

The Use of Cannabis as a Mood Stabilizer in Bipolar Disorder: Anecdotal Evidence and the Need for Clinical Research

The Use of Cannabis as a Mood Stabilizer in Bipolar Disorder: Anecdotal Evidence and the Need for Clinical Research

Lester Grinspoon, M.D. & James B. Bakalar

Published in *Journal of Psychoactive Drugs*, Volume 30 (2), April - June 1998, pp. 171-177.

Abstract-The authors present case histories indicating that a number of patients find cannabis (marihuana) useful in the treatment of their bipolar disorder. Some used it to treat mania, depression, or both. They stated that it was more effective than conventional drugs, or helped relieve the side effects of those drugs. One woman found that cannabis curbed her manic episodes; she and her husband have worked to make it legally available as a medicine. Others described the use of cannabis as a supplement to lithium (allowing reduced consumption) or for relief of lithium's side effects. Another case illustrates the fact that medical cannabis users are in danger of arrest, especially when children are encouraged to inform on parents by some drug prevention programs. An analogy is drawn between the status of cannabis today and that of lithium in the early 1950s, when its effect on mania had been discovered but there were no controlled studies. In the case of cannabis, the law has made such studies almost impossible, and the only available evidence is anecdotal. The potential for cannabis as a treatment for bipolar disorder unfortunately cannot be fully explored in the present social circumstances.

[EDITOR'S NOTE: The following article is based in part on materials that appear in the revised and expanded edition of the authors' book, *Marihuana, The Forbidden Medicine*, republished in 1997 by Yale University Press, New Haven and London. While the interviews have previously appeared in print, they provide a reference point for the authors' discussion of cannabis' potential role in the treatment of bipolar disorder as it appears in this theme issue. In their revised and expanded book, Grinspoon and Bakalar discuss a wide range of what they refer to as "Common Medical Uses" and "Less Common Medical Uses" for cannabis. The former include treatment for the nausea and vomiting of cancer chemotherapy, glaucoma, epilepsy, the muscle spasms of multiple sclerosis, paraplegia and quadriplegia, the weight loss syndrome of AIDS, chronic pain, migraine, rheumatic diseases, pruritus, PMS, menstrual cramps and labor pains, depression and other mood disorders. The latter include treatment for asthma, insomnia, antimicrobial effects, topical anesthetic effects, antitumor effects, dystonias, adult ADD, schizophrenia, systemic sclerosis, Crohn's disease, diabetic gastroparesis, pseudotumor cerebri, tinnitus, violence, PTSD, phantom limb pain, alcoholism and other addictions, terminal illness and aging.]

In bipolar or manic-depressive disorder, major depression alternates with uncontrollable elation, or mania. Symptoms of depression include loss of interest and pleasure in life, sadness, irrational guilt, inability to concentrate, appetite loss, lethargy, and chronic fatigue. Manic symptoms include sleeplessness, tirelessness (until exhaustion leads to a breakdown), and recklessly gregarious and expansive behavior, which sometimes turns to irritability, rage and paranoid delusions. Bipolar disorder is treated mainly with lithium salts and anticonvulsant drugs, which can have serious side effects. Thirty percent to 40% of patients with bipolar disorder are not consistently helped by or cannot tolerate standard medications. In the course of the authors' studies of the medical uses of cannabis (Grinspoon & Bakalar 1997), a number of sufferers were discovered who believed marihuana to be more effective than conventional anti-manic drugs, or who used it to relieve the side effects of lithium.

Our first account was written by a 47-year-old woman:

I was born on Friday, October 13, 1950, a few months before my father had his first serious bout with manic depression. My mother said he was taking valuable art objects they owned and throwing them down the trash chute in their New York apartment building.

I enjoyed my youth with a great deal of abandon. How much of this would be mood disorder I could not tell you. As a single person I didn't notice; I just rode the waves of emotional highs and lows and didn't think much about it. I was an old pro at this by the time I was 19 and met my husband. It was only through my association with him that I came to terms with my mood problems, although right before I met him I had checked myself in at a mental health clinic

complaining that I sometimes felt unable to concentrate on one thing at a time.

I think I was 22 years old when my troubles cropped up again. At one point my husband and I went to see a psychologist. We talked about my mood swings and spells of nervousness, anger, and depression. The tiniest negative thing happening would cause long-lasting rage, very hard to quell. We told the psychologist of my father's history, even longer and grislier by then. He must have been in every state mental institution along the East Coast. My grandmother, his mother, was wasting away by this time, losing her lifelong battle with chronic depression. I don't know much about her case except that she was chronically sad and starved herself to death after her husband passed away.

This man said my husband and I needed to lose weight; that was the extent of his advice. We did not see him much longer. By this time I was experiencing most of the symptoms I have today, although they have strengthened year by year. Sometimes I feel elated, exhilarated, with a great deal of energy. It sounds great, but you can get to be feeling so good that you scare the people around you, believe me! This is accompanied by light sleeping and nocturnal habits. I tend to become angry or aggressive when it is not appropriate, or just talk too loud. I often have a low self-image or feel sad. I sometimes have a hard time getting up to work, a heaviness that keeps me from moving. I get racing thoughts that make concentration hard. I have strong emotions that change rapidly. I tend to be physically clumsy. I develop unexplained skin rashes, and sometimes feel like I'm generating electricity and shooting it out my fingers and toes. My judgment is often poor.

It was in my early twenties that I first used cannabis for my condition. I had been exposed to it several times, the first when I was quite young. My mother had taken me to a mental health center after my initial signs of trouble as a child. After a group therapy session there, some of the other kids took me riding and gave me a joint. Nothing at all happened, and I concluded it must be a mild drug.

When I was exposed to it later, I would actually choose it over alcohol because it didn't have such strong and negative effects on me. This is how I discovered that it was effective against most of my symptoms. Suppose I am in a fit of manic rage—the most destructive behavior of all. A few puffs of this herb and I can be calm. My husband and I have both noticed this; it is quite dramatic. One minute out of control in a mad rage over a meaningless detail, seemingly in need of a strait jacket, and somewhere, deep in my mind, asking myself why this is happening and why I can't get a handle on my own emotions. Then, within a few minutes, the time it takes to smoke a few pinches—why, I could even, after a round of apologies, laugh at myself!

But this herb is illegal and I have a strong desire to abide by the law. My father was having great success with a new drug, lithium carbonate. I saw my father's physician and he recommended that I try it. I took lithium for six months and experienced several adverse side effects: shaking, skin rashes, and loss of control over my speech. But I would still be taking it if it had worked for me as it did for my father. It literally restored his life. I had gotten worse, if anything.

The combination of lithium side effects and increased manic depressive symptoms drove me back to the use of cannabis. Some years later I tried to go without it again, this time because of increased social pressure against illegal drug use. It was a very difficult time for my family. Whenever I started to become manic, my husband and son would get scared and cower, triggering rage and making matters worse. When depression struck it was a black funk on our household. And I can tell you from the experience with my father that this can really destroy a family. After a while the knowledge that a little bit of marijuana would help me so much became irresistible. At first I tried eating cannabis, but soon returned to smoking because I could control the dose better.

I don't at all consider myself a drug abuser. I am doing what any rational person in my position would do. Cannabis does not cure my condition and over the years it has probably continued to worsen. But with judicious use of this medicine my life is fine. I can control things with this drug that seems so harmless compared to the others I've tried, including tranquilizers as well as lithium. I am constantly concerned that I will be cut off from my supply of marijuana or caught with it in my possession. I feel my sanity may depend on it. Cannabis lessens what is troubling me and returns me to a more normal state. Often I do not experience a "high" at all, just a return to normal.

This patient's husband bears witness to the usefulness of cannabis:

I've been mates with my full-blown manic-depressive (M-D) wife for 26 years. Her father was the classic, well-studied and well-written-about manic-depressive, and she's the one who inherited it. She's lovely, and as I've always truthfully told her, she has the perfect personality, blemished only by M-D.

I've always been smooth-sailing. Smoking marijuana only makes me sleepy. I never use it. She requires it, or, I swear she'd be institutionalized just like her father. There wouldn't be any other way.

We've tried Marinol [dronabinol]. It works for her too, but to get the same effect as marijuana she must take 10 mg about six times a day, which costs about \$65 a day. What's worse is that it takes forty-five minutes to engage and tapers off within two hours maximum. Timing of capsule ingestion must be exact or the symptoms can print through. Marijuana [smoked] lasts a little longer and is smoother, and, most importantly takes effect quickly.

What does marijuana do for my wife? It "recenters" her personality and her interaction with the immediate family moves back into a normal range—no highs, no lows, at least not the highs and lows that are abnormally extreme and that you can tell are from a crazy person with active M-D. Narcoleptic drugs really "zone" her out, like a temporary lobotomy in a medicine bottle. Marijuana never does that! It normalizes, that's all. If there's an overdose, which is rare, it's not dangerous and is very short.

Yesterday we went downtown (one and a half hour's drive one way). However, going several hours without the medicine can be quite calamitous. The worst kind of getting along badly ensued. That's the exact nature of M-D. You tear at your mate with unfounded suspicions, accusations, insane bitterness—enough to make you hate each other. It makes no sense. That's why it's crazy behavior. If you're lucky, like my wife, your mate understands and gets you home right away to have a smoke. It used to be that you could take trips, but the police have cracked down so hard that you don't dare smoke a joint in the car.

I can bear witness to the probability of a near normal life situation for a manic-depressive if they've got good marijuana, a lifestyle that allows one to be home nearly always, and an understanding partner.

Here is the account of another woman with bipolar disorder who finds cannabis more useful than conventional medications:

I am a 35-year-old woman with severe manic depression. When I was growing up I was hypersensitive, cried all the time, and fought with my brothers and sister. My parents always said they had to handle me with kid gloves. I had more energy than most and used it to the hilt. I was an agile gymnast and one of the fastest swimmers in my school. I was also at the top of my class in algebra and good at art and creative writing. I used to stay awake at night and dream up stories.

Around age 14 my mood swings began to get more intense. I was agitated, restless, and constantly fighting at home. I lay awake at night and lost a lot of weight. Eventually I snapped and was sent to a mental hospital, where I was diagnosed as having manic-depressive disorder. They put me on lithium and told me I would have to take it the rest of my life. But lithium made me lethargic. I had trouble communicating and lost all my animation and creativity. Eventually I quit taking it. Recently I have also tried Tegretol [carbamazepine] and Depakote [valproic acid], neither of which helped.

Tegretol started a manic episode, and Depakote had some very bad side effects. I'd like to find something else, but I don't have health insurance or the money to spend trying out new medications.

Since the age of 14 I have had manic episodes regularly about once every six months. It would always start with not being able to sleep or eat. After two weeks I would just break down and seem to trip out into another world.

Usually I ended up in a mental hospital.

I smoked marijuana for the first time in high school and couldn't believe how good it made me feel. My normally chaotic emotions subsided and I had a sudden sense of calm, peace, and well-being. My perceptions of others and life changed dramatically. The world no longer seemed hostile but more within my control. I could sleep easily and actually had cravings for food. There were practically no side effects. When I had enough marijuana I would just naturally stop, because once you've gotten a certain effect you really don't want any more.

Only another manic-depressive using marijuana could possibly know how much this has changed the quality of my life. Although they don't know it, my family actually likes me better when I'm stoned than when I'm taking lithium or not taking anything. When I'm stoned they can predict my moods and actually get close to me. But I can't tell my family or the doctors because it's illegal. I have to live a double life to get along.

I've often tried to quit marijuana, but I have a manic episode every time. Last year I decided I could control my emotional ups and downs without marijuana, but it led to one of the worst episodes I've ever experienced. I had been having trouble sleeping as usual. I began to get super clear vision that a disastrous earthquake was going to hit Los Angeles. I was feeling so good I was sure I was right. Soon I had my roommate convinced that we didn't have much time and would have to buy as many supplies as possible and then leave. We thought that after the quake the New World Order would be implemented and everyone would have to take the number that Revelation talks about in the Bible. We planned to go to El Salvador, where her family lives, and hide out for the next three and a half years. Crazy! But I really believed it. I maxed out all my credit cards, quit my job, and packed up all my things, including disguises I thought we were going to need. Eventually I had to return home with no job and major bills.

I knew then and there that I would have to go back on marijuana. It's been seven months now since I resumed smoking marijuana, and I don't know what else to do. I have to choose between obeying the law and staying sick or breaking the law and being well.

J.P. is a 45-year-old health professional and the mother of a 20-year-old son:

In late 1994 and early 1995 my son Michael, age 18, began to go out of control. He was unable to sleep, attend school, or function in a normal fashion. He was running around nonstop, acting on impulse without any sense of normal judgment. He was in serious danger of accidentally harming himself or others. There was no way to reason with him, because he was unable to think or listen long enough to understand what you were trying to say. He had become a human time-bomb.

Then, on February 14, 1995, he had a full-blown psychotic manic episode and refused treatment. I had to petition a court to commit him to a psychiatric hospital in Portland, Maine, where he was given a diagnosis of manic-depressive disorder. Both Michael's father and my grandmother suffered from the same disorder, which is now called bipolar disorder.

During his nine days in the hospital (the time allotted by my insurance company) Michael was given lithium and Trilafon [perphenazine]. We were told that he would need lithium for the rest of his life. They explained that it worked very well in 60% of people with this disorder.

We returned home, and for the first month or two, the mania seemed to have ended. At the end of the second month the Trilafon was discontinued, but Michael was still taking a high dose of lithium. At that point he developed a rash on his neck and chest; he also had dark circles under his eyes, and he was incoherent most of the time. The lithium level in his blood was exactly where the doctor wanted it, but now he was acting like an Alzheimer's patient. He couldn't read or comprehend a paragraph, let alone finish school. He was detached from his surroundings and himself. There was no emotional content left in him. He was becoming unrecognizable. He had always been very much like [comedian] Robin Williams in personality and extremely athletic -- a skier, football player, and weight lifter. It was heartbreaking to watch him lose himself in a medicated stupor. I became convinced that lithium did not eliminate the disease but instead was drowning his brain so the symptoms could not be activated. I could still see tiny mood swings and moments of

complete restlessness, but in a body that was unable to become hypomanic.

Michael decided to cut his lithium in half. I knew this would be dangerous but I agreed that something had to be done. Soon he was more himself, laughing and talking and almost back among the living. Then he started to become more hypomanic, and I knew we were headed for trouble. He was back to the energy level of someone on high doses of speed, and this lasted for months. He was running through life like a high-bred stallion, while I was gathering everything ever written on manic-depressive disorder.

Then one day he came home and was perfectly normal in every respect. I thought that maybe he was in remission because the disease is known to do that, and I was thrilled at the possibility. Later that night he was back to full speed ahead, and all hope sank within me. This continued as the weeks passed. There would be times when he was perfectly normal, but only for short intervals. I could not figure it out. I started to chart his sleep pattern, his food intake, the kinds of foods, what chemicals he was subjecting himself to, and so on. Finally one day I discovered that he was smoking pot. Of course I freaked out. We talked about it at length and he told me point blank, "I only feel normal when I smoke a joint." By this time I was ready to blame the disease on his pot smoking. I was totally irrational about this. Michael and I fought constantly for a month about it. Finally he asked me to research cannabis and let him know what I found. I figured I would be able to find enough damaging information to put the subject to rest. The next week was my week of discovery. Not only could I not find what I was looking for, but I became convinced that there was no permanent damage, and that cannabis was actually helpful for people with mood disorders.

I went on-line on the computer to talk to other people suffering from bipolar disorder, and I was overwhelmed by first-person stories of the benefits that others had found.

The hardest part of this entire thing was rearranging my value system. I was raised to be a law-abiding citizen. Although I grew up in the sixties and had tried pot and inhaled, I was never a regular user because it was illegal. I raised Mike right. He was taught to respect elders, do what you are supposed to do, and above all follow the law.

It is hard enough to live with an 18-year-old during a naturally rebellious time, but to be forced to participate in an illegal activity is the absolute worst scenario. But that is exactly what I'm doing. Mike has been smoking pot for two months now. He does not smoke daily, but when the mania begins she smokes and within five minutes he is fine. He never appears to be "high," just happy and relaxed. We don't have to deal with mood swings anymore. He can work on his home-schooling program, and I don't doubt that he will finish by the end of summer. He has been repairing lobster traps with a friend and will be lobstering six days a week by the end of April.

At this point I expect to be arrested some day, because if Mike gets arrested, they will have to take me right along with him. I plan to grow a plant this summer for his use. I know I could end up in jail, but I also know that without some kind of medication that works, my son could end up in jail, institutionalized, or dead. What choice do I have?

Another account of cannabis use by a person with bipolar disorder emphasizes the reduction of lithium side effects:

I am 29 years old, born and raised in North Carolina. My academic background is in English literature, computer science, and law; I now work as a technology consultant and writer, although I am contemplating returning to graduate school. I am divorced. I am reasonably active in my community, though work takes much of my time these days.

I was first diagnosed with bipolar disorder about five years ago, when I was in law school (a psychiatrist also tentatively ventured this diagnosis during my undergraduate years), but I suspect that I have had a mood disorder for most of my life. I was certainly clinically depressed as early as age nine, and my first hypomanic episode occurred at 17. There is also a family history of mood disorders, especially on my mother's side. All three of her brothers had "mercurial" personalities, and they all experienced tremendous successes and notable failures in business. Their extravagance and outgoing personalities resemble my behavior while manic or hypomanic. Although none of them was formally diagnosed with a mood disorder, both my parents have been treated for clinical depression.

Before I was diagnosed and found the right treatment, I had the typical symptoms of bipolar disorder. During depressive phases I became withdrawn, uncommunicative, and preoccupied with suicide. I found it nearly impossible to function in school or at work. During hypomanic or manic phases I spent freely, traveled all over the country (and world), made poor personal and business decisions, engaged in risky sexual behavior, and so forth. The illness has caused me a great deal of personal pain as well as financial woes. I separated from my wife (who eventually divorced me) the summer before I was diagnosed. I've lost jobs, ruined friendships, and alienated members of my family. Fortunately, much of this damage has been repaired with time and understanding. I thank God that my ruined credit rating is the only apparent lasting harm.

Thanks to lithium and sensible therapy, including the judicious use of cannabis, I have been relatively stable and sane for the past three years, although my sleep is often disturbed and I still have (very much milder) hypomania and depression in much the same cyclic pattern as before.

I first used cannabis in my freshman year of college (1984). I preferred it to alcohol as an intoxicant, and used it a few times a week, almost always by smoking (I still prefer to take it that way). In retrospect, it seems clear to me that I was medicating myself for bipolar disorder even then. When depressed and anxious, I found that cannabis was soothing and enhanced my ability to enjoy life. When I was in a manic phase, it relaxed me and helped me get to sleep. I often felt as though I had so much energy inside me that I would jump out of my skin; the cannabis helped tremendously with that. But there was a downside. Manics have a big problem with impulse control, and cannabis seemed to exacerbate it. ("Drive to Canada? Great idea. Let's go!") It also ratcheted up my already overactive libido a notch or two, which wasn't the healthiest thing in the world.

When I was diagnosed and began treatment with lithium, I got almost immediate relief, but I also suffered from nausea, pounding headaches, hand tremors, and excess production of saliva. A friend suggested that I try getting high, reasoning that if cannabis helped chemotherapy patients deal with their nausea and discomfort, it might help me too. My doctor thought the idea was absurd but admitted that it would be safe to take cannabis together with lithium. So I tried it, and the results were remarkable. The hand tremors subsided, the headaches vanished, and the saliva factory resumed normal production levels. All I needed was one or two puffs on a marijuana cigarette. When lithium side effects get bad, the availability of cannabis has been an absolute godsend. It is also nice to be able to use cannabis as an intoxicant, knowing that, unlike the combination of lithium and alcohol, it cannot damage my kidneys.

Every one of the many thousands of Americans who use marijuana as a medicine runs a risk of being arrested. They have to worry about financial ruin, the loss of their careers, and forfeiture of their automobiles and homes. Some have an additional burden because mandatory school drug programs and Parents for a Drug-Free America advertisements have given their children an exaggerated idea of the dangers of using marijuana. Many of these children become concerned about the health and well-being of their marijuana-using parents. A few of those parents have been arrested because their worried children informed on them to the police officers who serve as instructors in the popular school drug program known as Drug Abuse Resistance Education (DARE).

The following accounts are by a 40-year-old software engineer and his 37-year-old wife, who suffers from bipolar disorder. He speaks first: My wife and I and our two boys live in Tyngsboro, Massachusetts. My wife was given a diagnosis of bipolar disorder in 1982 and has been taking lithium since 1992. She also uses marijuana for her symptoms. She has had six psychiatrists in the past 14 years and has been interviewed by many more. I have always told them that she uses marijuana regularly, and not one of them has told her to stop. They do not even seem to care or pay attention. I posted a question about this to the alt.support.depression.manic newsgroup on the Internet. I asked whether doctors knew something about marijuana but could not recommend it because of its illegality. The responses were varied, but most people who were manic-depressive said marijuana helped them, and one said that some doctors considered it effective in controlling mood disorders.

My wife functions much better when she uses marijuana. When she is hypomanic, it relaxes her, helps her sleep, and slows her speech down. When she is depressed and would otherwise lie in bed all day, the marijuana makes her more active. When she runs out of marijuana and can't get more, she becomes more irritable and hard to live with. Lithium is also effective, but it doesn't always keep her in control.

Our dilemma is that our 13-year-old has been through the DARE program and has learned about the evils of drugs and alcohol. He opposes all substance use, legal or illegal -- and I want it that way. But he knows that my wife uses marijuana and it "eats" at him, although he also knows about her illness and how marijuana helps. Understandably, all this confuses him. I believe that marijuana could help some people if it were made available as a prescription medicine. Certainly there are other health and social issues involved, and I can't decide what would be right for the country as a whole. All I know is that in this family it has relieved us all of much suffering. Now his wife:

I am 37, and I have been using marijuana for 20 years. I was diagnosed bipolar in 1982. I take lithium and Wellbutrin (bupropion), although I dislike these drugs. I've gained about 40 pounds since I started taking lithium, but otherwise there are no side effects.

My 13-year-old son knows about my illness. He has also known about my marijuana smoking for about five years. He realized what I was doing after he participated in the DARE program in school. It bothers me when he comes home and says they talked about drugs and he was thinking that his mother is "one of them," He doesn't want anyone to know his mother is a "druggie," and until now we've kept it as our secret. I don't think he would tell anyone, but I'm still afraid something might get out. Sometimes these programs use tricks to get kids to inform on their friends and relatives. They say, "If you really care about this person, the only way you can help them is to report them." My husband has talked to him about it. He has explained that lithium and the other medications I'm taking are drugs. He also explained that many legal drugs are far more dangerous than marijuana and that no one has ever died from using marijuana. But my son insists that if it is illegal, then it is wrong. This bothers me so much that I have considered stopping.

The trouble is that at times when I feel tired and rundown, just a couple puffs of marijuana bring me back to life. Sometimes I think it brings me to a level of normalcy that everyone else achieves naturally. At other times, when everything seems to be going like a whirlwind around me and I can't keep track of what I'm thinking about or saying or feeling, the marijuana just seems to slow the world down a bit. When I have trouble sleeping, it helps zone me out, but if I have trouble waking up it brings me to life. I don't like being thought of as a "drug-abusing mother," but I actually think I'm a better mom when I'm feeling in control because of marijuana. In some ways cannabis today is in a position analogous to that of lithium in 1949, when J. F. J. Cade, after observing its sedative effect on guinea pigs, administered it to patients suffering from "chronic and recurrent mania." His seminal paper, "Lithium Salts in the Treatment of Psychotic Excitement," presented ten one-paragraph case histories, and this compelling anecdotal evidence attracted the attention of psychiatrists around the world because there was no adequate treatment for bipolar disorder. In his paper Cade (1949) mentioned the need for "controlled observation[s] of a sufficient number of treated and untreated patients." In 1951, Noack and Trautner followed up by reporting on the treatment of another 30 patients with "mania alone." But they pointed out that not all patients improved, that many discontinued the treatment, and that "it does not appear to be justified to accept the lithium treatment of mania as invariably safe." (Noack & Trautner 1951).

In 1954, Schou and colleagues published a controlled study in which they alternated lithium and a placebo at two-week intervals. Lithium was clearly beneficial for 12 patients; 15 showed improvement that was "not as clearcut," and three did not improve at all. Schou and his colleagues found it "rather astonishing that [lithium's success] has failed to arouse greater general interest among psychiatrists." One explanation they offered was its slow therapeutic ratio. Another explanation was "the difficulties encountered in attempts to convey to others in a quantitative manner ... the effect of a new psychiatric therapy," i.e. to move beyond anecdotal data to controlled studies (Schou et al. 1954). But there was an even more compelling reason for the delay in lithium's acceptance in the United States. In this country, drugs are introduced by pharmaceutical companies which invest in the studies necessary for official acceptance. They do this because they receive a patent (in the 1950s, for 17 years) on the new drug which allows them to recoup their investment. Lithium salts, of course, could not be patented. Similar obstacles face the medical use of cannabis today. Lithium had a reputation for toxicity that grew out of its use as a salt substitute for cardiac patients in the 1940s. There were a number of deaths before its dangers were fully appreciated, and today blood levels are carefully monitored. Because of its nonmedical use, cannabis also has a reputation for toxicity, in this case undeserved. Lithium was unpatentable, and so is cannabis. Finally, like the evidence for lithium in 1949, the evidence for the therapeutic value of cannabis in bipolar disorder today is anecdotal. Although it has been repeatedly considered as a treatment for affective disorders in the Western medical literature since 1845, when Jacques-Joseph Moreau de Tours (1857) recommended it for melancholia, there is little in the medical literature on the use of cannabis as a mood stabilizer (see Parker & Wrigley 1950; Pond 1948; Stockings 1947).

Today drugs must undergo rigorous, expensive, and time-consuming tests to win approval by the Food and Drug Administration (FDA) for marketing as medicines. The purpose of the testing is to protect the consumer by establishing both safety and efficacy. First the drug's safety (or rather limited toxicity) is established through animal and then human

experiments. Next, double-blind controlled studies are conducted to determine whether the drug has more than a placebo effect and is at least as useful as an available drug. As the difference between drug and placebo may be small, large numbers of patients are often needed in these studies for a statistically significant effect. Because no drug is completely safe (nontoxic) or always efficacious, a drug approved by the FDA has presumably satisfied a risk-benefit analysis. When physicians prescribe for individual patients they conduct an informal analysis of a similar kind, taking into account not just the drug's overall safety and efficacy but its risks and benefits for a given patient and a given condition. The formal drug approval procedures help to provide physicians with the information they need to make this analysis.

But devotion to formal procedures may have caused us to undervalue anecdotal evidence. Regulators today are willing to accept the experience of physicians and patients as evidence of adverse effects but not as evidence of therapeutic effects (Lasagna 1985). Yet case histories and clinical experience are the source of much of our knowledge of synthetic medicines as well as plant derivatives. Controlled experiments were not needed to recognize the therapeutic potential of chloral hydrate, barbiturates, aspirin, curare, insulin, or penicillin. More recently, the uses of propranolol for angina and hypertension, diazepam for status epilepticus, and imipramine for childhood enuresis were discovered in the same way, although these drugs were originally approved by regulators for other purposes.

A related source of evidence is the experimental method known as the "N of 1" clinical trial or single-patient randomized trial. This is the kind of experiment used by Schou and his colleagues (1954), in which active and placebo treatments are administered in alternation or succession to a patient. The method is often used when large-scale controlled studies are impossible or inappropriate because the disorder is rare, the patient is atypical, or the response to treatment is idiosyncratic. Several patients the authors have encountered carried out somewhat similar experiments on themselves. They alternated periods of cannabis use with periods of no use and discovered that cannabis was effective.

The familiar deficiency of anecdotal evidence is the risk of counting successes and ignoring failures. If many people suffering from clinical depression take, say, St. John's Wort after unsuccessful treatment with conventional antidepressants and a few recover, those few stand out and come to attention. Bipolar disorder is a cyclical condition, so it is essential to avoid confusing natural remission with drug-induced improvement. At present we do not know how many patients with bipolar disorder would benefit from cannabis. The promising anecdotal evidence points to the need for more systematic clinical investigation, just as it did 50 years ago in the case of lithium.

Thousands of years of widespread use as well as recent research designed to discover toxic effects have made it clear that cannabis is an unusually safe drug. In fact, its long-term safety is better established than that of St. John's Wort. Yet unlike St. John's Wort, cannabis would be subject to government regulations that demand further time-consuming and unnecessary safety tests. The classification of cannabis as a Schedule I drug creates further obstacles to clinical research. But given the disinterest of pharmaceutical companies, there is no immediate prospect of such studies being funded even if the political obstacles are removed. We are left with the tantalizing possibility that cannabis (or one or more of its constituent cannabinoids) is useful in the treatment of bipolar disorder and the sad knowledge that in the present circumstances little can be done to explore that potential.

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