

The Lifevine Foundation

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Practicing Physicians
Medical Professionals
State of Washington

Dear Concerned Physician,

The patient presenting this letter to you has been diagnosed with Rheumatoid Arthritis. The Lifevine Foundation is a non-profit public education and legal assistance provider for medical marijuana patients and their physicians. We urge you to consider the following information when determining whether this patient will potentially benefit from the use of cannabis.

As you are probably aware, drug therapy for RA usually consists of the use of NSAID's, 5-ASA agents and various forms of corticosteroid. These drugs are used because of their ability to inhibit immune-induced inflammation. Immunomodulators may also play an important therapeutic role for the same reason.

NSAID's such as aspirin, ibuprofen, carprofen, naproxen, ketoprofen, ketorolac tromethamine, meclufenamate sodium, fenoprofen calcium and the various salicylates have analgesic benefits as well as being anti-inflammatory agents. However, it often takes months to determine the drug's effectiveness and they are not effective for all patients. Side effects include; headaches, liver function abnormalities, drowsiness, nausea, abdominal pain, vomiting, and diarrhea, anemia, platelet dysfunction, blood (or protein) in the urine, stomach pain and ulcers

5-ASA agents such as Sulfasalazine, Asacol, Pentasa, and Dipentum have limited effectiveness with some RA patients, and they may have some very serious side-effects including; kidney damage, nausea, loss of appetite, pancreatitis, hair loss, rash and fever, diarrhea, male infertility, anemia and leukopenia.

Corticosteroids are effective anti-inflammatory agents but adverse reactions are very common. Long-term use is not recommended because of the side effects. Insomnia, alterations of mood, night sweats, altered glucose metabolism, rounding of the face, development of a fatty neck hump, excessive hair growth, cataracts, osteoporosis, muscle weakness, hypertension, and osteonecrosis are some of the short and long term side effects

Immunomodulators such as 6-MP, Azathioprine, Cyclosporin, and Remicade, can be very expensive and have limited effectiveness in many patients. Side effects include; nausea, headache, numbness of extremities, excessive hair growth, pancreatitis, bone marrow depression, hepatitis, opportunistic infections, hypertension, seizures, kidney dysfunction and lymphoma.

Marijuana (Cannabis) is a powerful anti-inflammatory agent that has been shown to be particularly effective with immune-induced inflammation. Cannabis has the added advantage of easing, or even completely eliminating, the painful muscle cramping that may accompany a flare-up. Marijuana is an effective analgesic. Interestingly, 5-ASA's, corticosteroids and immunomodulators are indicated for Crohn's Disease and MS patients as well. Cannabis has been

demonstrated effective with both of these conditions. The Canadian Health Department (Health Canada) has listed Rheumatoid Arthritis as a debilitating medical condition that could potentially benefit from the use of medical marijuana. Please review the following data. The minimal side effects of cannabis will be discussed following the data.

Published Current Data (studies relevant to RA, short synopsis - complete articles are available)

1974, *Comprehensive Psychiatry*, Vol. 15, No. 6, Noyes and Barnes stated “There are indications that the active ingredients in marijuana may be an effective analgesic that is efficacious in functional pain”

1981, *Journal of Clinical Pharmacology*, Vol. 21, “Treatment of human spasticity with delta-9-tetrahydrocannabinol” Petro and Ellenberger found “THC can relieve a broad range of muscle spasms in humans and animals”

1986, *Pharmacological Review*, Vol. 38, No. 1 “Health Aspects of Marijuana” Hollister “Constituents of marijuana; CBC, olivitol, and cannoflavin all have marked anti-inflammatory properties.”

1988, *Inflammation*, Vol. 12 No. 4, “Analgesic and anti-inflammatory activity of constituents of cannabis sativa I” Formukong, Evans, and Evans “Cannabidol is more effective than aspirin in reducing inflammation” (Cannabidol or CBD, is one of the scores of cannabinoids found in marijuana other than THC)

1988, *European Archive of Psychiatry and Neurological Science*, Vol. 240 No. 1 (published in 1990, written in 1988) “Delta-9-tetrahydrocannabinol shows anti-spastic and analgesic effects in a single case double-blind trial” The trial compared Codeine, THC, and a placebo. The study found codeine and THC had comparable analgesic effects but only THC had a significant beneficial effect on spasticity and inflammation.”

1988, *International Journal of Clinical Pharmacology*, Vol. 34, No. 10, “The effect of orally and rectally administered delta-9-tetrahydrocannabinol on spasticity” Egli, Elsohly, Henn and Spiess. “THC was shown to relieve muscle spasms in human patients”

1988, *Journal of Psychoactive Drugs* Vol.20 (1:): 3-8, January-March, Hollister, L.E., “Marijuana and immunity” Cannabinoids found in marijuana are effective immunomodulators.

1991, *Pain* Vol. 47(1): 95-103, October Zeltser, R.; Seltzer, Z.; Eisen, A.; Feigenbaum, J.J.; and Mechoulam, R. “Suppression of neuropathic pain behavior in rats by a non-psychotropic synthetic cannabinoid with NMDA receptor-blocking properties”. The study found cannabis suppressed neuropathic pain which complicates many CNS diseases. Cannabis was effective when few available therapies provided even partial relief.

1993, *Advances in Experimental Medicine and Biology*, Vol. 335, 115-120 N. E. Kaminsky, “Evidence for a cannabinoid receptor in immunomodulation by cannabinoid compounds” Identifies the receptors and process that allows marijuana to be an effective immunomodulator.

1995. *Advances in Experimental Medicine and Biology* 373:103-113, Friedman, H.; Klein, T.W.; Newton, C.; and Daaka, Y.” Marijuana, receptors and immunomodulation.” The study suggested that the immunosuppressive effects of cannabinoids might be useful clinically; for example, in treating multiple sclerosis.

1997, *Science*, Vol.277, No. 5329, “Functional role of high-affinity anandamide transport as revealed by selective inhibition.” Beltramo and Piomelli. “Cannabinoid and non-cannabinoid compounds in marijuana reduce pain and inflammation.”

1997, *Anesthesia*, Vol. 52, No. 5, May, “Pain relief with oral cannabinoids in familial Mediterranean fever” Holdcroft, et al. This research paper done at Hammersmith Hospital in London confirmed cannabis’ analgesic effects in the first UK clinical trial. The paper states “Cannabinoids have analgesic and possibly anti-inflammatory properties but their clinical use has been restricted by legislation”

1997, Society for Neuroscience Conference, symposium syllabus published in Aug. '98 *Functional Role of Cannabinoid Receptors*, “Cannabinoids were shown to have a direct effect on the biochemical pain signals in the central nervous system, and to exhibit superior pain control to addictive opiate based narcotics. Cannabinoids prevented hyperalgesia and were shown to be particularly effective in the treatment of arthritis and other inflammation induced pain.

1998, *BW Healthwire*, January, ‘Pre-clinical studies show CT-3 reduces chronic and acute inflammation and reduces destruction of joints’ Atlantic Pharmaceuticals was evaluating CT-3, a cannabinoid derivative. The company reported “In recent studies, the agent was found to reduce inflammation and prevent the destruction of joint tissue.”

1998, *Pain* Vol. 75, 1 pp. 111-119 By Jennelle Durnett Richardson, Sonja Kilo, Kenneth M. Hargreaves, “Cannabinoids Reduce Hyperalgesia and Inflammation via Interaction with Peripheral CB1 Receptors”.

1998, *Journal of Neuroimmunology*, Dr. N. E. Kaminsky wrote, “These [cannabinoids] might be useful as immune modulators, perhaps to be used as anti-inflammatory agents“

1999, *National Academy of Science, Institute of Medicine*, “Marijuana and Medicine; Assessing the Science Base “ Executive Summary, “Conclusion: Scientific data indicate the potential therapeutic value of cannabinoid drugs, primarily THC, for pain relief, control of nausea and vomiting, and appetite stimulation;”

2000, *IACM-Bulletin of 25 June*, Dr. Franjo Grotenhermen (IACM): "We know from animal studies that THC inhibits the production of Th-1 cytokines such as IL-1, IL-2, and IFN-gamma and stimulates the production of Th-2 cytokines such as IL-4, IL-10, and TGF-beta. This would give reason for a causal therapeutic use of THC in certain autoimmune diseases that appear to be Th-1 mediated such as Crohn's disease, a form of chronic intestinal inflammation, and rheumatoid arthritis.”

2001, *Press release of the University of Kuopio of 17. September 2001*, Medical researchers of the University of Kuopio, Finland, investigated the effects of hemp seed oil on physical parameters in a double blind study with 14 subjects, who ingested either 30 ml hemp seed oil or linseed oil for a period of four weeks. Hemp seed oil resulted in statistically higher levels of GLA (gamma-linolenic acid) in the serum triglycerides and in the cholesteryl esters. Both oils showed statistically significant increases in blood levels of linoleic acid and alpha-linolenic acid. Increased serum levels of GLA might help explain beneficial effects in some chronic diseases such as allergies and rheumatoid arthritis, Dr Jace Callaway, one of the principal investigators said.

2001 *Journal of Cannabis Therapeutics*, Vol.1, #3, Broom, Sufka, El Sohly & Ross, “Analgesic and Reinforcing Properties of D9-THC-Hemisuccinate in Adjuvant-Arthritic Rats” The purpose

of this study was to investigate the antinociceptive and reinforcing effects of rectally administered D9-THC-HS in rats. Tests were conducted in two groups of animals: Complete Freund's adjuvant-inflamed animals (CFA) and non-inflamed controls. A hotplate test was administered to index hyperalgesia and possible analgesic effects of D9-THC-HS on thermal nociception. CFA animals demonstrated shorter latencies than non-inflamed animals. The highest dose of D9-THC-HS produced longer hotplate latencies. Additionally, the reinforcing properties of D9-THC-HS were evaluated using the Conditioned Place Preference (CPP) paradigm. D9-THC-HS produced an increase in preference scores in non-inflamed animals (positive reinforcement), but did not affect preference scores in CFA animals. These data suggest that D9-THC-HS has therapeutic potential and is unlikely to possess an abuse liability when used in the context of chronic pain.

Historical Data

- *The oldest medical text known to man was written over 5,000 years ago. The Chinese *Pen Ts'ao*, prescribed cannabis for rheumatism and digestive disorders among other illnesses.
- **The New English Dispensary* of 1764 recommended hemp to reduce inflammation.
- *In 1814, Nicholas Culpepper published his *Complete Herbal*, which included "allaying humors of the bowels" and "reducing inflammation" among the applications of cannabis.
- *Surgeon William O'Shoughnessy in his 1839 paper titled *On the preparation of the Indian Hemp* found that cannabis relieved rheumatism, convulsions and muscle spasms.
- *The 1854 *United States Dispensary* listed many uses for cannabis including "reduction of inflammation", "relax muscle contractions", "treatment of digestive disorders" and as "an analgesic and sedative"
- *Between 1840 and 1890 over 100 papers were published on the medical uses of cannabis.
- *Sir William Osler, known as the "father of modern medicine", proclaimed cannabis the best treatment for migraine pain in his authoritative 1915 textbook.
- *In 1937, when the Marijuana Tax Act was before Congress The American Medical Association protested vehemently, Dr William C. Woodward, the AMA's counsel, testified that the bill would deprive Americans of one of the most useful drugs known to medicine. He also complained that the only reason there hadn't been a larger public outcry was because the Act referred to the Mexican slang "marijuana" and not to cannabis, which everyone understood was a medicine

Side Effects

There has never been a reported death from overdose of marijuana. There has never been a death or permanent health effect reported from long-term heavy use of marijuana. Side effects include; a slight increase in heart rate, slight hypotension (lowering of blood pressure), increased appetite, and of course, a mild euphoric effect. There are "no deleterious effects on the normal cardiovascular system" as a result of these side effects according to a 1997 WHO report. An Australian National Drug Strategy report states "Tolerance to the cardiovascular effects develop within 7-10 days in persons receiving daily doses of THC".

The euphoria also is subject to the effects of tolerance. Any effects on coordination and cognition dissipate within 7-10 days of daily use. However marijuana's effects continue to aid with the patient's stress reduction and to alleviate the other emotional problems that RA patients often suffer from. Many patients find cannabis far superior to Valium, Serax, Elavil, or Sinequan; all are commonly prescribed to RA sufferers. Please contact the Lifestone Foundation for published data regarding the anti-anxiety and anti-depressant properties of cannabis.

Risks

The most obvious risk of smoking marijuana, is, of course, the risk incurred smoking any vegetable material. There are several factors to consider when determining this risk. If your patient is not suffering from an additional digestive disorder and they are able to keep food digesting for two hours, the patient may choose to eat their cannabis and avoid all smoking risks. Other smoking methods such as vaporizers (which heat the cannabis to a temperature high enough to “vaporize” the cannabinoids on the surface of the marijuana without igniting the vegetable matter) may minimize the smoking risks.

The carcinogenic ingredients in both tobacco and cannabis are primarily the tars that reside in both plants - not the THC or other cannabinoids of cannabis. The main difference in the incidence of development of lung cancer is a matter of exposure to these tars, which is overwhelmingly greater with tobacco than with cannabis.

It takes 20 - 25 pack/years or more (1 pack/year = smoking 1 pack of cigarettes/day for 1 year.) for most tobacco-induced lung cancers to develop. 20 - 25 pack/years worth of cigarettes = 150,000 to 200,000 cigarettes. Of all those people who smoke 1 pack/day or more of tobacco cigarettes for all of their adult lives, only from 1 in 5 (20%) will actually develop tobacco-induced lung cancer.

Most patients who use marijuana medicinally develop their illness in mid to late life, and start smoking marijuana medicinally only when their projected remaining life span is already relatively short. Light medical marijuana users - (1-2 joints/day) in one year would smoke 365 - 730 joints; in ten years - 3650 - 7300 joints. In order to reach the equivalent of 200,000 cigarettes it would take them 270 years, at which time 1/5 of them might develop a cancer.

Very heavy use of medicinal marijuana may amount to 10 joints/day. In one year they would smoke roughly 3,650 joints; in ten years- 36,500 joints It would take them 54 years to smoke the equivalent of 200,000 tobacco cigarettes, at which time 1/5 of them might develop a cancer. These figures assume large (1 gm) joints are being smoked - similar in size to a tobacco cigarette

Tobacco smoke is a bronchial constrictor known to penetrate the lung's smaller peripheral air passages and causes inflammation of the lung's absorbent microphages. Tobacco causes blockages which leads to emphysema. Dr. Donald Tashkin, a federally sponsored pulmonologist and professor of medicine at UCLA Medical School has determined that marijuana smoke acts as a bronchial dilator and suppresses inflammation of the lung's macrophages. In a 1997 UCLA study involving 394 participants Tashkin noted “Neither habitual long-term marijuana smokers nor intermittent marijuana smokers exhibited any significantly different rates of decline in lung function. No differences were noted between even quite heavy smoking and non-smoking of marijuana.” In contrast, the tobacco-only smokers in the study experienced a rapid decline in lung function during the eight years this study ran. The study also found no connection between marijuana and tobacco smoking in those subjects who smoked both. The evidence from this exhaustive real-world study indicates that the pulmonary health of marijuana smokers is no different from that of the general population.

Other risks include physical or psychological dependence. These risks are far lower than with any other psychotropic drug. The addictive properties of marijuana are far lower than caffeine, ephedrine, or benzodiazepines (like Valium). Marijuana is similar to chocolate in it's potential for dependency. Unlike alcohol, nicotine, opiates, barbiturates, amphetamines, cocaine or chocolate, marijuana does not effect the dopamine receptors of the brain. There is no physical withdrawal.

Unlike steroids and other pharmaceuticals, one can cease use immediately; there is no need to “taper down” dosages.

Conclusion

There is compelling evidence that cannabis is an effective anti-inflammatory, analgesic and anti spasmodic agent. These properties are indicated for patients suffering from RA. Five thousand years of recorded medical use, has shown no long-term consequences. Side effects from the use of medical marijuana are much milder than the side effects of the traditional drugs used to treat RA. Most patients who use cannabis report they are able to substantially reduce or even eliminate the use of their prescription medications. Marijuana also has recognized antiemetic, anti-anxiety, anti-depressant and stress reducing qualities, which many RA patients find beneficial. Patients without prescription insurance find the ability to grow their own medicine at little or no cost to be an additional benefit.

RCW 69.51A states that for a patient to qualify for use of medical marijuana, their physician must find that “It is their medical opinion that the *potential* benefits of the medical use of marijuana would *likely* outweigh the health risks for this patient.” We urge you to sign the enclosed “Documentation of Medical Authorization to Possess Marijuana for Medical Purposes in Washington State.” The Washington State Medical Association has prepared this document for use by our state’s physicians. The link between stress and RA flare-ups is well established. Eliminating the stress induced by the fear of arrest by patients who currently use marijuana for their symptoms is one more benefit of the medical marijuana act.

Report by Bruce Buckner