# Cannabinoid in E-Cigarettes, And Its Effect on Lung

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**Abstract**:

Cannabinoids are highly inducing chemical substance derived from Cannabis sativa plant. The two main types of cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), in which the former type (THC) is the most commonly used one. THC produces "strong" psychoactive effects to the consumer, which is described as making a person "high". Electronic cigarettes or e-cigarettes (e-cigs) are newly emerged pen-sized devices used to vapor nicotine e-liquids or cannabinoid e-liquids. The e-liquid or as named commercially e-juice  can contain: nicotine, tetrahydrocannabinol (THC) and cannabinoid (CBD) oils, and other substances, flavorings, and additives. Vaping is the process of heating the e-liquid to produce its vapor/aerosol which is inhaled by the consumer. "E-cigarette or Vaping Product Use-Associated Lung Injury (EVALI)" is the name given to the newly identified dangerous lung disease which is caused by vaping e-cigarettes contained THC. Cannabinoids cause also chronic bronchitis, emphysema, asthma, or chronic obstructive pulmonary disease (COPD).

An outbreak reported by Centers for Disease Control and Prevention (CDC) in the United States in Aug. 2019 and reached its peak in Sep. 2019. The patients have respiratory, gastrointestinal and constitutional symptoms. Most of patients suffer from shortness of breath and fever which quickly arose in many different states in the U.S. the researchers and physicians have noticed one linked factor between those cases which is: all patients have reported that they used e-cigarettes or vaping products. THC has been detected in most of the EVALI case samples tested by FDA. 15% of patients were under 18 years old and 37% of them were 18 to 24years old. 50% of EVALI patients who were reported to use THC-containing products, informed that 78% has acquired their products from informal sources only, as family, friends, online dealers or other unknown sources. There is no way to avoid EVALI disease except that you must consider refraining from use of all e-cigarette or vaping products. Avoid e-cigarettes and vaping products which contain tetrahydrocannabinol (THC), which is a high-inducing chemical substance. Ill prognosis of EVALI disease is due to lack of long-term data, patients have died from EVALI and because of the quick progression of the disease and its fatality within few days. Treatment of EVALI depends on providing broad-spectrum antibiotics in combination with steroids, in addition to regular testing of lung function and pulse oximetry.

## Introduction:

"Cannabinoids" is defined as any chemical substance that can attach to cannabinoid receptors of the body and brain and produce its effect, regardless to its chemical structure or origin and have the same effect or similar effect which is produced by Cannabis Sativa plant. The endo-cannabinoid system affects many important functions and responsible for regulating a number of activities, such as mood, memory, sleep and appetite. There are 3 main types of cannabinoids that people use which are: recreational, medicinal and synthetic. Researchers have found that cannabis plant can produce from 80 to 100 cannabinoids and about 300 non-cannabinoid chemicals. [1]

There are 2 main types of cannabinoids which are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), in which the former type (THC) is the most commonly used one. THC is a chemical substance which is responsible for the psychoactive effect of Cannabis plant. THC produces "strong" psychoactive effects to the consumer, which is described as making a person "high". In contrast, CBD is thought to have anti-psychoactive effects, which means that it controls or moderates the effects of THC as high-mood and anxiety. [1]

"E-cigarette or Vaping Product Use-Associated Lung Injury (EVALI)" is the name given by the centers for Disease Control and Prevention (CDC) to the newly identified dangerous lung disease which is caused by vaping. Vaping includes a device categorically called e-cigarette, but it may be named commonly as vape pens, mods or tanks. Its mechanism of action depends on heating up a small amount of the vaping liquid and turning it into an inhaled vapor. Most of vape liquids –which are also called commercially as e-juice or e-liquid- contain base substances as propylene glycol and glycerol, in order to create the vapor. "Nicotine" and "artificial flavors" are added to the base ingredient. Analysis of commercial vaping liquid samples have showed harmful "acetals" which is produced due to interaction between flavoring chemicals with the base ingredients. [3]

Electronic cigarettes or e-cigarettes (e-cigs) are newly emerged pen-sized devices used to vapor nicotine e-liquids or cannabinoid e-liquids. E-cigs have other commercial names as vapes, e-hooks, vape pens, tank systems, mods and ENDS (electronic nicotine delivery systems). It depends on heating complex ingredients to produce its active constituents and the feel the effect of nicotine or cannabinoids, according to the used e-liquid. Vaping is the process of heating the e-liquid to produce its vapor/aerosol which is inhaled by the consumer. Figure (1) shows the different shapes and types of e-cigarettes or vaping products, which is filled with THC-containing vaping liquids. [2][5]

*Figure (1): different shapes and types of e-cigarettes or vaping products. [1]*

## Statement of the problem

The problem of the study can be noticed in almost all ages and both sexes around the world. Vaping has become a dangerous phenomenon affecting children, youth and adults of both sexes. The prevalence of EVALI disease is strongly related to THC-containing vaping liquids. We have to advise the users of e-cigarettes about its dangers and focus on the point that it is not less dangerous than the regular cigarettes as thought by most of the consumers, and they are not avoiding the diseases caused by regular cigarettes.

## Objectives

This research aims to focus on the following points:

1. Definition and composition of cannabinoids.
2. Discuss the effect of THC on lung.
3. Define EVALI disease and its symptoms.
4. Discuss the EVALI outbreak in Aug. 2019.
5. Recommendations of FDA and CDC.

## Research Questions

The researcher is concerned to answer the following questions:

1. What are cannabinoids and its sources?
2. What is the mechanism of action of e-cigarettes and vaping products?

3. What does EVALI mean?

4. What are the symptoms of EVALI?

5. What are FDA recommendations about vaping products?

6. How can the person avoid being infected with EVALI?

## Discussion

Tetrahydrocannabinol (THC) and cannabidiol (CBD) are found to be the direct cause of EVALI disease, due to its presence in many documented cases as a linked factor between patients. Using of cannabinoid derivatives in vaping liquids are found to be linked to other lung diseases, as chronic bronchitis, emphysema, asthma, or chronic obstructive pulmonary disease (COPD). General effects of heavy regular using of THC-containing vaping products range from short-term problems as attention, memory and learning problems, to long-term problems as psychosis, anxiety, suicidal attempts, depression, and substance use disorder. The following table shows the different commercial products of cannabinoids used in vaping products and its ambient heating temperatures. [2][3]

| Compound | Temp. | Information |
|---|---|---|
| THC | 155°C / 311°F | This is thought to be the best temperature for vaping THC, which induces senses of euphoria and relaxation. |
| CBD | 165°C / 329°F | CBD, famous for its medical benefits, is able to counter side effects of THC, such as anxiety. |
| Delta-8-THC | 175°C / 347°F | This cannabinoid is very similar to THC, but it is more stable and less psychoactive. |
| CBN | 185°C / 365°F | CBN is believed to break down THC and have a calming effect. |
| CBE | 195°C / 383°F | This temperature is intented to show the maximum medical temperature. |
| Benzene | 205°C / 401°F | Benzene is a carcinogen. Warning: Harmful toxins are released as from this temperature. |
| THCV | <220°C / 428°F | THCV has been shown to moderate the psychoactive effects of THC, but more research is required. |
| CBC | 220°C / 428°F | This cannabinoid has anti-inflammatory and anti-fungal properties. |

*Table (1): Vaping temperatures of cannabinoids.*

In general, researchers were concerned in the last two decades about studying cannabinoids and endo-cannabinoid system since discovering of the cannabinoid receptors (CB1 and CB2) in many areas of the human body in 1980s. Studying the cannabinoid system is about explaining the impact of cannabinoids on the lungs and how it effects on lung functions regulation. Histological examination of lung tissues of patients who were died suddenly from marijuana (Cannabis) smoking, the researchers found macrophage infiltration in the lung with presence of fibrosis with lymphocytes. Marijuana smoking -or its derivatives as THC or CBD- is known to induce effects on lung functions which are not found in tobacco smoking. The adverse effects include lung damage, in addition to cellular damages in cells exposed to marijuana smoke or cannabinoids. [4]

Histopathological picture of EVALI disease shows hyperemia in the bronchial airways, hyperplasia of goblet and basal cells, and cellular disorganization is found in over 50% of cannabinoid smokers. Epithelial hyperplasia is the most common finding. Also, pathologists have found greater incidence and severity of bronchiolitis, alveolar cell hyperplasia with atypia and fibrosis in cannabinoids smokers. Most of patients have acute to sub-acute clinical picture with bilateral pulmonary opacities. Histopathological picture of acute lung injury caused by vaping include acute fibrinous pneumonitis, diffuse alveolar damage or organizing pneumonia and associated with bronchiolitis (see figure 2). All pictures in figure (2) show foamy macrophages and pneumocyte vacuolization. Neutrophils are predominant character in EVALI cases as neutrophils are the first line of immunity defense in case of pathogens, inflammation and strange aerosols. Recent researches suspect presence of exogenous lipoid pneumonia in consumption of THC-containing products, but none of our pictures have lipoid pneumonia. [4][6]
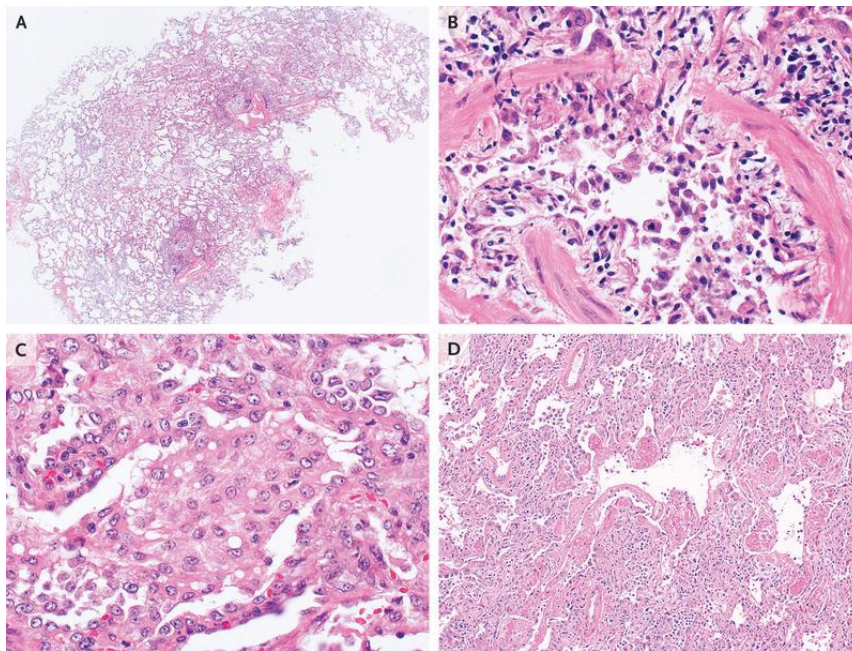
*Figure (2): Histopathological picture of EVALI. [6]*

EVALI outbreak:

An outbreak reported by Centers for Disease Control and Prevention (CDC) in the United States in Aug. 2019 and reached its peak in Sep. 2019. The patients showed symptoms of lung injury, some of them reported their clinical signs within few days and the others have developed the signs over several weeks. The symptoms do not appear as lung infection. The clinical signs include the following: [2][3]

1- Respiratory signs: including cough, shortness of breath, or chest pain.
2- Gastrointestinal signs: including nausea, vomiting, stomach pain, or diarrhea.
3- Tachycardia: include rapid heartbeats.
4- Non-specific constitutional signs: as fever, chills, or weight loss.
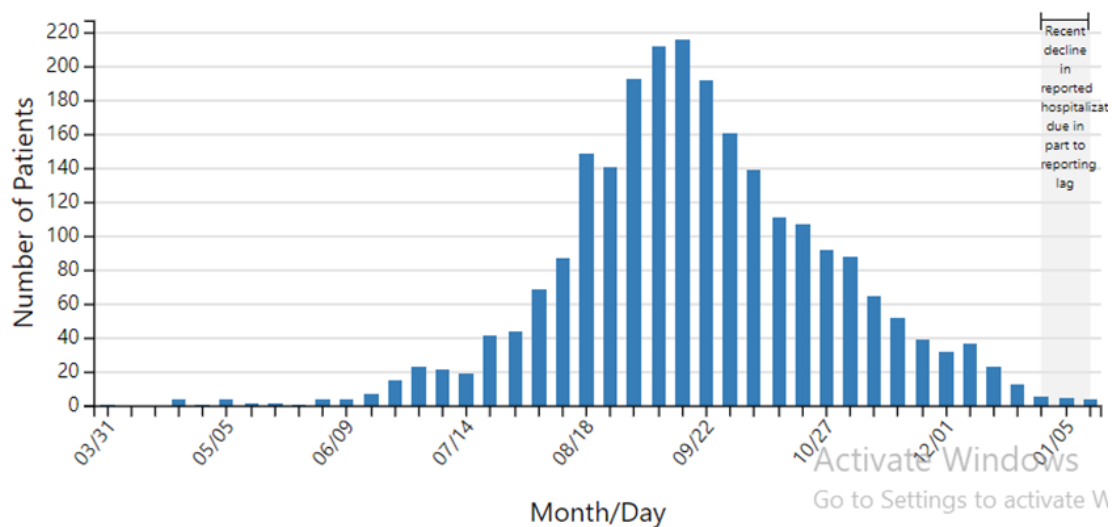
*Figure (3): Dates of symptom onset and hospital admission for patients with EVALI in the U.S in the period of 31 Mar. 2019 till 18 Jan. 2020. [2]*

The disease is firstly identified by the CDC in Aug. 2019 when the health department officials were working across the country for studying cases of severe or fatal lung infections that have occurred suddenly to healthy persons. Most of patients suffer from shortness of breath and fever which quickly arose in many different states in the U.S. the researchers and physicians have noticed one linked factor between those cases which is: all patients have reported that they used e-cigarettes or vaping products. THC has been detected in most of the EVALI case samples tested by FDA. [3]

The latest data gathered from CDC (as of January 14, 2020) that the median age of patients was 24 years old. 15% of patients were under 18 years old and 37% of them were 18 to 24years old. 82% reported using THC-containing products, while 33% reported exclusive use of THC-containing products. 66% were male consumers. 50% of EVALI patients who were reported to use THC-containing products, informed that 78% has acquired their products from informal sources only, as family, friends, online dealers or other unknown sources. Examination of bronchoalveolar lavage (BAL) fluid samples showed presence of THC substance, also the same substance is found in the autopsy tissue specimens of EVALI patients. 94% of EVALI patients aged 13–17 years acquired THC-containing products only from informal sources. [2]

Vitamin E acetate is strongly linked to the EVALI outbreak. The FDA researchers have found vitamin E acetate in the product samples, while state laboratories found vitamin E acetate in patient lung fluid samples. Examination of lung fluid samples of individuals not having EVALI do not show presence of vitamin E acetate in these samples. Even it was thought that "vitamin E acetate" appears to be involved in this vaping-related disease, but the investigations showed that there is no single ingredient responsible for causing EVALI and cannabinoid derivatives are strongly involved in causing EVALI cases. Normally, vitamin E acetate is taken orally in form of vitamin supplement or applied locally on skin, but it is found that it may interfere with normal lung functions if it inhaled. [2][3]

It is unclear till now how could those cases developed or why, even how the case could be life threatening in this short time which can cause the lungs to stop functioning altogether. EVALI cases investigation have showed that most of the patients have used vaping liquids containing additional substances as THC, cannabinoid (CBD) oil, and vitamin E oil (vitamin E acetate). A CDC investigator said that THC containing products particularly which are obtained off the street or from other informal sources as friends, family members, in-person or illicit dealers played a major role in the outbreak. [3]

The total number of hospitalized EVALI cases reached 2,711 cases in Jan 21, 2020. The number is reported by CDC from all 50 states of U.S, with number of deaths reached to 60 deaths. After Sep. 2019 there is gradual decline but the problem is still persistent. The reasons behind this decline are thought to be as follows:

- Increased public awareness of the risk associated with using THC-containing e-cigarette, or vaping product, as a result of the rapid public health response.
- Removal of vitamin E acetate from some products.
- Law-enforcement actions related to some illicit or online products.

## Conclusion

Ill prognosis of EVALI disease is due to lack of long-term data, patients have died from EVALI and because of the quick progression of the disease and its fatality within few days.

Treatment of EVALI depends on providing broad-spectrum antibiotics in combination with steroids, in addition to regular testing of lung function and pulse oximetry (which is estimation of blood oxygen level), and continue examining of lung function tests for 1 to 2 weeks after the patient is discharged from hospital to ensure complete recovery and avoid its recurrence. CDC and FDA recommend people not to use THC-containing e-cigarette and vaping products particularly from informal sources like friends, family, or online dealers. Any person who is using e-cigs or vaping products recently and have any symptom of EVALI disease that was mentioned before must go directly to his/her physician or healthcare provider in order to have the correct and accurate diagnosis, and take the right treatment for the case.

## Recommendations

THC use is associated with wide range of health negative effects, especially in prolonged frequent use. The best way to avoid potentially harmful effects is to avoid or take-off any THC-containing e-cigarette or vaping products. CDC and FDA officials recommend everyone to: [2][3]

1- Avoid e-cigarettes and vaping products which contain tetrahydrocannabinol (THC), which is a high-inducing chemical substance derived from Cannabis Sativa plant (marijuana).

2- Avoid mixing additional substances to vaping liquids or gels, because when heating these ingredients together it will produce extremely dangerous end products.

3- Avoid using products obtained off the streets.

4- Youth and pregnant women should NEVER use all types of e-cigarettes and vaping products.

5- FDA advised that adults who are using nicotine-containing e-cigarettes or vaping products should NOT return to smoking, and they must contact their healthcare provider if they had done.

6- Youth or adults who never used to smoking (tobacco products) should NOT start using e-cigarettes or vaping products.

7- In general, there is no way to avoid EVALI disease except that you must consider refraining from use of all e-cigarette or vaping products.

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