

**Information for CPS, Probation, etc.
on Marijuana "Addiction" and Marijuana & Driving**

Are there are so-called "addictive levels of cannabis"?

The concept that "blood levels of THC" are related to its euphoric or psychomotor side effects of cannabinoids is not true. Further, the idea that there are "addictive levels" or some similar construction of speech also does not make scientific sense.

Let's explore some of the reasons:

- (1) By the usual and most widely accepted definitions, there is no addiction to cannabis,
- (2) Blood levels of THC are principally related to how recently it was consumed
- (3) Blood levels of THC and its metabolites are unrelated to the level of euphoria, dysphoria and/or "impairment" a person feels and/or demonstrates
- (4) The definition and meaning of addiction is a moving target. This is likely because it was originally a highly questionable propaganda concept appropriate by the notorious Harry Anslinger (first director of the Federal Bureau of Narcotics) the terms was developed to apply to heroin. Applying the term to any other substance is questionable at best. The term addiction is better replaced by terms such as specific drug dependence. Even then, the use of a therapeutic substance under a physician's approval is another matter.

• Addiction? No!

For decades U.S. government reports never referred to marijuana as addictive. Now that the movement for marijuana reform has grown, the government has chosen to counter-attack with fear by distorting and changing the definition of addiction. The DEA's citations for its sources of authority in naming marijuana as an "addictive" drug include no research or studies supporting its claim.

The allegation that cannabis 'is addictive' has been repeatedly contradicted by past experience and present scientific research. Drug addiction means physical dependence and withdrawal, always assuming that such terms still mean anything at all, and cannabis possesses neither.

You can love your car and you can love your mother, but the same word, “love” has very different meanings in context. The same applies to vague terms like “addiction,” “drug dependence” and “chronic use.” Let’s examine this whole addiction area a little closer:

In discussing the hallmarks of addiction, NIDA scientist Jack E. Henningfield, Ph.D., assigned five qualities to substances by which to measure relative addictiveness:

Dependence – how difficult it is for the user to quit, the relapse rate, the percentage of people who eventually become dependent, the rating users give their own need for the substance, and the degree to which the substance will be used in the face of evidence that it causes harm. This is physical dependence.

Withdrawal – the presence and severity of characteristic withdrawal symptoms, involved in physical dependence.

Tolerance – how much of the substance is needed to satisfy increasing cravings for it, and the level of stable need that is eventually reached. Involved in physical dependence.

Reinforcement – a measure of the substance’s ability, in human and animal tests, to get users to take it again and again, and in reference to other substances, involved in physical dependence.

Intoxication – though not usually counted as a measure of addiction in itself, the level of intoxication is associated with addiction and increases the personal and social damage a substance may do.

- **Mild Dependence**

The U.S. Institute of Medicine studied medicinal cannabis at the behest of the White House. In 1999 they released a voluminous scientific review of marijuana and health. The IOM completely debunked cannabis addiction. The Institute of Medicine report points out the relatively mild nature of marijuana. It is a well-documented fact that once a cannabis consumer decides to give it up, which usually happens between ages 25 and 34, that almost all do so with no or little difficulty. In most cases those who continue have an obvious medical use. There is a growing body of evidence that marijuana can be used to help counter other drug addictions. Marijuana use shows promise and can assist persons fighting addiction. Diana Cichewicz at Virginia Commonwealth University has recently shown that THC blocks the development of tolerance and withdrawal in

experimental animals (Cichewicz and Welch 2002). Clinicians in 19th America and Europe knew the same thing.

The IOM report said there is a very low incidence of cannabis "dependence." They reasoned, "Millions of Americans have tried marijuana, but most are not regular users ... [and] few marijuana users become dependent on it." In fact, authors of the report found that less than 10 percent of marijuana users ever exhibit symptoms of dependence (as defined by the American Psychiatric Association's DSM-III-R criteria). By comparison 15 percent of alcohol users, 17 percent of cocaine users, and a whopping 32 percent of cigarette smokers statistically exhibit symptoms of drug dependence. So this "dependence" is hardly a significant issue, particularly in view of the position of Francis Young, FDA Administrative Law Judge who said in 1988, after a two (2) year FDA rescheduling hearing, that cannabis was one of the safest therapeutic agents known to mankind. (Note: He recommended rescheduling cannabis out of Schedule I.)

- Withdrawal

The Institute of Medicine further concluded, "Experimental animals that are given the opportunity to self-administer cannabinoids generally do not choose to do so, which has led to the conclusion that they (e.g., cannabinoids) are not reinforcing or rewarding." It should come as little surprise then that most recreational cannabis users voluntarily cease their marijuana smoking by their late 20s or early 30s, often citing health or professional concerns and/or the decision to start a family. Contrast this pattern with that of the typical tobacco smoker, many of whom begin as teens and continue smoking daily for the rest of their lives.

Observable "withdrawal" symptoms attributable to marijuana are also exceedingly rare and mild. They are less severe than symptoms from withdrawing from coffee. Again the Institute of Medicine says that these symptoms are "mild and short-lived" particularly when compared to the profound physical withdrawal symptoms of other drugs, such as alcohol or heroin. The IOM concluded that these so-called withdrawal symptoms are extremely unlikely to persuade former smokers to re-initiate their marijuana use.

The evidence for these conclusions is substantial. The results of the research conducted on regular users of cannabis and tobacco by the Canadian government's Commission of Inquiry into the Non-Medical use of Drugs speak volumes. When asked whether they would rather give up cannabis or tobacco if they had to choose, they all replied that they would prefer to give up tobacco. But when they were asked to do so, by the end of the first day they all opted to give up cannabis after all, being unable to cope with the terrible withdrawal symptoms. A comparative study of cannabis and alcohol produced similar results.

A study by Dr. Reese Jones, a critic of medicinal cannabis, was designed in the hopes of demonstrating withdrawal symptoms from THC. He placed volunteers on 210 mg. of Marinol (drabinol-synthetic Δ^9 THC) a day for 30 days and at the end of 30 days the THC was stopped abruptly. This is a formula calculated to maximize any drug's withdrawal symptoms. He was disappointed to find only mild withdrawal symptoms in individuals taking these large doses of synthetic Δ^9 -THC under laboratory conditions (this daily dose of 210 mg. of synthetic Δ^9 -THC, is equivalent to 20-40 joints of natural marijuana).

Leo E. Hollister's "Health Aspects of Marijuana" from the *Pharmacological Review*, 1986, Vol. 38, No. 1 provides a lengthy overview objectively evaluating what the pharmacologist peer-reviewed research said about cannabis as of 1986. His conclusion can be summarized by his statement that "generally toxicity studies of cannabis and its constituents lead to the inescapable conclusion that it is one of the safest drugs ever studied this way."

Chronic user studies in Jamaica (Comitas et al., 1976), revealed no deficits in worker motivation or production. Two studies of brain computerized tomography (CT scan) refuted prior claims of heavy use producing cerebral atrophy (co et al., 1977; Kuehnle et al., 1977). With respect to behavior, Hollister refuted the tenet that depicted Cannabis as a contributor to violent and aggressive behavior. Concerning addiction, he noted minimal withdrawal symptoms of nausea, vomiting, diarrhea, and tremors in some experimental subjects after very heavy chronic usage. Such effects were brief and self-limited.

Marijuana is not considered an addictive drug. A more appropriate question would be whether marijuana is relatively more or less of a health risk compared to other drugs available for the treatment of a particular medical condition or symptom. As FDA Administrative Law Judge Young stated, marijuana is one of the safest therapeutic agents known to man.

Compared to nicotine, heroin, cocaine, alcohol, and caffeine, marijuana was ranked by Dr. Henningfield as the least "addictive." In creating dependence, producing withdrawal symptoms, and leading to the development of tolerance, marijuana ranked lower than all four other substances. In reinforcement, marijuana ranked at the same level as caffeine. Marijuana's highest quality was in intoxication, where it was ranked fourth below alcohol, heroin, and cocaine, respectively.

The use of cannabis does not lead to physical dependence; cessation of use is not followed by withdrawal symptoms, and consequently THC is not addictive. In 1953, Thompson & Proctor summed up the attitude of the great majority of the medical profession stating that 'the use of cannabis does not give rise to biological

or physiological dependence and discontinuance of the drug does not result in withdrawal symptoms.' In 1976 Stephen Szara of the U.S. NIDA categorically stated that 'the question of physical dependence ... has been answered with a flat no. No physical dependence, of the type seen in opiates, has been seen in man and this is true even today."

Here are the conclusions of some Greek scientists who have looked into the matter. Despite what they concede, not one of them has ever made a public stand even for the decriminalization of cannabis, much less for its legalization.

- In contrast to opiates, prolonged use of hashish presents no physical syndrome of chronic poisoning. (Yannis Ayoutandis, Professor of Forensic Medicine)
- Tolerance and physical dependence apparently do not arise from the use of cannabis, hashish or marijuana. (Dionyssios Varonos, Professor of Pharmacology)
- The organism apparently does not become habituated [to hashish], for the dose does not have to be increased. Nor is physical dependence observed, as with addictive drugs that is to say no withdrawal symptoms are observed. (Yorgos Logaras, Professor of Pharmacology)
- Long-term consumption of cannabinoids has not been correlated with the development of physical dependence. (Marios Marselos, Professor of Pharmacology)
- Cannabis does not cause biological dependence. (Kostas Stefanis, Professor of Psychiatry)
- [Hashish] does not cause habituation, it does not develop physical dependence. (Andreas Davaroukas and Yannis Souretis, Surgeons General)

• There is No Relationship Between Blood Levels and Psychomotor Impairment

The basic problem with trying to link the blood level of cannabinoids or their metabolites with level of impairment is that, unlike alcohol, cannabinoids' concentration in bodily fluids has no clear correlation to their activity in the brain. Urine tests of THC and/or metabolites are clearly useless for the obvious reason that they lag hours and days behind actual exposure. Blood concentrations are somewhat more useful in that they can at least help determine whether one has used marijuana recently. As noted in the references cited by Kevin, high levels of blood THC, (≤ 10 ng/ml), are a good telltale sign of having used marijuana in

the last hour or two. The problems are that (1) blood levels are highly variable and (2) have no clear-cut relation to actual impairment, i.e., “being under the influence.”

This was aptly illustrated in the most realistic study on marijuana and driving to date, HWJ Robbe’s “Influence of Marijuana on Driving,” (Institute for Human Psychopharmacology, Univ. of Limburg, Maastricht, 1994; sponsored by the U.S. National Highway Transportation Safety Administration). In this study, drivers were dosed with marijuana and observed while actually driving on the road in the Netherlands. Robbe looked at the blood THC of the subjects and found the following:

“Plasma Concentrations of the Drug: Though consumed dose differed little between subjects, THC and THC-COOH (e.g., metabolite) varied enormously. Thirty minutes after smoking 300 micrograms/kg, for example, THC ranged between 1.6 and 29.6 ng/ml...” “Drug Plasma Concentrations and Driving Performance”: One of the program’s objectives was to determine whether it is possible to predict driving impairment by plasma concentrations of THC and/or its metabolite, THC-COOH. The answer is very clear: it is not. Plasma of drivers showing substantial impairment in these studies contained both high and low THC concentrations; and, drivers with high plasma concentrations showed substantial, but also no impairment, even some improvement...”

The authoritative Consensus Report of NIDA’s Research Technology Branch (“Drug Concentrations and Driving Impairment (JAMA, Nov. 8, 1985 – Vol. 254 #18) said:

“What is known about correlations between driving impairment and drug concentration? – Except for ethanol, determinations of drug concentrations in body fluids are at present of limited value for establishing driving impairment...”

Although this report dates from 1985, its conclusions are still valid.

In a forensic review (Mason et al., 1985), the issue of marijuana’s effect on driving was addressed, and it was indicated that isolated reports of adverse outcomes secondary to impairment by Cannabis as a sole inebriant were rare. The authors concluded that there was no suitable correlation between plasma or blood levels of THC and the degree of apparent impairment a human might exhibit.

The blood concentration of THC is meaningless as any predictor of psychomotor effect. Dr. Barry Beyerstein of Simon Frazer University said, "The relationship between THC (the psychoactive ingredient in marijuana) levels in blood and impairment of eye-hand coordination, reaction time and other components of driving skill is not a straightforward one. Also, individual differences of impairment among different users are so great that it would be very difficult to set a fair legal standard of impairment that would apply to everyone." This is the same conclusion which the U.S. Department of Transportation reached.

"A finding of 20 ug L of THC in plasman (10 ug/L in blood) probably indicates that marijuana was smoked with the hour and with 10 uL plasma within two hours. THC concentrations greater than 50 ug L indicate smoking within 20 minutes. Concentrations of THC-COOH THC metabolite. It is unlikely that a range of plasma THC concentrations could be reliably equated with impaired performance.

Solowij (1998) states that blood plasma levels of THC of 10-15 ng/ml are suggestive of recent consumption but determining just how recent use was is not possible. A more precise measure is the ratio of THC to THC-COOH. If THC-COOH levels are greater than THC, use was probably more than 30 minutes ago but only in naive users.

• **Science, Cannabis and Driving**

As to cannabis having a clear adverse affect on driving, that also does not hold up to scientific scrutiny. Going back prior to the NIDA consensus report and the Robbe study, the Nixon Marijuana Commission concluded that there is no conclusive evidence that cannabis impairs driving. This was in part based on studies by Crancer et.al. for the Washington State Highway Department, a similar study done at UCLA, and another at Boston University. Crancer found that, "Simulated driving scores for subjects experiencing a normal social 'high' and the same subjects under control conditions are not significantly different. However, there are significantly more errors for alcohol-intoxicated than for control subjects."

This assessment is affirmed by the FDA approved package insert language for Marinol that driving and operating heavy equipment after use of synthetic Δ^9 THC is permissible. The package insert states that patients receiving treatment with Marinol should be specifically warned not to drive, operate machinery, or engage in any hazardous activity until it is established that they are able to tolerate the drug and to perform such tasks safely.

According to research by British scientists, a moderate amount of cannabis may actually improve driving performance. A group of 20 drivers aged 21-40 participated in a driving simulator test. Ten of them smoked the equivalent of

about half a cannabis cigarette. Subjects under cannabis scored superior than the sober subjects in most of the tasks, including reaction time and number of collisions. Simon Smith Wright, director of the laboratory where the studies were conducted, said "The results of our test clearly show that a small or moderate amount of cannabis is actually quite beneficial to someone's driving performance."

A story published in January 2004 in Britain's Evening News characterized the results this way:

"A group of 20 volunteers participated in the study, which tested respondents' performance on a video game that simulated driving. Half of the drivers played the game after smoking the equivalent of half a marijuana cigarette. The results showed that for those who had smoked...cannabis, 80 percent demonstrated superior reaction times; 60 percent finished a lap faster; 70 percent experienced a lower number of collisions; 60 percent reached a higher level in the game."

National Highway Safety Study 1993

According to the National Highway Traffic Safety Administration study titled "Marijuana and Actual Driving performance" (published November 1993), "THC's adverse effects on driving performance appear relatively small" and "Evidence from the present and previous studies strongly suggests that alcohol encourages risky driving, whereas THC encourages greater caution."

According to this study, it is not possible to conclude anything about a driver's impairment on the basis of his/her plasma concentrations of THC and THC-COOH determined in a single sample.

A 1993 study of cannabis and driving (Robbe & O'Hanlon, 1993) which was sponsored by the U.S. National Highway Safety Traffic Administration included a review of the literature. The authors' comments in summary of their literature review and of their own results include the following:

The foremost impression one gains from reviewing the literature is that no clear relationship has ever been demonstrated between marijuana smoking and either seriously impaired driving performance or the risk of accident involvement. The epidemiological evidence, as limited as it is, shows that the combination of THC and alcohol is over-represented in injured and dead drivers, and moreso in those who actually caused the accidents to occur. Yet there is little if any evidence to indicate that drivers who have used marijuana alone are any more likely to cause serious accidents than drug-free drivers.

The U.S. Transportation study results were more than confirmed by a 1998 Australian study of 2500 injured drivers which found that drivers who use marijuana are less likely to cause road accidents than drunk drivers or even drug-free drivers. This goes even further than the Australian Government Report (1996) "There is no controlled epidemiological evidence that cannabis users are at increased risk of being involved in motor vehicle or other accidents."

A study from Tilburg, The Netherlands reported in May 2004, "Researchers at the St. Elisabeth Hospital in the Netherlands estimated the association between drug use and motor vehicle accidents by conducting a prospective observational case-controlled study. Cases were drivers involved in road crashes requiring hospitalization. Controls were drivers recruited at random while driving on public roads.

Authors found that driver's risk for road trauma significantly increased with the use of benzodiazepines and alcohol. Increased risks, although not statistically significant, were also assessed for drivers using amphetamines, cocaine, or opiates. The authors concluded that,

"No increased risk for road trauma was found for drivers exposed to cannabis."

- **Second Hand Cannabis Smoke**

The possible dangers of second-hand smoke is a dubious proposition. This is largely because there does not appear to be any significant cancer risk from even first-hand cannabis smoking. A study by Kaiser Permanente of 66,000 patient charts comparing cancer rates in cannabis smokers to non-cannabis smokers found no difference in cancer rate between the two groups. Dr. Donald Tashkin of UCLA, whose work is often erroneously cited to support the canard that cannabis smoke is a worse irritant to the bronchial tree than tobacco smoke, actually found the opposite. In comparing the irritation to the bronchial tree of research monkeys by 29 components of tobacco smoke to similar components in cannabis smoke, tobacco was more irritating in 28 instances. The one exception was where the tobacco smoke he found that was five times component caused almost 0 irritation and almost zero for cannabis smoke. Tashkin himself has said on more than one occasion that he does not know of a single case of cancer caused by smoking cannabis.

- **FDA Administrative Law Judge – The Last Word**

In 1988 action was initiated through the FDA to reclassify marijuana to Schedule 2, potentially making it available for prescription to patients. The FDA Administrative Law Judge, Francis Young, reviewed a tremendous amount of testimony from patients, scientists, and politicians in rendering his ruling.

Although a medical indication of marijuana for migraine was not considered, its use was approved as an anti-emetic, an anti-spasticity drug in multiple sclerosis and paraplegia, while its utilization in glaucoma was considered reasonable. He stated, "By any measure of rational analysis marijuana can be safely used within a supervised routine of medical care."

So there you have it - I send this to the patient so that she or her attorney could educate the court and hopefully provide her attorney with a higher comfort level about the safety of medicinal cannabis. I closed by saying that in addition the findings of the FDA by Administrative Law Judge Young, we have the FDA's approval of Marinol (synthetic $\Delta 9$ THC). Marinol (dranabinol) is far more dysphoric than cannabis. GW Pharmaceuticals (manufacturer of Sativex - tincture of cannabis - which is about to be approved by Health Canada and distributed by Bayer) This is because the cannabiniols (CBDs) in cannabis counter the euphoric impact of THC. Marinol is all THC. So one of the best supports for the safety of cannabis is the fact that Marinol is used by tens of thousands with no concern by CPS, and with the approval of the FDA.

I hope you found the foregoing useful. I would be happy to discuss any of this in greater detail should that be of further assistance.

Sincerely yours,

David Bearman, M.D.