

















A SMOKING GUN?

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THE IMPACT OF CANNABIS SMOKING ON RESPIRATORY HEALTH

INTRODUCTION

Cannabis is the most widely consumed illegal drug in the UK. Recent media coverage has focused on the public and political debate around issues such as reclassification of cannabis and how the police should deal with those who sell or are found to be in possession of varying amounts of the substance.

What has been consistently missing from the public debate on the safety or otherwise of cannabis as compared to other illegal drugs is the impact of smoking cannabis on respiratory health and the possible link with nicotine addiction in the form of tobacco smoking.

This report sets out to identify existing scientific and medical research on cannabis smoking and respiratory health. It identifies what conclusions it is possible to draw from the existing evidence and highlights gaps in our knowledge which require further research.

The aim of this report is to ensure that those taking part in the debate on cannabis and those engaged in promoting health education to our young people have the fullest possible information on the medical and scientific evidence of the impact of cannabis smoking on respiratory health.

Many young people will make decisions about whether they wish to use cannabis or not – regardless of its legal status. We have a duty to ensure that they do so with full knowledge of the risks associated with smoking cannabis.



Cannabis sativa leaf

Image by LPX, © 2002 Erowid.org



SUMMARY OF FINDINGS AND RECOMMENDATIONS

Whilst there is a wealth of research into the health impact of tobacco smoking, there is relatively little on the effects of cannabis smoking.

Research investigating whether the inhalation of cannabis smoke causes damage to the lungs and airways focuses on whether this effect is independent of the effects of tobacco smoke or not. In general, the studies indicate that there is an increased negative health impact on those who smoke cannabis compared to those who do not smoke at all. When cannabis is smoked together with tobacco then the effects are additive. However, what is not clear is whether it is the addition of the cannabis or the tobacco which is more harmful or whether this is the result of the combined effects of equally harmful substances.

Some key findings emerge from the research:

- Studies comparing the clinical effects of habitual cannabis smokers versus non-smokers demonstrate a significantly higher prevalence of chronic and acute respiratory symptoms such as chronic cough and sputum production, wheeze and acute bronchitis episodes.
- 3-4 cannabis cigarettes a day are associated with the same evidence of acute and chronic bronchitis and the same degree of damage to the bronchial mucus membrane as 20 or more tobacco cigarettes a day.
- The cannabis smoked today is much more potent than that smoked in the 1960s. The average cannabis cigarette smoked in the 1960s contained about 10mg of tetrahydrocannabinol (THC), the ingredient which accounts for the psychoactive properties of cannabis, compared to 150mg of THC today. This means that longitudinal studies carried out in the 1960s and 1970s may not be indicative of the effects of cannabis cigarettes smoked today.
- Cannabis tends to be smoked in a way which increases the puff volume by two-thirds and depth of inhalation by one-third. There is an average fourfold longer breath-holding time with cannabis than with tobacco. This means that there is a greater respiratory burden of carbon monoxide and smoke particulates such as tar than when smoking a similar quantity of tobacco.
- Cannabis smoking is likely to weaken the immune system. Infections of the lung are due to a combination of smoking-related damage to the cells lining the bronchial passage (the fine hair-like projection on these cells filter out inhaled microorganisms) and impairment of the principal immune cells in the small air sacs caused by cannabis.
- The evidence concerning a possible link between cannabis smoking and Chronic Obstructive Pulmonary Disease (COPD) has not yet been conclusively established. A number of studies indicate a causal relationship between the two whereas others contradict these findings.
- Research linking cannabis smoking to the development of respiratory cancer exists although there have also been conflicting findings. Not only does the tar in a cannabis cigarette contain many of the same known carcinogens as tobacco smoke but the concentrations of these are up to 50% higher in the smoke of a cannabis cigarette. It also deposits four times as much tar on the respiratory tract as an unfiltered cigarette of the same weight. Smokers of cannabis and tobacco have shown a greater increase in cellular abnormalities indicating a cumulative effect of smoking both.
- The THC in cannabis has been shown to have a short-term bronchodilator effect. This has led to suggestions that THC may have therapeutic benefits in asthma. However, the noxious gases, chronic airway irritation or malignancy after long term use associated with smoking would seem likely to negate these benefits.

RECOMMENDATIONS

From a clinical perspective the main effects of smoking cannabis on the lungs are increased risk of pulmonary infections and respiratory cancers. Benzpyrene, a known constituent of the tar of cannabis cigarettes has been shown to promote alterations in one of the most common tumour suppressor genes, p53, hence facilitating the development of respiratory cancer. Gene p53 is thought to play a role in 75% of all lung cancers.

The British Lung Foundation recommends a public health education campaign aimed at young people to ensure that they are fully aware of the increased risk of pulmonary infections and respiratory cancers associated with cannabis smoking.

The increased potency of the cannabis smoked today compared to the cannabis smoked 20-30 years ago suggests that earlier studies may underestimate the effects of cannabis smoking. In addition the lack of conclusive evidence concerning the link between cannabis smoking and Chronic Obstructive Pulmonary Disease (COPD) underlines the need for further research.

The British Lung Foundation recommends that further research is undertaken to take into account the increased potency of today's cannabis and to establish what link (if any) there is between COPD and cannabis smoking.

THE BRITISH LUNG FOUNDATION (BLF)

On average, one person in every family has a lung disease, like asthma, COPD, lung cancer or TB. The BLF helps them by:

- Providing information to the public on lung conditions and all aspects of lung health in clear, easily understandable language
- Supporting those living with a lung condition, their carers and families through the Breathe Easy Club, a nationwide network of local voluntary support groups and
- Finding solutions to lung disease by funding world-class medical research. Since its inception, the BLF has given £15.5 million to medical projects.

If you want to know more about the BLF, contact us via any of the details below. We rely entirely on voluntary support to fund out information leaflets, support groups and medical research.

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THE EFFECT OF CANNABIS SMOKING ON RESPIRATORY HEALTH

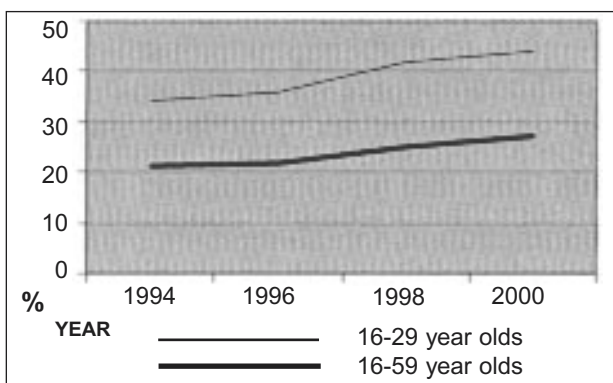
1. SCOPE OF THIS REPORT AND BACKGROUND

This report surveys the current medical and scientific research into the direct effects of smoking cannabis – both alone and in combination with tobacco – on the smoker's respiratory health. The report is divided into two parts. The first part outlines the constituents of cannabis, the amount of cannabis smoked and the dynamics of smoking cannabis compared with tobacco. The second part surveys the findings of the existing published research into the biological effects on respiratory health of cannabis which is smoked, both in the short-term and long-term. Full references to the individual publications are included at the end of the report.

Prevalence of cannabis smoking in UK

Cannabis is the most widely consumed illegal drug in the UK by gross weight (it is estimated that 486,224kg were consumed in 1998 – this is roughly the weight of 7,000 people put together)¹. It is often smoked together with tobacco although it can also be ingested in the form of 'hash cookies' or taken as cannabis oil.

Percentage of people in England and Wales to have 'ever' taken cannabis



Source: Annual Report on the UK Drug Situation 2001, Drug Scope, London

Constituents of cannabis

The smoke from the same quantity of cannabis and tobacco contains the same constituents and quantities of chemicals known to be toxic to respi-

ratory tissue as tobacco smoke, apart from nicotine^{2 3}. The smoke includes carbon monoxide, bronchial irritants, tumour initiators, tumour promoters and carcinogens⁴. Tar from cannabis cigarettes contains up to 50% higher concentrations of the carcinogens benzantracenes and benzpyrenes⁵ than tobacco smoke^{6 7 8}.

There are three main species of cannabis: *Cannabis sativa*, *Cannabis indica* and *Cannabis ruderalis*. The plant is also known as hemp. As a drug of abuse it is either taken in the form of herbal cannabis (marijuana), which consists of the plant's dried leaves and female flower heads, or as cannabis resin (hashish), which is the resin secreted by the leaves and flower heads and may be compressed into blocks.

Cannabis contains over 400 compounds including 60 different cannabinoids (plant derivatives unique to cannabis) the most abundant of which is tetrahydrocannabinol (THC). This accounts for the psychoactive properties of cannabis. It is highly soluble in fats and rapidly absorbed in the respiratory and gastrointestinal tract lining. The intoxicating effects depend on the way in which cannabis is taken – blood concentrations after oral ingestion are only about 25-30% of those obtained when cannabis is smoked⁹. About 50% of the THC in a cigarette of herbal cannabis is inhaled in mainstream smoke, nearly all of which is absorbed through the lungs, rapidly entering the bloodstream and reaching the brain within minutes.

A greater amount of tar is inhaled from the cannabis cigarette butt rather than its tip. There is also a higher concentration of carbon monoxide and THC in the smoke from the butt end. Carbon monoxide produces high concentrations of carboxyhaemoglobin in the blood¹⁰, which interferes with the transport of oxygen around the body. This is likely to be due to decreased filtration of insoluble particles and differential burn rates. The clinical implication of this is that smoking cannabis cigarettes down to the butt is more harmful than smoking a similar quantity of cannabis cigarettes to a longer butt length.

Other cannabinoids which interact with THC -

although are not actually psychoactive in themselves, are cannabidiol and cannabitol. The amounts and proportions of the various cannabinoids in each plant vary from strain to strain, and can be adjusted by breeding.



Cannabis is often smoked with tobacco
Image by sciencephoto.com

Amount of cannabis smoked

THC is present in varying concentrations in the stalks, leaves, flowers and seeds of the plant as well as the resin secreted by the female plant. This has an impact on the potency of different cannabis preparations. Furthermore, sophisticated cultivation has increased the potency of cannabis products over the last 20 years. Whereas the average cannabis cigarette of the 1960s and 1970s contained about 10mg of THC, today it may contain up to 150mg of THC, or 300mg if laced with hashish oil¹¹. This means that the modern cannabis smoker may be exposed to greater doses of THC than in the 1960s and 1970s^{12 13}, which in turn means that studies investigating the long-term effects of smoking cannabis have to be interpreted cautiously.

Cannabis and tobacco

Cannabis resin, the most commonly used form of cannabis in the United Kingdom, is often smoked mixed with tobacco. Although this can confound research on the respiratory effects of smoking pure cannabis, the well-documented consequences of smoking tobacco need therefore also to be considered in the evaluation of the effects of cannabis smoking on respiratory health.

It has been calculated that smoking 3-4 cannabis cigarettes a day is associated with the same evidence of acute and chronic bronchitis and the same degree of damage to the bronchial mucus membrane as 20 or more tobacco cigarettes a day^{14 15}.

Dynamics of smoking cannabis vs tobacco

Significant differences have been noted in the dynamics of smoking cannabis and tobacco including an approximately two-thirds larger puff volume, a one-third greater depth of inhalation and a fourfold longer breath-holding time with cannabis than with tobacco¹⁶. This means that there is a greater respiratory burden of carbon monoxide and smoke particles than when smoking a similar quantity of tobacco. Similarly with tar, it has been estimated that smoking a cannabis cigarette results in a fourfold greater amount of tar inhaled and retention in the respiratory tract or one-third more tar than smoking a tobacco cigarette¹⁷. This is due to the longer breath holding time for cannabis and differences in filtering characteristics of the two types of cigarette.



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2. EFFECTS OF SMOKING CANNABIS ON RESPIRATORY HEALTH

The British Medical Association estimates that smoking a cannabis cigarette containing only herbal cannabis leads to an approximately fivefold increase in blood carboxyhaemoglobin concentration (which is formed by carbon monoxide reacting with the oxygen carrying particle haemoglobin in red blood cells, thereby reducing the transport of oxygen)¹⁸.

Within minutes of smoking cannabis significant decreases in airway resistance and increases in specific airway conductance have been observed in healthy individuals, which persist for at least one hour¹⁹. This is caused by THC which has subsequently been investigated for its possible therapeutic use in diseases such as asthma (see below).

From a clinical perspective, the main effects of smoking cannabis on the lungs are pulmonary infections and respiratory cancer.

Immune responses

Several studies indicate that smoking cannabis has a negative effect on the immune system. THC has been shown to decrease the function of several white blood cells (T cells, natural killer cells and macrophages) that help protect the lungs against micro-organisms²⁰. Alveolar macrophages in particular are important in regulating lung immunity and their central location in the lung's air sacs means that they are exposed to very large amounts of cannabis smoke.

Twice as many alveolar macrophages as normal have been found to be produced in the lungs of cannabis smokers and three times as many in cannabis & tobacco smokers²¹. These macrophages have been found to be considerably larger and contain more ingested particles than is the case in non-smokers²². They are also functionally impaired in that they are less likely to kill tumour target cells²³ and a variety of common fungal organisms and bacteria such as *Candida*

*albicans*²⁴ and *Candida pseudotropicalis*²⁵ (can cause thrush), *Legionella pneumophila*²⁶ (can cause pneumonia) and *Staphylococcus aureus*²⁷ (can cause food poisoning). Macrophagal ability to produce a variety of chemicals that play a key role in the immune response to infection and malignancy has also shown to be impaired²⁸.

A decreased immune function may explain why there appears to be an association between cannabis use and opportunistic bacterial and fungal pneumonias in patients with cancer²⁹ and transplant^{30 31} patients as well as those with human immunodeficiency virus (HIV) infection³².

Inflammation

Visual inspection of the central airway of cannabis smokers has shown increased redness, swelling and mucus secretion by comparison to non-smokers³³. Smoking tobacco in conjunction with cannabis appears to have an additive effect^{34 35}. An increase in the number and size of small blood vessels and replacement of the normal ciliated surface lining cells (ie those with hair-like projections) by mucus-secreting cells have also been observed.



Cannabis tar contains up to 50% more carcinogens than tobacco smoke

Image by sciencephoto.com

This may explain why cannabis smokers tend to suffer from chronic cough and phlegm as there may not be sufficient ciliated cells to remove the mucus from the airways.

Chronic Obstructive Pulmonary Disease (COPD)

COPD is an umbrella term for conditions such as emphysema and chronic bronchitis. The evidence that COPD is mostly smoking-related is already well established. Currently more than 32,000 people die from COPD every year in the UK.

There is a lot of evidence that the long-term effects of habitual cannabis smoking include a significantly higher prevalence of chronic and acute respiratory symptoms such as chronic cough, chronic sputum production, wheeze and acute bronchitis episodes^{36 37 38 39} by comparison to non-smokers. There is evidence of a cumulative effect of smoking cannabis and tobacco in two studies^{40 41} although not in another⁴².

Some studies indicate that young cannabis smokers may be at risk of developing obstructive airway disease in later life^{43 44}. This is supported by animal studies in which dogs⁴⁵, monkeys⁴⁶ and rats^{47 48} have been exposed to varying doses of cannabis for 12-30 months and suffered damage to the smaller airway which is a major site of injury in tobacco-related COPD as well as acute and chronic pneumonia. However, other studies contradict a causal relationship between smoking cannabis and COPD^{49 50 51}. Regular cannabis smoking has been associated with emphysema in some studies^{52 53} but not so in others^{54 55}. These studies are, however, non-conclusive as they did not distinguish between smoking only cannabis and smoking cannabis together with tobacco. They also only involved a relatively small number of participants. A further study involving rats exposed to increasing doses of cannabis for six months did not display any evidence of emphysema although this was the case in rats exposed to tobacco smoke⁵⁶.

Further research in this area is necessary to provide more conclusive results.

Respiratory cancer

More people in the UK die of lung cancer than from any other cancer – more than 34,000 every year.

As already mentioned, the tar from a cannabis

cigarette contains many of the same (and even higher concentrations of) carcinogenic compounds found in cigarette smoke and deposits four times as much tar on the respiratory tract in comparison to an unfiltered cigarette of the same weight. This amplifies the exposure of cannabis smokers to particles that are known to be involved in the development of lung cancer.

There are several case studies (over 75) reporting cancers of the aero-digestive tract in young adults with a history of cannabis use^{57 58 59 60 61 62 63}. These are rare in adults under 60, although their exact cause is not clearly identifiable as many of the cases also used alcohol and tobacco. A retrospective study undertaken in the US⁶⁴ did not find a link between smoking cannabis and tobacco-related cancers but it has been suggested that the time span investigated may not have been enough to study long-term effects⁶⁵. There is clearly a need for more epidemiological research in this area.

As it is, the development of cancer is a multistep process comprised of sequential alterations in



More Britons die from lung cancer than from any other type of cancer

Image by Dr. Andrew Miller, Mayday Hospital, Croydon

genomic DNA (the genetic material contained in cells) which are promoted and/or interact with environmental and genetic factors. It is therefore often not clear what the exact cause of a particular cancer may be.

Research suggests that cannabis might contribute to cancer by manipulating the genetic makeup of cells. For lung cells to transform into cancerous cells, a specific combination of genes that regulate cell growth must be activated (in the case of onco-



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genes, which can produce tumours) and/or mutate (in the case of tumour suppressor genes). THC has been shown to increase the production of a chemical particle (CYP1A1) that is responsible for causing benzpyrene (a constituent of cannabis smoke) to promote alterations in one of the most common tumour suppressor genes, p53 thereby facilitating the development of respiratory cancer^{66 67}. The genetic information on this particular gene is translated into a chemical particle in 11% of individuals who smoke cannabis and tobacco⁶⁹. It is also thought that the gene plays a role in 75% of all lung cancers⁶⁸. Other studies looking at the effect of tar in cannabis smoke on animals^{70 71 72} also indicate a correlation between cannabis and respiratory cancer.

An increase in cellular abnormalities has also been observed in cannabis smokers by comparison to non-smokers^{73 74}. Abnormalities include an increase in the production of mucus-producing (goblet) and reserve cells, transformation of ciliated cells into cells that resemble skin (squamous metaplasia), an accumulation of inflammatory cells and abnormalities in the cell nuclei. Nuclear alterations and squamous metaplasia have been described as precursors to the development of lung cancer in tobacco smokers⁷⁵. In addition, smokers of cannabis and tobacco have shown a greater increase in cellular abnormalities indicating an additive effect.

Other lung conditions

There have been isolated reports of spontaneous pneumothorax (breaches of the lungs causing gas in the lung cavity leading to compression of the lungs) and pneumomediastinum (breaches of the lungs causing gas in the cavities of the respiratory tract) associated temporally with the use of cannabis^{76 77 78} and thought to be caused by deep inhalation of cannabis smoke to enhance absorption of THC and hence the intoxication caused by it⁷⁹. Deep inhalation coupled with direct pulmonary toxicity from components in cannabis in susceptible smokers has also been implicated with the formation of large lung bullae (watery blisters) in the upper respiratory area⁸⁰.

Contamination of cannabis

There has been a report of chronic cannabis smoking leading to necrotizing pulmonary granulomata (changes in the lungs at cellular level which may prevent the lungs from working properly)⁸¹ due to possible fungal contamination of cannabis.

Oral soft tissues

The effects of tobacco smoking on oral soft tissues have been well documented but there is little data available on the effects of cannabis smoking. However, there are some case reports that heavy cannabis use is associated with cancer of the tongue^{82 83} and larynx⁸⁴.

Health care utilization by cannabis smokers

This has been assessed in an epidemiological study in which cannabis smokers who had never smoked tobacco were compared with non-smokers⁸⁵. Frequent cannabis smokers showed a slight increase in outpatient visits for respiratory and other illnesses compared with non-smokers as well as a small increased risk of hospitalization.

Potential therapeutic benefits

The bronchodilator effects of THC in cannabis have also been found in the case of asthmatics with mild to moderate airway obstruction although not to the same extent as in healthy people⁸⁶. This has led to suggestions that THC might have therapeutic benefits in asthma. However, the noxious gases, chronic airway irritation or malignancy after long-term use associated with smoking would seem likely to negate these benefits over the long term. Oral intake of THC has also shown to cause unwanted side-effects such as central nervous system intoxication and an excessive increase in heart rate^{87 88}. Furthermore, tolerance to the bronchodilator effects of THC has been demonstrated after several weeks of use⁸⁹.

The study was funded through the UK Department of Health, Section 64 Grants (VOF 1138/05A). All views expressed are those of the authors and not necessarily of the Department of Health.

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- Study carried out in New Zealand. A cohort of 943 young adults (21 year olds) was studied using standardised symptom questionnaires and spirometry. 9.7% of the cohort were regular marijuana smokers. They reported more wheezing, exertional dyspnoea, nocturnal awakenings with chest tightness and morn-



ing sputum production than non-smokers (increases ranging from 61 – 144%). Prevalence of these symptoms was similar to that found in smokers of 1-10 cigarettes per day.

³⁷ Bloom, JW, Kaltenborn, WT, Paoletti, P, et al, 1987, Respiratory effects of non-tobacco cigarettes, *Br Med J* 295, 1516-1518

Study carried out in Arizona on 15-40 year olds. 54 marijuana only smokers, 56 marijuana and tobacco smokers, 20 tobacco only smokers and 502 non-smokers were investigated. Marijuana smokers reported significantly more sputum and wheeze than non-smokers. An additive effect of marijuana and tobacco on chronic respiratory symptoms was noted.

³⁸ Tashkin, DP, Coulson, AH, Clark, VA, et al, 1987, Respiratory symptoms and lung function in habitual, heavy smokers of marijuana alone, smokers of marijuana and tobacco, smokers of tobacco alone and non-smokers, *Am Rev Respir Dis* 135, 209-216

Study carried out in California. 144 daily marijuana only smokers were compared with 135 smokers of both marijuana and tobacco, 70 smokers of tobacco only and 97 non-smokers. Marijuana smokers had a significantly higher prevalence of chronic cough, chronic sputum production, wheeze and acute bronchitic episodes than non-smokers. No significant differences were found between the prevalence of symptoms of chronic and acute bronchitis between marijuana smokers and tobacco smokers. This was despite a marked disparity in the amount of each substance smoked per day: 3 joints of marijuana vs more than 20 cigarettes of tobacco. Similarly, no additive effects of marijuana and tobacco were noted.

³⁹ Gong, H, Fligel, S, Tashkin, DP, Barbers, RG, 1987, Tracheobronchial changes in habitual heavy smokers of marijuana with and without tobacco, *Am Rev Respir Dis* 136, 209-216

Flexible fibreoptic bronchoscopy was performed in 29 habitual, heavy marijuana smokers aged between 25 and 45 and control groups. The prevalence of respiratory symptoms and pulmonary function abnormalities was generally higher in smokers although no significant differences were found between smokers of marijuana only, tobacco only or both together. However, 91% of the smokers in all three groups revealed airway hyperemia and other visible abnormalities. All smokers had damaged cells in their bronchial epithelium. Squamous metaplasia was observed in all smokers of tobacco and marijuana, significantly different to smokers of tobacco or marijuana alone and non-smokers. A direct cumulative effect of marijuana and tobacco smoking was not established.

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