Respiratory complications of drug abuse

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Learning objectives

To describe the imaging findings of respiratory complications of recreational drug abuse, emphasizing those radiologic patterns that might point to a concrete aetiology.

Background

Illicit drugs of common use include opioids, cocaine, amphetamines and derivatives, cannabis, inhaled volatile agents ("poppers") and industrial solvents such as toluene.

Recreational drug use and abuse has increased markedly in almost all European countries in recent years, and the trends in use of each substance and the methods of administration have also evolved.

Prevalence of cannabis use is by far the highest among illicit drugs in the general population. EU reports reveal that it has been used at least once by around 74 million Europeans. It is estimated that around 22.5 million Europeans have used cannabis in the last year, whereas 12 million did it in the last month [1].

Cocaine remains the second most used illicit drug in Europe. Consumption rates soared in the late 1990s and early 2000s in many European countries, especially in the UK and Spain, with prevalence numbers twice above the European average. This is particularly important as cocaine appears to be involved in the majority of drug-related hospital emergencies. In Spain, for example, the national reporting system of hospital emergencies found that in 2006 cocaine was the substance most frequently reported - 59%, followed by cannabis (31%), sedatives (28%) and heroin (22%). These figures show a significant change in trends, as heroin was involved in an estimated 61.5% of drug-related hospital emergencies in 1996. In the USA, cocaine is also the most commonly used illicit drug among patients seen in hospital emergency departments and the most frequent cause of drug-related deaths reported by medical examiners [2].

As for opioids, heroin use seems to stabilise or even subtly increase in most European countries after a downward trend in the late 1990s and early 2000s.

Finally, trends in amphetamine and ecstasy use seem to follow quite a similar pattern to that of cannabis.
Drug use is one of the major causes of death and health problems among young people in Europe \[^1\]. The potential complications involve almost any body organ and imaging frequently plays a vital role in their detection and characterization. Such complications depend basically on the pharmacologic effects of the drug used, the physical, mechanical and microbiologic effects derived from the method of administration, and the nature of the substances mixed with the drug. Imaging techniques may demonstrate sequelae after the use of most of the drugs mentioned, which include cardiovascular, respiratory, abdominal, neurologic and musculoskeletal complications \[^3\].

Radiologic findings in these cases are usually non-specific. However, at the time a patient presents with a complication derived from recreational drug abuse in either an acute or chronic setting, the underlying cause may stay unknown as a result of the social stigma of drug consumption and its illicit nature. Radiologists therefore assume a key role in the work-up of these patients as they may be the first to suggest the diagnosis. For this reason it is essential that radiologists should be aware of and familiar with the imaging spectrum of drug abuse.

**Imaging findings OR Procedure details**

**Airway injury**

Nasal septum perforation due to ischemic necrosis is a common complication of chronic cocaine use, as the septal mucosa and supporting cartilage and bone seem to be especially sensitive to local drug-induced vasoconstriction. A more aggressive intranasal and pharyngeal destructive process mimicking the clinical and radiologic picture of other necrotizing midfacial lesions (midline granuloma disease and Wegener granulomatosis) may also be triggered by heavy cocaine use \[^4\] (figure 1). Thus, history of cocaine abuse should be sought when these diagnoses are being considered because of the therapeutic implications.

Cocaine smokers usually develop bronchitis, sinusitis and epiglottitis, due to inhalation of some adulterants or filler agents mixed with the drug or by combustion of flammable solvents added in drug production. Sometimes, upper respiratory tract thermal injuries may induce bronchospasm, especially in asthmatic patients, or result in tracheal stenosis \[^5\].
**Pneumonia**

Bacterial pneumonia is more likely to happen in intravenous (IV) drug users and cocaine or cannabis smokers than in the general population. IV drug use frequently involves exposure to contaminated drugs and needles, skin colonization by unusual microorganisms from prior hospitalizations and changes in normal bacterial flora due to self-medication with antibiotics. Cocaine alters alveolar macrophage function and causes a decrease in cytokine production ending up in a weakened local immune response \[^2, 5\]. Its local anesthetic effect in pharynx may also lead to aspiration events. The same may occur with opiates owing to its consciousness-altering effect. Chest X-Ray images in patients with aspiration pneumonia usually show involvement of the dependent portions of the lung in the supine position (posterior segments of the upper lobes and apical segments of the lower lobes), and alveolar opacities with or without volume loss are often seen (figures 2, 3, 4 and 5). Recurrent pneumonia may result in bronchiectasis.

Lipoid pneumonia may occur after aspiration of volatile organic compounds such as amyl and butyl nitrites (commonly known as "poppers") during attempted inhalation \[^3\].

**Pulmonary edema**

Sympathomimetic effects of some drugs such as cocaine, amphetamines and its derivatives -MDMA or "ecstasy" and so- may cause cardiogenic pulmonary edema by inducing coronary vasoconstriction and secondary acute coronary episodes (ranging from transient ischaemia to large transmural myocardial infarction). These events lead to myocardial disfunction and severe peripheral vasoconstriction with transient left ventricular failure and may trigger some kinds of arrhythmia \[^6, 7, 8\]. Imaging features of both drug-induced and non drug-induced cardiogenic pulmonary edema are indistinguishable and include cardiomegaly, peribronchovascular and interlobular septal thickening, pleural effusions and, when severe, central perihiliar airspace foci of increased opacity representing alveolar edema.

Non-cardiogenic pulmonary edema may be induced by several drugs. Though opiates are the agents most commonly involved, it has also been reported with cocaine, amphetamines and its derivatives. Physiopathology remains unclear, though direct endothelial damage is believed to play a key role in the ultimately increased pulmonary capillar permeability. Heroin is also thought to trigger some degree of neurogenic edema due to its central neurologic effects \[^2, 3, 9, 10\]. Radiography and CT images usually
show different degrees of bilateral perihilar alveolar opacities with or without thickened septa and ground glass infiltrates. In opposition to cardiogenic pulmonary edema, pleural effusions and cardiomegaly are usually absent (figure 6). Atypical manifestations, including unilateral or dominant interstitial edema, may occur [10].

Classically, clinical and radiographic findings resolve rapidly, often within hours after stopping drug use.

**Pulmonary hemorrhage**

It usually appears in cocaine smokers, due to rupture of bronchial vessels or direct toxic effect on alveolar-capillary membrane [2].

Chest radiography may display uni or multifocal areas of increased opacity with normal heart size and minimal or no effusions (figures 7, 8 and 9). As in the case of drug-induced pulmonary edema, imaging abnormalities clear rapidly after cessation of use of the responsible agent, though chronic hemorrhages have been reported, and occult lung hemorrhage is a common finding at autopsy (in an estimated 30% of subjects who died suddenly from cocaine overdose) [11]. Pulmonary hemorrhage, non-cardiogenic edema and "crack lung" (see ahead) may be radiographically indistinguishable [9].

"Crack lung" / cocaine-induced eosinophilic lung injury

Smoked free-base cocaine form (commonly referred to as "crack") may induce an acute clinical syndrome characterised by fever, dyspnea, productive cough and hypoxemia. It is thought that in a first contact cocaine may behave like an antigen, prompting IgE production. After a second exposure some compounds (histamine, serotonin, eosinophil chemotactic factor and others) are released into the blood stream shortly after drug consumption, triggering acute alveolar injury [5]. At radiography, it manifests as diffuse, multifocal or peripheral airspace opacities (figures 10, 11, 12 and 13), usually impossible to differentiate from non-cardiogenic edema or pulmonary hemorrhage findings, and up to 40% of patients present a variable degree of peripheral eosinophilia [2]. It also clears rapidly after drug cessation and may show a good response to corticosteroid therapy.
**Talcosis and other pulmonary granulomatosis**

Talc (magnesium silicate) is an insoluble filler used in several oral medications to bind the active medicinal agent. Methadone and methylphenidate -among others- usually contain it. When these oral tablets containing talc are ground up, dissolved and injected into bloodstream, talc particles embolize small lung vessels leading to occlusion and secondary pulmonary hypertension \[9, 12\]. Talc particles may then reach the pulmonary interstitium, where they prompt a foreign-body reaction with eventual fibrosis.

Talcosis is rare in nasal drug use, though it may occur in chronic talc-containing drug inhalation.

At chest radiography, talcosis appears as small nodular opacities in the middle and upper areas of the lungs that keep growing in chronic consumption and may coalesce in late stages to form conglomerate masses. These sometimes high-attenuation masses resemble progressive massive fibrosis seen in some pneumoconiosis (silicosis) \[2, 13\]. High resolution CT may also reveal numerous small nodules, ground-glass attenuation, lower-lobe predominant panacinar emphysema and mediastinal lymphadenopathy. These patterns are often seen in combination.

Other fillers such as cellulose, cornstarch, cotton fibers or cork may also induce a foreign-body granulomatous reaction when taken intravenously or inhaled. The most usual radiographic pattern includes numerous small nodules, often in centrilobular distribution, with a "tree-in-bud" appearance in HRCT images \[9\].

**Pulmonary thromboembolic disease**

Injecting drug use is a risk factor for deep vein thrombosis \[14, 15\]. Deep vein thrombosis in IV drug users may end up in pulmonary thromboembolism, which may be detected with CT pulmonary angiography as filling defects in pulmonary arteries \[3\].

Septic emboli may occur as a consequence of septic thrombophlebitis, right-sided cardiac valve endocarditis or direct injection of microorganisms into the blood stream along with the drug.

Radiographic findings consist of multiple round ill-defined peripherally-located opacities which evolve into true variable-sized nodules that may cavitate (figures 14 to 19). These small lung abscesses may rupture into the pleural space leading to empyema,
pyopneumothorax or even bronchopleural fistula formation \cite{3}. Lesions may be found in different evolutive stages as a result of repeated thromboembolic events.

**Pulmonary hypertension**

The mechanism by which heroin and especially cocaine use may induce pulmonary hypertension is complex and multifactorial. Foreign particle embolization (talc or other fillers, see *talcosis*) affecting pulmonary small and medium-sized vessels may play a key role \cite{2}. Besides, smoked cocaine may induce an intense pulmonary vasoconstriction, along with in situ thrombotic phenomena. High levels of endothelin-1 and endothelium-derived vasoconstrictor peptide have been found in bronchoalveolar lavage fluid from chronic cocaine smokers \cite{16}. Imaging features at chest X radiography are non-specific and do not differ from those found in other causes of pulmonary hypertension (figures 20 and 21).

**Emphysema**

A striking pattern of large upper lobe bullae formation has been reported in regular marijuana smokers and less commonly in cocaine smokers and IV drug addicts \cite{3}. Although most of these patients are also usual tobacco smokers, their young ages and relatively short smoking history suggest other mechanisms taking part in disease development may exist (figure 10). Direct pulmonary toxic effects of drugs and other combustion products of the smoked mixture, pleural pressure swings and airway barotrauma brought about by the high inspiratory pressures produced in drug smoking have been invoked \cite{3,17}. Most frequent findings at pathologic examination of the lungs of IV drug abusers include angiothrombosis, intra and extravascular foreign-body particles and areas of inflammation adjacent to the bullae \cite{18}.

IV abuse of oral methylphenidate has been linked specifically to the development of lower lobe panlobular emphysema in up to 86% of cases. Imaging features resemble closely those of #-1 antitrypsin deficiency and consist of large lung volumes with lower-lobe hyperlucency at chest radiography and lower-lobe predominant simplification of the pulmonary architecture at HRCT \cite{13,19} (figures 22 to 26). Although oral methylphenidate tablets contain talc, its IV administration induces panacinar emphysema much more
frequently than the upper-lobe predominant micronodular pattern usually found in
talcosis, probably indicative of a direct methylphenidate-related toxic effect \cite{13, 19}.

**Pneumothorax**

Pneumothorax and less commonly pneumomediastinum, pneumopericardium or
subcutaneous emphysema are well-known complications of cocaine and cannabis
smoking. Smokers usually take deep inhalations followed by Valsalva manoeuvres in an
attempt to improve drug diffusion and absorption, which may result in intra-alveolar high
pressures and eventual alveolar wall rupture \cite{5}. Other mechanisms include severe cough
triggered by cocaine smoke inhalation, attempted subclavian or jugular vein puncture in
IV drug users, rupture of drug-related pre-existing bullae or rarely rupture of peripheral
pulmonary drug-related abscesses \cite{3}.

**Others**

Respiratory failure secondary to biopsy-proven bronchiolitis obliterans with organizing
pneumonia has been reported in young crack cocaine smokers, with diffuse bilateral
alveolar opacities at chest radiography which are virtually indistinguishable from those of
cryptogenic organizing pneumonia \cite{11}.

Marijuana and cocaine smoking have been found to induce a carcinogenic effect on the
bronchial epithelium, placing drug users at a higher risk of developing lung cancer \cite{2}.
These effects are thought to be synergistic with those of tobacco.

**Images for this section:**
Fig. 1: Non-healing midline destructive lesion in a heavy cocaine user. Extensive bone and soft-tissue destruction affecting nose, nasal cavity and pharynx may be seen in this axial image from a contrast-enhanced CT scan of the head and face.
Fig. 2: Figure 2. Aspiration pneumonia in a polydrug user. Chest radiography shows bilateral air-space opacities in dependent lung regions (posterior segment of right superior lobe, apicoposterior segment of left superior lobe and posterior segments of left inferior lobe).
Fig. 3: Figures 3, 4 and 5: Necrotizing pneumonia in a heroin user. Posterior-anterior (3) and lateral (4) chest radiographs and chest CT scan axial image (5) show inferior left lobe air-space consolidation, with cavitation and associated pyopneumothorax due to bronchopleural fistula. Both intraparenchymal and pleural air-fluid levels may be appreciated.
Fig. 4: Figures 3, 4 and 5: Necrotizing pneumonia in a heroin user. Posterior-anterior (3) and lateral (4) chest radiographs and chest CT scan axial image (5) show inferior left lobe air-space consolidation, with cavitation and associated pyopneumothorax due
to bronchopleural fistula. Both intraparenchymal and pleural air-fluid levels may be appreciated.

**Fig. 5:** Figures 3, 4 and 5: Necrotizing pneumonia in a heroin user. Posterior-anterior (3) and lateral (4) chest radiographs and chest CT scan axial image (5) show inferior left lobe air-space consolidation, with cavitation and associated pyopneumothorax due to bronchopleural fistula. Both intraparenchymal and pleural air-fluid levels may be appreciated.
Fig. 6: Non-cardiogenic pulmonary edema. Anterior-posterior chest radiograph reveals diffuse air-space consolidation and ground-glass opacity in a young patient who was brought to our Emergency Department after a heroin and cocaine overdose.
Fig. 7: Pulmonary hemorrhage. Posterior-anterior chest radiograph revealed bilateral perihilar ground-glass opacities in a young male with a history of cocaine use and hemoptysis due to alveolar hemorrhage.
Fig. 8: This chest radiograph belonging to the patient in figure 7 was taken 24 hours later and showed improvement with significant clearance of pulmonary infiltrates.
Fig. 9: Chest CT scan of the same patient, which was obtained on the same day as the radiograph in image 8, demonstrated diffuse ground-glass opacities with interlobular septal thickening.
Fig. 10: "Crack lung" in a patient with a history of cocaine abuse who came to our Service with sudden-onset dyspnea and hypoxemia after smoking cocaine. CX-Ray on figure 10 shows diffuse ground-glass opacities very difficult to differentiate from those appearing at pulmonary edema or hemorrhage. Bronchoalveolar lavage found eosinophilia. 24 hours later the parenchymal shadowing had partially resolved (figure 11).
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Fig. 12: "Crack lung", same patient. CT scan image in figure 12 demonstrates diffuse air-space disease, with parenchymal areas of consolidation and ground-glass opacity. A few days later (figure 13) almost complete resolution of the radiographic abnormalities could be appreciated.
Fig. 13: "Crack lung", same patient. CT scan image in figure 12 demonstrates diffuse air-space disease, with parenchymal areas of consolidation and ground-glass opacity. A few days later (figure 13) almost complete resolution of the radiographic abnormalities could be appreciated.
Fig. 14: Figures 14 and 15. Septic emboli in a young IV drug user who came to our Institution because of fever and postration. Posterior-anterior chest radiograph image (14) shows multiple ill-defined peripherally-located nodules consistent with septic embolization. Cavitation of previous nodules and new-onset lesions may be seen in a chest radiograph taken seven days later (15).
Fig. 15: Figures 14 and 15. Septic emboli in a young IV drug user who came to our Institution because of fever and prostration. Posterior-anterior chest radiograph image (14) shows multiple ill-defined peripherally-located nodules consistent with septic embolization. Cavitation of previous nodules and new-onset lesions may be seen in a chest radiograph taken seven days later (15).
Fig. 16: Figures 16, 17, 18 and 19. Bilateral ill-defined nodules consistent with septic embolization in a heavy IV polydrug user with previous tricuspid valve endocarditis and vague complaints (16). Figure 17 shows chest radiographic evolution two months later. Pre-existing nodules had partially resolved and new-onset nodules and left pleural effusion could be appreciated. Figures 18 and 19: chest CT scan obtained at the same time as the radiograph in figure 17 demonstrated multiple peripheral nodules and nodular ground-glass opacities, as well as left loculated pleural effusion.
Fig. 17: Figures 16, 17, 18 and 19. Bilateral ill-defined nodules consistent with septic embolization in a heavy IV polydrug user with previous tricuspid valve endocarditis and vague complaints (16). Figure 17 shows chest radiographic evolution two months later. Pre-existing nodules had partially resolved and new-onset nodules and left pleural effusion could be appreciated. Figures 18 and 19: chest CT scan obtained at the same time as the radiograph in figure 17 demonstrated multiple peripheral nodules and nodular ground-glass opacities, as well as left loculated pleural effusion.
**Fig. 18:** Figures 16, 17, 18 and 19. Bilateral ill-defined nodules consistent with septic embolization in a heavy IV polydrug user with previous tricuspid valve endocarditis and vague complaints (16). Figure 17 shows chest radiographic evolution two months later. Pre-existing nodules had partially resolved and new-onset nodules and left pleural effusion could be appreciated. Figures 18 and 19: chest CT scan obtained at the same time as the radiograph in figure 17 demonstrated multiple peripheral nodules and nodular ground-glass opacities, as well as left loculated pleural effusion.
Fig. 19: Figures 16, 17, 18 and 19. Bilateral ill-defined nodules consistent with septic embolization in a heavy IV polydrug user with previous tricuspid valve endocarditis and vague complaints (16). Figure 17 shows chest radiographic evolution two months later. Pre-existing nodules had partially resolved and new-onset nodules and left pleural effusion could be appreciated. Figures 18 and 19: chest CT scan obtained at the same time as the radiograph in figure 17 demonstrated multiple peripheral nodules and nodular ground-glass opacities, as well as left loculated pleural effusion.
Fig. 20: Pulmonary hypertension in a young male with a history of heavy cocaine use who asked for assistance because of dyspnea. Chest CT scan image at the level of the pulmonary artery bifurcation shows an enlarged pulmonary trunk measuring over 29 mm, a finding that is consistent with central pulmonary hypertension. Ill-defined foci of parenchymal consolidation in dependent portions of both lungs could be appreciated despite the mediastinal window. After the bronchoalveolar lavage results (which confirmed eosinophilia) and a rapid favourable evolution, a diagnosis of "crack lung" was made.
Fig. 21: Chest CT image at the level of the heart ventricles belongs to the patient in figure 20 and reveals pathologic right ventricular chamber enlargement consistent with pulmonary hypertension and secondary right ventricular cardiomyopathy.
**Fig. 22:** Figures 22, 23 and 24. Chest MDCT scan axial image (22) shows bilateral large-sized peripheral bullae in a 33-year-old heavy marijuana smoker. Sagital (23) and MiniP coronal (24) images reveal the apical predominance of this type of emphysema.
Fig. 23: Figures 22, 23 and 24. Chest MDCT scan axial image (22) shows bilateral large-sized peripheral bullae in a 33-year-old heavy marijuana smoker. Sagital (23) and MiniP coronal (24) images reveal the apical predominance of this type of emphysema.
**Fig. 24**: Figures 22, 23 and 24. Chest MDCT scan axial image (22) shows bilateral large-sized peripheral bullae in a 33-year-old heavy marijuana smoker. Sagital (23) and MiniP coronal (24) images reveal the apical predominance of this type of emphysema.
**Fig. 25:** Figures 25 and 26. #1 antitrypsin deficiency-like panlobular emphysema in a young male with a history of IV polydrug administration which included oral methylphenidate. Both lung-windowed (25) and MiniP (26) CT scan axial images demonstrate lower lobe-predominant simplification of the pulmonary architecture as well as abnormal low attenuation areas of the lung parenchyma.
Fig. 26: Figures 25 and 26. #1 antitrypsin deficiency-like panlobular emphysema in a young male with a history of IV polydrug administration which included oral methylphenidate. Both lung-windowed (25) and MiniP (26) CT scan axial images demonstrate lower lobe-predominant simplification of the pulmonary architecture as well as abnormal low attenuation areas of the lung parenchyma.
Conclusion

Recreational drug use has considerably risen worldwide in recent years, bringing about high consumption rates in most European countries. Consumption thus poses a substantial public health problem nowadays as it constitutes a major cause of morbidmortality among young European population. In fact, illicit drug use results in an important number of emergency department attendances. Medical consequences of drug abuse are diverse and include complications in almost any body organ, respiratory ones being among the most common.

Imaging techniques play a critical role in the detection and characterization of such complications. Radiologic findings of pulmonary drug-related diseases are often non-specific, though some patterns may strongly point to drug consumption in a given clinical setting, thus enabling clinicians to settle earlier and more accurate, aetiology-based therapeutic strategies.

Being aware of the dimension of the problem and taking all the formerly mentioned issues into account, we think it is essential for radiologists to be familiar with the physiopathology, clinical manifestations and imaging features of these complications.

Personal Information

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