Lung disease induced by drug addiction

Drug abuse refers to the non-medical "recreational" use of drugs, some of which results in physical or psychological dependence. Alcohol and nicotine are available legally and represent by far the most common form of drug abuse. The adverse effects on health and, more specifically, the respiratory consequences of cigarette smoking are widely recognised and represent a major burden on any health care system. Illicit use of drugs is widespread in some sections of society. The major health problems are largely the consequence of transmitted infection, especially HIV and hepatitis, which occurs in intravenous drug abusers who share needles. Here the AIDS-related respiratory consequences are widely known and include opportunistic infections, tuberculosis, and Kaposi's sarcoma.

There are several other potential adverse pulmonary effects of illicit drugs. Since these are relatively uncommon or unreported, many physicians are unlikely to encounter them unless they are working in areas where there is widespread drug abuse. Problems may arise as a direct consequence of the pharmacological effects of the drug, or be associated with the method by which it is administered. In general, drugs can be administered either orally, inhaled, or given parenterally, usually by the intravenous route. It is not surprising that ingested drugs are generally safer, whilst injected drugs carry the greatest health risk. Drugs which are inhaled are those most likely to result in respiratory symptoms. Various methods of inhalation are employed including nasal inhalation in powder form (for example, cocaine hydrochloride), smoking or igniting and inhaling the vapour (for example, marijuana, free-base cocaine (crack), and heroin), or inhaling the fumes from volatile substances (glue sniffing). The three classes of drugs most likely to cause respiratory problems include cocaine, marijuana, and opiates.

Cocaine

Cocaine is a stimulant drug which has been used in various forms for over 1000 years. It is extracted from the leaf of the shrub *Erythroxylon coca*. Casual or occasional cocaine abusers tend to inhale it in powder form, while more habitual users resort to intravenous use or smoking free-base cocaine. In western society it is available in two main forms. Cocaine hydrochloride is a crystalline salt available in solid form (rock), in smaller pieces (flake), or as powder. Casual users tend to resort to nasal inhalation (sniffing, snorting, tooting) although, being water soluble, it can also be used intravenously. In the mid 1980s free-base cocaine (crack) was developed and has now become the most popular form for many cocaine users. This is a waxy substance and, unlike cocaine salt, is readily vaporised. It can thus be smoked, often in special pipes, resulting in a rapid "high" since the inhaled cocaine comes in contact with a large surface area for absorption.

Inhalation of cocaine powder has long been recognised as a cause of ischaemia and necrosis of the nasal mucosa and sinuses, but respiratory problems arise more frequently from smoking free-base cocaine. Some of these problems might reasonably be anticipated from knowledge of the method of administration. Thus, the high levels of carbonaceous material found in sputum or lavage material are likely to result from the inhalation of non-volatile impurities present when crack is heated. The most common acute respiratory symptom, which usually develops within 1–2 hours of inhalation, is a cough productive of blackened sputum. Although acute bronchospasm has been reported, breathlessness and wheeze are relatively uncommon, even in habitual cocaine smokers. Chest discomfort, which occurs shortly after inhalation, is also commonly reported and, although it may have pleuritic features, the causal mechanism is uncertain. Haemoptysis occurs in about 5% of patients but is usually small in volume and transient. Thermal injury to the airway has been reported but is only likely to arise when ether is being used to extract free-base cocaine from an aqueous solution of the cocaine salt. The vigorous method of inhaling cocaine is likely to be responsible for a degree of barotrauma resulting in a number of reports of associated pneumomediastinum or pneumothorax.

Other acute effects on the lung parenchyma are also reported, although the clinical picture is variable and underlying mechanisms are not clearly understood. Syndromes described include eosinophilic infiltrates, diffuse alveolar haemorrhage, bronchiolitis obliterans with organising pneumonia, and pulmonary oedema. There are several reports of an acute illness which develops within a few hours of inhaling cocaine, the predominant clinical features of which are breathlessness, cough, and fever.

Chest radiographs have shown diffuse alveolar or interstitial infiltrates, but there seems to be no characteristic pattern. All patients had evidence of hypoxic respiratory failure and required additional inspired oxygen or assisted ventilation. One common but not invariably finding is the presence of a peripheral blood eosinophilia and, when taken, biopsy samples show an eosinophilic infiltrate in the bronchial mucosa or lung parenchyma. Despite an initial assumption that the illness was infective in origin, no organisms have been identified. In two patients there was spontaneous resolution, whereas in several others improvement was coincident with the introduction of steroids. The clinical features are compatible with a hypersensitivity reaction and the syndrome has recurred following the repeated use of cocaine.

Other syndromes are anecdotal. Murray et al reported a case, demonstrated on the lung biopsy sample, which was
associated with a significant haemoptysis and acute alveolar haemorrhage.\textsuperscript{13} Interstitial fibrosis was also present and it is of note that the patient also had a blood eosinophilia. A further case showed histological changes compatible with bronchiolitis obliterans organising pneumonia which occurred after inhaling cocaine.\textsuperscript{16} Clinical resolution followed steroid treatment. Cucco et al reported a case in which alveolar infiltrates resolved within 36 hours. In the presence of a normal lung biopsy sample it was assumed that the changes were due to pulmonary oedema.\textsuperscript{17}

None of the patients suffering from acute effects is reported to have sustained any long term sequelae. The main physiological effect of chronic cocaine abuse is a reduction in gas transfer, although the results are unlikely to be clinically significant.\textsuperscript{18} A possible mechanism is that of injury to the alveolar capillary membrane, a hypothesis supported by the increased clearance of inhaled technetium-99m labelled DTPA aerosol from the lungs of chronic cocaine users.\textsuperscript{19} Vascular changes in the form of pulmonary arterial medial hypertrophy have been shown pathologically.\textsuperscript{20}

Marijuana
Marijuana (cannabis) was first introduced to western Europe in the 19th century for its potential therapeutic effects in the treatment of epilepsy, asthma, and migraine. There is some evidence to suggest that it is an effective antiemetic for the control of nausea and vomiting related to chemotherapy. More commonly, cannabis is a frequently used "social" drug in which physical dependence is rarely encountered. Preparations are smoked, eaten, or drunk.

Cannabis is derived from Cannabis sativa, a native plant of Asia now grown all over the world. Sticky resin from the leaves and stem is the main source of the active compounds of which delta-9-tetrahydrocannabinol (delta-9-THC) is the major active pharmacological constituent. It is highly lipid soluble and rapidly absorbed from the respiratory and gastrointestinal mucosa. The bioavailability from smoking is 15–20% compared with approximately 6% orally. Smoking produces rapid effects within a few minutes of inhalation, whereas ingestion takes 1–3 hours before its effects are apparent.

Inhaled cannabis produces a degree of bronchodilatation in small airways and has been implicated as beneficial in the treatment of asthma. However, smoking marijuana is likely to have more detrimental than beneficial effects on the lungs. After chronic use it impairs gas exchange as shown by a reduction in single breath carbon monoxide diffusing capacity.\textsuperscript{21} This is similar in degree to that seen with tobacco smoking, but there may be an additional impairment in individuals who smoke tobacco and cannabis. Smoking a cannabis cigarette results in an approximately fivefold greater increase in carboxyhaemoglobin concentration than with a tobacco cigarette, with increases in the inhaled tar content and the amount retained in the respiratory tract.\textsuperscript{22} Deeper inhalation techniques and longer inspiratory times may partly explain these observations.

As with any material that is smoked, regular smoking of cannabis will cause bronchitis and squamous metaplasia of the tracheobronchial epithelium.\textsuperscript{23–27} The long term consequences of cannabis smoking are not clear as prospective epidemiological studies are not available. However, there is circumstantial evidence to suggest that emphysema and bronchogenic carcinoma may be associated with regular smoking of marijuana.\textsuperscript{28} Fatal invasive aspergillosis has been associated with smoking contaminated marijuana used illicitly as an anti-emetic in immunocompromised individuals.\textsuperscript{29, 30}

Opiates
Opioid analgesics abused for pleasurable or recreational purposes are numerous and include heroin, morphine, dextromoramide, pethidine, and pentazocine. The potent narcotic analgesic fentanyl and its analogues have been synthesised and sold as heroin substitutes. The most potent opioid analgesics are injected intravenously or smoked, although it should be remembered that body packing is an increasing hazard.

Characteristics features of overdose include impaired consciousness and respiratory depression. Non-cardiogenic pulmonary oedema is well recognised in association with increased capillary permeability.\textsuperscript{31} It is not clear whether this occurs as a result of a direct toxic effect on capillary membranes or secondary to tissue hypoxia. There are case reports of unilateral oedema of the lung associated with heroin overdose which may suggest a toxic effect related to the site of exposure.\textsuperscript{32} Overdoses of opiates are known to precipitate bronchospasm. Following repeated inhalations an acute eosinophilic pneumonia has been recorded.\textsuperscript{33} Presentation was with reduced lung volumes, airways hyperresponsiveness, diffuse pulmonary infiltrates, and bronchoalveolar lavage eosinophilia. Resolution occurred on abstinence and treatment with corticosteroids.

The intravenous abuse of heroin is associated with a different profile of lung injuries. Asymptomatic pulmonary vascular abnormalities have been detected on lung perfusion scanning,\textsuperscript{34} probably related to drug-induced pulmonary embolic disease which clearly may have long term sequelae. Bullous degeneration has been reported following intravenous opiate abuse.\textsuperscript{35} This usually presents with localised chest pain possibly due to air trapping. Bullae more usually occur in the upper lobes. Pulmonary atelectasis is a recognised complication of intravenous heroin use.\textsuperscript{36} This usually presents with fever, respiratory distress, and diffuse pulmonary infiltrates, and the presence of talc granulomas can be confirmed histologically. They originate from impure mixtures of injected opiates on the street.

Conclusions
It is difficult to obtain accurate information as to the prevalence of respiratory effects of drug abuse, especially those used illicitly. Minor symptoms are likely to go unreported. More seriously ill patients may be unwilling to volunteer information regarding drug abuse and a high index of suspicion is required. Illicit drugs are frequently adulterated and contain a variety of impurities and additives. Epidemiological studies are fraught with problems because many drug abusers will resort to a variety of drugs. Long term follow up studies are equally difficult and, even in those which have focused on chronic drug abusers, the duration of use has been a few years at most. Thus, a drug such as cannabis which is regarded as relatively harmless could, in the long term, have greater health risks than cigarette smoking. Much of the current information comes from the American literature where drug abuse is far more prevalent. However, British physicians should not be complacent and an awareness of potential problems is a prerequisite to their recognition.

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