

C.T.S./CANNABINOID TOXICITY SYNDROME: ITS RELATIONSHIP TO PERSISTENT "NEUROLOGIC DISORGANIZATION", SHORTLIVED THERAPEUTIC RESPONSIVENESS, AND CHRONIC ILL HEALTH. METHODS OF DRUG ("POT") DETOXIFICATION.

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ABSTRACT. The damaging effects of cannabis consumption are briefly presented from an overview of exhaustive, current research findings. Relationships between cannabinoid toxicity, "neurologic disorganization" and chronic ill health are hypothesized. Methods of treating active or latent cannabis-toxic patients to enhance therapeutic responsiveness and reduce chronic biomechanical instability are discussed.

INTRODUCTION

Despite the fact that thousands of articles on marijuana have appeared internationally in medical journals over the last 15 years, few physicians ever consider cannabis-related health problems on a day to day basis. (Cannabis and cannabinoids will be used somewhat interchangeably in this paper, although technically cannabis contains some 60 cannabinoids, delta 9-THC being the most psychoactive.) That active cannabis consumption can be damaging to several physiological processes is widely documented in research literature⁽¹⁻⁵⁾. The concept that cannabis can exert persistent damaging effects in the human organism (other than genetic) long after its use has stopped (latent effects), however, has generally not been recognized, and is a primary consideration of this paper.

CTS is a symptom complex observed clinically over several years and defined by this author to help explain a constellation of health disorders which very possibly occur in a considerable percentage of the population between adolescence and early middle age.

Individuals detected suffering from cannabis toxicity have repeatedly used cannabis in the past, although they may not have been heavy users. Also, they may be current users of the drug at the time they are seeking medical care. Two types of cannabis toxicity will be described: the acute and latent stages. The latent stage is particularly interesting due to the fact that it can manifest after (sometimes years after) marijuana use has been completely stopped.

General practitioners tend to overlook the issue of how marijuana consumption (past or present) may be affecting patients' health because the whole subject of cannabis use has been clouded on the one hand by academic controversy and on the other hand by emotional appeals of both individuals favoring its recreational use and those vehemently opposed to the drug. In an authoritative work on health effects of marijuana, Health et al. Note that "Each time sound data have been presented which indicate the drug might be injurious to health, there have been rebuttals, the critics usually claiming the study lacked adequate controls. Typical arguments have been that subjects participating in the study

used drugs in addition to cannabis sativa or that the pathology would have developed in the absence of cannabis use" ⁽³⁾

Further, it is important to note that some holistic health practitioners assume that because they emphasize in their practice the importance of healthy life styles, they are not treating the type of individual that would be a candidate for CTS. A cursory review of the statistics of marijuana use among adolescents and young adults over the last two decades should dispel this notion on the basis of the sheer volume of individuals that have used or are using the drug, if nothing else.

Before defining the syndrome, general information will be briefly presented relating to the prevalence of marijuana use, the metabolism of Cannabis, its toxicology and pharmacology.

In the interests of the burgeoning numbers of chronically ill, it is hoped that this paper will encourage a greater awareness of Cannabis' related health problems (especially of Latent Cannabinoid Toxicity) and wider clinical appreciation of the marijuana detoxification measures suggested here.

OCCURRENCE OF CANNABIS USE

Trend studies of cannabis use in U.S.A., Canada, Australia, and Norway show that marijuana consumption has dramatically increased in the last 15-20 years. "For example, only 6.7% of students in Canada in 1968 but 31.7% in 1979 used Cannabis. Annual household surveys in the U.S.A. showed that the percentage of young people (aged 12 to 17) who smoked cannabis increased from 15% in 1971 to 22% in 1977. ...Currently there are some signs of stabilization in rates of use. The latest studies of high school seniors by Johnston et al. Showed no increase in use in 1980 and 1979 over 1978..." (Smart, R.G. ⁽⁵⁾)

Nicholi (6) reports that "recent surveys indicate that approximately 60% of high school seniors have smoked marijuana and approximately the same percentage of college students. ...Within the college age group, the 18-25 year olds, some **21 million use the drug with about 40% of this group having used it a minimum of a hundred times**" (emphasis mine).

PHARMACOLOGY, TOXICOLOGY AND METABOLISM OF CANNABIS - AN OVERVIEW

A tremendous number of experimental studies have demonstrated the potentially far-reaching negative effects of cannabis on experimental animals and humans. Adverse finds suggest, and in some instances prove, that marijuana ⁽⁷⁾:

1. Diminishes growth and body weight.
2. Decreases gastric acid secretion, causing hypochlorhydria.
3. Causes chromosomal aberrations and mutagenicity.
4. Impairs synthesis of macromolecules.

5. Depresses T-lymphocyte, B-lymphocyte and macrophage activity.
6. Seriously disturbs male and female endocrine balance.
7. Causes CNS dysfunction, altering cognitive-perceptual and psychomotor activities.
8. Invades and becomes sequestered in fatty tissues and organs throughout the body. Due to its strong lipophilicity, its noxious influence could persist for long periods of time.
9. 97% of blood born delta 9-THC is bound mainly to protein, especially Low Density Lipoproteins.
10. Radiolabelled THC accumulates particularly in the lungs, liver, kidney, heart, gut, spleen brown fat, and mammary glands. THC also accumulates in several endocrine glands such as the adrenal cortex, thyroid and pituitary. There is a high uptake by the tissues, common for highly lipophilic compounds (Harvey, D.J., ⁽²⁾)
11. Cannabis has marked lipophilic properties, which aid its rapid passage across lipoprotein membranes in the lung and in the vascular system. Cannabinoids appear to disrupt the structure and function of biological membranes (Mellors, A. ⁽¹⁾)
12. "THC has excitatory as well as depressant effects on spinal pathways of the rat and of polysynaptic reflexes of the nonhuman primate. ...The ambivalent
13. effects of THC are also observed on EEG records which display patterns of desynchronization under effects of the drug" (Nahas, Gabriel G. ⁽²⁾)
14. THC reduces the number of lymphocytes and uptake of nucleic acids by lymphocytes in the adrenal medulla. THC has reportedly caused decrease in the weight of the thymus gland in experimental animals (Albert, et al. ⁽⁴⁾)
15. In man Cannabis smoking suppresses circulating levels of (FSH) and (LH) accompanied by a decrease in the amount of Testosterone. Cannabis appears to act on the testes directly (Nogawa, T. et al. ⁽⁴⁾) in female primates it is likely that THC directly suppresses hypothalamic/pituitary activity (Smith, C.G. et al. ⁽⁴⁾).
16. Leukocyte and sperm cell nuclear chromatin is altered under the effects of Cannabis (Issidorides, M.R. et al. ⁽¹⁾)

METABOLISM

At the time of peak psychoactivity, brain concentrations of THC are quite low, estimated at less than 1% of the intravenous administered dose (Harvey, D.J. ⁽²⁾)

In experimental animals THC non-competitively inhibits brain MAO by interacting with the lipophilic moiety of the enzyme or its membranal microenvironment.

THC is extensively metabolized by liver enzymes (working to change it into metabolites which the body would hope to more easily handle) (Wall, M.E. et al. ⁽⁴⁾)

EXCRETION

In humans, about 70% of the dose of "pot" is excreted during the first week. The pattern that emerges from studies on the metabolism, distribution and excretion of THC is similar to typical lipophilic drugs, which are rapidly taken up by the tissues, particularly fat. "Although metabolism is both rapid and extensive, elimination is mainly governed by slow release of the drug sequestered in deep body compartments" (Harvey, D.J.⁽²⁾)

CHARACTERIZATION OF CANNABINOID TOXICITY SYNDROME (CTS)

CTS is a pan symptomatic disorder. Due to cannabinoids' ability to infiltrate, sequester, and negatively influence diverse areas of the human organism, they have the potential of disrupting the body's homeostatic mechanisms, especially at the level of the CNS. Once this has happened, physiological and psychic breakdown by attrition can occur from any number of chronic stressors, which are encountered by individuals living in modern industrial societies. The mental pre-disposition and constitutional or genetic inheritance will govern which systems or organs break down in a given case. Therefore, specific mechanisms establishing the causal relationship between marijuana consumption and manifestation of any particular disorder are hard to define.

Nevertheless, several signs have been observed in clinical practice by this writer which indicate that a given patient may be experiencing CTS. Over the last five years, Dr. Davis has treated at least 50 previously refractory cases (suffering from diverse complaints) the success of which principally depended on recognizing and helping the patient diminish cannabis toxicity. In most cases, the patient had made no association whatsoever between marijuana consumption and the onset of orthopedic and other complaints. As far as patient interview and physical exam can establish, none of the patients presented for examination under the immediate influence of drugs, although some had consumed marijuana within the previous 24 hours. The characterization of CTS in this paper is a composite of factors seen in several model cases.

CTS can include effects of acute intoxication, which have been widely described in medical literature (Brill, H. et al. ⁽²⁾). Generally speaking, however, there is a small likelihood of seeing acutely intoxicated patients in general practice. Non-habituated patients that have previously scheduled office visits (and who would show obvious signs of intoxication) are apt to refrain from drug use prior to seeing their doctor. Clinically, therefore, CTS primarily involves:

1. Chronic users habituated to Cannabis who experience acute episodes of distress, presumably by passing the end point of the body's ability to compensate to the noxious influence of a persistent chemical stressor.

2. Periodic users that may not have consumed the drug for several days or weeks, and
3. Individuals who relate that they have stopped smoking "pot", and may not have consumed it for months or years.

Interestingly, the latter frequently exhibit persistent weaknesses in the body's compensatory and homeostatic mechanisms. These weaknesses lead to chronic physical complaints that most physicians would dismiss as being psychosomatic or ephemeral dyspathies. Diagnostic signs in the latter, the latent state of CTS - designated as Latent Cannabinoid Toxicity (LCT) - are subtle and can easily evade detection. (Psychiatric tests do identify numerous psychopathological effects of chronic cannabis consumption, which are believed to be reversible, disappearing after drug use has stopped.) The possibility of identifying latent effects of past Cannabis use is significant in light of the findings of a recent, authoritative WHO report ⁽⁵⁾ pg. 41):

"Because of the sequestration of cannabinoids, THC or its biologically active metabolites could theoretically accumulate in fatty tissues during chronic or intermittent administration (Jones, 1980). This accumulation would not be measurable by determinations of blood levels of cannabinoids, and has not, as yet, been demonstrated in human tissue samples. In humans, cumulative behavioral or physiological effects have not been demonstrated under conditions of controlled administration of up to three months duration, although the simultaneous development of tolerance may have masked this phenomenon (Jones 1980). In animals, cumulative toxicity ...has been observed at doses relevant to those consumed by human chronic users. The possible occurrence of cumulative toxicity in humans, therefore, is a question that should be examined."

GENERAL SIGN OF CTS

1. Deep seated and persistent tendency toward "neurologic disorganization" or "switching" as defined in the field of Applied Kinesiology ⁽⁸⁾.
2. Loss of musculoligamentous tone and inability to maintain therapeutic musculoskeletal manipulative corrections (even with nutritional support.)

SIGNS OF THE ACUTE STATE OF CTS

1. Profound anxiety experienced by the patient over loss of previous relatively normal musculoskeletal integrity, attended by severe pain, spasm and the feeling that weight bearing structures (pelvis, lumbar spine, neck/shoulders) will "give out" or collapse.
2. Moderate as well as severe (and occasionally bizarre) antalgic positions, in the most extreme cases resembling a combination of Intervertebral Disc Syndrome antalgia and torticollis.

SIGNS OF THE LATENT STATE OF CTS (aka Latent Cannabinoid Toxicity LCT)

1. Transient/mild or deep sense of depression and apprehension, mood swings, apathy.
2. Poor attention span - tendency to confuse sides of the body and proper execution of commands in physical examination.
3. Similarity to and increased propensity of association with chronic ill-health syndromes such as: functional hypoadrenia, blood sugar handling stress, Candida albicans allergy, immunodepression, fatty acid metabolism problems, etc.

CASE REPORT # 1

Acute CTS - *Mr. R, a 28 year male Caucasian, came to my office as a new patient on a Monday. He was heavy set, about 6'2" tall, 230 pounds. He was extremely distressed about an injury he had sustained two weeks previously while working at his janitorial job. He had never had back problems before. After he had finished mopping, his low back and shoulder muscles began to tighten. Without abating, the spasms continued to worsen in the next week such that he assumed an antalgic position that made him twist in deformity. In my office, he literally began to weep, asking what was going to happen to his body - would he be paralyzed.*

On temporary disability leave, Mr. R. had visited a neurologist and an orthopedist. He had been prescribed bedrest the previous week, and Fiorinal/Codeine III (30 mg. Codeine/tablet) to relieve pain and anxiety. He took the medication several days with no relief. In fact, the Saturday before seeing me, he took "at least 6 pain pills". He felt he was still getting worse, so on Sunday he took nothing. His condition continued to worsen on Sunday.

Since this case was reminiscent of CTS, I asked Mr. R. if he was presently using or if he had ever used recreational drugs. He related that he had used "pot" for years and that he had smoked a lot of it the previous week to relax his muscle spasms. He had smoked six "joints" on Saturday and Sunday to "handle it." I told him I had seen cases where marijuana had caused orthopedic problems, and mentioned that he would have to stop if he wanted the pain to go away.

I asked Mr. R. if he could lie on the examining table. He said he was in too much pain. No strong indicator muscles could be found for weight bearing Applied Kinesiological muscle testing.

Following a procedure that I have seen work several times before in chronic musculoskeletal instability, I recommended that he take 1 tsp. of a powdered Basil preparation I had made up with each meal and before bed, and return the next day.

To my astonishment, his antalgia and anxiety had almost entirely disappeared. He was then able to undergo routine AK diagnostic workup and treatment. He said he would continue the Basil and stop "pot". He called on Thursday to tell me he felt quite well. He wasn't "smoking dope". He did not return to the office.

Since Mr. R.'s case, several musculoskeletal and other complex conditions have been greatly helped by using a tableted preparation of highly bioactive species of organically grown Basil ⁽⁹⁾.

EXPERIMENTAL RESEARCH EVIDENCE SUPPORTING CTS

The varying and potentially far reaching negative biochemical influence of cannabinoids cannot help but encourage one to try to discover if Cannabis consumption is causally associated with many of the chronic ill-health syndromes seen so frequently in practice today, problems which could very possible be centrally mediated, i.e. at the brain level. Experimental evidence does support this possibility.

Evidence in support of "Neurologic Disorganization", "Ocular Lock" and "Switching":

- W.W. Just et al. ⁽¹⁾ report: "Brain autoradiographs (using labeled cannabinoids) showed that gray matter was more heavily labeled than white matter. Apart from this gross distribution, however, some brain structures contained higher levels of radioactivity than gray matter in general. Most of these structures are involved in the processing of visual and acoustic information and in motor control (emphasis mine) ...The visual pathway displayed high concentrations of radioactivity..."

It was further noted that six hours after introduction of labeled THC into the live animal, brain levels of THC, in general, diminished, but the midbrain and medulla oblongata maintained rather high levels of radioactivity.

- Robert G. Heath et al. ⁽³⁾ report that in non-human primates that showed lasting EEG changes consequent to moderate or heavy smoking of marijuana, consistent brain ultrastructural changes were observed. Pathologic changes were: (1) in the morphology of the synapse; (2) in the volume density of the rough endoplasmic reticulum; (3) in the nuclei, characterized by the presence of a large number of intranuclear inclusions. Greatest pathology was noted in the septal region, the hippocampus and amygdala.
- P. Etevenon ⁽³⁾ reports that permanent subcortical EEG changes can be observed in limbic structures and sensory thalamic nuclei of monkeys that have undergone 3 monts of exposure to marijuana via a "smoking machine".

C. J. Hillard et al. ⁽⁴⁾ remark that THC has an extremely high affinity for brain synaptosomal membranes and "exerts a wide range of effects on membrane associated systems as well." For example, THC has been shown to affect neurotransmitter uptake systems and membrane-bound enzyme systems which "suggest that a mechanism of THC action could be a primary alteration in the physical properties of the phospholipid bilayer of the membrane which secondarily affects membrane associated macromolecules."

Gabriel G. Nahas ⁽²⁾ states: "Acute as well as chronic manifestations of cannabis intoxication will result from exposure to nanomolar (10^{-9} M) concentrations of this (drug) and of its many metabolites, sustained in vital organs for hours, days or years. Neutral fat deposits represent a major storage buffer compartment for the THC and limit exposure of

the brain and other tissues to low but sustained concentrations of the drug." The fact that activity of the drug can be achieved with such a small concentration likely indicates that its action is on or close to receptor sites (Maureen Bronson et al. ⁽⁴⁾).

There is ample evidence to suggest that cannabinoids (and by extension, other noxious lipophilic substances) could chemically induce "neurologic disorganization" over time by sequestering strategically in the CNS.

That Cannabis can aggravate tendencies toward schizophrenia is well established in psychiatric literature. There is clear evidence in AK between the relationship of "neurologic disorganization" and schizophrenia - a further tie between disruption of fundamental neurologic mechanisms and invasive chemical substances in marijuana.

EVIDENCE LINKING ACTIONS OF CANNABINOIDS AND FUNCTIONAL HYPOADRENIA:

- Orthostatic hypotension was induced in human experimental subjects by marijuana inhalation ⁽¹⁰⁾.
- The number of lymphocytes in the adrenal is diminished under the influence of THC, and could possibly initiate adrenal autoimmune dysfunction.
- Cannabinoids selectively sequester in the adrenals, and may persist over time.
- Blevins and Regan ⁽¹⁾ point out that some cannabinoids and their metabolites have chemical structures that resemble cholesterol. This has strong implications with respect to the interactions between the cannabinoids and all membranes of and within the cell, and could represent an additional source of stress on the adrenal during steroid synthesis.

MARIJUANA AND PREDISPOSITION TO FUNGAL INFECTION:

- Introduction into the lungs of *Aspergillus* by contaminated marijuana cigarettes has been reported (F.S. Tennant ⁽⁵⁾) and may not be an uncommon occurrence. The pathway of entry of airborne pathogens via the lungs is facilitated due to Cannabis' considerable destructive effects on lung macrophages and general physiology. This could weaken the body's resistance to opportunistic organisms such as *Candida*.

MARIJUANA IN RELATIONSHIP TO FATTY ACID METABOLISM

- With reference to cannabinoids, D.J. Harvey ⁽²⁾ states that "the exact nature of the material accumulated in the tissues is largely unknown, although...studies...do indicate that a substantial portion is THC itself. The 11-hydroxy metabolite has been found in brain and other tissues including fat... A substantial portion of the drug, particularly at later times, appears to be in the form of fatty acid conjugates..."

MANAGEMENT OF CTS

Well trained holistic chiropractic physicians already have at their disposal the tool necessary for managing CTS. The obvious prerequisite to management is identifying the problem.

1. Patients with unusual or chronic symptoms should routinely be asked "Have you ever or are you now using recreational drugs - marijuana?"
2. If CTS does exist, the physician must have a strategy to try to mobilize sequestered drug residues by increasing circulation of biological fluids. Musculoskeletal manipulation and/or cranial-sacral respiratory therapy are ideal for this purpose.
3. Channels of elimination should be kept open. A high roughage diet helps move toxic bile out of the body more quickly.
4. Specific nutritional supplemental therapy should be initiated. While conventional vitamins and minerals can be helpful, in this author's opinion, nothing approaches the effectiveness of bioactive Basil.⁽⁹⁾

BASIL & DRUG DETOX - POSSIBLE MODES OF ACTION

In the course of Dr. Davis' research in medicinal plant therapy and ethnomedicine, it was discovered that Basil was used in ancient India and Egypt, among other places, to detoxify Hashish (a potent concentration of marijuana.) This led the author to try to empirically evaluate its usefulness in clinical practice. Several years of application have confirmed its utility. As a therapeutic plant its usefulness is specific against Cannabis, but it should also be utilized in the case of sequestration of other lipophilic, noxious chemicals, when AK reflex testing or independent clinical knowledge dictate.

The mode of action of Basil is complex due to its numerous essential oils, polysaccharides, minerals, vitamins and other constituents. Its medicinal properties are listed as: aromatic, diaphoretic, stimulant, carminative, expectorant, and stomachic⁽¹¹⁾.

Perhaps Basil's strongest therapeutic force comes from the fact that it is also able to penetrate fatty tissue, but in a benevolent way. Chemically, the isoprene and phenylpropanoid constituents of the essential oils of Basil are quite similar to the cannabinoids in Marijuana. Basil's essential oils might solubilize cannabinoid residues.

For millennia in India, Basil has always been planted around temples. It is respected as a holy herb.

CONCLUSION

Beyond finding and fixing somatic problems, one of the great joys of healing is the ability to help restore the patient's mental order and harmony of spirit. To this end, an ancient remedy - the benevolent herb, Basil - makes a unique contribution.

SUMMARY

1. CTS is a constellation of health disorders more prevalent than one might assume.

2. AK procedures give physicians particular insight into identifying and successfully treating patients with toxic problems from Cannabis that very likely might be missed or misdiagnosed.
3. Administration of tableted bioactive species of Basil ⁽⁹⁾ to individuals in both the acute and latent stages of CTS can bring dramatic improvement.
4. The possibility that ⁽¹⁾CTS can serve as a model for deleterious effects of lipophilic noxious chemical substances other than cannabinoids should be considered.

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