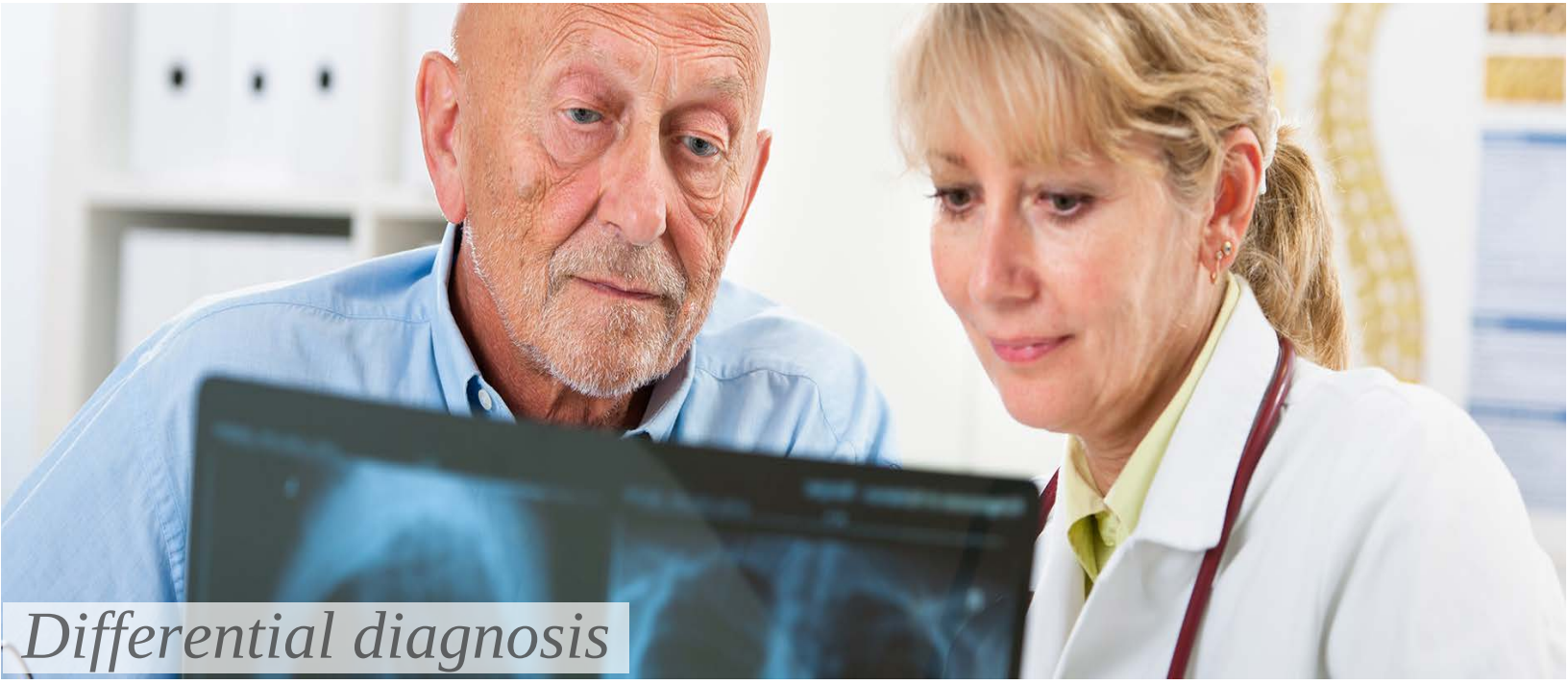
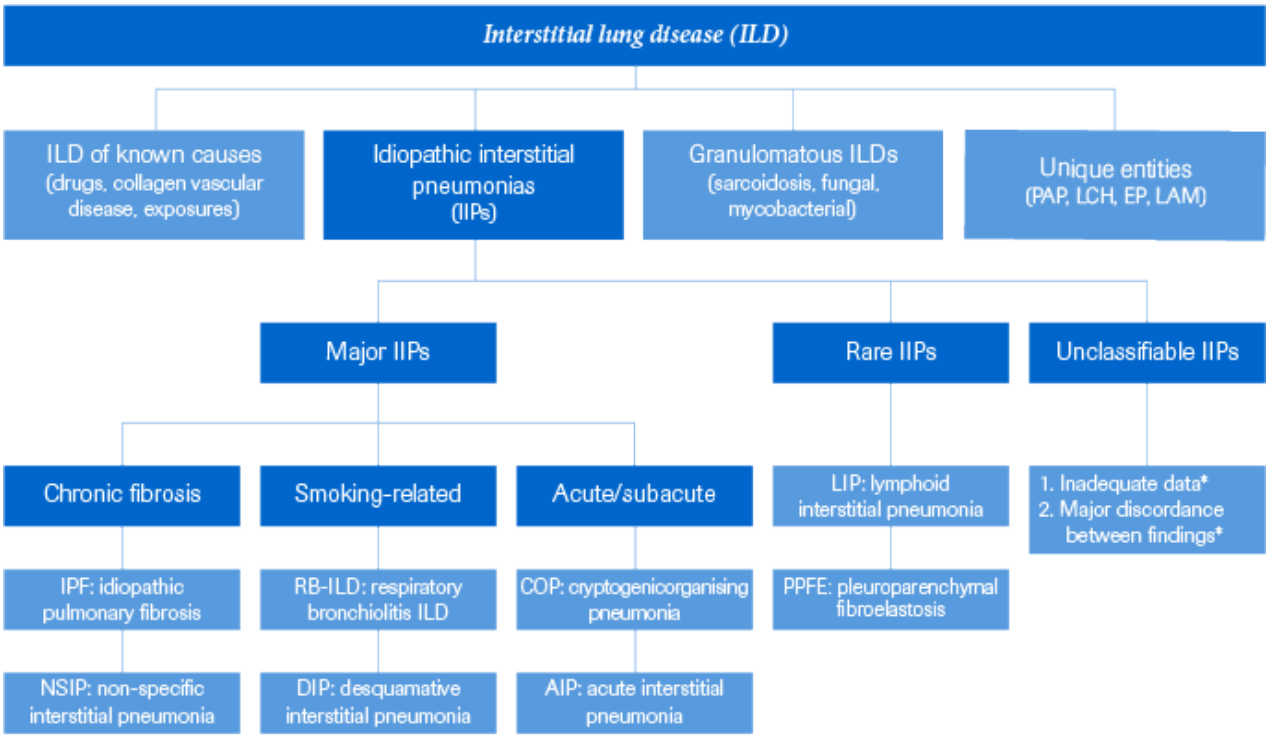


Differential diagnosis

Idiopathic pulmonary fibrosis (IPF) is part of a large family of idiopathic interstitial pneumonias (IIP), one of four subgroups of interstitial lung disease (ILD). Differential diagnosis is required to define the specific disease amongst related ILDs as well as other conditions with similar presentations.[1,2]

IPF is a form of IIP[3]



** Causes of unclassifiable idiopathic interstitial pneumonia include (1) inadequate clinical, radiologic or pathologic data and (2) major discordance between clinical, radiologic and pathologic findings.*

EP, eosinophilic pneumonia; LAM, lymphangioleiomyomatosis; LCH, Langerhans' cell histiocytosis; PAP, pulmonary alveolar proteinosis.

To begin making a diagnosis, a complete clinical assessment is required, including a full physical work-up and an in-depth patient history (medical, familial, occupational and environmental).[1,2,4]

It is important to understand the radiological and histopathological features that separate different fibrotic lung diseases.[1] This is especially vital in certain situations where the treatment of one disease (e.g. immunotherapy for hypersensitivity pneumonitis) can worsen treatment outcomes in patients with another disease, such as IPF.[4]

Features suggestive of non-IPF fibrotic lung disease[1,4-8]

Non-specific interstitial pneumonia

- Radiological
  - Symmetrical bilateral ground glass opacities with fine reticulations
  - Lack of macroscopic honeycombing
- Other
  - Presence of auto-antibodies if secondary to an underlying connective tissue disease

Hypersensitivity pneumonitis

- Radiological
  - Areas of decreased attenuation
  - Centrilobular nodules
  - Mid-upper lobe predominance
- Histopathological
  - Cellular interstitial pneumonia
  - Multinucleated giant cells or granulomas situated around bronchioles

Desquamative interstitial pneumonia

- Radiological
  - Ground glass opacities
  - Restrictive pattern on PFTs
  - No scarring fibrosis

Respiratory bronchiolitis (ILD)

- Radiological
  - Diffuse fine nodular or reticular changes on chest CT
  - Combined obstruction end restriction on pulmonary function tests

Cryptogenic organising pneumonia

- Clinical
  - Systemic manifestation of weight loss, fever, joint symptoms and rash are more common
- Radiological
  - Patchy consolidation, isolated nodules or infiltrative reticulation on chest CT

Asbestosis

- Radiological
  - Plaques and/or significant pleural thickening
  - Limited extent
- Histopathological
  - Pleural abnormalities
  - Asbestos bodies
  - Bronchial wall fibrosis
  - Fibroblastic foci infrequent

Sarcoidosis

- Radiological
  - Fibrosis, linear opacities and traction bronchiectasis predominantly in the perihilar regions and upper lobes
  - Conglomerate masses of fibrosis in the posterior part of the lungs
  - Small well-defined nodules with a perilymphatic distribution
- Histopathological
  - Non-caseating granulomas with a characteristic perilymphatic distribution

Connective tissue disease

- Radiological
  - Bronchiectasis far from fibrotic areas
  - Signs of pulmonary hypertension disproportionate to the extent of fibrosis
  - Pleural or pericardial effusion
  - Oesophagus or bone abnormalities
- Histopathological
  - Dense perivascular collagen
  - Extensive pleuritic
  - Lymphoid aggregates with germinal centre formation
  - Prominent plasmacytic infiltration

BAL in differential diagnosis

Bronchoalveolar lavage (BAL) is a useful addition to other diagnostic tools when a number of differential diagnoses are possible.[4] The procedure collects cells from a small area of the lung via a bronchoscope—the proportions of different cell types collected can inform a potential diagnosis or help to rule out some diagnoses.[1,4,9] The use of BAL on its own is non-specific for particular ILDs when taken in isolation; but when assessed in conjunction with other clinical and radiological findings, it can assist in narrowing diagnosis. This may also avoid some patients having to undergo a lung biopsy.[4,9]

BAL is of particular use in differentiating IPF from hypersensitivity pneumonia (HP), as chronic HP can mimic IPF so closely in clinical and radiological factors.[1,4,9] BAL provides cell profiles extracted from the lungs that are known to be different between the two diseases.

BAL profiles for IPF differential diagnosis[4,10,11]

IPF

- Moderately increased neutrophil count (10-30% of total cells); increase seen in 70-90% of patients
  - With or without eosinophil count increase; increase seen in 40-60% of patients
- Neutrophil count usually twice as high as eosinophil count
- Moderately increased (<30%) lymphocyte count; seen in 10-20% of patients
  - An isolated marked increase in lymphocytes is inconsistent with IP

Hypersensitivity pneumonia

- Highest total cell count and highest lymphocyte count of all ILDs
- Cell count yield from 100 mL BAL: >20 million
  - Lymphocytes exceeding 50% of total cell count
- Lymphocyte increase less prominent in patients with radiological aspects of fibrotic UIP or non-specific IP
- Increase in activated T-cells
- Decreased CD4/CD8 ratio
- Neutrophil count may transiently increase during an acute episode

Asbestosis

- High counts of asbestos bodies are more likely in patients with asbestosis

Sarcoidosis

- Elevated total cell count
- Predominantly lymphocytes
- Eosinophil and neutrophil percentage close to normal
- Absence of plasma cells

Rheumatoid arthritis (connective tissue disease)

- Highly variable and non-specific
- Increase in either lymphocytes or granulocytes
- Lymphocytes more prominent than in systemic sclerosis

Importance of the MDT

Due to the complexities of diagnosing IPF, involvement of the entire multidisciplinary team (MDT) is important. As clinical, radiological and histopathological data all have to be analysed to make an accurate assessment, the pulmonologist, thoracic radiologist and thoracic histopathologist need to work closely together. An experienced MDT is able to provide a more accurate diagnosis, minimising uncertainty by providing integration of each data set.[1,12-14]

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