# Imaging of Smoking and Vaping Related Diffuse Lung Injury

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**KEYWORDS**

• Smoking-related lung injury • EVALI • Crack lung • Respiratory bronchiolitis • Langerhans cell histiocytosis

**KEY POINTS**

- Smoking-related lung injury demonstrates a range of clinical presentations and radiologic findings.
- Variable imaging findings reflect a variety of possible substances inhaled and pathologic mechanisms for lung injury.
- Radiologists should be familiar with acute and subacute patterns of smoking-related lung disease and EVALI to ensure timely diagnosis and treatment.

## INTRODUCTION

Smoking, whether of tobacco or other substances, is one of the most common causes of lung injury. Multiple mechanisms are responsible for smoking-related lung injury, including direct and indirect effects of toxins. Particle size, chemical makeup and solubility, inhaled volume, and presence of contaminants also play a substantial role in determining the effects of the exposure.[1] Given these factors, it is not surprising that the findings of smoking-related lung injury may overlap. The timeline of the patient's initial symptoms and presentation can play an essential role in diagnosis and management. Therefore, this review organizes the patterns of lung injury from inhaled toxins based on acuity of presentation: the acute category consisting of acute eosinophilic pneumonia, synthetic marijuana, e-cigarette or vaping product use–associated lung injury (EVALI), and illicit drug use; the subacute category comprising Langerhans cell histiocytosis (LCH) and the respiratory bronchiolitis (RB) and desquamative interstitial pneumonitis (DIP) disease spectrum; and lastly the chronic category including smoking-related fibrosis and emphysema.

## WHEN TO SUSPECT SMOKING-RELATED LUNG INJURY

An accurate and comprehensive patient history is a powerful resource for the clinician and radiologist, helping narrow the differential diagnosis to smoking-related and other inhalational lung diseases, particularly in the acute setting. Thus the radiologist should consider lung injury from an inhaled toxin when acute clinical decompensation occurs in the absence of infection and cardiac dysfunction. In this setting, imaging features are often nonspecific. For example, acute lung injury may present with diffuse centrilobular nodules that might otherwise be suggestive of infection. Lung injury may also mimic pulmonary edema with central ground-glass opacities, interlobular septal thickening, and pleural effusions.

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## ACUTE PRESENTATIONS

### Acute Eosinophilic Pneumonia

#### Patient presentation

Acute eosinophilic pneumonia is caused by multiple etiologies, including infections, drug reactions, and inhalation of illicit drugs. However, there remains to be a close association of acute eosinophilic pneumonia with cigarette smoking, particularly when there is an increase in smoking habits. Patients with smoking-related acute eosinophilic pneumonia are most commonly young men in their 20s to 40s, presenting with acute febrile illness and impaired respiratory function that may mimic acute respiratory distress syndrome (ARDS).[2]

#### Pathophysiology

Although the mechanisms of lung injury for acute eosinophilic pneumonia have yet to be fully determined, the pathology stems from the recruitment of eosinophils and their degranulation of proteins that promote inflammation and lung injury. Although peripheral eosinophils remain within the normal range, pulmonary eosinophilia greater than 25% is seen on bronchioloalveolar lavage (BAL), distinguishing this entity from ARDS in which neutrophilia is seen on BAL.[2]

#### Imaging

Diagnosis of acute eosinophilic pneumonia is guided by the Philit criteria, which include acute respiratory symptoms of less than 1 month, pulmonary opacities on thoracic imaging, pulmonary eosinophilia (>25% eosinophils on BAL), and absence of other pulmonary eosinophilic diseases.[2] Thoracic imaging reveals multifocal or diffuse ground-glass opacities, sometimes with superimposed consolidation and interlobular septal thickening as seen in **Fig. 1**. Small to moderate pleural effusions may also be present.[3] Although the radiographic findings may mimic ARDS or pulmonary edema, accurate diagnosis for acute eosinophilic pneumonia is imperative. Rapid response to corticosteroid treatment is a hallmark of the disease; the clinical course can result in death without timely treatment.[2]

### Synthetic Marijuana

#### Patient presentation

Developed to simulate the cannabis effect, synthetic cannabinoids are mood-altering chemicals that were initially sprayed onto dry plant material, which could then be smoked. Lung injury related to this practice may be considered in adolescents and young adults who present with compromised respiratory function and altered mental status.[4] These substances are now also used in electronic cigarette and vaping devices, and the findings in that setting are described with other vaping-related lung diseases.

#### Pathophysiology

Although the exact mechanism is unknown, injury to the endothelium of the airway most likely precipitates an immune response that triggers inflammation, damaging surrounding normal lung tissue. Histology from patients who smoked synthetic cannabinoids demonstrated plugs of granulation tissue centered around the bronchioles (organizing pneumonia) and foci of acute lung injury.[4,5]

#### Imaging

Although the pulmonary manifestations of synthetic marijuana have not been fully investigated, case reports have demonstrated diffuse centrilobular nodules and tree-in-bud opacities, which parallel the histology of an airway-centered injury as seen in **Fig. 2**. In addition, patterns of organizing pneumonia, including areas of superimposed patchy consolidation, have also been observed. Synthetic marijuana use may also result in cardiac dysfunction, and as such the imaging manifestations of pulmonary edema may also be present.[4]

### E-Cigarette or Vaping Product Use–Associated Lung Injury

#### Patient presentation

EVALI has emerged as a deadly trend, particularly among young patients in whom cigarette smoking is being supplanted by the use of vaping products. Like other inhalational injuries, EVALI is a diagnosis of exclusion. Patients are often young and present not only with respiratory symptoms and chest pain, but also with nonspecific signs including gastrointestinal symptoms. Most cases of EVALI are attributable to inhalation of nicotine or marijuana/THC derivatives. This customization is an alluring but deadly feature of electronic cigarettes. Severe cases may result in intensive care unit level care and a minority of patients have died of EVALI.[6]

#### Pathophysiology

As with any inhaled toxin, the body's response to electronic cigarettes creates a cascade of immune responses that ultimately culminates in inflammation and leads to lung injury. Histology has demonstrated airway-centered lung injury. However, the exact mechanism of injury is poorly understood, possibly because of the wide variety of contents seen in electronic cigarettes.[6] Everything regarding electronic cigarettes can be personalized, from the type of compound that is vaporized, particle size, inhaled quantity and duration, and so

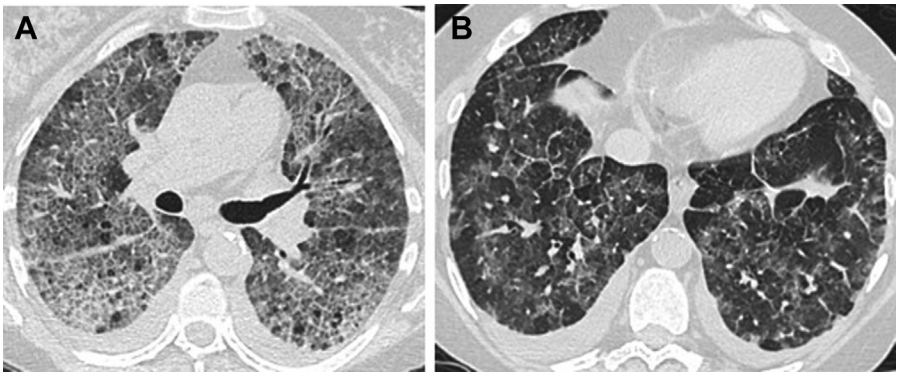


**Fig. 1.** A 57-year-old previously healthy woman with acute eosinophilic pneumonia attributed to smoking tobacco. She was admitted for acute respiratory failure and underwent computed tomography (CT), which shows bilateral ground-glass opacitiesand small pleural effusions as seen in Panel A. Imaging also included smooth interlobular septal thickening, best illustrated in Panel B. The diagnosis was confirmed at surgical lung biopsy and the patient quickly improved after initiation of corticosteroid treatment.

forth. The most common findings of EVALI at pathology include organizing pneumonia and diffuse alveolar damage. Acute eosinophilic pneumonia and diffuse alveolar hemorrhage may also be seen.[6]

### *Imaging*

The inherent variability of exposures with these devices results in a wide range of mechanisms that can lead to lung injury and thus variability in imaging presentation. Although organizing pneumonia can demonstrate a wide variety of imaging presentations, the pattern seen in the setting of EVALI tends to be somewhat less variable. Patients often present with bilateral symmetric ground-glass opacities with associated septal thickening, often resulting in a crazy paving pattern. Subpleural sparing is commonly present. There may also be sparing along the peribronchovascular interstitium.[6,7]

Patients with a diffuse alveolar damage pattern of injury may present with a more severe clinical and imaging presentation, including lower lobe–predominant consolidation and volume loss as seen in **Fig. 3**B. Findings may overlap with those of organizing pneumonia with peribronchovascular ground-glass opacities, for example please refer to **Fig. 3**C. Patients may also demonstrate a crazy paving pattern as seen in **Fig. 3**A.[6,7] Less commonly, patients with EVALI may also present with diffuse centrilobular nodules as depicted in **Fig 3**D. This pattern likely reflects airway-centered organizing pneumonia (similar to synthetic marijuana). Pulmonary hemorrhage is a rare manifestation with bilateral ground-glass opacities or consolidation.

## *Cocaine*

### *Patient presentation*

Crack cocaine is the highly addictive precipitant solid form of cocaine that is evaporated at high temperatures and smoked, causing neurologic and cardiovascular symptoms and throat

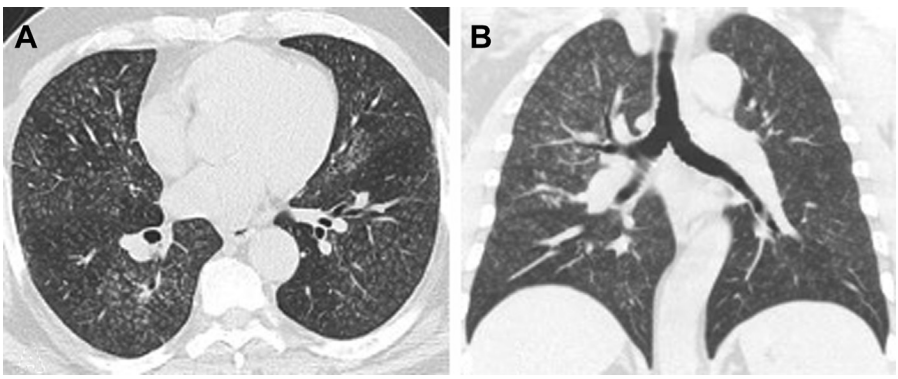


**Fig. 2.** (*A, B*) Diffuse bilateral centrilobular nodules in a patient with history of smoking synthetic marijuana.

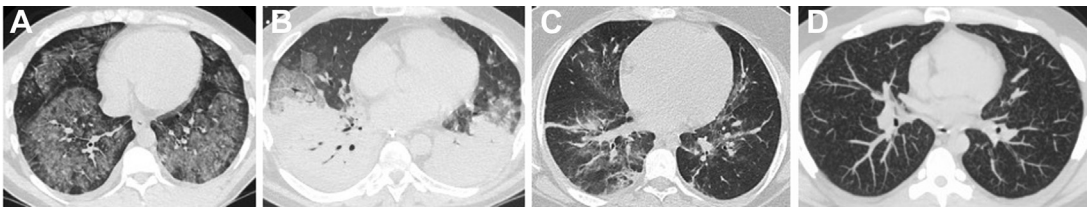


**Fig. 3.** Spectrum of imaging findings from four different patients with EVALI. (*A*) Bilateral ground-glass opacities and crazy paving. (*B*) Dependent consolidation from lung injury. (*C*) Mild peribronchovascular ground-glass opacities and linear consolidation consistent with organizing pneumonia. (*D*) Axial maximum intensity projection image showing diffuse centrilobular nodules in a 40-year-old man who vaped THC.

tightness or pain, chest pain, dyspnea, hemoptysis, and cough with black sputum.[8] Specifically, "crack lung" is used to describe an acute respiratory compromise that manifests within 48 hours of use and associated with ancillary symptoms, such as fever and hemoptysis.[9]

### *Pathophysiology*

"Crack lung" comprises diffuse alveolar damage and alveolar hemorrhage. Pulmonary hemorrhage can occur at the level of the airways with bleeding of the bronchial and tracheal vessels or from destruction of the capillary alveolar interface.[8] In a histologic review of 52 autopsies from patients that tested positive for cocaine, 58% showed acute pulmonary hemorrhage (**Fig. 4**) and 40% showed chronic pulmonary hemorrhage with hemosiderin-laden macrophages.[10]

### *Imaging*

Although the mechanism for damage to the capillary alveolar membrane in crack lung is not fully characterized, the resulting increase in permeability leads to increased edema fluid in the alveolar spaces, which was seen in 77% patients in the previously mentioned histologic review.[10] Although the increased permeability can account for the noncardiogenic pulmonary edema, impaired cardiac function from cocaine-induced myocardial ischemia can also result in cardiogenic pulmonary edema. The radiologic findings of pulmonary edema include interlobular septal thickening, perihilar opacities, effusions, and parenchymal consolidation or ground-glass opacities with possible subpleural sparring as seen in **Fig. 5**. Ground-glass opacities with subpleural sparing is a common feature in "crack lung."[11] Images in patients with diffuse alveolar hemorrhage demonstrate diffuse opacities without geographic predilection, predominantly ground-glass in attenuation with or without superimposed areas of consolidation, and occasionally with superimposed interlobular septal thickening giving rise to a "crazy paving" appearance.

Other radiologic abnormalities that may be seen in association with inhaled cocaine include pneumothorax or pneumomediastinum from barotrauma, findings of organizing pneumonia, bronchiolitis obliterans, and pulmonary eosinophilia.[8]

## *Heroin*

### *Patient presentation*

Although typically injected intravenously, heroin can also be inhaled or smoked, often in conjunction with cannabis. At an inpatient rehabilitation center, a

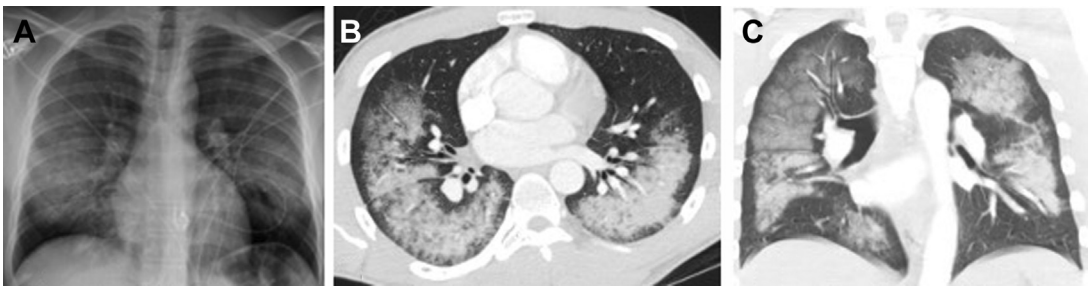


**Fig. 4.** (*A*) Bilateral central opacities in a patient presenting for acute shortness of breath after smoking crack cocaine. (*B, C*) CT finding of that same patient; central ground-glass opacities with subpleural sparing and superimposed confluent areas of consolidation and interlobular septal thickening. Findings compatible with significant pulmonary edema.

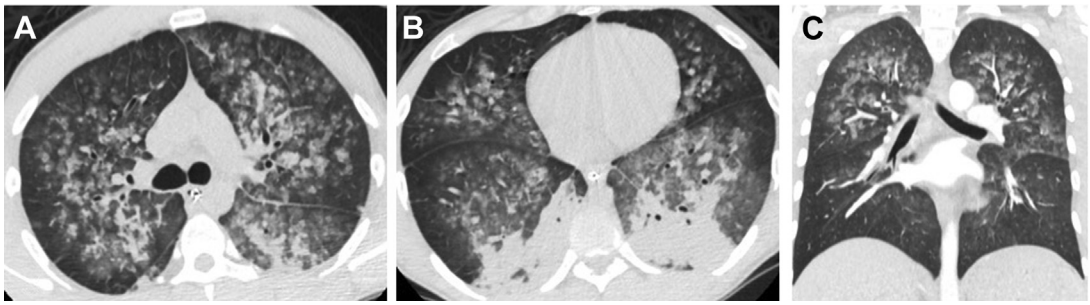


**Fig. 5.** (*A, B*) A 33-year-old homeless man who presented with respiratory failure bloody secretions. He was a regular cocaine user and admitted to recently smoking heroin before admission. CT images show symmetric ground-glass opacities, dependent consolidation, and smooth interlobular septal thickening. These findings were believed to represent a combination of permeability edema and hemorrhage in the context of bloody secretions. (*C*) A 24-year-old man who presented with lung injury from smoking the gel out of a fentanyl patch. He was hypoxic to 89% on room air and coughing up blood at the time of presentation. CT was negative for pulmonary embolism but showed symmetric bilateral ground-glass opacities attributable to smoking fentanyl. Patient's symptoms improved and he was discharged the following day.

sample of 300 heroin users were assessed and 70.3% of them were smokers of heroin laced with cannabis.[12] Patients often mistakenly believe that smoking heroin rather than administering it intravenously removes the addictive and destructive nature of heroin. Reports of patients smoking fentanyl have also been described.[13] Clinical signs include mental status change and euphoria, nausea, vomiting, dyspnea, cough, fevers, and depressed respiratory function. Compromised respiratory status often occurs acutely.[14]

### *Pathophysiology*

Similar to cocaine, heroin is associated with damage to the capillary alveolar interface, resulting in increased permeability. In addition, the neurologic response to heroin itself may also provoke neurologic pulmonary edema. Regardless of the pathophysiology, noncardiogenic pulmonary edema is a common manifestation of heroin and opioid use, whether through inhalation or intravenous injection.[1] Heroin is also a stimulator of mast cells, which release histamine and trigger bronchospasm.[14]

### *Imaging*

Imaging in patients with heroin or other opiate inhalation may demonstrate classic findings of pulmonary edema and lung injury. Other histologic manifestations that may be seen in these patients include eosinophilic pneumonia and, rarely, alveolar proteinosis, which have been reported in case reports.[15]

## SUBACUTE PRESENTATIONS

### *Pulmonary Langerhans Cell Histiocytosis*

### *Clinical presentation*

Pulmonary LCH is highly associated with smokers and more commonly seen in young adults ranging from 20 to 40 years of age. Although nearly all patients with pulmonary LCH have a personal history of smoking or prolonged exposure to secondhand smoke, only a minority of patients with smoking history actually develop pulmonary LCH, implying a possible genetic predisposition.[16,17] In a review of 20 lobectomy specimens from patients with a smoking history, only one patient had the histologic findings of LCH. This contrasts with the 18 patients who had RB, which is described in the following section.[18]

There is a broad clinical presentation and course for LCH; patients may be asymptomatic, present with vague symptoms of dyspnea and cough, or succumb to severe respiratory compromise. Pneumothorax is a classic complication and can prompt the initial clinical presentation. Patients with more advanced disease and symptoms may require steroid therapy or even lung transplantation.[16]

### *Pathophysiology*

LCH is the abnormal proliferation and accumulation of Langerhans cells, a subset of dendritic cells that are identified through their characteristic Birbeck granules or X-bodies. These cells are the immune protectors of the respiratory tract; therefore, they are predictably increased in smokers, reflecting an immune-mediated inflammatory response.[17]

### *Imaging*

Biopsy is used for definitive diagnosis but can often be avoided in patients who demonstrate "classic" imaging findings and mild symptoms that are managed with smoking cessation. Therefore, it is imperative that the radiologist be familiar with the imaging patterns of LCH. The recruitment and accumulation of the dendritic cells along the

airways manifest as airway-centered nodules, which develop central lucencies that may expand and evolve into irregular, thick-walled cysts as the inflammation progresses.[17] The presence of cysts that may rupture into the pleural spaces results in the propensity for pneumothorax. Sparing of the costophrenic angles is the radiologic hallmark of this disease. In early phases of the disease, small nodules less than 10 mm tend to predominate (**Fig. 6**A). Cysts are seen in all phases but often suggest a more advanced disease state.[16] Extensive cystic parenchmymal destruction can create a "burnt out" appearance as seen in Fig. 6B and 6C. LCH may also be observed in conjunction with other smoking-related lung diseases.

## Respiratory Bronchiolitis and Desquamative Interstitial Pneumonia

### Clinical presentation

Respiratory Bronchiolitis (RB), respiratory bronchiolitis with interstitial lung disease (RB-ILD), and desquamative interstitial pneumonia (DIP) represent a spectrum of disease, seen in the same patient population and representing different distributions of similar macrophages. These histologic patterns are typically seen in smokers and management primarily consists of smoking cessation. RB is characterized by the accumulation of airway-centered macrophages without clinical symptoms. When patients exhibit clinical manifestations, such as abnormal pulmonary function tests, shortness of breath, or cough, the term RB-ILD is applied.[19] In a cohort of 109 surgically confirmed cases of RB, 98% were smokers. Smoking cessation can potentially alleviate the symptoms and reverse the lung injury in most cases. In that same cohort, RB remained in one-third of patients after 5 years of smoking cessation.[20] DIP is associated with alveolar accumulation of macrophages. Its clinical manifestations include cough, clubbing of the fingers, and shortness of breath with a slight male preponderance.[21]

### Pathophysiology

The pathophysiology of RB and DIP involves the accumulation and migration of macrophages as a response to the inflammation incited by the inhalation of smoking toxins. These macrophages engulf and remove the toxins, turning their cytoplasm into a tan color hue, earning the nickname "smokers' macrophages." In RB and RB-ILD, the studding of the airways with these colored macrophages gives rise to centrilobular nodules. In DIP, those tan-colored macrophages extend from the airways and fill the alveolar spaces. Alveolar wall fibrosis and concurrent inflammation may be present in both pathologies. Because DIP is merely an extension of RB and both diseases stem from smoking, it is common for both pathologies to coexist with histologic and radiographic overlap.[17]

### Imaging

Like other smoking-related lung injury patterns, RB presents radiographically as ill-defined, centrilobular nodules with an upper lobe–predominance (**Fig. 7**). The upper lung–predominant distribution may be attributed to the more robust lymphatic drainage system in the lower lungs, allowing for better clearance of the particles.[17] For reasons unknown, these centrilobular nodules do not cavitate or progress into cysts, a distinguishing feature from LCH. As in other small airway diseases, mosaic attenuation may be seen.

Because DIP involves the accumulation of smokers' macrophages in the alveolar spaces, this radiographically translates into the nonspecific pattern of symmetric ground-glass opacities interposed with normal areas of lung parenchyma. However, despite the aforementioned robust lower lung lymphatic system, these ground-glass opacities tend to be basilar predominant (**Fig. 8**). Cystic changes and emphysema may also be seen; however, honeycombing is unusual. The fibrosis pattern in DIP consists of symmetric wall thickening of the alveoli without destruction of the lung architecture, mirroring the nonspecific interstitial pneumonia pattern in histology.[19]

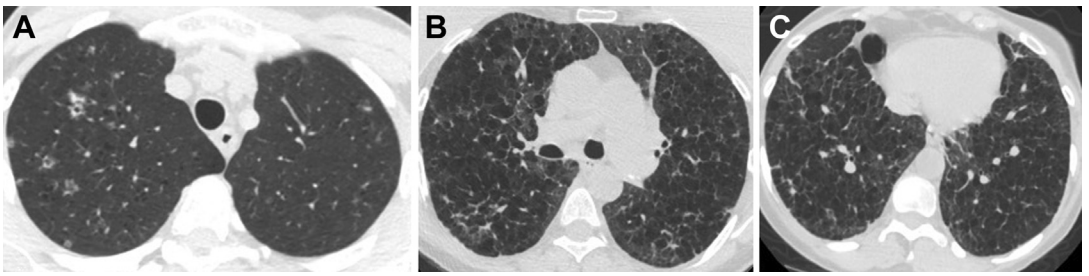


**Fig. 6.** Patients with known LCH. (*A*) Early manifestations of LCH with upper lung–predominant centrilobular nodules, some of which show cavitations. (*B, C*) Patient with advanced or "burnt out" LCH with extensive cystic parenchymal destruction.

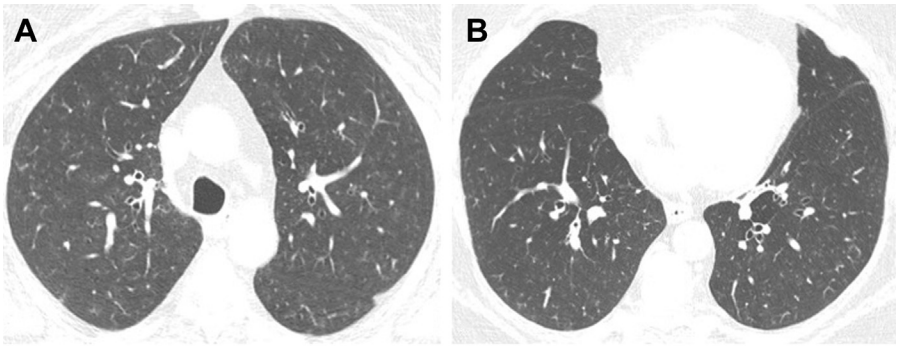


Fig. 7. (*A, B*) Diffuse centrilobular nodules in a patient with a long-standing history of smoking and suspected RB-ILD.

## CHRONIC LUNG DISEASE
### *Smoking-Related Interstitial Fibrosis*

#### *Patient presentation*

The importance of diagnosing smoking-related interstitial lung fibrosis (SRIF), also referred to as airspace enlargement with fibrosis or RB with fibrosis, lies in its different prognosis from that of other forms of fibrosis, specifically idiopathic pulmonary fibrosis (IPF).[22] It is therefore important to distinguish these entities, although the distinction is challenging for the clinician, radiologist, and pathologist. In contrast to IPF, there have been no reports of significant clinical impairment related to SRIF. In fact, studies have described SRIF (**Fig. 9**) in patients without clinical suspicion for ILD.[18]

#### *Pathophysiology*

Although it is not surprising that the toxic effects of cigarette smoking can cause fibrosis, the pathophysiology of SRIF is poorly understood but probably multifactorial. Cigarette toxins promote inflammation, recruit and accumulate immune cells, and cause the release of cytokines and growth factors. Specifically, nicotine is a suspected culprit because it can induce cell damage, incite inflammation, and initiate collagen production. These combined effects likely play a role in the pathogenesis of SRIF.[21] Histologically, SRIF consists of alveolar wall thickening with increased collagen accumulation. In contrast to IPF, SRIF is distinguished by overall preserved lung architecture and lack of temporal variability.[18]

#### *Imaging*

Even in the presence of the histologic findings of fibrosis, patients may have normal imaging on high-resolution computed tomography. In patients with abnormal imaging, findings typically include a background centrilobular nodules and

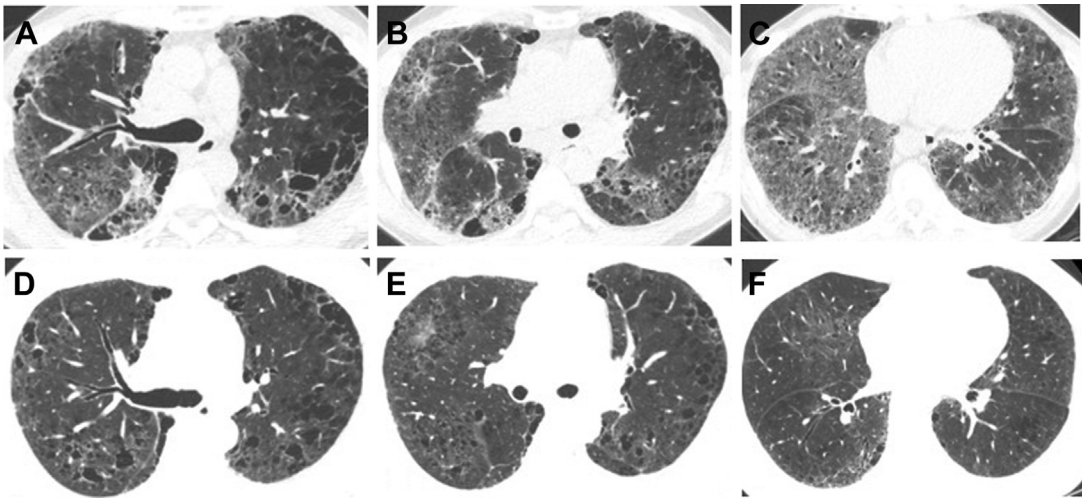


Fig. 8. (*A–C*) Diffuse basilar-predominant ground-glass opacities are seen in a patient with suspected DIP in the setting of emphysema. After smoking cessation and short-term treatment of steroids, there is significant decrease in the ground-glass opacities (*D–F*), which is expected in DIP.

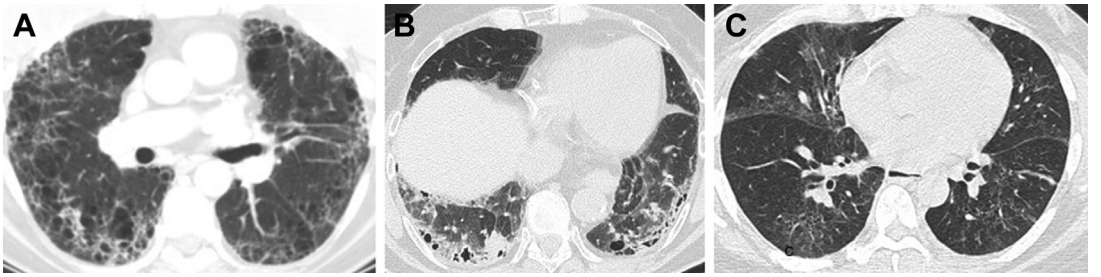


**Fig. 9.** (*A*) Findings of SRIF with reticulation and ground-glass opacities on a background of emphysema and respiratory bronchiolitis. Pathology showed bronchiolocentric fibrosis suggestive of SRIF. (*B*) Patient with ground-glass opacities, reticulation, and cystic changes found to be distal lobular airspace enlargement on histology. (*C*) Separate patient that also had histology suggestive of SRIF with ground-glass opacities as the predominant findings.

ground-glass opacities (reflecting RB spectrum disease) and upper lung–predominant emphysema with concurrent reticulation.[21] Although SRIF and usual interstitial pneumonia differ in their clinical presentation, progression, and management, distinguishing between the two pathologies is challenging, especially because they can share radiologic features, such as honeycombing, and both are seen in conjunction with emphysema. Chae and colleagues[23] advocated for the location of emphysema and honeycombing and their relationship with respect to each other as helpful tools for the radiologist; honeycombing bordering to emphysema, uneven areas of honeycombing, and absence of honeycombing in the upper lungs all favor SRIF over usual interstitial pneumonia.

## Emphysema

### Clinical presentation

Emphysema is a ubiquitous disease among smokers causing significant clinical impairment and respiratory compromise. Patients present with cough, dyspnea on exertion, and abnormal pulmonary function tests including increased total lung capacity and decreased forced expiratory volume in 1 second.[24]

### Pathophysiology

Smoking causes airway-centered injury that progresses to alveolar destruction through a cascade of inflammatory pathways that lead to cellular destruction and remodeling mediated by immune cells, cytokines, oxidative stress, and extracellular matrix proteolysis. Emphysema related to smoking is predominantly centrilobular in distribution, although paraseptal emphysema (**Fig. 10**) may also be seen. On histologic review, there is destruction of the alveolar walls with enlargement of the airspaces.[25]

### Imaging

Focal areas of lucency without perceptible walls are the hallmark imaging findings of emphysema. In smokers, these focal lucencies are usually centered around the airways, otherwise described as centrilobular in location. These lucencies can merge as the disease process progresses and form bullae. Alternatively, these lucencies may be located in the periphery near the pleural spaces, giving rise to paraseptal emphysema.[25] The pulmonary vessels are diminutive in the areas of emphysema further decreasing the attenuation of the affected areas, because the lung directs blood flow away from areas of hypoxia to areas of preserved ventilation to promote effective vascular gas exchange.

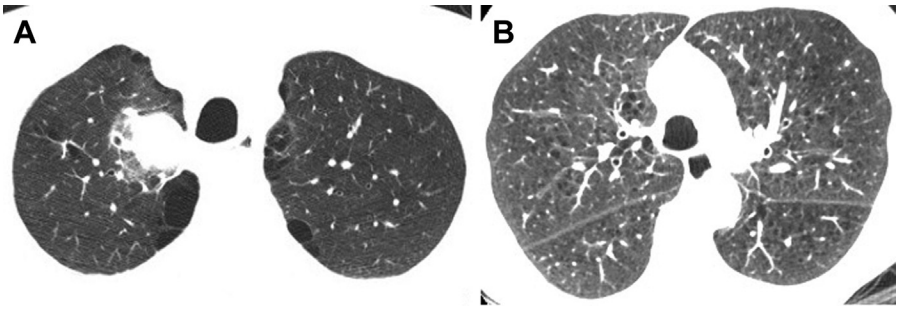


**Fig. 10.** (*A*) Subpleural lucencies reflecting paraseptal emphysema. (*B*) Centrilobular emphysema.

**Table 1**
**Summary table**

| Presentation | Disease Entity | Mechanism of Injury | Common Imaging Findings |
|---|---|---|---|
| Acute | Acute eosinophilic pneumonia | Recruitment of eosinophils and release of degranulation proteins | Multifocal or diffuse ground-glass opacities, ± superimposed consolidation or ground-glass opacities. |
| | Synthetic marijuana use | Airway-centered injury, organizing pneumonia | Apical-predominant centrilobular nodules. Patchy consolidation, crazy paving. |
| | EVALI | Variable: organizing pneumonia, diffuse alveolar damage, acute eosinophilic pneumonia, diffuse alveolar hemorrhage | Ground-glass opacities with septal thickening (crazy paving), subpleural sparing. May demonstrate lower lobe–predominant consolidation. |
| | Crack lung | Diffuse alveolar damage, alveolar hemorrhage | Diffuse ground-glass opacities, ± superimposed consolidation, occasional crazy paving. |
| | Heroin inhalation | Damage to the capillary alveolar interface | Findings of pulmonary edema: ground-glass opacities with interlobular septal thickening. ± pleural effusions. |
| Subacute | LCH | Langerhans cell proliferation and associated inflammatory response | Irregular centrilobular nodules. Thick-walled, irregular cysts. Sparing of the costophrenic angles. |
| | RB | Macrophage accumulation along the airways | Ill-defined apical-predominant centrilobular micronodules. |
| | DIP | Macrophage accumulation in the alveolar spaces | Bilateral lower lung–predominant ground-glass opacities. |
| Chronic | Emphysema | Inflammatory cascade resulting in alveolar destruction | Lucencies without perceptible walls, which may be centrilobular or paraseptal in distribution. |
| | SRIF | Poorly understood mechanism resulting in alveolar wall thickening and collagen accumulation | Basal- and peripheral-predominant septal thickening. May demonstrate ground-glass opacities. With or without imaging findings of other smoking-related lung disease. |

## SUMMARY

Smoking-related lung injury comprises a broad spectrum of pathologies that can share overlapping imaging features, making diagnosis challenging to the radiologist and clinician. Furthermore, the category of smoking-related lung injury has also evolved to include pathologies that extend beyond nicotine cigarette smoking to include inhalation of illicit drugs and electronic cigarettes. Despite these challenges, imaging remains a powerful clinical tool that can aid in diagnosis and prognosis by expediting appropriate treatment. By categorizing smoking-related lung injury based on the timeline and acuity of the patient's symptoms, we hope to improve the radiologist's understanding of the pathophysiology and imaging features of smoking-related lung injury (Table 1).

## CLINICS CARE POINTS

- Acute presentations are uncommon with cigarette smoking and more common with related inhalational injuries.
- Centrilobular nodules and ground-glass opacities are nonspecific findings that may be seen in the acute setting but are also commonly seen in subacute smoking-related lung diseases.
- Chronic smoking-related lung injury tends to have an insidious clinical presentation.

## DISCLOSURE

The authors have nothing to disclose.

## REFERENCES


1. Mégarbane B, Chevillard L. The large spectrum of pulmonary complications following illicit drug use: features and mechanisms. Chem Biol Interact 2013;206(3):444–51.
2. De Giacomi F, Vassallo R, Yi ES, et al. Acute eosinophilic pneumonia. Causes, diagnosis, and management. Am J Respir Crit Care Med 2018;197(6):728–36.
3. Jeong YJ, Kim K-I, Seo IJ, et al. Eosinophilic lung diseases: a clinical, radiologic, and pathologic overview. RadioGraphics 2007;27(3):617–37.
4. Berkowitz EA, Henry TS, Veeraraghavan S, et al. Pulmonary effects of synthetic marijuana: chest radiography and CT findings. AJR Am J Roentgenol 2015;204(4):750–7.
5. Kourouni I, Mourad B, Khouli H, et al. Critical illness secondary to synthetic cannabinoid ingestion. JAMA Netw Open 2020;3(7):e208516.
6. Kligerman S, Raptis C, Larsen B, et al. Radiologic, pathologic, clinical, and physiologic findings of electronic cigarette or vaping product use-associated lung injury (EVALI): evolving knowledge and remaining questions. Radiology 2020;294(3):491–505.
7. Kligerman SJ, Kay FU, Raptis CA, et al. CT findings and patterns of e-cigarette or vaping product use-associated lung injury: a multicenter cohort of 160 cases. Chest 2021;160(4):1492–511.
8. Restrepo CS, Carrillo JA, Martínez S, et al. Pulmonary complications from cocaine and cocaine-based substances: imaging manifestations. Radiographics 2007;27(4):941–56.
9. Giacomi FD, Srivali N. Cocaine use and crack lung syndrome. QJM 2019;112(2):125–6.
10. Bailey ME, Fraire AE, Greenberg SD, et al. Pulmonary histopathology in cocaine abusers. Hum Pathol 1994;25(2):203–7.
11. Chong WH, Saha BK, Austin A, et al. The significance of subpleural sparing in CT chest: a state-of-the-art review. Am J Med Sci 2021;361(4):427–35.
12. Morgan N, Daniels W, Subramaney U. Smoking heroin with cannabis versus injecting heroin: unexpected impact on treatment outcomes. Harm Reduct J 2019;16(1):65.
13. Tambe V, Desai P, Kondapi D, et al. 1156: Inhaled fentanyl leading to diffuse alveolar hemorrhage. Crit Care Med 2019;47(1):555.
14. Radke JB, Owen KP, Sutter ME, et al. The effects of opioids on the lung. Clin Rev Allergy Immunol 2014;46(1):54–64.
15. Chapman E, Leipsic J, Satkunam N, et al. Pulmonary alveolar proteinosis as a reaction to fentanyl patch smoke. Chest 2012;141(5):1321–3.
16. Suri HS, Yi ES, Nowakowski GS, et al. Pulmonary Langerhans cell histiocytosis. Orphanet J Rare Dis 2012;7:16.
17. Kligerman S, Franks TJ, Galvin JR. Clinical-radiologic-pathologic correlation of smoking-related diffuse parenchymal lung disease. Radiol Clin North Am 2016;54(6):1047–63.
18. Katzenstein AL, Mukhopadhyay S, Zanardi C, et al. Clinically occult interstitial fibrosis in smokers: classification and significance of a surprisingly common finding in lobectomy specimens. Hum Pathol 2010;41(3):316–25.
19. Elicker BM, Kallianos KG, Jones KD, et al. Smoking-related lung disease. Semin Ultrasound CT MR 2019;40(3):229–38.
20. Fraig M, Shreesha U, Savici D, et al. Respiratory bronchiolitis: a clinicopathologic study in current smokers, ex-smokers, and never-smokers. Am J Surg Pathol 2002;26(5):647–53.
21. Margaritopoulos GA, Harari S, Caminati A, et al. Smoking-related idiopathic interstitial pneumonia: a review. Respirology 2016;21(1):57–64.
22. Watanabe Y, Kawabata Y, Kanauchi T, et al. Multiple, thin-walled cysts are one of the HRCT features of airspace enlargement with fibrosis. Eur J Radiol 2015;84(5):986–92.
23. Chae KJ, Jin GY, Jung HN, et al. Differentiating smoking-related interstitial fibrosis (SRIF) from usual interstitial pneumonia (UIP) with emphysema using CT features based on pathologically proven cases. PLoS One 2016;11(9):e0162231.
24. Newell JD Jr. CT of emphysema. Radiol Clin North Am 2002;40(1):31–42, vii.
25. Yoshida T, Tuder RM. Pathobiology of cigarette smoke-induced chronic obstructive pulmonary disease. Physiol Rev 2007;87(3):1047–82.