Brief Review

Beyond pneumonoconiosis: Recently described occupational interstitial lung diseases

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SUMMARY. Recent technological innovations have resulted in the introduction of new substances in different manufacturing procedures. Unfortunately, lack of knowledge of the adverse effects of some novel substances has led to the development of interstitial lung disease (ILD) among exposed workers. Exposure to diacetyl can cause bronchiolitis obliterans ("popcorn lung"), while exposure to nylon flock, Acramin-FWN, indium-tin oxide, biomass fuels or nanoparticles is associated with ILD. In addition, hypersensitivity pneumonitis can occur after exposure to additives in animal feed. Finally, new applications of substances already known to be hazardous can result in the occurrence of ILD in exposed workers. *Pneumon 2010, 23(3):297-300.*

Key words:
- occupational interstitial lung disease
- work-related pulmonary fibrosis

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INTRODUCTION

The term 'occupational interstitial lung disease' usually refers to a number of pneumonoconioses, i.e. interstitial lung disease (ILD) due to exposure to inorganic substances, such as asbestos, in the workplace. The identification of hazardous substances and the understanding of the biological consequences of exposure resulted in a significant reduction of the prevalence of these disorders. The development of new technologies, however, has resulted in the introduction of new substances, or new applications of substances already known to he hazardous[1]. At first, new cases of ILD were often considered to be of idiopathic origin, which emphasizes the importance of seeking information about the occupational and environmental exposure to possibly hazardous substances in the medical history.

This review explores all recent reports of ILD of occupational origin, the occurrence of which was associated with exposure to novel substances

1. Bronchiolitis Obliterans due to diacetyl exposure

Diacetyl is a chemical of low molecular weight, used as a food additive to give a flavour of butter. Recent reports have associated diacetyl use with

bronchiolitis obliterans, a condition frequently referred to as "popcorn lung" because the first outbreaks of cases were reported among workers involved in the mixing and packaging of that product.[2] Individuals with other diacetyl exposure scenarios, such as work in confectionery, also appear to be at risk.[3,4]

The prognosis differs significantly from the bronchiolitis obliterans of the "silo-filler's lung", which is reversible and responds well to early treatment with steroids. In contrast, the prognosis in diacetyl-caused bronchiolitis obliterans is much worse, as a more insidious constrictive pattern develops, resulting in a condition that can be life-threatening and may require lung transplantation.

Apart from diacetyl exposure, bronchiolitis obliterans can be caused by an Asian herbal medicine derived from Sauropus.[5] In addition, an outbreak of bronchiolitis obliterans was recently reported among small craft boat builders who were using styrene containing "gelcoat" as a coating for fibreglass hulls[6].

2. Flock-associated ILD ('Flock-Workers Lung')

Lymphocytic bronchiolitis of occupational exposure was first reported among manufacturing workers heavily exposed to nylon flock (i.e., very short synthetic nylon fibres used in nonwoven applications)[7]. The first cases to be reported were initially described as desquamative pneumonia[8] and were attributed to an unspecified toxin exposure, rather than to the flock fibres. As subsequent cases emerged, the pathological findings appeared to be better characterized as lymphocytic bronchiolitis and peribronchiolitis, and were linked with exposure to flock.

Workers exposed to flock made of polyethylene, polypropylene, and rayon are also at risk of developing lymphocytic bronchiolitis[9-11]. The predominant risk factors are the short length of the synthetic fibres and the performance of work processes that generate substantial concentrations of airborne fibres.

The latency of flock-workers' ILD ranges between a few months and several years. It usually presents with gradually progressive dyspnoea, dry cough and constitutional symptoms. Some patients also demonstrate work-related symptoms, especially early in the process[7,12]. Pulmonary function tests typically reveal restriction and reduced diffusion. The most common findings on high resolution computed tomography (HRCT) of the chest are diffuse ground glass changes and centrilobular nodules giving an overall appearance very similar to hypersensitivity pneumonitis[13] Removal from exposure and corticosteroids comprise the recommended treatment[12-14].

3. Ardystil syndrome

Ardystil syndrome is a severe form of organizing pneumonia that was first described in textile workers exposed to a certain spray paint containing the chemical Acramin- FWN[15,16]. The syndrome latency ranges from one month to one year. Typical symptoms include epistaxis, dyspnoea, cough, and chest pain[17,18]. The prognosis is poor, as the lung disease is often severe and progressive, despite steroid treatment, leading in some cases to death[17].

4. ILD due to indium-tin oxide

Exposure to indium-tin oxide, a metal alloy used in the manufacture of liquid crystal or plasma flat panel display units, has been linked to alveolitis and pulmonary fibrosis among production workers.[19] The first reports of this novel form of pneumoconiosis came from Japan, where the majority of such manufacturing industries is concentrated,[19,20] but additional cases can occur through exposure during the recycling of these devices.

A recent report from Turkey describes the cases of interstitial lung disease among cottage industry workers lining copper pots with tin[21]. Although tin exposure is linked to a "benign" pneumoconiosis, this case cluster had CT findings suggestive of respiratory bronchiolitis-interstitial lung disease (RB-ILD).

The reported latency ranges from one to 5 years. Longer exposure and higher serum indium levels have been linked with more severe disease. HRCT findings include ground glass appearance, centrilobular nodules and emphysema[19,20,22] Histopathological examination reveals peribronchiolar fibrosis, foreign body giant cells and intraalveolar accumulation of macrophages containing brown particles composed of indium[20,22].

5. ILD due to nanoparticles

There is rising concern over the potential human respiratory health effects of a spectrum of engineered nanomaterials, particularly nanotubules and nanoparticles[23]. The seriousness of this potential new threat has been confirmed by a recent outbreak of severe pulmonary-pleural disease, with histopathologically confirmed, nanoparticle-laden epithelial cells, in factory workers who were heavily exposed to an aerosolized polyacrylate mixture. The histological examination revealed nanoparticles in the epithelial and mesothelial cells and in the pleural fluid[24].

6. ILD due to biomass fuels

It is already known that use of biomass fuels results in the occurrence of chronic obstructive pulmonary disease (COPD) in non-smoking women and lower respiratory tract infections in children[25]. There have also been reports of development of ILD after exposure to burning of biomass fuels, a condition known as "hut lung".[25,26] Bronchoscopy reveals a large number of anthracotic pigments in the airways. These pigments are also found in the interstitial tissue on histopathological examination. The patients develop progressive cough and dyspnoea, and their pulmonary function tests indicate a mixed disorder[27]. The chest X-ray shows reticulonodular or nodular infiltrates with preservation of the lung volume[27]. On HRCT the distribution of the nodules is seen to be centrilobular[28]. In advanced disease, massive lung fibrosis and cor pulmonale develop[26,27].

7. Hypersensitivity pneumonitis after exposure to animal feed

Phytoset, a relatively new additive in animal feed has been reported to be responsible for causing hypersensitivity pneumonitis[29].

8. Novel routes of exposure for established causes of ILD

Numerous substances of which the adverse effects on the respiratory system have been known for a long time continue to have novel applications, resulting in the occurrence of different lung disorders. An example of this is the epidemic of silicosis (which is considered a preventable disease) in Turkey among workers in jeans-manufacturing companies due to the sandblasting procedure that gives a “distressed” look, popular for consumer retailing[30].

CONCLUSIONS

Clinical physicians play an important role in diagnosing the abovementioned novel conditions; they should always be aware that the development of ILD may be due to workplace exposure to a hazardous substance. The diagnosis requires a high degree of clinical suspicion, and a detailed occupational and environmental history. Pharmaceutical treatment is similar to that for other forms of ILD, but in this case of occupational exposure the management includes removal from further exposure. What is more important though, is for measures to be taken for primary and secondary disease prevention, in

Table I. Recently described interstitial lung diseases of occupational origin

Risk factor	Disease	Occupational exposure
Diacetyl	Bronchiolitis obliterans	Food industry (especially popcorn manufacturing)
Nylon, polyethylene, polypropylene, rayon flock fibres	Lymphocytic bronchiolitis	Synthetic flock manufacturing
Acramin-FWN (synthetic spray paint)	Organizing pneumonia (Ardystil Syndrome)	Textile workers
Indium-tin oxide	Pulmonary fibrosis, alveolitis	Production of flat panel display units
Nanoparticles	Pulmonary fibrosis with pleural effusion	Nanoparticle aerosols
Biomass fuels	Interstitial lung disease	Domestic use for heating, cooking
Phytoset (Additive in animal feed)	Hypersensitivity pneumonitis	Animal breeding
Sand	Silicosis	Blue jeans manufacture

order to stop the occurrence of these diseases among the working population.

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