

# Does Smoking Marijuana Contribute to the Risk of Developing Lung Cancer?

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Lung cancer has emerged as the most common cause of cancer-related death in men and women in the United States (Edmondson, 2008; Swaney, 2002). Marijuana, a product of the *Cannabis sativa* plant, is the most frequently used illegal substance in the United States (Mehra, Moore, Crothers, Tetrauld, & Fiellin, 2006). The question explored here is whether evidence links marijuana use to lung cancer development.

Tobacco use was known to Native Americans, but the first recorded harvest of a tobacco crop in North America was in 1611 in the Jamestown colony (Cruz et al., 1998). Marijuana has a world history that dates back to 4000 BC, when it was grown in China for the hemp fibers. Oral traditions from China list medical uses for marijuana as far back as 2700 BC (Zuardi, 2005). Marijuana use in the United States dates to the early 1900s, when it was used as a cure for morphine addiction (Cruz et al., 1998). Marijuana primarily is obtained from the leaves and flower heads of the female *Cannabis sativa* plant. The active ingredient is delta-9 tetrahydrocannabinol (THC), with the highest content found in the flower heads and decreasing in concentration from the stems down to the seeds (Campbell, 1999; Hall & Solowij, 1998).

## Biologic Damage

Tashkin (2001) cited studies showing a relationship between smoking marijuana and potentially serious damage to the epithelium of the central airway, present in the absence of clinical or physiologic evidence of lung disease. Immunohistopathologic studies from the University of California, Los Angeles, showed

overexpression in marijuana users of Ki-67 (a cell proliferation marker), epidermal growth factor receptor, and *p53* (a suppressor gene that becomes altered in cancer states), suggesting a biologic basis for increased risk of lung cancer. Tashkin also reported that different concentrations of THC stimulate formation of reactive oxygen species in cells that are exposed to smoke from the distal end of the “joint,” indicating that cell damage is caused by toxic gas in the smoke. THC exposure also may cause changes in alveolar macrophages that are crucial to the lung’s immune defense system. The damage may be caused by impairment of proinflammatory cytokines, interferon- $\gamma$ , and granulocyte macrophage-colony-stimulating factor production. Tashkin proposed that marijuana and tobacco together appear to produce an additive effect on bronchial epithelial histopathology and concluded that regular marijuana use could potentially predispose an individual to pulmonary infection and respiratory cancer.

Mehra et al. (2006) also discussed a THC-induced cellular proliferation in a murine-based (mouse) model, suggesting that tumor growth is caused by inhibition of antitumor immunity from a cannabinoid-2 receptor-mediated pathway. A literature review conducted by Mehra et

al. included two case control studies of marijuana users who did not smoke tobacco. The control studies demonstrated more metaplastic cells, macrophages, pigmented macrophages, and columnar cell presence in marijuana smokers who did not smoke tobacco. The two studies also demonstrated that alveolar macrophages from marijuana smokers alone, or in combination with tobacco use, were more

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likely to show DNA damage, although these alveolar changes were not statistically significant. Another study reviewed by Mehra et al. showed decreased levels of glutathione and a dose-dependent THC content and reactive oxygen species generation. Mehra et al. concluded that alveolar macrophages exposed to marijuana smoke were less tumoricidal and had an increased likelihood of damaging DNA; therefore, marijuana smokers are more likely to have basal, goblet, and squamous cell hyperplasia; stratification; cell disorganization; nuclear variation; increased nuclear cytoplasmic ratio; basement membrane thickening; squamous cell metaplasia; mitotic figures; abnormal expression of Ki-67; and increased epidermal growth factor receptor compared

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