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Kelsey Noble

*Clarkson Family Medicine*

Julia Griffin

*Creighton University*

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## Early Onset Bullous Emphysema Associated with Polysubstance Use

### Abstract

The burden of COPD in the United States is tremendous. This disease is not only among the leading causes of mortality annually, but also takes a heavy financial toll.<sup>1</sup> Bullous emphysema is a severe variant of COPD. The primary identified risk factor for bullous emphysema is tobacco use; however, the impact of other substances is not clearly delineated.<sup>2</sup> This case presents a patient diagnosed with severe bullous emphysema at age 33 with substantial disease progression over the course of 12 years associated with much scarcer tobacco use than would be expected but a prominent history of methamphetamine and marijuana use.

Marijuana and amphetamine-type stimulants are the most widely used illicit substances in the world, and prevalence of both are increasing in the United States. In 2020, an estimated 14.2 million Americans had a marijuana use disorder and 1.5 million had a methamphetamine use disorder.<sup>3-7</sup> A better understanding of how these substances may contribute to development and progression of chronic lung disease, both individually and perhaps synergistically, is necessary to guide discussions with patients and inform effective public health efforts.

### Keywords

COPD, Bullous Emphysema, Methamphetamine, Marijuana, Tobacco

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# Early Onset Bullous Emphysema Associated with Polysubstance Use

Kelsey Noble<sup>1</sup>, Julia Griffin<sup>2</sup>

<sup>1</sup>Clarkson Family Medicine, Nebraska Medicine, Omaha, NE

<sup>2</sup>Creighton University, Omaha, NE

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## Abstract

The burden of COPD in the United States is tremendous. This disease is not only among the leading causes of mortality annually, but also takes a heavy financial toll.<sup>1</sup> Bullous emphysema is a severe variant of COPD. The primary identified risk factor for bullous emphysema is tobacco use; however, the impact of other substances is not clearly delineated.<sup>2</sup> This case presents a patient diagnosed with severe bullous emphysema at age 33 with substantial disease progression over the course of 12 years associated with much scarcer tobacco use than would be expected but a prominent history of methamphetamine and marijuana use.

Marijuana and amphetamine-type stimulants are the most widely used illicit substances in the world, and prevalence of both are increasing in the United States. In 2020, an estimated 14.2 million Americans had a marijuana use disorder and 1.5 million had a methamphetamine use disorder.<sup>3-7</sup> A better understanding of how these substances may contribute to development and progression of chronic lung disease, both individually and perhaps synergistically, is necessary to guide discussions with patients and inform effective public health efforts.

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## Introduction

Bullous emphysema is a subset of COPD associated with particularly high mortality. Primary risk factors have long been considered tobacco use and, particularly in early onset disease, alpha-1 antitrypsin deficiency. Numerous case studies have suggested a link between marijuana use, crack cocaine use, IV drug use and development of COPD but these are still considered less important causes.<sup>2</sup> In the case presented herein, our patient smoked both marijuana and methamphetamine regularly, but had a relatively minimal history of tobacco use compared to many patients diagnosed with bullous emphysema. Alpha-1 antitrypsin levels were within normal limits, leading us to suspect that his polysubstance use contributed substantially to his severe early onset disease.

## Case

A 46 year-old male, with a 13 year history of chronic bullous emphysema and extensive tobacco, marijuana, and methamphetamine use, presented to our clinic for dyspnea. Three days prior the patient had been seen in another local ED, diagnosed with a pneumothorax with chest-tube placement, and treated for pneumonia and pulmonary-bullous abscesses. The clinic x-ray shown in Figure 1 showed large right-sided bullous emphysema with leftward mediastinal shift of structures, similar to his past imaging studies. However, there was a new right-sided pleural effusion as well as large air-fluid levels within the right sided bulla suggestive of infection and developing abscess. The patient was directly admitted to the hospital, where he was found to have an elevated white blood cell count and procalcitonin, consistent with suspected infection. Due to his extensive disease and subsequent high risk of bronchopleural fistula development, drainage was avoided and he was started on vancomycin, cefepime and doxycycline, subsequently narrowed to ceftriaxone and metronidazole. He demonstrated rapid clinical improvement and was discharged on six weeks of oral antibiotics with subsequent resolution of infection and return to his baseline 1-2 L oxygen requirement. Trelegy and albuterol inhalers were also started. At follow up a year after his hospitalization, the patient was remarkably stable. He admitted that after a period of a few months' abstinence, he had resumed smoking about a pack of cigarettes every 3 days as well as vaping nicotine 2-3 x weekly, though he denied smoking marijuana or methamphetamine. He was asymptomatic, breathing comfortably on room air and no longer requiring supplemental oxygen, despite having no medical follow up for 11 months and having discontinued his Trelegy inhaler a few months prior due to his ongoing complex social situation. He was advised on smoking cessation, to resume his prescribed medications, and scheduled for appropriate follow up with the assistance of social work to help with transportation.

It is significant to comment on this patients' polysubstance use, as it provides a salient discussion for our case. Our patient had approximately a 25 pack-year tobacco history and a 20 year marijuana use history prior to diagnosis of bullous emphysema in 2009.

While he continued to smoke both tobacco and marijuana until his recent hospitalizations, his bullous emphysema appears to have been relatively stable. Additionally, he began smoking methamphetamine frequently in 2015. Imaging demonstrates significant progression of his disease from 2013 to 2021, as demonstrated in Figures 2 and 3. The long history of tobacco and marijuana use and progression of his disease corresponding with onset of heavy methamphetamine use makes this a unique case as we consider the impact of polysubstance use on bullous emphysema.

## Discussion

COPD related health care costs were \$32.1 billion in 2010, with 76% of those costs paid by public insurance, and have since increased.<sup>1</sup> A better understanding of risk factors for COPD could help us to better screen patients, detect disease earlier and provide more accurate information to patients, as well as enhance understanding of pathophysiology impacting disease development.

Lung pathology in heavy marijuana users, especially with development of bullae, is well documented in the literature, but clarification regarding dose dependency and synergistic risk factors is needed.<sup>8-13</sup>



**Figure 1.** Patient x-ray with right-sided bullous emphysema, leftward mediastinal shift, and right-sided pleural effusion



**Figure 2.** Chest x-ray in 2013 demonstrating early onset severe bullous emphysema

Interestingly, multiple studies have demonstrated that smoking marijuana does not impair FEV1 in a similar fashion to tobacco, thus suggesting that the injurious mechanism that results in increased risk of emphysema and/or bullae may be unique.<sup>10,14</sup> Case reports associating cocaine use and development of bullous emphysema or bronchial hypereactivity are also abundant in the literature.<sup>15-21</sup> Contributions of methamphetamine use to development of chronic lung disease are not as well detailed, however it is reasonable to think that there may be a similar mechanism of injury as with other strong sympathetic activators as these substances share many physiologic effects. In our patient's case, he reported having discontinued methamphetamine use several months prior to acute flaring of his disease after a several year period of heavy use, raising the possibility that perhaps long term abuse of strong sympathetic activators may even cause changes in adrenergic receptors within the respiratory system that predispose users to withdrawal associated respiratory complications. Additionally, it's possible that disease associations with substance use are attributable to inhalation of contaminants or barotrauma associated with deep inhalation.

In addition to physiologic effects, substance misuse has substantial secondary impact on patients' ability to access and appropriately use the healthcare system. A 2020 study reported significantly worsened outcomes in chronic lung disease among patient's with substance misuse, and a decrease in healthcare utilization associated with treatment of substance dependence, which is very consistent with our patient's case to date.<sup>22</sup>



**Figure 3.** Chest x-ray in 2021 demonstrating disease progression

## Conclusion

Chronic lung disease represents a substantial cost in the United States, both in terms of cost to patient's quality of life and financial and energy costs to the healthcare system. There has been a great deal of association between substance use disorders and development or progression of chronic lung disease, but the details of these associations are unclear. As substance use disorders continue to increase in our population, further study to clarify the contributions of substance use to chronic lung disease is needed to help clarify messaging to patients, understanding of physiology and eventually, more effective management of these pathologies. ■

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