Physician Recommended Marijuana:  
Contraindications & Standards of Care  
A Review of the Literature

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*Primum non nocere.* This is the physician's first rule: whatever treatment a physician prescribes to a patient—first, that treatment must not harm the patient.

According to the Institute of Medicine: Marijuana and Medicine: Assessing the Science Base

1. Marijuana is not a benign substance as previously believed
2. Smoked crude marijuana has no medical value and is contraindicated in general
3. Numerous studies suggest that marijuana smoke is an important risk factor in the development of respiratory disease.
4. While early literature suggests some potential benefits if marijuana for the treatment of glaucoma, nausea, and muscle spasms, by today’s standards there are much better and safer drugs available.
5. The psychological effects of cannabinoids, such as anxiety reduction, sedation, and euphoria, can influence their potential therapeutic value. Those effects are potentially undesirable for certain patients and situations.

The report concluded that short-term use of smoked marijuana (less than six months) for patients with debilitating symptoms (such as intractable pain or vomiting) must meet the following conditions:

- Failure of all approved medications to provide relief has been documented.
- The symptoms can reasonably be expected to be relieved by rapid-onset cannabinoid drugs.
- Such treatment is administered under medical supervision in a manner that allows for assessment of treatment effectiveness.
- Treatment involves an oversight strategy comparable to an institutional review board process that could provide guidance within 24 hours of a submission by a physician to provide marijuana to a patient for a specified use.

The Institute of Medicine has concluded that smoking marijuana is not recommended for any long-term medical use, and their subsequent report declared that, “marijuana is not modern medicine.” Additionally, the American Medical Association, the National Cancer Institute, the American Cancer Society, and the National Multiple Sclerosis Society do not support the smoked form of marijuana as medicine and see it as contraindicated in general.

According to the American Medical Association (AMA)

AMA recommends that marijuana be retained in Schedule I of the Controlled Substances Act. AMA believes that the NIH should use its resources and influence to support the development of a smoke-free inhaled delivery system for marijuana or delta-9-tetrahydrocannabinol (THC) to reduce the health hazards associated with the combustion and inhalation of marijuana.
According to the American Society of Addiction Medicine (ASAM)

Marijuana is a mood-altering drug capable of producing dependency. Its chief active ingredient is delta-9-Tetrahydrocannabinol, but there are many other ingredients. Marijuana has been shown to have adverse effects on memory and learning, on perception, behavior and functioning, and on pregnancy.

Persons suffering from alcoholism and other drug dependencies should be educated about the need for abstinence from marijuana and its role in precipitating relapse, even if their original drug of choice is other than marijuana. Treatment programs providing addictions treatment for chemically dependent patients should include tests for cannabinoids with other drug test panels and consider test results when designing treatment plans.

According to the British Journal of Psychiatry (178: 101-106. 2001)
1. Cannabis is not, as widely perceived, a harmless drug but poses risks to the individual and to society.
2. Long-term cannabis use carries respiratory, cardiovascular and other health risks.
3. Cannabis also has immunosuppressant and endocrine effects although the clinical significance of these is still not clear.
4. There is considerable evidence, that performance of attention, memory and ability to process complex information in heavy, chronic cannabis users remains impaired even when they are not actually intoxicated.

**Discovery of the Endocannabinoid System**
The human body has an *endocannabinoid system*. This system is involved in regulating metabolism, appetitive behaviors, blood pressure, glycemic control, immune response, and reward. Within this system, there are receptors sites, called *cannabinoid receptor sites*. There are at least 2 of these receptors called CB1 and CB2. There are neurotransmitter-like substances that activate the system called *endocannabinoids*.

**The Metabolic Syndrome, Obesity, and Diabetes**
Overactive CB1 receptor sites is associated with the *metabolic syndrome*, which includes high blood pressure, insulin resistance, increase in visceral fat, cholesterol imbalance, and elevated triglycerides. All of these symptoms are associated with cardiac risk, diabetes, and obesity. Overactive CB1 receptors sites are also associated with compulsive behaviors including alcoholism and drug addiction including smoking, and compulsive eating. THC and other cannabinoids within the cannabis plant activate CB1 receptor sites. Therefore, THC, or any other drug that is an agonist at CB1 receptor sites, seem contraindicated for patients with symptoms of the metabolic syndrome, i.e. hypertension, diabetes, obesity, hypertriglyceridemia, eating disorders or other compulsive behaviors.

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**Immune System**
The endocannabinoid system plays a role in the human immune system. Endocannabinoids are immunomodulators. That is, they can either increase or decrease antibody response to infection and do so through CB2 receptor sites found throughout the immune system. For patients with compromised immune systems, further imbalances of antibody response or inhibition of lymphocyte capability is dangerous and is therefore contraindicated in general.

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**Psychosis and Schizophrenia**
A recent review of observational studies supports the view that cannabis use can increase the risk of psychotic illness. This review reported an increase in risk of psychosis of about 40% in a pooled analysis of participants who had ever used cannabis. All the studies that examined the increase in risk in relation to cannabis exposure showed a dose-response relationship, with a 50% - 200% increase in risk. Although the individual lifetime risk of psychotic disorders is less than 3%, the authors conclude that there is now enough evidence to inform cannabis users of the increase in risk because exposure to this drug is so common.

There is research evidence showing that a higher frequency of cannabis use was predictive of psychotic relapse after controlling for medication adherence, other substance use and duration of untreated psychosis.
A follow-up of participants in the Baltimore Epidemiological Catchment Area Study (approximately 15 years later) found that cannabis smokers with no baseline depressive symptoms were four times more likely than those with no cannabis use diagnosis to have depressive symptoms at follow up. Suicide ideation and anhedonia were common symptoms. Subsequently, data from the National Comorbidity Survey suggested a possible causal role in the development of Major Depressive Episode (MDE).

Recent research finds that first episode schizophrenia patients who use cannabis show a more pronounced brain volume reduction over a 5-year follow-up than patients with schizophrenia who do not use cannabis. In the research, the schizophrenics who used marijuana over the five years since their first break were found to have lost significantly more gray matter than abstaining schizophrenics. This study suggests that some of the detrimental effects of cannabis on the course of illness may be explained by its effect on the progression of brain changes in schizophrenia.

Previous functional imaging studies have found reduced left hippocampal activation during cognitive performance in cannabis users, and there is evidence to suggest that hippocampal abnormalities in psychiatric disorders such as schizophrenia are more prominent in the left hemisphere. These findings converge to suggest that the left hippocampus may be particularly vulnerable to the effects of cannabis exposure and may be more closely related to the emergence of psychotic symptoms.

These findings challenge the widespread perception of cannabis as having limited or no neuroanatomical sequelae.

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**Addiction**
In addiction, there are major involvements of the endocannabinoid system in general brain reward functions and drug abuse. First, natural and synthetic cannabinoids and endocannabinoids can produce
rewarding effects in humans and laboratory animals. Second, activation or blockade of the endogenous cannabinoid system has been shown to modulate the rewarding effects of psychoactive drugs. Third, most abused drugs alter brain levels of endocannabinoids in the brain. In addition to reward functions, the endocannabinoid system is involved in the ability of drugs and drug-related cues to reinstate drug-seeking behavior. THC produces rewarding effects in humans and non-human primates. A diagnosis of substance abuse/dependence would therefore contraindicate medical marijuana.

Medical Marijuana and Addiction Treatment Programs
Within addiction treatment programs, it is especially important to have clear thinking on this topic. The California Society of Addiction Medicine (CSAM) (California Society of Addiction Medicine News, 1997) recommends that all physicians who recommend cannabis should adhere to the accepted standards of practice, as cited in their January 1997 issue of Action Report:

- History and physical examination of the patient
- Development of a treatment plan with objectives
- Provision of informed consent, including discussion of side effects
- Periodic review of the treatment’s efficacy
- Proper record keeping that supports the decision to recommend the use of marijuana

In the case of smoked marijuana by physician recommendation, there is conflict between two principles:

1) Abstinence is defined as no abuse of psychoactive substances, and taking properly prescribed medication as directed. (this principle is also known as ‘don’t play doctor.’)
2) Addiction treatment programs provide environments that are safe for recovering patients, and avoid known triggers to relapse.

A flexible approach includes getting a release to talk with the prescribing physician and determining, if possible, whether acceptable standards of care were followed. This includes a request for records.

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