

# Quality Resource Guide

## Oral Complications of Cannabis Use

### Author Acknowledgements

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### Educational Objectives

Following this unit of instruction, the practitioner should be able to:

1. Discuss the medical diseases and disorders for which medical marijuana has been studied.
2. Understand why changes in the oral cavity related to cannabis use have assumed greater significance for oral health care providers.
3. Be familiar with the literature on the relationship of cannabis use and the risk for oral squamous cell cancer (OSCC).
4. Be familiar with the literature on the relationship of cannabis use and the risk for dental caries and periodontal disease.
5. Understand the limitations and shortcomings of studies that have examined the relationship of cannabis use to oral disease.

MetLife designates this activity for **1.0 continuing education credits** for the review of this Quality Resource Guide and successful completion of the post test.

The following commentary highlights fundamental and commonly accepted practices on the subject matter. The information is intended as a general overview and is for educational purposes only. This information does not constitute legal advice, which can only be provided by an attorney.

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## Introduction

The effects of cannabis on the oral cavity and the provision of dental care for cannabis users have become relevant topics for oral health care providers because of liberalization of state laws regulating the use of recreational marijuana and expansion of the use of marijuana for medical reasons.

Cannabis is considered a flowering herb, and while the number of species is debated, the species *Cannabis sativa* is accepted as the Latin name of the plant. Cannabis contains several bioactive chemicals collectively referred to as cannabinoids. Among the most important of these is tetrahydrocannabinol (THC), which has psychoactive properties. When cannabis is used for its psychoactive effects, it is most often smoked or ingested. Another important component is cannabidiol (CBD), which does not have psychoactive effects. CBD is available in a variety of preparations, including oils, creams and sprays, and is also included in some beauty products.

Cannabis use can be divided into medicinal uses, industrial applications and use as a recreational drug. Cannabis preparations used as medical and recreational drugs include both the dried flower (referred to as marijuana), as a resin (hashish) and as different types of oils. Industrial applications have centered on use of the stem fibers (known as hemp) from the cannabis plant for a variety of different purposes, including paper and textiles. As a fiber, hemp is more durable than cotton.

The medical uses of cannabis include a range of symptoms associated with various diseases and disorders.<sup>1</sup> These include:

- nausea and vomiting as a side effect of cancer chemotherapy
- improving appetite in persons with HIV/AIDS
- chronic pain
- spasticity due to multiple sclerosis/paraplegia
- depression
- anxiety disorders
- sleep disorders
- psychosis
- glaucoma
- Tourette syndrome

This review of the literature determined that there was evidence that cannabinoids had a beneficial effect in the treatment of chronic pain and spasticity, and the quality of evidence was moderate. There was low quality of evidence supporting the use of cannabinoids in the treatment of nausea/vomiting and adverse effect of cancer chemotherapy, appetite enhancement and weight gain in persons with HIV/AIDS, and as a treatment for sleep disorders and Tourette syndrome.

A subsequent review<sup>2</sup> noted an expanded number of possible uses for cannabis/cannabinoids, which highlighted potential benefits in the treatment of disorders noted in the earlier review (nausea and vomiting associated with cancer chemotherapy, treatment of anorexia in different patient groups including HIV/AIDS, multiple sclerosis and for chronic pain). This review also included the potential application in other disorders, such as irritable bowel syndrome, post-traumatic stress disorders, drug abuse and even some ocular diseases.

The focus on the use of cannabis in the treatment of chronic pain was recently emphasized in a systematic review.<sup>3</sup> High ratio THC:CBD products were associated with improved short-term management of chronic pain, but dizziness and sedation were reported as adverse side effects.

Considering that cannabis used for medicinal purposes is ingested or smoked, and that it is often smoked when used for recreational purposes, the potential impact of cannabis on the oral cavity is a concern for oral health care providers. Cannabis use is now approved for medical use in 41 states, and for recreational purposes in 23 of those states.<sup>4</sup> In the future, other states are sure to follow. Therefore, oral health care providers will see an increased number of patients who are users and must be aware of the potential adverse effects on the oral cavity.

## The Effect of Cannabis Use on the Oral Soft Tissues

A study of oral cytology that included cannabis smokers, tobacco smokers and non-smoking controls demonstrated degenerative changes

in epithelial cells, suggestive of human papillomavirus (HPV) infection, in smears from both tobacco and cannabis users. This was not seen in the control smears. In addition, smears from the cannabis users demonstrated a greater number of bacterial cells as compared to controls.<sup>5</sup> An animal study that examined wound healing following systemic exposure to CBD demonstrated that treated animals did not differ from controls in the size of the wound but did demonstrate a reduced inflammatory response three days after wounding. This difference was not seen seven days after wounding.<sup>6</sup> Further, xerostomia has been reported as a side effect of cannabis use,<sup>7</sup> as has inflammation of the uvula.<sup>8</sup>

A cell function study focused on the effect of cannabis on gingival epithelial cell function.<sup>9</sup> The adverse effects were seen in regard to increased apoptosis and autophagy, and were suggested to increase susceptibility to gingivitis and periodontitis.

These data suggest some limited alterations in the oral soft tissue response in cannabis users. The effect of cannabis on specific oral diseases and disorders (oral cancer, dental caries, periodontal diseases) has also been studied and is discussed below.

## Cannabis Use and Oral Cancer

Considering the relationship of cigarette smoking and other exposures to tobacco to the development of oral cancer, the relationship of cannabis use and smoking marijuana to oral cancer has been examined.

An early case series reported six cases of head and neck cancer in younger patients, all of whom regularly smoked marijuana. This study was published in the otolaryngology literature, and as a case series, the prevalence in a general population is not available.<sup>10</sup> However, this report alerted both dental and medical providers to this potential risk.

A case-control study reported on the risk for oral squamous cell cancer in persons under the age

of forty-five.<sup>11</sup> Compared to controls without oral cancer, the affected adults reported exposure to alcohol and tobacco, with smoking for a long period of time (at least 21 years) being associated with a significantly elevated risk (OR = 2.1). Though cannabis was included as a potential risk, it was not an independent risk factor, but may have a contributing role. An expanded study from these same investigators, cannabis again was not identified as an independent risk factor for oral squamous cell carcinoma.<sup>12</sup>

Human papilloma virus (HPV) infection has been identified as a risk factor for oral and pharyngeal cancer in younger individuals<sup>13</sup> and a study of oral HPV infection (high-risk subtypes) with men who have sex with men who were either HIV positive or HIV negative<sup>14</sup> indicated a higher percentage of oral HPV infection in individuals who were HIV positive (23.9%) versus HIV negative (9.4%). Recent use of cannabis was identified as a risk factor for HPV infection. While not linking cannabis use and oral cancer, this suggests a possible indirect association of cannabis and oral cancer.

*An expanded discussion of human papilloma virus infection may be found in the MetLife QRG – Redding S: HPV and Oral Cancer.*

Two reports examined the relationship between cannabis use and head and neck cancer, provided additional, interesting information that adds to earlier studies suggesting an indirect link between cannabis use and oral cancer. In the first,<sup>15</sup> a meta-analysis that included six articles did not find a statistically significant association of lifetime use of cannabis and head and neck cancer (OR = 1.02; p = 0.72). In the other, cannabis (marijuana) exposure was defined as current (weekly) use.<sup>16</sup> Cancer patients who used cannabis tended to use less tobacco and had a higher prevalence of HPV-associated oropharyngeal cancer. Further, there was a predominance of cancers in the oropharynx for marijuana users, versus a broader distribution of the location of the disease in non-users.

These data suggest that there is no definable direct relationship between cannabis use and oral squamous cell cancer (head and neck cancer) but cannabis use may have a contributing role

mediated by HPV infection. It is important to point out a shortcoming of these studies. While cigarette smoking can be quantified by determining pack-years, there is no generally accepted means of quantifying marijuana/cannabis use.

## Cannabis Use and Dental Caries

The literature examining the relationship between cannabis use and dental caries is not extensive. A review of systemic and oral effects of cannabis use stated that cannabis users have poor oral health and that users are at increased risk for both caries and periodontal disease.<sup>17</sup> A study from Switzerland did not identify any differences in caries risk between young adults (18-25 years) who were cannabis users and those who did not use cannabis but were tobacco users.<sup>18</sup> They note the potential for an increased caries rate in cannabis users associated with hyposalivation as well as neglect of routine oral hygiene.

Confirming the potential importance of cannabis use being associated with a reduction in salivary flow, the association of the use of e-cigarettes, cannabis smoking and tobacco smoking by high school students on xerostomia was studied and revealed that frequent dry mouth (5%), and occasional dry mouth (54%) occurred in all three groups as compared to controls who did not have these habits.<sup>19</sup> Dry mouth also increased with more frequent use of these products. When the new data was adjusted for potential confounders, only frequent use of cannabis (odds ratio = 3.17) and frequent use of smoked tobacco (odds ratio = 1.92) were associated with greater frequency of recurring dry mouth. Considering the importance of normal salivary flow as protection against dental caries, these data indicate one potential reason for increased caries rate among those who smoke cannabis.

A study of the oral health of adolescents (13-18 years of age) in Nevada compared marijuana and tobacco users to those adolescents who did not use either tobacco or marijuana. Here, the combined use of smoking tobacco and marijuana was considered. The extent and severity of caries was greater in smokers than non-users, with marijuana apparently having an even

more pronounced adverse effect than tobacco smoking.<sup>20</sup> Again, it is emphasized that the effect of reduced self-care should be considered as a major determinant of dental disease in some recreational marijuana users.

## Cannabis Use and Periodontal Diseases

Tobacco smoking is a primary risk factor for periodontitis, and consequently, the impact of cannabis use/marijuana smoking on periodontal status has been examined.

A general review of the effect of recreational drug use on periodontal health emphasized that behavior and personal as well as professional oral health must be considered when determining the effect of cannabis/marijuana on oral health.<sup>21</sup>

An animal study examined the effect of marijuana smoke on alveolar bone loss. A ligature-induced model was used and animals that were exposed to marijuana smoke demonstrated greater bone loss, and reduced bone density, versus unexposed animals.<sup>22</sup>

Clinical studies of the effect of exposure to cannabis on the periodontium generally suggest that cannabis is a risk factor for periodontal disease. A number of reports of large cohorts provide an indication of the magnitude of this effect. A study from New Zealand evaluated a birth cohort (born at a single hospital between April 1972 and March 1973).<sup>23</sup> Health examinations were conducted at various time points and an oral examination was performed at 26 and 32 years. Participants were stratified by cannabis usage into none (293 individuals), some (428 individuals) and high (182 individuals) exposure. Increased attachment loss between the two examinations was observed for 6.5%, 11.2% and 23.6%, respectively, of the three groups. After controlling for known periodontal disease-associated risk factors (including tobacco smoking, plaque accumulation and lack of regular dental visits), the relative risk of different adverse periodontal outcomes ranged between 1.6 and 3.1. Of interest, while smoking tobacco was observed to be an important risk factor for periodontitis, cannabis exposure was also an independent risk factor for periodontal destruction.

An evaluation of the relationship of cannabis exposure and periodontal diseases in U.S. adults, using data from the 2011-2012 NHANES study, found that probing depth and clinical attachment loss were greater in individuals who self-reported to be frequent users of cannabis.<sup>24</sup> Frequent use of cannabis for recreational reasons was associated with advanced periodontitis (odds ratio = 1.7,  $p=0.002$ ). Of note, this cannabis-periodontitis relationship was still observed after correction for a range of variables, including race/ethnicity, tobacco use and diabetes mellitus.

Data from these two studies<sup>23,24</sup> suggest that cannabis use is a risk factor for periodontitis, and a recent systematic review and meta-analysis concluded that cannabis use is “associated with a higher prevalence of periodontitis”.<sup>25</sup> A recent review also concluded that evidence strongly suggests that marijuana users are at increased risk for periodontitis, but little is understood about the exact host response or microbial mechanisms that are responsible for this increased risk.<sup>26</sup> In that regard, a small clinical study identified two pro-inflammatory mediators (interleukin 17-A and 23) that were in higher concentration in saliva from marijuana smokers with periodontitis than cigarette smokers with periodontitis.<sup>27</sup> However, it is important to note that not all studies are in agreement. No association was observed in an adolescent population of cannabis-users in Chile.<sup>28</sup> In summary, the published data that has examined the relationship of recreational cannabis use and oral disease suggests that cannabis is an independent risk factor for periodontitis. What is also clear is that this relationship requires further study, as important variables such as exposure to cannabis requires a quantitative measure (equivalent to pack-years for cigarette smoking) to truly define this relationship. Further, adherence to oral hygiene procedures (self-care) and utilization of professional dental services are other important variables that need to be considered in future studies. At this time, however, awareness on the part of oral health care providers is certainly warranted.

## Clinical Considerations When Treating Patients Who Smoke Marijuana

A number of studies have explored special clinical considerations when providing dental care to patients who use marijuana, as well as some possible therapeutic uses for marijuana derived products as part of care management.

A review cautioned that an interaction between marijuana and local anesthetics containing epinephrine may be associated with severe sequelae.<sup>29</sup> A pilot study examined the success of local anesthesia with 1:100,000 epinephrine in individuals identified as chronic users of marijuana and nonusers. Successful anesthesia was achieved in 61% of those who used marijuana and 88% of those that did not. These results approached significance ( $p=0.07$ ). There was no difference between the groups in terms of onset or anesthesia duration.<sup>30</sup>

The CBD component of marijuana has been studied for its efficacy in treating a variety of oral disorders, including gingival inflammation and burning mouth syndrome.<sup>31</sup> In an in-vitro study, cannabinoid-containing mouthrinses were shown to have antimicrobial activity comparable to 0.2% chlorhexidine.<sup>32</sup> Furthermore, 0.1% CBD-containing patch was shown to have a beneficial effect on recurrent aphthous ulcers, reducing the size of the ulcers and reducing the healing time. An analgesic effect was also reported.<sup>33</sup> Further, a specially-prepared extract of cannabis was shown to improve the symptoms of burning mouth syndrome. The preparation was well tolerated, and the authors indicated the need for a larger placebo-controlled trial to define efficacy.<sup>34</sup>

## Summary

At present, there are no generally accepted guidelines to assist oral healthcare provider in asking their patients about recreational drug use. However, all health questionnaires should contain a question about such use. Cannabis/marijuana use for medical purposes should be disclosed when the patient is asked about prescription and non-prescription drug use.

It can be suggested that if upon completion of the oral examination, the extent and severity of oral disease is not commensurate with the patient's age or other personal factors, the oral healthcare provider can state this fact and ask the patient about other risk factors including recreational drug use. Further, since cannabis can be delivered in a variety of ways (*i.e.*, sublingual drops), it is essential that providers perform a comprehensive oral examination and have all relevant patient information to properly identify, diagnose and treat oral diseases.

Inquiring about substance abuse, including heavy cannabis/marijuana use, presents a dilemma for oral healthcare providers. However, it is essential that reasons for a greater than expected oral disease burden be identified, and that modifiable risk factors be modified. Issues associated with personal privacy, especially if the patient is underage complicate this matter. However, improving oral health/health is the primary responsibility of oral healthcare providers, and a comprehensive understanding of all relevant patient-related information is critical to achieve the desired outcome.

As additional states legalize the use of cannabis/marijuana for medical and recreational use, further research will be performed to answer a wide range of questions. It is essential that oral health care providers both be aware of newly published data and thoroughly evaluate patients who self-identify as using these drugs.

In the three years since the first edition of this Quality Resource Guide was published, earlier findings have been confirmed, specifically that cannabis is a risk factor for periodontitis. Further, some additional aspects of the cannabis-oral health and disease relationship have been introduced. Examples include cannabis-derived products have been identified as having antimicrobial/antiplaque activity,<sup>32</sup> and can be used by patients with burning mouth syndrome.<sup>34</sup>

Problems in defining the relationship of cannabis use to oral disease exist, and include the lack of a reliable measure of exposure (equivalent to pack years for smoking cigarettes) as well as variation in phytocompound concentration in different products. The need for well-designed clinical studies remains a concern.<sup>35</sup>

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## POST-TEST

Internet Users: This page is intended to assist you in fast and accurate testing when completing the “Online Exam.” We suggest reviewing the questions and then circling your answers on this page prior to completing the online exam.

(1.0 CE Credit Contact Hour) Please circle the correct answer. 70% equals passing grade.

1. **Tetrahydrocannabinol (THC) and cannabidiol (CBD) are the two most important components of cannabis. Which of the following is TRUE regarding THC and CBD:**
  - a. Both chemicals have psychoactive properties.
  - b. THC has psychoactive properties but CBD does not.
  - c. THC does not have psychoactive properties but CBD does have these effects.
  - d. THC and CBD act synergistically.
2. **Medical uses of the cannabis plant include all the following symptoms except:**
  - a. nausea and vomiting
  - b. inflammation
  - c. anxiety
  - d. sleep disturbances
3. **At present, the focus of attention for the clinical use of medical marijuana is:**
  - a. post-traumatic stress disorder
  - b. gastrointestinal disease of hypermotility
  - c. chronic pain management
  - d. psychiatric disorders
4. **Human papilloma virus (HPV) infection is greater in cannabis users compared to non-users. Studies examining the effect of cannabis use on oral cancer suggest that HPV infection may play a role in explaining any increased risks in persons using cannabis.**
  - a. Both statements are true.
  - b. The first statement is true, the second is false.
  - c. The first statement is false, the second true.
  - d. Both statements are false.
5. **Which statement is true regarding the relationship between cannabis use and the risk of oral squamous cell cancer (OSCC):**
  - a. Cannabis use is a risk factor for OSCC.
  - b. OSCC tends to occur in patients who are older, and generally do not use cannabis.
  - c. Cannabis use is associated with the use of tobacco, so separating the effects of both on the risk for OSCC is not possible.
  - d. There is no definable, direct relationship between cannabis use and the risk for OSCC.
6. **Based on the available literature, which statement is true regarding the caries risk in persons who use cannabis?**
  - a. There is a direct link between cannabis use and the risk for caries in adolescents.
  - b. The cannabis-dental caries association is likely modified by hyposalivation and neglect of routine oral hygiene measures.
  - c. All adolescents with a high caries rate should be asked about cannabis use.
  - d. A component in cannabis can be metabolized by the bacterium *Streptococcus mutans*, leading to acid production.
7. **Which of the following is true regarding the study of the relationship between cannabis use and the risk for periodontitis?**
  - a. The data is not robust but suggests that cannabis use is a risk factor for periodontitis.
  - b. The data is robust, suggesting that cannabis use is a risk factor for early-onset forms of periodontitis.
  - c. The data is not robust and suggests that cannabis use is not a risk factor for early-onset forms of periodontitis.
  - d. The data is robust and suggests that cannabis use is associated with increased gingival inflammation.
8. **The effect of cannabis use on the oral cavity is complicated by a lack of a means of quantifying total cannabis exposure. Another important complicating factor is the difficulty in evaluating the effect of reduced personal and professional care in heavy cannabis users.**
  - a. Both statements are true.
  - b. The first statement is true, the second is false.
  - c. The first statement is false, the second is true.
  - d. Both statements are false.
9. **Which of the following statements is true regarding asking a dental patient about cannabis use;**
  - a. Dental providers must fully understand all factors that influence the occurrence of oral/dental disease.
  - b. When possible, modifiable risk factors for oral disease should be modified.
  - c. Medical-legal concerns must be carefully considered.
  - d. All the above
10. **Which of the following is true regarding guidelines to assist oral health care providers when asking patients about recreational drug use?**
  - a. There are generally accepted guidelines for oral health care providers to use.
  - b. All health questionnaires should contain a question about recreational drug use.
  - c. Oral health care providers are required to contact a local law enforcement agency if illegal drug use is suspected.
  - d. Advice and counseling regarding recreational drug use is the responsibility of oral health care providers.

