

Mini Review**Cannabis Smoking And The Lung**Donald E Greydanus¹, Jasmine Alsukhon¹ and Andrey Leonov^{1*}¹Department of Pediatric & Adolescent Medicine Western Michigan University Homer Stryker M.D. School of Medicine 1000 Oakland Drive
Kalamazoo, MI 49008-1284. USA**Abstract**

Health effects of cannabis use has been a point of controversy on multiple fronts, from media to legislature to medicine. Here we review cannabis-associated respiratory adverse effects and underline the importance of comprehensive approach to patients who use or consider using cannabis.

Introduction

The scientific term, Cannabaceae, is the name of a group of flowering plants (angiosperm) of which Cannabis is the genus name with three subgroups or species: *Cannabis sativa*, *C. indica*, and *C. ruderalis*. Cannabis (marijuana, pot) is the most common illicit drug in the United States and is produced mainly from the *C sativa* plant due to its high concentration of its addictive agent, delta-9-tetrahydro-cannabinol [1].

The euphoric effects of cannabis that have led to its popularity continues from adolescence through adulthood [1]. There is a strong lobbying effort currently underway from pro-cannabis groups to allow more use of cannabis legally. Unproven claims of medical benefit serve as part of the driving force behind such efforts [1,2]. While modest therapeutic effects have been demonstrated in conditions such as chemotherapy-induced nausea and vomiting, chronic pain, multiple sclerosis-associated spasticity, the evidence of health benefits in other conditions is inadequate [3]. Multiple states in US have legalized use of marijuana for medical purposes and some states have legalized it for recreational use.

One of the concerns raised about smoking cannabis is that acute and chronic adverse effects of the respiratory tract may develop. Separating out effects of cannabis can be difficult since cannabis smokers often smoke tobacco as well [4]. Multiple products from natural plant or synthetic cannabis exists. Various ways to use cannabis and its products have been described, including pipe and cigarette smoking, water-pipe smoking, ingestion, vaporizing or applying to skin or mucosal surfaces as topical preparations [3]. In this article we review potential negative effects of cannabis in the respiratory and pulmonary structures that may occur in some persons who utilize this drug for recreation and/or anticipated medicinal benefit.

Toxic Chemicals of Cannabis

The Cannabis plant contains over 450 chemicals that include known carcinogens (such as benzopyrene and polycyclic aromatic hydrocarbons), some of which are at greater levels than found in tobacco smoke [5]. Other chemicals found in this plant include terpenoids, phytol, phytocannabinoids and others. There are over 60 phytocannabinoids in the cannabis plant including delta-9-tetra-hydrocannabinol (THC), cannabinol (CBN; THC metabolite), cannabidiol (CBD; THC isomer), cannabigerol (CBG), tetrahydrocannabivarin (THCV; THV) and cannabichromene (CBC) [1,2].

Aluminum, which is found in both cannabis and tobacco smoke, accumulates in pulmonary fluids leading to higher levels in other organs. This, as some research suggest, contributes to pulmonary as well as neurological sequel observed in cannabis and tobacco smokers [1,6].

Allergic/Immunologic and Pulmonary Considerations

Inhalation of cannabis induces a risk of addiction which can lead to frequent and persistent smoking [1]. Regular or heavy cannabis smoking can lead to generalized airway inflammation that includes respiratory epithelial cell damage and alveolar macrophage injury involving nitric oxide as well as cytokine impairment. Inflammation-induced airway dysfunction and pulmonary infections can result from such cannabis-induced changes [7, 8]. Effects on the pulmonary system are summarized

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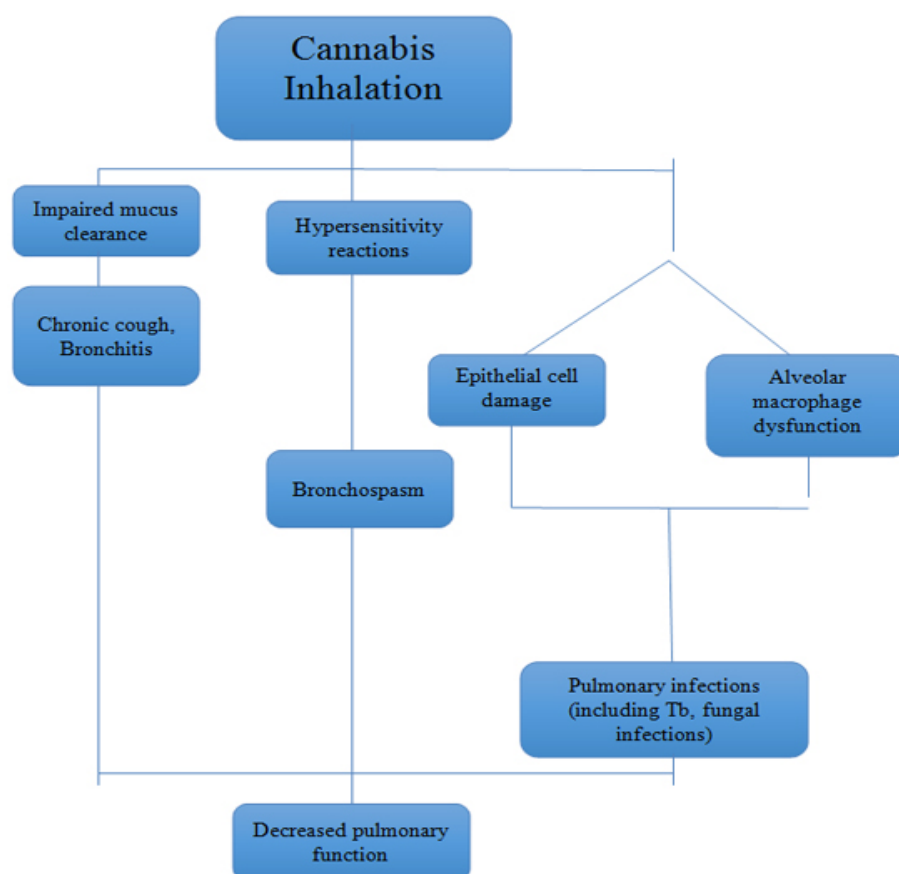
in Figure 1. Some persons can be allergic to certain components of the cannabis plant and immediate-type hypersensitivity can be identified with cannabis skin tests and specific IgE levels. Allergic cross-reactivity exists with tomato, banana, apple, cherry and nuts, which is known as Cannabis-Fruit/Vegetable syndrome. Cannabis also cross reacts with tobacco and some plant derived alcoholic beverages [9-15]. Hempseed ingestion has a potential to induce anaphylaxis in humans [16]. Allergic reactions can be triggered by active or passive exposure to cannabis. Pulmonary inflammatory response to various cannabis exposures, ranging from smoking to chronic hemp dust exposure in hemp workers, manifests with chronic respiratory symptoms and decline in lung function [17-20].

Pulmonary Infection

Pulmonary infections can occur in part due to cannabis-alteration of fungicidal and antibacterial activity of alveolar macrophages [8,21].

An increased risk for pulmonary tuberculosis is seen in those using a shared marijuana water pipe and tuberculosis outbreaks have been seen with hot-boxing (closed car cannabis smoking with peers) [22-24].

Smoking cannabis contaminated with fungal spores can result in pulmonary fungal infections such as pulmonary aspergillosis from the inhaled molds [25-27].



Increased risk for pulmonary disorders has been well described in cannabis smokers (Table 1).

Table 1. Pulmonary Health Effects by Cannabis Inhalation

Chronic pulmonary inflammation, cough and bronchitis
Increased pulmonary infections
Decreased pulmonary function
Allergic reactions and anaphylaxis
Pneumoconiosis
Alveolar hemorrhage
Potential for lung cancer

Cough, Bronchitis, and More

Cannabis smokers have increased risk for respiratory disorders that includes chronic cough, bronchitis and decline in lung function [1,2,17,28-37]. Magnitude of risk is related to the levels and chronicity of exposures. In one study of 5,115 adult males who smoked cannabis, those with lower level of exposure did not have decreased pulmonary function, but higher levels of exposure were associated with decreased lung function [38]. Chronic bronchitis characteristic of chronic cannabis users can improve with cessation of pot smoking [39]. Pulmonary damage can occur with cannabis smoking that may be complicated by tobacco smoking [1]. One cannabis joint is equated to 2.5-5 cigarettes in terms of potential lung injury [21]. This chronic use can have adverse effects on respiratory tissue including bronchodilation, hyperinflation, airway obstruction, chronic cough, and bronchitis (acute or chronic) [8, 22- 24,40,41].

Other potential complications in adults, especially for those whose cannabis smoking is complicated by tobacco smoking, include bullous emphysema (chronic obstructive lung disease), pneumo thorax, pneumo-mediastinum and pulmonary dysplasia [1,40,41]. Hemoptysis may occur if the smoked cannabis is made with silicon dioxide micro-particles [42].

The granulomatous lung inflammation called talcosis can occur if the smoked cannabis contains sufficient amounts of talcum dust; this is an unusual form of pneumoconiosis [43]. Dust disease has been well-known in hemp workers for decades [18-20].

Death by Cannabis

Death in a 19-year old male from fatal alveolar hemorrhage has been seen after he smoked cannabis using a homemade water pipe ("bang"); the underlying mortal blow was probably acid anhydrides that were released after incomplete burning of the pot that was in contact with homemade plastic material [44]. Death may also occur in immune-compromised persons who smoke cannabis contaminated with fungal spores [25-27]. Smoking synthetic cannabis can lead to death from respiratory depression [1,45].

Cannabis and Cancer

Anecdotal reports of upper and lower respiratory airway cancers are found in the literature; these include a small cell lung cancer in a 22-yr old who smoked one cannabis joint three times a week for three years and a 26-year old male with small cell lung cancer who had "considerable" cannabis exposure [23, 46-48]. Studies of cannabis smokers are complicated by a history of co-smoking tobacco, thus assessment of the risk of cancer is difficult and research results are controversial, with some studies suggesting higher and some studies suggesting lower risk in comparison to data in tobacco users [49-51].

A study in Sweden looked at 49,321 males aged 18 to 20 years in 1969/1970 and followed them through 2009; Cox regression analyses with an *n* of 44,284 concluded that those with heavy cannabis use (as defined as over 50 times lifetime use of cannabis) had a twofold risk for developing lung cancer over this 40-year period in contrast to those with a risk from tobacco and alcohol use [52]. Additional research also suggests a twofold risk of developing lung cancer for regular or heavy adult cannabis smokers [5].

Conclusions

The risk is compounded by often co-existent tobacco smoking that also leads to production of sputum, large airway inflammation, increased airway resistance, and hyperinflation. Chronic use from adolescence into adulthood has many adverse effects on the brain, lungs, heart, and other structures; thus, teenagers are advised to neither smoke cannabis nor tobacco.

Cannabis smokers who do not stop should smoke as infrequently as possible and avoid tobacco use. Unfortunately, the addictive properties experienced by many cannabis smokers and the concomitant use of addicting tobacco results in the potentially chronic and heavy use of both substances over many years. Such use can lead to considerable respiratory adverse effects as well as damage of other human organs.

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