

Cannabis and Schizophrenia

Schizophrenia is caused by a damaged gene or an insult in the womb or infancy that results in malfunction when the brain develops and gets exposed to hormones produced in adulthood. What role, if any, does cannabis play in this process? We asked Lester Grinspoon, MD.

"There is now sufficient evidence to warn young people that using cannabis could increase their risk of developing a psychotic illness later in life," according to a paper in the *Lancet* July 28.

The "evidence" was produced by an exercise in statistics. The authors (no MDS among them) searched databases for relevant studies and then analyzed 35 of them deemed worthy. They claim to have "adjusted for about 60 different confounding factors, including other substance use, personality traits, socio-demographic markers, intellectual ability and other mental health problems." They concluded that people who have used cannabis face a 40% higher risk of psychosis, and that heavy use increases the risk to 50-200%.

Political Context

The British government has been re-considering the legal status of cannabis, which in 2004 was moved from Class B to Class C—a less dangerous drug category with less onerous penalties for growers, distributors and users. Prohibitionist forces—notably the big drug companies and law enforcement—protested. In 2005 the Advisory Council on the Misuse of Drugs reviewed the medical literature, held hearings and concluded that Class C indeed was the appropriate category. The Council's report stated "for individuals, the current evidence suggests, at worst, that using cannabis increases the lifetime risk of developing schizophrenia by 1%." The latest *Lancet* paper is being played as a trump card to that report:

Classification of Drugs in the UK
Class A (most harmful) includes cocaine, heroin, ecstasy and LSD.
Class B (intermediate) includes amphetamines, barbiturates and codeine.
Class C (least harmful) includes cannabis, benzodiazepines, anabolic steroids, and GHB.

- "Weed May Make You Go Psycho" —*Daily Mail*
- "Smoking Just One Cannabis Joint Raises Danger of Mental Illness by 40%" —*Daily Telegraph*
- "Cannabis Use Doubles Chance of Psychosis" —*The Independent on Sunday*

The *Independent on Sunday* supplemented its coverage of the *Lancet* paper with a survey headed "50 Top Experts Confirm Mental Health Risk." The IoS has led the campaign to return cannabis to Class B. Their poll does not and literally could not "confirm" the risk posed by cannabis, it can only "confirm that most believe..." as the story explains: "A poll of more than 50 of the world's leading authorities on drugs and mental health, confirms that most believe cannabis, and particularly its stronger variant, skunk, pose significant health risks and increase users' susceptibility to psychosis and schizophrenia."

We sought a 51st opinion from Lester Grinspoon, MD, professor of psychiatry emeritus at Harvard who has been studying marijuana since 1967 and is the co-author of *Schizophrenia: Pharmacotherapy and Psychotherapy* and other textbooks. "It is hard to refute a study that alleges certain things are going to

happen in the years ahead," he says, "but smoking marijuana does not cause schizophrenia."

Grinspoon and the psychiatric establishment agree that schizophrenia is caused by a damaged gene or an insult in the womb or infancy that results, when the brain develops and gets exposed to hormones produced in adulthood, in an organic malfunction. There ensues a break with reality, sometimes accompanied by visual hallucinations or "voices." Very often the break has an apparent "precipitating event," says Grinspoon, "—a serious automobile accident, loss of a loved one, an alcoholic binge a bad reaction to LSD or even, I imagine, to marijuana. But it's important to distinguish between 'precipitating event' and 'cause.'"

Can those teenagers at risk for schizophrenia be warned that cannabis should be avoided? Grinspoon responds, "We have no way of identifying a pre-schizophrenic individual."

The *Lancet* paper is "a meta-analysis of studies that are themselves flawed," says Grinspoon (who discredited some of them himself). "It greatly exaggerates the risk to the individual."

According to Grinspoon, the cannabis-causes-psychosis line is disproved

by the absence of "even a blip in the incidence of schizophrenia in the US after millions of people started smoking marijuana in the 1960s." The incidence of schizophrenia in adults is about 1% worldwide and seemingly independent of whether or not cannabis use is widespread in a given country.

A meta-analysis published in the *Lancet* in 2004 (Macleod, et al) stated, "Cannabis use appears to have increased substantially amongst young people over the past 30 years, from around 10% reporting ever use in 1959-70, to around 50% reporting ever use in 2001 in Britain and Sweden. If the relation between use and schizophrenia were truly causal and if the relative risk was around five-fold, then the incidence of schizophrenia should have more than doubled since 1970. However, population trends in schizophrenia incidence suggest that incidence has either been stable or slightly decreased over the relevant time period."

This sweeping, common-sense refutation of a causal link can only be gotten around by defining currently available cannabis as a new and different drug—which is what the prohibitionists are doing with their "skunk" appellation.

But the increase in THC content is not a sudden phenomenon, it has occurred over the course of decades (documented in the U.S. by DEA analysis of confiscated cannabis). The incidence of schizophrenia has not risen correspondingly. Nor has the widespread use of Marinol—synthetic THC available in the US since 1987—resulted in a higher incidence of schizophrenia.

Unmentioned in the media response to the *Lancet* paper of July 28 is the fact that Prohibition has prevented growers from developing cannabis strains high in cannabidiol (CBD), a component of the plant that counters the anxiety- and confusion-producing effect that THC exerts on some people.

The Unambiguous Dangers of Cannabis

According to John Macleod (lead author of the *Lancet's* 2004 meta-analysis), "It is unfortunate that the debate around whether cannabis causes schizophrenia has become conflated with the debate around the legal status of cannabis, and that this question has come to dominate discussions around the appropriate public-health response. The public-health case for prevention of cannabis use by young people is strong, irrespective of whether use also causes schizophrenia."

And what does Macleod see as "the public-health case" against young people using cannabis? "Most users seem to smoke cannabis with tobacco," he writes. "Cannabis use can actually lead to initiation of tobacco use, reinforce toxic effects of tobacco, and make abstinence from tobacco more difficult. Moreover, in most jurisdictions, cannabis use exposes young people to risks of criminalisation that could have additional consequences for their health."

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juana website (www.rxmarihuana.com) where you will find a published paper on this topic under the Publications Section, and in the section on Shared Experiences a number of accounts written by bipolar users who have found marijuana more useful than conventional medicines.

Unfortunately, while you will not find many physicians who are familiar with the possibility that in some patients suffering from this disorder, it would appear to be the "medicine of choice" because for these people it works best and it is surely less toxic than conventional medicines. It is also, even with the prohibition tariff, often less expensive. While I cannot assure you that it will be useful to your son (although he has some experience which suggests that it is) it is unlikely to be harmful to him. It would be best if he could find a psychiatrist who would be willing to follow him as he explores this possibility.

If after looking at the material mentioned above you have questions, I will be glad to try to answer them. Your son suffers from a very difficult disorder and I hope that you will find these suggestions helpful.

Sincerely yours,
Lester Grinspoon, MD

One reason "bipolar" diagnoses are soaring

A million kids in the U.S. are now diagnosed with "Bipolar Disorder," which used to be known as "Manic Depression" and occurred only in adults. On "Sixty Minutes" Sept. 30 Katie Couric did a jailhouse interview with the mother of a four-year-old girl named Rebecca Riley who died from an overdose of pharmaceutical drugs prescribed for Bipolar Disorder. Rebecca's parents are charged with murder. Her mother had taken Rebecca at age two-and-a-half to a psychiatrist at Tufts-New England Medical Center who labeled her bipolar and soon had her on a stew of Seroquel, an "unconventional antipsychotic," Depakote, an anticonvulsant, and Clonidine, a blood pressure drug. On the fatal night Rebecca had the sniffles; her mother gave her Children's Tylenol Plus Cough & Runny Nose and, when she couldn't sleep, half a Clonidine. She was dead by 6 a.m.

Tufts-New England issued a statement: "The care we provided was appropriate and within responsible professional standards." Couric quoted Dr. Kifuji's lawyer to the same effect: "she was just practicing mainstream psychiatry." Couric then went to "one of the



Dr. Joseph Biederman of Harvard Medical School has promoted "Bipolar" from a rare disorder to a common one.

leading proponents of the diagnosis of bipolar disorder in children, whose research Dr. Kifuji said had influenced her. He is Dr. Joseph Biederman, professor at Harvard and head of child psychopharmacology at Mass General Hospital."

Harvard's Biederman has influenced not just Dr. Kifuji but the entire field of child psychiatry. He is the most cited author of "scientific" papers on ADD/ADHD (thanks to which 5 million American kids are on strong stimulants) and has done more than anyone to promote "Bipolar" from a rare disorder to a common one. Biederman has a stern manner, and speaks in a German-sounding accent. His parents were Czech, he grew up in Argentina.

Couric asked how a million kids came to be labeled bipolar. Biederman said, "The idea is rare if you define it in very strict ways. Our contribution has been to describe the many ways that this condition may emerge in children that may make it a little bit more diagnosable and less rare than people have thought about it."

Dr. Biederman's contribution has been to widen the customer base for the pharmaceutical manufacturers, which is why he's so well-funded and highly positioned within psychiatry. Couric, to her credit, explained that the bipolar diagnosis for adults used to involve extreme mood swings that can last for months. "Dr. Biederman's definition for children, though, is much broader. It emphasizes extreme irritability and at least four other symptoms such as recklessness, sleeplessness and hyperactivity." Cut to Biederman behind his desk: "The average age of onset is about four. It's solidly in the preschool years."

Tod Mikuriya, MD, was the antithesis of Biederman—his polar opposite.

See "Cannabis as a first-line treatment for childhood mental disorders," page 7.

Surprising Cases Involving Cancer Patients

By Jeffrey Hergenrath, MD

It is well known that cannabis use helps cancer patients bolster appetite and reduce the nausea brought on by chemotherapy. My experience as a physician specializing in cannabis therapy suggests that cannabis also has *direct* anti-cancer properties. Some patients with metastatic cancers find that regular use of cannabis is associated with stopping or reducing the spread of cancer. Here are three case reports involving patients with confirmed diagnoses of metastatic cancer.

1. Glioblastoma multiforme — an aggressive brain tumor countered by cannabis

P.J., a 50-year-old man, was still enjoying motorcycle riding and surfing when he began having right parietal headaches with increasing frequency and severity in the spring of 2003. Within three weeks from the onset of pain, P.J. saw his primary-care doctor, who advised OTC pain medications. A few weeks later the pain worsened and he began to drop things from his hands and slur his speech. On hearing this the doctor sent him to the ER for a brain scan. P.J. was found to have a large stage-4 brain tumor, subsequently diagnosed as a glioblastoma multiforme. P.J. got his brain surgery in July '03 followed by radiation therapy; he was also referred to a study group at a major teaching hospital. Now, more than four years since his surgery, P.J. continues to improve despite the ominous prognosis with the diagnosis of glioblastoma multiforme. Untreated patients are found to live about three months from diagnosis. Treated patients have a median survival of 10-12 months. In the best case scenario people with this tumor are alive at 18 months and apparently very few are still alive after five years.

What's different in P.J.'s case is that everyday he eats at least five cannabis capsules that he prepares for himself. The cannabis helps P.J. with his appetite and sense of well-being.

Of great interest is the fact that he has been seizure-free and there has been no recurrence of the tumor on his follow-up brain scans, MRI and PET scans (conducted three or four times per year since 2003). Just back from a road trip to visit family, P.J. is out riding his bicycle on the rural roads with increasing confidence and he has re-applied for his driver's license.

2. Neuroblastoma countered by cannabis

"Prognosis of relapsing and refractory neuroblastoma is uniformly fatal" —neuroblastoma research team

Nick was 6 years old when diagnosed with Stage 3 neuroblastoma, later diagnosed as Stage 4 relapsing refractory neuroblastoma. He was enrolled in a metastatic neuroblastoma study group at UCSF for state of the art therapy. After about two and a half years all of his cohort group had died and Nick was in trouble. He had undergone numerous surgeries and numerous rounds of chemotherapy and radiation therapy. He had been a year on naso-gastric tube feedings and a year on TPN, total (IV) parenteral nutrition. Fearing they were losing him, his parents took 9-year-old Nick to Tod Mikuriya, MD, a pioneer in cannabis therapy. At the recommendation of Dr. Mikuriya, Nick's parents began using cannabis for his pain, appetite, anxiety, and sleep. No medications worked as well as cannabis for these symptoms, according to Nick. He was referred to me at age 11 when his family moved to my town. He continued to use cannabis frequently as needed for pain, nausea, loss of appetite, and mental ease. Nick's cancer went into remission when he was 13 years old.

Last year at the age of 16 Nick died of sepsis from a perforated bowel—a complication of the extensive scarring and organ damage from his many surgeries and treatments. A few of the oncologists and research scientist wanted to know what Nick's parents had done differently since they had never seen remission after such widespread refractory disease and prolonged treatment. When Nick's mother asked if this was a good time to talk about cannabis, the researchers fell silent, as this course of action was unacceptable in the clinical trial protocols. Despite the fact that their son had survived this cancer the use of cannabis could not be discussed for fear of compromising the cancer study. Nick's oncologist acknowledged that he had "bought many years of life" by using cannabis. The neuroblastoma researchers may still invite Nick's mother to speak at a neuroblastoma conference in the future, but for now his remission has not been attributed to his cannabis use. A website tells his story:

<<http://www.nicksnow.com>>

3. Metastatic melanoma countered by cannabis

DS is a 53-year-old woman who at the age of 27 had a malignant melanoma removed from her left arm. She reports that the mole was misdiagnosed by her physician as a benign lesion that could be treated topically. The lesion was left to grow for more than a year until it was recognized as stage-3 melanoma. Seven years elapsed until a metastatic melanoma was found in her esophagus. Eighty percent of her stomach was removed and reconnected to her esophagus. Eight months later a metastasis was found in her left ovary. Then another tumor on the right ovary and fallopian tube. Surgery, radiation treatments and chemotherapy were all used in an effort to stop the spread of the tumors. Despite BCG melanoma antigen therapy at UCLA and Interlukin-2 therapy at the City of Hope, tumors returned in her thigh and several other bone sites. More surgeries, radiation and chemotherapy ensued. Her course was further complicated by a new problem with seizures. A dermoid tumor was found in her brain. It too was treated with conventional therapy and anti-convulsant medication.

Then a simple, lifesaving change occurred. DS and her 14-year-old son moved to my town in northern California where she believed she would live out her life in a peaceful community. At the suggestion of her son, who had done research on the internet, she got her recommendation to use cannabis and began doing so daily for her pain and failing health. The melanoma metastases stopped and her health improved. She has been stable for the past 10 years with no additional conventional chemotherapy or anticonvulsant medications. Happy and healthy, she is working as a life coach specializing in yoga and nutrition.

Discussion:

These cases in which the use of cannabis is associated with reduced aggressiveness of highly malignant cancers are in accord with recent findings about the body's endocannabinoid system. Researchers have established that activation of the CB1 and CB2 cannabinoid receptors promote cell death and reduce cell growth in many types of cancer. Cannabinoids have been shown to inhibit angiogenesis—the formation of new blood vessels required by tumors for growth. Cannabidiol (CBD), an important cannabis constituent, has been shown to potently inhibit a cancer gene and protein Id-1, a key regulator of the spread of breast cancer. CBD is the first non-toxic exogenous agent that can significantly decrease Id-1 expression in breast cancer cells leading to down-regulation of tumor aggressiveness, thus inhibiting the metastasis of aggressive human breast cancers. We also know that Id-1 has been found at higher levels in other forms of cancer.

What is extremely promising about this research is that if CBD can inhibit Id-1 in breast cancer cells, then it may also prove effective at stopping the spread of cancer cells in other forms of the disease, such as ovarian, colon, brain, melanoma, and prostate cancer where these genes and proteins are found.



Cannabis for Bipolar Disorder?

To the Editor:

I have a 22-year-old son who was diagnosed with bipolar disorder (type 2). From age 16.5 to 18 he was on various different medications which mostly sedated him. He has done better off his meds than on.

He smokes marijuana at times & tells me that when he smokes he sleeps well (instead of being up for days), has good dreams instead of nightmares, feels "normal," can converse & enjoy social activities without being self absorbed or self conscious.

My initial reaction is —this is illegal, that is not true, etc. However, as I read more information it seems that possibly this is true?? It would be sad if there was something that could help him and we closed our minds to it. Most of the research seems to be directed toward marijuana causing mental illness & little or none on the treatment of....

I am just beginning to look into this but already have hit a number of dead ends. We live in Missouri & I don't think that helps! I got your name from your article on the obituaries of Tod Mikuriya, MD.

On Being Called a "Potdoc"

By Randolph Clarke, MD

I'm a family doctor in East Contra Costa County (Antioch). My practice consists of full-spectrum family medicine here in my hometown. I am used to being the "go-to" doctor for my patients (around 3,000), used to dealing with their many different medical problems. The patients coming for my approval to use cannabis are different in that (1) they usually have their own primary care doctor (through Workers Comp, Kaiser, Veterans Administration, etc.) and (2) I am acting as a "consultant" when issuing cannabis approvals (as opposed to primary care provider).

I wrote my first cannabis approval around 1998 for one of my patients who inquired about its medical use for pain and muscle spasm related to multiple sclerosis. I would tend to write a few approvals a year for my established patients until 2006 when I undertook a review of the medical cannabis literature and made some inquiries with the established clinicians (mainly through the Society of Cannabis Clinicians). I listed my practice through NORML, and am now doing an average of 10 approvals/week. (I see about 125 patients/wk in the practice overall).

Most of my referrals have come from the NORML website and word-of-mouth. The dispensaries know I am here, obviously, and do send patients.

The basic relationship of doctor to patient is otherwise the same and includes a presumption of competence and confidentiality. My records are maintained under the same conditions and subject to HIPPA laws.

Another difference in my cannabis patients is that they are overall sicker and suffer more medical disability than the average person in my practice. I have seen a mix of cannabis-savvy and cannabis-naive patients, which surprised me.

I have had the privilege of attending nurses, managers, science teachers, financial advisors who have provided me with many tales of failed prescription drug therapies, adverse side effects from standard treatments, and who have "re-discovered" cannabis for its medicinal use having tried it as a youth for recreation.

When I provide an "Approval" for medical marijuana, I also provide access for follow-up, and an implied commitment to that patient—same as my other patients. To me, that means that my Hippocratic oath applies to any interactions.

I am still a rookie in this area but I follow Frank Lucido's guidelines and have had nothing but good experience dealing with my cannabis patients.

In my previous practice I didn't have to learn nearly as much from my patients before I could make sense of what I was hearing from them; nor did I have to deal with as much ambient misinformation from other sources. That's not to say that there wasn't always the ongoing problem of trying to separate the apparently true from the probably false among the many contending ideas that always seemed to be competing within what can be thought of as the clinical commons — always a marketplace, but one that was destined to become far more competitive (and correspondingly less principled) in our modern era.

Would you be a source of any help for me? If so, I appreciate it very much.

Margaret Mickens, Joplin, MO

Response from Lester Grinspoon, MD

O'Shaughnessy's has asked me to reply to your e-mail concerning your son's use of marijuana. I should introduce myself as a professor of psychiatry emeritus at Harvard who has been studying marijuana since 1967. Most recently I have been interested in furthering its renaissance in Western medicine as a remarkably useful and safe therapeutic in the treatment of a wide variety of symptoms and syndromes. While recently more and more attention is being given to its usefulness in other medical situations, little note has been made of anecdotal accounts of its usefulness to people who suffer from bipolar disorder. Should you wish to read more about this utility, I would suggest you take a look at the second edition of *Marijuana, the Forbidden Medicine* by myself and James B. Bakalar (Yale University Press, 1997) and my medical mari-

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