gave a more secure effect than other sedatives and hypnotics, that it contributed to the cure of delirium tremens, and that it gave patients the rest during which spontaneous cure could develop, especially in cases of puerperal mania; later, he doubted more negative reports and claimed that they were based on experiments conducted with a lack of “sharpness.” A few years later, the eminent psychiatrist Richard von Krafft-Ebing said the drug was excellently suited for use in cases of psychoneurosis.

If we compare this with the indications for the use of cannabis in influential medical journals such as the American Journal of Insanity and the Lancet between 1860 and 1890, we notice similar indications mentioned. Cannabis was claimed to be an effective prescription against insomnia, more certain and better than opium or wine, sometimes successful in cases of delirium tremens and melancholia, and one of the most reliable painkillers. Not only acute mania but also religious mania and puerperal mania had been cured with cannabis. Cannabis indica was a more effective sedative and hypnotic than opium, concluded the psychiatrist Thomas Clouston after experiments in the innovative West Riding Lunatic Asylum in 1870.

But though the indications for the use of chloral hydrate were similar to those of cannabis, the positive acclaim for chloral hydrate was, in its quantitative and qualitative dimensions, definitely something new. In the overenthusiastic manner in which chloral was embraced by the medical profession there is more to be found than a recognition of its therapeutic efficacy. A large measure of enthusiasm for a new drug is an important characteristic of the first phase of a Seige cycle and reflects more than limited professional interests. We suggest that professional interests obtain their enthusiasm and momentum by linking up with a broad cultural process that has become inherent in modern medicine:

51. Liebreich, Chloralhydrat (n. 45), pp. 53–69.
the recurrent hailing of wonder drugs. These wonder drugs are received not only as medication—whether or not they are in fact "magic bullets" (like, for example, penicillin), they become awesome cultural symbols of the healing power of modern medicine. They carry a message of hope that the gap between the promises and expectations of medicine and the realities of sickness and death finally will be bridged. In 1881, T. H. Huxley forecast that "sooner or later, the pharmacologist will supply the physician with the means of affecting, in any desired sense, the functions of any physiological element of the body"; this hope, expressed at the seventh international medical congress in London, was surely intended to include "mental physiology" as well.56

This kind of optimism accounts for the overwhelming enthusiasm for chloral hydrate, first in Germany and then in Britain, France, and the Netherlands. Liebreich spoke of one case where chloral hydrate induced sleep "as if by magic," where all other means (bromide, opium, chloroform, wrapping up in ice, and straitjacket) had failed.57 At first the high price, the limited availability, and the extreme variations in quality restricted the expansion of demand for the drug, but these problems were quickly solved.58 Chloral certainly was not "pushed" initially by pharmaceutical companies; rather, the first impetus seems to have come from academic pharmacology and psychiatry. But pharmaceutical companies such as Schering and Merck quickly took stock of developments. Within months of Liebreich's introduction, the price of chloral had come down by eleven-twelfths; it has been claimed that Schering produced as much as 500 kg a week.59 Chloral became more popular than its alternatives, opium, bromides, or nightshade extracts. The consumption of the much-advertised "medicinal drink" Siroop de Chloral de Follet became very popular in the Netherlands, Belgium, and France.60 The Lancet reported that from the end of 1869 to the beginning of 1871, 1,200 kg of chloral had been

57. Liebreich, Chloralhydrat (n. 45), p. 69.
59. Linde, "Chemie und Schlaf" (n. 58), p. 64.
60. Pharmaceutisch Weekblad, 1875, 12 (12): 1; Nederlandsch Tijdschrift voor Geneeskunde, 1875, 11: 409.
imported into England, enough for half a million doses. In the summer of 1870, the daily production of chloral in Germany had risen to 150 kg, enough for more than seventy thousand doses.

Chloral and “The Living Death”

The intense enthusiasm for chloral from the very beginning marks an essential difference from the career of cannabis. It seems to be a characteristic element of the “modern” era of psychopharmacology—but modern or not, the careers of all therapeutic drugs enter a second phase of critical reappraisal. These first two phases of a Seige cycle can be co-existent for long periods. In the case of chloral, enthusiasm continued for more than three decades, notwithstanding the appearance of the first negative reports within a few years after 1869—but in the course of the 1870s, the second phase of its Seige cycle became more and more apparent. Not only was the velocity of these transformations much faster than in the case of cannabis, the ups and downs of the Seige cycle were also much steeper: not only was chloral hailed with more initial enthusiasm, but in its second phase it was also perceived as more dangerous than was cannabis in its own second phase.

Numerous studies were reported on problems of growing tolerance, physiological and psychological side effects, contrary reactions, individual variations in response, and finally the rise of dependence as a consequence of “chronic chloral abuse.” The latter was especially a source of anxiety in general practice and an important factor causing reactions against chloral use. In 1884 an English textbook reported an “enormous number of people [who] habitually take chloral.” In the first Dutch study on “chloralism,” the syndrome was discussed together with alcoholism and morphinism. Appearing in 1886, the study warned against the psychoses that could result from the consumption of larger doses of chloral: “Especially hysterical, neurasthenic individuals often suffer chloral very badly and become even more exalted [resulting in] states very similar to drunkenness, anxiety attacks, sometimes delirium with hallucinations.” For German pharmacologist Louis Lewin, the image of chloral as a miracle drug among the medical profession had by 1899 changed

64. Medawar, Power and Dependence (n. 48), p. 64.
into the "most dangerous of all hypnotics": in his view it was better not to treat insane patients at all than to treat them with chloral, and he was concerned about chloral-containing "knockout drops" that were sold in American drugstores.\textsuperscript{66} The danger of chloralism pervaded the medical and public spheres. For example, in a popular novel from 1897 one of the chief characters, a psychiatrist, uses chloral in a depressed mood to induce sleep, and observes: "I must be careful not to let it grow into a habit."\textsuperscript{67} Addiction to chloral was regarded as a business opportunity by quacks, who began to promote purported cures for what were regarded as the "living dead." In the nostrum ads we find chloralism clustered together with alcoholism and morphphinism.\textsuperscript{68} But despite this changing public image, with the most publicized affair involving the poisoning of the famous actress Sarah Bernhardt, chloral remained in use in medical practice. There are indications that in the Netherlands, consumption of the drug rose again after 1875.\textsuperscript{69} Until after the Second World War, chloral kept its place in the medicine cabinet in people's homes.\textsuperscript{70} We perceive here the third phase of its Seige cycle. As argued above, in this phase it is not so much the case that a consensus has been reached about acceptable uses of the drug, or that final criteria for these uses have been generally accepted; rather, the attention of professional and public discussions shift to other, newer drugs. The older drug disappears from the spotlight without actually disappearing from medical or public use. Chloral hydrate remained a substantial and useful intervention in medical practice, but lost its "newsworthiness" in the medical and public media.

One of the underlying factors that sustained the use of chloral despite its detrimental side effects and its loss of attention was economics: it had become cheaper than new and alternative medicines. The tempo of drug innovation by pharmaceutical companies picked up in the early 1900s with the continuous introduction of new barbiturates; for example, Veronal was created as a new and at first "miracle-promising" alternative

\textsuperscript{66} Lewin, \textit{Nebewirkungen} (n. 22), p. 125.
\textsuperscript{67} Bram Stoker, \textit{Dracula}, chap. 8.
to chloral. Chloral went out of the spotlight, although at the same time problems of dosage and the unpleasant taste were to a great extent solved and the drug continued to be used in asylums. As recently as 1965, a Dutch textbook placed chloral next to other sedatives and tranquilizers on an equal footing as far as “hypnotic activity” and “undesirable side effects” were concerned.71 Yet, to reemphasize, chloral was no longer the focus of intense symbolic activity that it had been in the 1870s. This cultural activity shifted to other drugs—first to the barbiturates, and then in the 1950s to the benzodiazepines. In the process, the attention given to chloral in scientific and clinical research also diminished.

Conclusion

On the basis of a comparison of the career paths of cannabis and chloral hydrate, however different in terms of their social and cultural contexts, we have argued that in both cases the dynamics of the Seige cycle become manifest: expanding use of the therapeutic drugs and high expectations of their effects upon their introduction are followed by rising criticism and disappointments, ending in a final phase of diminished attention, contracting use and limited application, and removal from the spotlight. It also becomes obvious that a history of a drug in isolation is too limited: drugs are always in competition with one another. Further, these cycles are not limited to psychoactive drugs, but are applicable to all kinds of therapeutic drugs.72

These cyclical career paths, however, are not static essences or ahistorical categories that unchangingly determine the course of drug use. On the contrary, as we have shown, the dynamic of a Seige cycle may differ significantly from one drug to another. In the case of cannabis and chloral hydrate, the duration and magnitude of the peaks and valleys of the phases of the cycle are clearly different: for cannabis they are much “flatter” than for chloral. The cycles become especially pronounced when the therapeutic drug is combined with the hypersymbolic manufacture of an icon and is received as a “wonder drug,” “miracle cure,” or “magic bullet,” as occurred with chloral hydrate. With chloral, a swift and enthusiastic acclaim in different countries was accompanied by new forms of mass production, mass marketing, and mass consumption of therapeutic drugs. As a product of the new laboratory sciences it became an icon of the increasing healing powers of modern medicine. In the process of

circulating between bench, bedside, and the public sphere, it aroused expectations that were amplified beyond measure, thereby yielding the label “wonder drug.” Chlora hydrate incorporated the promise of healing of a new scientific medicine while being at the same time an organic part of a new configuration of industry, scientific medicine, media, and consumers. We therefore designate this drug as “modern” compared to the “premodernity” of cannabis.

But have we really established here all the commonalities between the contexts and national settings, and can we go on to the differences? Clearly, more research into the details of Seige cycles and their meanings is needed. There are indications that these cycles show phase differences when we look at different sections of mental health care: asylums, extra-mural psychiatry, general practice, and the large but often neglected field of “self-medication.” Nor can we neglect the differences in national settings. By taking a comparative approach toward the courses and contexts of various Seige cycles, the significance of the scientific, political, economic, and cultural factors involved in shaping drug careers can be established. The causal influence of these factors cannot be assumed to be equal across cases. Differences in the influences of specific factors in different sections of mental health care can plausibly be accepted, but they need to be confirmed in future historical research that examines a larger series of cases than we have done in this article.

The Seige cycle is a general concept, but more specific concepts will also need to be developed. For example, we have seen in the case of cannabis the significance of governmental regulations in framing the Seige cycle. This kind of specificity will need to be clarified in studies using multiple-case comparison designs, instead of the simple two-case contrast approach employed in this article. In this way, the concept of the Seige cycle can become programmatic, connecting a history of psychopharmacology of the long run with multiple case histories of the medium and short run.

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