Interstitial lung diseases, also known as diffuse parenchymal lung diseases (DPLD), are a group of disorders involving the distal lung parenchyma. Diffuse parenchymal lung diseases are classified into four main groups, of which idiopathic interstitial pneumonias (IIP) are an important group of diseases. The terminology of idiopathic interstitial pneumonia is often confusing and it is called idiopathic pulmonary fibrosis (IPF) in the United States, cryptogenic fibrosing alveolitis (CFA) in the United Kingdom or idiopathic interstitial pneumonia in Japan. The landmark classification of chronic interstitial pneumonia was proposed by Leibow and Carrington in 1969. The new classification proposed by the American Thoracic Society (ATS) and the European Respiratory Society (ERS) has seven histological patterns: (i) usual interstitial pneumonia (UIP); (ii) non-specific interstitial pneumonia (NSIP); (iii) organizing pneumonia (OP); (iv) diffuse alveolar damage (DAD); (v) respiratory bronchiolitis (RB); (vi) desquamative interstitial pneumonia (DIP) and (vii) lymphoid interstitial pneumonia (LIP). The histological pattern of usual interstitial pneumonia is now reserved for the entity that is described as idiopathic interstitial pneumonia or cryptogenic fibrosing alveolitis. Idiopathic pulmonary fibrosis or cryptogenic fibrosing alveolitis is a distinctive type of chronic fibrosing interstitial pneumonia of unknown cause limited to the lungs in which a surgical lung biopsy shows a histological pattern of UIP. All other patterns proposed by the ATS/ERS are considered as separate entities.

**ABSTRACT**

Interstitial lung diseases, also known as diffuse parenchymal lung diseases (DPLD), are a group of disorders involving the distal lung parenchyma. Diffuse parenchymal lung diseases are classified into four main groups, of which idiopathic interstitial pneumonias (IIP) are an important group of diseases. The terminology of idiopathic interstitial pneumonia is often confusing and it is called idiopathic pulmonary fibrosis (IPF) in the United States, cryptogenic fibrosing alveolitis (CFA) in the United Kingdom or idiopathic interstitial pneumonia in Japan. The landmark classification of chronic interstitial pneumonia was proposed by Leibow and Carrington in 1969. The new classification proposed by the American Thoracic Society (ATS) and the European Respiratory Society (ERS) has seven histological patterns: (i) usual interstitial pneumonia (UIP); (ii) non-specific interstitial pneumonia (NSIP); (iii) organizing pneumonia (OP); (iv) diffuse alveolar damage (DAD); (v) respiratory bronchiolitis (RB); (vi) desquamative interstitial pneumonia (DIP) and (vii) lymphoid interstitial pneumonia (LIP). The histological pattern of usual interstitial pneumonia is now reserved for the entity that is described as idiopathic interstitial pneumonia or cryptogenic fibrosing alveolitis. Idiopathic pulmonary fibrosis or cryptogenic fibrosing alveolitis is a distinctive type of chronic fibrosing interstitial pneumonia of unknown cause limited to the lungs in which a surgical lung biopsy shows a histological pattern of UIP. All other patterns proposed by the ATS/ERS are considered as separate entities.

**INTRODUCTION**

Interstitial lung diseases, also known as diffuse parenchymal lung diseases (DPLD) are a group of disorders involving the distal lung parenchyma. Hamman and Rich in 1944 described several cases of “diffuse interstitial fibrosis of the lungs” which were rapidly progressive and fatal within a few weeks or months. Many cases of diffuse pulmonary fibrosis with a chronic course were then described. These cases were thought to be the chronic stage of Hamman–Rich syndrome and were termed as “idiopathic pulmonary fibrosis”. Subsequent studies had shown that Hamman–Rich syndrome had no chronic stage and the condition similar to this is now termed as acute interstitial pneumonia (AIP). There are more than 200 diseases with lung interstitial involvement with similar clinical, physiologic and radiographic manifestations. The important causes/categories of interstitial lung diseases are listed in Table 1. These disorders affect not only the interstitium, but also the airspaces, peripheral airways and vessels along with their respective epithelial and endothelial linings. Diffuse parenchymal lung diseases (DPLD) are classified into four groups: (1) DPLD of known causes; (2) idiopathic interstitial pneumonias (IIP); (3) granulomatous DPLD and (4) DPLD with well defined clinicopathologic features (Table 2).

**IDIOPATHIC INTERSTITIAL PNEUMONIAS**

The terminology of idiopathic interstitial pneumonias (IIP) varies from country to country and is often confusing. It is called idiopathic pulmonary fibrosis (IPF) in the United States, cryptogenic fibrosing alveolitis (CFA) in the United Kingdom or idiopathic interstitial pneumonia in Japan. In our country, it is termed either as IPF or CFA.

The landmark classification of chronic interstitial pneumonia was proposed by Leibow and Carrington in 1969. They described five types of chronic interstitial pneumonias: (i) usual interstitial pneumonia (UIP), (ii) bronchiolitis obliterans with interstitial pneumonia (BIP), (iii) desquamative interstitial pneumonia (DIP), (iv) lymphoid interstitial pneumonia (LIP) and (v) giant cell interstitial pneumonia (GIP). Subsequently, Katzenstein and Muller and Colby provided classifications that retained UIP and DIP as distinct entities and added new entities such as respiratory bronchiolitis associated interstitial lung disease (RB–ILD), bronchiolitis obliterance organizing pneumonia (BOOP), acute interstitial pneumonia (AIP), and non-specific interstitial pneumonia (NSIP). The terms GIP and LIP were omitted from their classifications because GIP was found to be associated with hard metal pneumoconiosis and LIP was found to develop into...
In order to avoid confusion in the terminology of IIPs, a new comprehensive clinical-radiographic and pathologic classification is provided by the American Thoracic Society (ATS) and the European Respiratory Society (ERS). The classification proposed by the ATS/ERS has seven histological patterns: (i) usual interstitial pneumonia (UIP); (ii) organizing pneumonia (OP); (iii) diffuse alveolar damage (DAD); (iv) respiratory bronchiolitis (RB); (v) desquamative interstitial pneumonia (DIP) and (vi) lymphoid interstitial pneumonia (LIP). The histological patterns that conform to the final clinicoradiologic-pathologic diagnosis are provided in Table 4. The term UIP is generally reserved for patients in whom the lesion is idiopathic which is currently referred to as either IPF or CFA. Idiopathic pulmonary fibrosis or idiopathic pulmonary fibrosis with acute interstitial pneumonia (AIP) is generally used interchangeably with UIP. However, the term UIP is recommended by the ATS/ERS classification system for patients with usual interstitial pneumonia.

In Table 3, the previous classifications of idiopathic interstitial pneumonias by different investigators are listed. These classifications include:

- I. Classification by Leibow and Carrington
  - Usual interstitial pneumonia
  - Desquamative interstitial pneumonia
  - Bronchiolitis obliterans interstitial pneumonia
  - Lymphoid interstitial pneumonia
  - Giant cell interstitial pneumonia

- II. Classification by Katzenstein
  - Usual interstitial pneumonia
  - Desquamative interstitial pneumonia/respiratory bronchiolitis interstitial lung disease
  - Acute interstitial pneumonia
  - Non-specific interstitial pneumonia

- III. Classification by Muller and Colby
  - Usual interstitial pneumonia
  - Desquamative interstitial pneumonia
  - Bronchiolitis obliterans organizing pneumonia
  - Acute interstitial pneumonia
  - Non-Specific interstitial pneumonia

In Table 4, the new classification of idiopathic interstitial pneumonias is presented. The classification includes:

- Usual interstitial pneumonia
- Organising pneumonia
- Diffuse alveolar damage
- Respiratory bronchiolitis
- Desquamative interstitial pneumonia
- Lymphoid interstitial pneumonia

CFA is therefore a distinctive type of chronic fibrosing interstitial pneumonia of unknown cause limited to the lungs in which a surgical lung biopsy shows a histological pattern of UIP. All other histopathologic patterns (DIP, NSIP, RB-ILD, AIP, COP, and LIP) are considered separate entities and should not be included in the group of patients with IPF. Pathologic features of the chronic idiopathic interstitial pneumonias are given in Table 5.

**USUAL INTERSTITIAL PNEUMONIA (UIP)**
This is characterized by marked fibrosis with insidious onset, slow progression and poor prognosis. There is patchy involvement with areas of marked fibrosis, and areas of less fibrosis and more inflammation. It often progresses to end-stage disease or “honey-comb” lung. The distribution is frequently subpleural and paraseptal. It has a heterogeneous appearance at low magnification with alternating areas of normal lung, interstitial inflammation, fibrosis and honeycomb change. The interstitial inflammation consists of alveolar septal infiltrate of lymphocytes, plasma cells and histiocytes and is associated with hyperplasia of Type II pneumocytes. Smooth muscle hyperplasia is commonly seen in areas of fibrosis and honeycomb change.

**NON-SPECIFIC INTERSTITIAL PNEUMONIA (NSIP)**
Non-specific interstitial pneumonia is characterized by the uniform appearance of interstitial inflammation mainly with lymphocytes, and rarely with plasma cells in all areas of the biopsy specimen. Two patterns of NSIP are described: cellular pattern and fibrosing pattern. Mild to moderate interstitial chronic inflammation with Type II pneumocyte hyperplasia is seen in cellular pattern. Fibrosing pattern can lead to dense or loose interstitial fibrosis that lacks the temporal patchy features of UIP. The lung architecture in fibrosing pattern may appear lost on examination of hematoxylin and eosin stained sections, but there is preservation of elastic stains.

**CRYPTOGENIC ORGANISING PNEUMONIA (COP)**
Intraluminal organizing pneumonia in the distal air-spaces (bronchioles, alveolar ducts and alveoli) is the characteristic finding in cryptogenic organizing pneumonia. There is mild interstitial inflammation with patchy distribution and preserved lung architecture. The same entity is also referred to as bronchiolitis obliterans organizing pneumonia (BOOP). However, the term cryptogenic organizing pneumonia is preferred.

**RESPIRATORY BRONCHIOLITIS ASSOCIATED INTERSTITIAL LUNG DISEASE (RB-ILD)**
Respiratory bronchiolitis associated interstitial lung disease is found in cigarette smokers. There is focal bronchiolar-alveolar macrophage accumulation and the macrophages are usually pigmented. The macrophages are seen within first- and second-order respiratory bronchioles. There is only mild bronchiolar fibrosis and chronic inflammation. It is rarely symptomatic and is associated with minor small airway dysfunction. It has been suggested that desquamative interstitial pneumonia is a more extensive form of RB-ILD.

**DEQUAMATIVE INTERSTITIAL PNEUMONIA (DIP)**
There is only mild interstitial fibrosis and the macrophages are uniformly distributed predominantly in the alveoli. The alveolar macrophages are non-pigmented as opposed to the pigmented macrophages seen in RB-ILD. Many consider that it represents the end of a spectrum of RB-ILD because of its similar pathology and association with cigarette smoke, both active and passive.

**LYMPHOID INTERSTITIAL PNEUMONIA (LIP)**
There is diffuse interstitial infiltration of T lymphocytes which may be grouped into germinal centers. There is predominant alveolar septal distribution.

**ACUTE INTERSTITIAL PNEUMONIA (AIP)**
The original description of Hamman-Rich syndrome falls in this category and it is a rare fulminant form of lung injury presenting acutely usually in a previously healthy individual. There is diffuse alveolar damage (DAD) and this is indistinguishable from acute respiratory distress syndrome (ARDS) caused by sepsis and shock. The term AIP is reserved for cases of unknown cause. Histological features reveal exudative, proliferative and or fibrotic phases of diffuse alveolar damage. There may be patchy or diffuse airspace organization. Focal or diffuse hyaline membranes may also be seen.
A small subset of patients with interstitial pneumonia remains unclassified even after extensive clinical radiological and/or pathologic evaluation.

REFERENCES