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CHEST

# Marijuana and Lung Disease

Q26 Q1 *Donald P. Tashkin, MD*

As marijuana smoking prevalence increases in the United States, concern regarding its potential risks to lung health has also risen, given the general similarity in the smoke contents between marijuana and tobacco. Most studies have found a significant association between marijuana smoking and chronic bronchitis symptoms after adjustment for tobacco. Although reports are mixed regarding associations between marijuana smoking and lung function, none have shown a relationship to decrements in $FEV_1$ and few have found a relationship to a decreased ratio of $FEV_1$/FVC, possibly related to an association between marijuana and an increased FVC. A few studies have found a modest reduction in specific airway conductance in relation to marijuana, probably reflecting endoscopic evidence of bronchial mucosal edema among habitual marijuana smokers. Diffusing capacity in marijuana smokers has been normal, and two studies of thoracic high-resolution CT scan have not shown any association of marijuana smoking with emphysema. Although bronchial biopsies from habitual marijuana smokers have shown precancerous histopathologic changes, a large cohort study and a pooled analysis of six well-designed case-control studies have not found evidence of a link between marijuana smoking and lung cancer. The immunosuppressive effects of delta-9 tetrahydrocannabinol raise the possibility of an increased risk of pneumonia, but further studies are needed to evaluate this potential risk. Several cases series have demonstrated pneumothoraces/pneumomediastinum and bullous lung disease in marijuana smokers, but these associations require epidemiologic studies for firmer evidence of possible causality. CHEST 2018; ■(■):■-■

**KEY WORDS:** chronic bronchitis; lung cancer; lung function; marijuana; smoking; tobacco Q5

Marijuana is the second most commonly smoked substance in our society after tobacco. According to US national surveys, after an initial decline in marijuana use from 1990 through 2005 among adults ≥ 18 years of age, its use prevalence increased markedly over the following 10 years.[1] This surge in use was most notable among those 40 to 59 years of age, and by 2014 to 2015, 12.9% of all adults reported using marijuana within the last year. More potentially concerning has been the increase in daily or near-daily use from 5.1% to 7.6% over roughly the same time interval among individuals ≥ 12 years of age.[2] This rise in use prevalence has been accompanied by changing perceptions regarding the risks and benefits of marijuana use that are likely related to the legalization of marijuana for medicinal use by 29 states in the United States and for recreational use in seven states as of 2017.

The smoke of marijuana contains many of the same volatile and particulate

**ABBREVIATIONS:** AM = alveolar macrophage; ROS = reactive oxygen species; THC = delta-9 tetrahydrocannabinol

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components found in tobacco smoke, including a variety of chemicals (phenols, aldehydes, acrolein, etc) that are injurious to lung tissue, and carcinogens, including benzpyrene and benzanthracene.[3,4] The major exceptions are nicotine, found only in tobacco, and delta-9 tetrahydrocannabinol (THC), the major psychoactive ingredient, and a number of THC-like compounds, namely cannabinoids, in marijuana. In view of the similarity in the smoke contents of marijuana and tobacco, the increasing use of marijuana in our society, particularly on a daily or near-daily basis, raises concern regarding a potential link between marijuana smoking and the well-known deleterious effects of regular tobacco smoking on the lung, particularly regarding increased risks for developing COPD and lung cancer. Complicating this public health issue is the observation that most marijuana smokers also smoke tobacco, requiring methods of analysis that control for concomitant tobacco use and examine possible interactive effects and/or restricting the analysis to a comparison of marijuana smokers alone vs nonsmokers of any substance. The aim of this article is to review the evidence mainly from the limited number of publications largely based on observational cohort studies that have systematically addressed these concerns. In addition, findings from case series and other observational studies pertaining to a possible link between marijuana and other forms of lung disease, including pneumothorax/pneumomediastinum, bullous lung disease, and pneumonia risk, will also be reviewed. Although increasing numbers of users of marijuana are adopting other modes of use than smoking (eg, vaping, ingestion of edibles), little information concerning the impact of these alternative modes of use on lung health is available. Therefore, the focus of this review will be confined to smoked marijuana.

## Marijuana and Symptoms of Chronic Bronchitis

Ten cross-sectional or prospective cohort studies have examined the association between marijuana use and chronic respiratory symptoms (mainly cough, sputum, wheeze, and/or dyspnea) after adjusting for tobacco or comparing the marijuana-only users with nonsmokers.[5-14] The findings are shown in Table 1. Despite the heterogeneity of the populations studied regarding age, amount of marijuana smoked, the presence of concomitant tobacco smoking (controlled for in the analysis), and geographic location, the results reveal general, albeit incomplete, agreement regarding a significant association of marijuana use with symptoms of chronic bronchitis (cough, sputum, and wheeze). The notable exceptions were the studies of Tan et al[11] and Morris et al,[14] which included older subjects who may not have smoked as much marijuana as their younger counterparts. In addition, Tan et al[11] appeared to find an interaction between marijuana and tobacco such that the smokers of both substances were more likely to have chronic respiratory symptoms than the smokers of either substance alone. On the other hand, a similar interaction was not reported by other investigators. In addition, one study showed an increased incidence of acute bronchitic episodes over the previous 3 years in habitual marijuana smokers compared with nonsmokers.[6] Somewhat consistent with the latter findings, a large prospective cohort study in Northern California found that a subgroup of 452 frequent marijuana smokers who reported never smoking tobacco had a significantly increased risk of outpatient visits for respiratory illnesses than 450 nonsmoking control subjects.[15] As part of another cohort study in upstate New York, investigators interviewed 749 participants at 14, 16, 22, and 27 years of age and found a significant association of marijuana use with self-reported respiratory problems (not specifically defined) occurring by their late twenties. However, the analysis was not adjusted for concomitant tobacco use.[16] Two longitudinal studies have shown at least partial resolution of chronic respiratory symptoms in marijuana smokers who quit smoking marijuana.[13,17] In one of these studies, resolution of symptoms occurred only in those former marijuana smokers who did not also smoke tobacco.[17]

Bronchoscopic studies performed in habitual smokers of marijuana alone (n = 40), tobacco alone (n = 31), marijuana plus tobacco (n = 44), and never smokers (n = 53) provide a clue as to the possible underlying mechanism for the association of marijuana use with chronic bronchitic symptoms.[18] Bronchial mucosal biopsies revealed widespread histopathologic changes in the bronchial mucosa in marijuana smokers alone that were comparable with those in the tobacco-only smokers, consisting of destruction of the ciliated columnar bronchial epithelial cells and their replacement by mucus-secreting surface epithelial (goblet) cells or reserve cells (Fig 1).[18] An increase in mucus secretion in the face of an impairment in the mucociliary escalator could contribute to cough as an alternative mechanism to cleanse the

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