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The classification, natural history and radiological/histological appearance of idiopathic pulmonary fibrosis and the other idiopathic interstitial pneumonias

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ABSTRACT: The idiopathic interstitial pneumonias (IIPs) are a heterogeneous group of rare interstitial lung diseases (ILDs) or diffuse parenchymal lung diseases, which, as their name implies, are of unknown aetiology. The past 10 yrs have seen important advances in the classification of the IIPs into idiopathic pulmonary fibrosis (IPF) and its corresponding histopathological pattern of usual interstitial pneumonia (UIP), plus six non-IPF IIP subtypes.

The present article will look at the current classification of IIPs, arising from the Consensus Statement of the American Thoracic Society and European Respiratory Society, and discusses the importance of differential diagnosis of IPF from the non-IPF IIP subtypes, especially nonspecific interstitial pneumonia. Diagnosis of IIPs is a dynamic process involving close collaboration between pulmonologists, radiologists and pathologists.

Increasingly accurate diagnosis of IPF has been made possible by the use of high-resolution computed tomography (HRCT) and refinements in surgical lung biopsy. In IPF, a lung HRCT will typically reveal irregular reticular opacities, traction bronchiestasis and, most importantly, peripheral honeycombing. In contrast, histological examination shows evidence of UIP manifesting as typically subpleural and paraseptal established fibrosis, often with honeycomb changes, associated with mild chronic inflammation and varying numbers of fibroblastic foci in continuity with the edges of areas of established fibrosis.

Despite these advances, obtaining a consistent and uniform diagnosis of idiopathic interstitial pneumonias is difficult, with studies showing significant disagreement in the diagnosis of interstitial lung diseases between academic centres of expertise and community-based clinicians. Greater interaction between academic and community clinicians, together with improved education, is needed to bridge this gap.

KEYWORDS: Idiopathic pulmonary fibrosis, nonspecific interstitial pneumonia, usual interstitial pneumonia

The idiopathic interstitial pneumonias (IIPs) are a heterogeneous group of rare interstitial lung diseases (ILDs) characterised by damage to the lung parenchyma arising from the effects of inflammation and fibrosis. While the interstitium is the primary site of injury in IIPs, the airspaces, peripheral airways and vessels are also commonly involved [1].

As a group, the IIPs are distinct from ILDs of known aetiology, such as collagen vascular diseases, inherited disorders (tuberous sclerosis, Hermansky-Pudlak Syndrome, neurofibromatosis, metabolic storage disorders and familial pulmonary fibrosis) and diseases due to drug, occupational and environmental exposures, as well as from unknown causes, such as granulomatous diseases (sarcoidosis and hypersensitivity pneumonia), iatrogenic conditions and unique entities such as Langerhans cell granulomatosis, lymphangioleimyomatosis, alveolar proteinosis and idiopathic capillaritis [2].

The present article will look at the current classification of the IIPs and the importance of distinguishing usual interstitial pneumonia (UIP) associated with idiopathic pulmonary fibrosis (IPF) from other IIPs, especially in the context of clinical studies.

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CLASSIFICATION AND NATURAL HISTORY OF IIPS

Before the International Consensus Statement on IIPs was formed by the American Thoracic Society (ATS) and the European Respiratory Society (ERS) [2], there was a notable lack of consistency in the classification of IIPs, although attempts at classifying IIPs date back to the late 1960s [3]. At present, following the publication of the guidelines, IIPs are now subdivided simply into IPF and non-IPF IIPs (table 1). This is an important bifurcation point in the classification of IIPs, since IPF is both diagnostically and prognostically distinct from non-IPF IIPs. As currently defined, IPF is not a systemic disorder but a distinctive type of chronic fibrosing interstitial pneumonia of unknown aetiology, limited to the lungs and associated with a surgical lung biopsy (SLB) showing a histological pattern of UIP [2]. The ATS/ERS classification emphasises the distinction between the morphological pattern of UIP, identified by imagers and pathologists, and the associated idiopathic clinical syndrome, to which the term IPF is applied when potential causes of the UIP pattern (*e.g.* collagen vascular disease and hypersensitivity pneumonia) have been excluded. Although IPF remains relatively uncommon, there is epidemiological evidence to suggest that incidence is increasing in both the USA and the UK. GRIBBIN *et al.* [4] documented a change in incidence from 27.3 to 67.8 cases per million over the period 1991–2003. Whether this increase in incidence is due to greater awareness of the disease on the part of pulmonary and general physicians, or to environmental factors, remains to be established.

IPF, the most common of the IIPs [2], typically occurs in people aged $\geqslant$50 yrs. It has an insidious onset characterised by unexplained dyspnoea, especially on exertion, and nonproductive cough that develops over a period of ~3 months [5, 6]. In most patients, IPF follows a progressive course, eventually leading to peripheral oedema and right heart failure. With 5-yr mortality approaching 70% [7], prognosis is poor, worse in fact than most other ILDs [6]. Prognosis is particularly poor in patients with pre-existing IPF who develop an acute exacerbation or deterioration in their condition over a very short period of time [8]. Such patients, in whom there is no evidence of an identifiable cause such as infection, cardiovascular or thrombotic disease, display: rapid worsening in dyspnoea and hypoxia within 1 month of presentation; new pulmonary alveolar infiltrates on chest radiographs or high-resolution computed tomography (HRCT) scans; and diffuse alveolar damage superimposed on the more chronic changes of UIP on histology [9].

In contrast to IPF, the non-IPF IIPs cover a spectrum of disorders that include desquamative interstitial pneumonia (DIP), respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), acute interstitial pneumonia (AIP), cryptogenic organising pneumonia (COP), lymphoid interstitial pneumonia (LIP) and nonspecific interstitial pneumonia (NSIP; table 1) [2, 10]. Understanding of NSIP is still evolving, and it appears that many cases are likely to be due to or associated with several aetiologies, including collagen vascular diseases, hypersensitivity pneumonia and drug toxicity, whilst truly idiopathic cases are relatively rare [10]. Its presence in the classification scheme is justified by the fact that NSIP is characterised by a much more favourable prognosis in comparison with IPF [7]. Importantly, patients with NSIP are often responsive to treatment with corticosteroids, unlike their IPF counterparts (table 2) [10]. Clearly, differentiating IPF from NSIP and other non-IPF IIPs is an essential part of the differential diagnosis of IIPs.

DIAGNOSIS OF IIPS

Accurate diagnosis of IPF is essential in light of the prognostic differences that exist between the IIPs. Currently, clinical diagnosis of IIPs is based on a detailed medical history together with a physical examination. Indeed, early recognition of IPF often starts with a high level of clinical suspicion and good clinical acumen. Chest radiographs and lung function tests follow. HRCT is performed in those patients in whom IIP is suspected. As discussed in detail below, HRCT is now an integral part of the diagnostic process for IIPs (fig. 1), an iterative process in which pulmonologists, radiologists, thoracic surgeons and pathologists all play a key role. Although radiological diagnosis by HRCT may eliminate the need for SLB in as many as 50% of patients with IIP [11, 12], histological diagnosis by SLB remains the definitive procedure for excluding other disease processes that can mimic IPF, particularly hypersensitivity pneumonia [2].

Clinically, IPF is strongly suspected in any patient aged $\geqslant$50 yrs presenting with unexplained dyspnoea on exertion that has been present for a period of $\geqslant$3 months, and with evidence of bibasilar, inspiratory ''velcro-like'' crackles on chest auscultation. In addition to the presence of at least three of these minor diagnostic criteria, patients must meet all four

TABLE 1 Classification of the idiopathic interstitial pneumonias (IIPs)

	Clinicopathological diagnosis	Histological patterns
IPF	IPF/cryptogenic fibrosing alveolitis	Usual interstitial pneumonia
Non-IPF IIPs	Nonspecific interstitial pneumonia (provisional)	Nonspecific interstitial pneumonia
	Cryptogenic organising pneumonia	Organising pneumonia
	Acute interstitial pneumonia	Diffuse alveolar damage
	Respiratory bronchiolitis interstitial lung disease	Respiratory bronchiolitis
	Desquamative interstitial pneumonia	Desquamative interstitial pneumonia
	Lymphoid interstitial pneumonia	Lymphoid interstitial pneumonia

IPF: idiopathic pulmonary fibrosis. Modified from [2] with permission from the publisher.

TABLE 2 Distinguishing clinical and radiographical features of idiopathic pulmonary fibrosis and nonspecific interstitial pneumonia

	Idiopathic pulmonary fibrosis	Nonspecific interstitial pneumonia
Duration of illness	Chronic (>12 months)	Subacute to chronic
Frequency of diagnosis	47–64%	14–36%
Treatment	Poor response to any treatment	Corticosteroid responsiveness
Prognosis	50–70% mortality within 5 yrs	<15% mortality in 5 yrs
Chest radiograph	Bilateral reticular opacities in lower zones; volume loss plus honeycombing	Bilateral hazy and reticular opacity
HRCT	Peripheral, subpleural, basal predominance; reticular opacities; honeycombing; traction bronchiectasis; architectural distortion	Peripheral, basal, symmetrical; ground-glass attenuation; consolidation; traction bronchiectasis; lower lobe volume loss
Key histological features	UIP pattern	NSIP pattern: cellular, fibrotic

HRCT: high-resolution computed tomography; UIP: usual interstitial pneumonia; NSIP: nonspecific interstitial pneumonia.

major criteria, these include: 1) the exclusion of other known causes of ILD; 2) abnormal pulmonary function tests with evidence of restriction and impaired gas exchange; 3) bibasilar reticular abnormalities with minimal ground-glass opacities on lung HRCT; and 4) transbronchial lung biopsy or bronchoalveolar lavage without features to support an alternative diagnosis [6]. While a normal chest radiograph does not exclude the presence of IPF, radiographic evidence of reticular opacities, reduced lung volume and honeycombing is highly suggestive. An alternative diagnosis to IPF is more likely if there is radiographic evidence of confluent alveolar opacities, pleural disease or significant lymphadenopathy.

HRCT IN THE DIAGNOSIS OF IIPS

The introduction of HRCT has had a major impact on the diagnosis of ILDs. HRCT is part of the standard of care in all but a small proportion of patients for whom chest radiograph findings are definitive [6]. Its primary role is to separate patients with UIP from those with less specific findings associated with NSIP and other non-IPF IIPs.

In a patient with fibrotic lung disease, the HRCT will typically reveal evidence of reticular abnormality, characterised by a fine, lace-like network of lines, often accompanied by subpleural irregularity, architectural distortion, traction bronchiectasis and honeycombing. Architectural distortion is an inevitable consequence of moderate or advanced fibrosis, along with crowding of vessels and lower lobe volume loss. Traction bronchiectasis is also a useful indicator of fibrotic lung disease. The most valuable indicator of fibrotic lung disease is honeycombing, which manifests as clusters of cysts that lie in single or multiple layers in the subpleural region of the lungs. Ground-glass opacity is relatively uncommon in patients with fibrotic lung disease, and more commonly indicates an inflammatory, potentially treatment-responsive condition, such as hypersensitivity pneumonia, DIP or respiratory bronchiolitis. However, when ground-glass opacity is associated with a fine reticular abnormality or traction bronchiectasis, a fibrotic lung condition such as NSIP or UIP should be considered.

Imaging criteria for the diagnosis of UIP on HRCT includes the presence of a bilateral, predominantly basal, predominantly subpleural reticular abnormality. Although reticular abnormality is usually the most salient feature, this can be seen in any fibrotic diffuse lung disease, and thus is fairly nonspecific for UIP. Honeycombing, however, is a much more specific feature of UIP (fig. 2). Additional important criteria for UIP include absence or paucity of ground-glass abnormality as well as absence of nodules, consolidation and cysts. The absence of lobular mosaic attenuation or air trapping is also important, as these findings should strongly suggest the diagnosis of chronic hypersensitivity pneumonia [13]. On serial computed tomography (CT) evaluation of patients with UIP, ground-glass abnormality (when present) tends to progress inexorably to a more reticular pattern with architectural distortion, while areas of reticular abnormality also tend to progress and increase over time. Areas of honeycomb cysts tend to enlarge and increase in extent, suggesting that HRCT is useful not only for radiological diagnosis but also for identifying disease progression in UIP.

A succession of studies has found that when radiologists make a first-choice diagnosis of UIP they are correct in 85–90% of cases. A confident diagnosis of UIP, based on typical CT features, including honeycombing, has a positive predictive value of >90% [11, 12, 14–16].

However, some 30–50% of cases of histologically confirmed UIP remain in which a confident radiological diagnosis cannot be made and these cases will continue to be diagnosed by SLB. The critical element in accurate diagnosis of UIP is the presence or absence of lower lobe honeycombing. The presence of honeycombing on lung HRCT correlates well with the presence of honeycombing on lung biopsy and can be used both to predict the diagnosis and indicate the likely prognosis. In a study of 91 patients with suspected IPF, HUNNINGHAKE *et al.* [17] found that lower-lobe honeycombing was present in 79% of those with UIP compared with 25% of those without; by far the strongest predictive factor for the presence of UIP on HRCT (table 3). In the study by HUNNINGHAKE *et al.* [17], radiologists were confident of their diagnosis in 52 (57%) patients. A confident diagnosis of UIP was correct in 26 (96%) out of 27 patients and a confident diagnosis of non-UIP was correct in 21 (84%) out of 25 patients.

Although the presence of lower-lobe honeycombing is among the most valuable criteria for distinguishing between UIP and

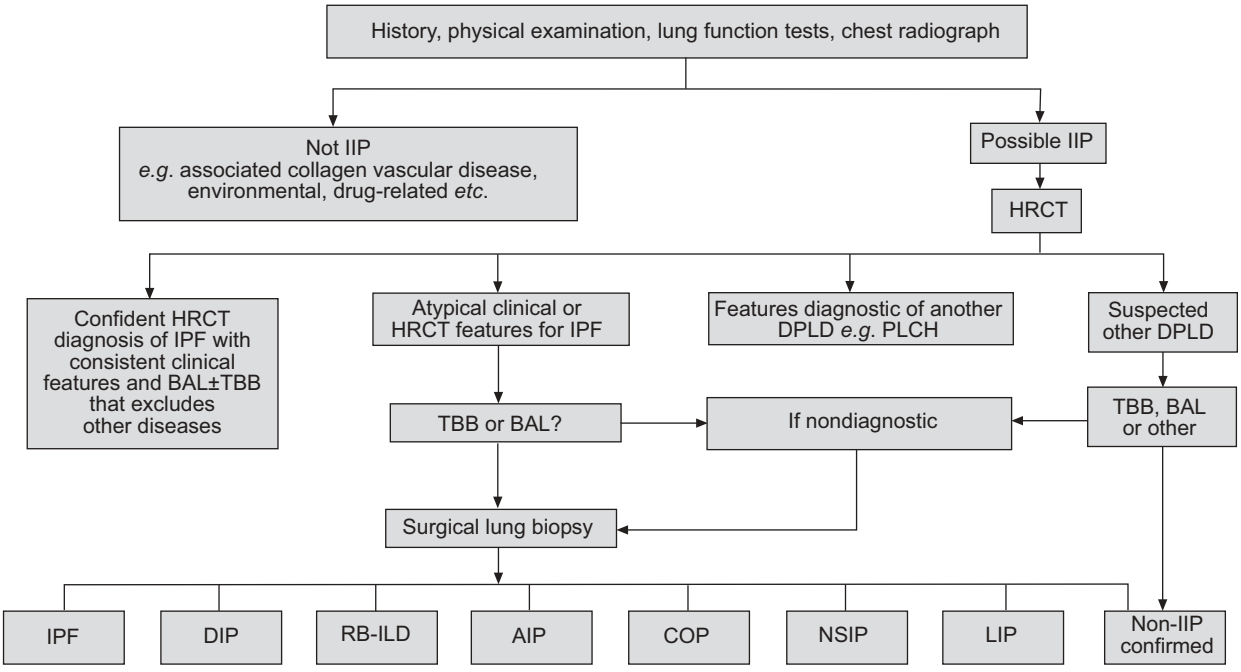

FIGURE 1. Procedure for the diagnosis of interstitial lung diseases. IIP: idiopathic interstitial pneumonias; HRCT: high-resolution computed tomography; IPF: idiopathic pulmonary fibrosis; BAL: bronchoalveolar lavage; TBB: transbronchial biopsy; DPLD: diffuse parenchymal lung diseases; PLCH: pulmonary Langerhans cell histiocytosis; DIP: desquamative interstitial pneumonia; RB-ILD: respiratory bronchiolitis-associated interstitial lung disease; AIP: acute interstitial pneumonia; COP: cryptogenic organising pneumonia; NSIP: nonspecific interstitial pneumonia; LIP: lymphoid interstitial pneumonia. Modified from [2] with permission from the publisher.

NSIP, studies have identified a substantial number of cases in which the HRCT features of histological UIP and histological NSIP overlap. The proportion of such patients is projected to rise as fewer typical UIP cases are subject to SLB. In a study of 96 patients, of whom 73 had a histological diagnosis of UIP, FLAHERTY *et al*. [18] found that 27 (37%) of these patients had a definite radiological diagnosis of UIP, 20 (27%) had an indeterminate radiological diagnosis and 26 (36%) had a definite radiological diagnosis of NSIP. In the 23 patients with histologically confirmed NSIP, there were no radiological diagnoses of UIP, five (22%) indeterminate cases and 18 (78%) definite cases of NSIP [18]. Median survival was notably poorer in the 27 patients with HRCT-confirmed UIP than in those with a histological diagnosis of UIP and an atypical HRCT for UIP (median survival: 2.08 and 5.76 yrs, respectively). These findings suggest that a positive radiological diagnosis of UIP with honeycombing confers an adverse prognosis.

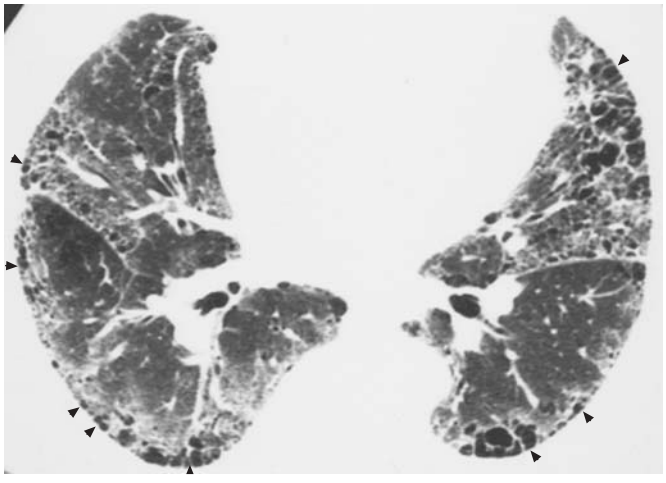

FIGURE 2. A computed tomography image through the lower lungs in a patient with idiopathic pulmonary fibrosis showing predominantly subpleural honeycombing (arrowheads).

While a confident clinical diagnosis of IPF can be obtained from clinical and radiological findings in $\geqslant$50% of patients, any patient with an atypical clinical presentation or with an indeterminate or atypical HRCT needs a histologically confirmed diagnosis. SLB provides a similar diagnostic yield to traditional open lung biopsy (thoracotomy) but with much lower comorbidity. To maximise diagnostic yield, surgical biopsies need to be obtained from more than one lobe and from at least two to three sites based on HRCT evidence, avoiding tips of the lingula and right middle lobe [19]. They should also include samples of apparently normal and abnormal lung parenchyma.

IMAGING PATTERNS IN OTHER FORMS OF IIPS

NSIP often has a recognisable appearance on HRCT, characterised by basal predominant ground-glass and reticular abnormality, usually associated with traction bronchiectasis and lower-lobe volume loss [10]. Sparing of the immediate subpleural region can help distinguish this entity from UIP. Use of such criteria in a recent study resulted in a positive predictive value of 90% for a confident HRCT diagnosis of NSIP [13].

RB-ILD and DIP, both smoking-related lung diseases, are characterised by a combination of ground-glass abnormality

TABLE 3 Multivariate analysis of factors associated with a confirmed pathological diagnosis of usual interstitial pneumonia

HRCT finding	OR (95% CI)	p-value
Irregular lines upper lobe	6.28 (1.80–21.89)	0.004
Honeycombing lower lobe	5.36 (1.58–18.22)	0.007

HRCT: high-resolution computed tomography; OR: odds ratio; 95% CI: 95% confidence interval. Modified and reproduced from [17] with permission from the publisher.

and centrilobular nodularity. The ground-glass abnormalities tend to be patchier in RB-ILD and more diffuse in DIP [20]. Another useful clue to DIP is the presence of small cysts within the areas of ground-glass abnormality.

The organising pneumonia pattern, as its name would suggest, is characterised by the salient feature of consolidation, often multifocal and sometimes migratory [21]. There may be associated ground-glass abnormality. The distribution is usually either subpleural or peribronchovascular, and bronchial dilation may be present.

The features of AIP are the same as those of acute respiratory distress syndrome (ARDS), characterised by patchy consolidation in the dependent lung, with ground-glass abnormality in less dependent areas [22]. Some patients with AIP have honeycombing, perhaps indicating underlying UIP [23]. In the organising or fibrotic phases of AIP, traction bronchiectasis may develop.

Ground-glass abnormality is the salient feature of LIP. However, a more specific feature, seen in a substantial proportion of cases, is the presence of discrete thin-walled cysts [24].

HISTOLOGICAL PATTERNS IN UIP AND OTHER FORMS OF IIPS

As mentioned previously, the current ATS/ERS consensus classification of the IIPs recognises seven separate clinicopathological diagnoses, each of which has a corresponding histopathological pattern (table 1) [2].

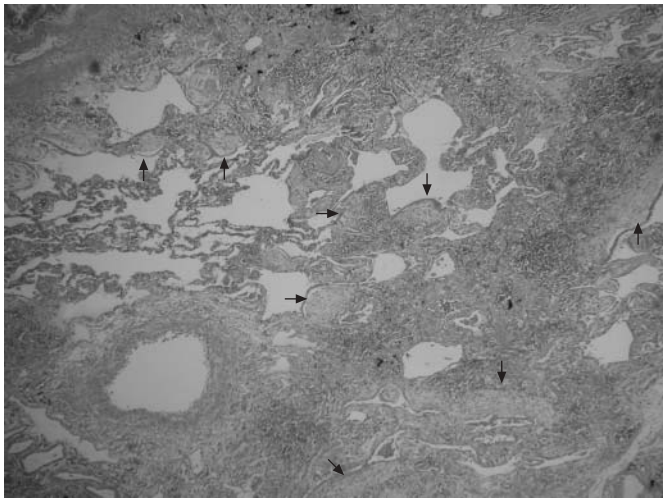

FIGURE 3. Histology slide demonstrating fibroblastic foci (arrows), a cardinal feature of usual interstitial pneumonia.

UIP is the defining histological pattern of IPF. That said, while the majority of cases of UIP are seen in this context, it is not unique to IPF but may also occur in connective tissue diseases (such as scleroderma), asbestosis and hypersensitivity pneumonia. In a surgical lung biopsy from a patient with UIP, low-power examination reveals fibrotic zones of dense collagen with a typically subpleural and paraseptal distribution, a sharp demarcation between normal lung and abnormal honeycomb lung, and comparatively little nonspecific chronic inflammation when compared with other IIPs [2]. On higher magnification, varying numbers of fibroblastic foci, a cardinal feature of UIP, are evident (fig. 3). These appear as areas of loose fibroblastic proliferation, either re-epithelialising or de-epithelialising, that are highly interconnected on sequential sectioning. It is a reactive rather than a malignant process. The fibroblastic foci are of lower vascularity than the intra-alveolar foci of fibroblastic proliferation seen in organising pneumonia and inflammatory cells are typically seen in areas of established fibrosis rather than the fibroblastic areas. These findings, amongst others, have led to the view that, although inflammation still has a role in pathogenesis, there may be significant epithelial–mesenchymal interaction in UIP as a response to repetitive alveolar epithelial injury and an altered alveolar microenvironment.

The histopathology of NSIP, a term first used by KATZENSTEIN and FIORELLI [25] in relation to the IIPs, is characterised by diffuse involvement of abnormal lung by varying amounts of inflammation and/or fibrosis. Initially, three groups of NSIP patients were identified. Group I: those with a cellular interstitial pneumonia but little or absent fibrosis; group II: those with a mixture of inflammation and fibrosis; and group III: those with predominant fibrosis. The ATS/ERS consensus classification narrowed these groups down to two types, cellular and fibrotic [2]. Histologically, the fibrosis seen in NSIP is diffuse unlike the patchy involvement seen in UIP and the fibroblastic foci (a key pathological feature of UIP) are inconspicuous or absent [2, 10].

Historically thought of as early-stage IPF, DIP is now considered a separate entity within the non-IPF IIPs. It has also been considered a more extensive form of the smoking-related IIP, RB-ILD, with pigmented macrophages diffusely filling the alveolar spaces throughout the lungs compared with the bronchocentric macrophage accumulation seen in RB-ILD. However, while nearly all cases of RB-ILD occur in smokers, there are probably 10–20% of DIP cases that occur in never-smokers with an idiopathic disease. Moreover, there is more eosinophilia, follicular hyperplasia and fibrosis in DIP than in RB-ILD, and no difference in histology between smokers and nonsmokers with DIP [26]. Therefore, since some cases of DIP are truly idiopathic, there is a strong case for considering DIP a distinct clinicopathological disease entity within the current IIP classification.

Diffuse alveolar damage is the histological pattern seen in ARDS but the clinicopatholical disease is termed AIP when idiopathic. Histologically, the disease progresses from purely congestion and oedema at its earliest phase, through the exudative phase with prominent hyaline membranes and then the organising phase when organising pneumonia predominates, with a

TABLE 4 Diagnostic agreement between academic physicians and community-based physicians in 39 patients with diffuse parenchymal lung diseases

	Clinicians		Radiologists		Pathologists	
	Academic	Community	Academic	Community	Academic	Community
HRCT alone	0.28	0.20	0.59	0.38	0.57	0.14
History plus clinical	0.32	0.23	0.41	0.34	NA	NA
Clinician/radiologist discussion	0.37	0.27	0.45	0.40	0.53	NA
Clinician/radiologist/ pathologist discussion	0.62	0.47	0.55	0.31	0.53	0.14
Consensus	0.71	0.44	0.55	0.32	0.57	0.41

Data are presented as kappa scores. HRCT: high-resolution computed tomography; NA: data not available. Adapted from [29] with permission from the publisher.

fibrotic stage showing a pattern of NSIP in the few patients with long-term survival but residual fibrosis.

Organising pneumonia in an idiopathic setting is termed COP and histologically shows intra-alveolar polypoid buds of granulation tissue, which are typically of greater vascularity than the fibrotic foci seen in UIP. There is a variably intense associated nonspecific interstitial chronic inflammatory cell infiltrate but generally no interstitial fibrosis. However, some cases of organising pneumonia progress to established interstitial fibrosis and these cases can sometimes be difficult to distinguish from UIP, especially in cases with an acute exacerbation. Multidisciplinary review of such cases is especially important. The presence of fibrosis is an adverse prognostic indicator.

The seventh histological pattern is LIP, which is becoming increasingly rare because pathologists are now likely to preferentially classify milder cases as cellular NSIP. However, LIP is still considered a separate histological and clinicopathological entity within the non-IPF IIPs, and there are some patients who have a specific phenotype, often with cysts in the lung, associated with their dense lymphoid infiltrate. In reality these cases are rarely, if ever, idiopathic and typically will have an associated collagen vascular disease or an associated immune deficiency, either congenital or acquired.

DIAGNOSIS OF IIPS IN CLINICAL PRACTICE

A precise diagnosis of IIPs is reached by close consultation between pulmonologists, radiologists and pathologists. Since the histological patterns identified by pathologists permit better separation of the IIPs than HRCT, they serve as the basis for the classification of the IIPs into IPF and non-IPF IIPs. Although historically there has been a lack of confidence in the diagnostic and predictive value of pathology in the diagnosis of IIPs [2], recent studies suggest that the interobserver variation between pathologists in the diagnosis of diffuse parenchymal lung diseases is within acceptable levels. Kappa values are in the range of 0.75 for sarcoidosis, 0.70 for organising pneumonia and 0.59 for UIP. Even for NSIP, a diagnosis that is still provisional, the weighted kappa value was 0.4, where 0.4–0.6 is considered satisfactory, 0.6–0.8 good and >0.8 excellent [27].

Diagnosis of the IIPs is a progressive process, in which the level of agreement between clinical disciplines tends to increase as additional information is provided. For example, in a study of 58 patients with suspected IIP who underwent biopsy, the radiological diagnosis changed in up to 50% of cases when pathological evaluation was provided, while a diagnosis based on clinical and imaging features changed in ~35% of cases. Conversely, the pathological diagnosis changed in ~20% of cases when clinical and imaging information was provided [28]. Studies have also looked at the consistency in diagnosis of IIPs between community and tertiary referral centres. In one such study, FLAHERTY *et al.* [29] undertook a retrospective analysis of diagnostic data that had been collected prospectively from 39 patients with suspected IPF. The clinical information included results of pulmonary function tests, lung HRCT and SLB. These data were prospectively assessed in a step-wise manner by a team of academic pathologists, radiologists and clinicians and a team of community clinicians, pathologists and radiologists. Results showed that among academic clinicians the kappa scores increased as more diagnostic data became available, whereas with community clinicians there was negligible change (table 4). Thus, despite discussions within the community team, the initial diagnosis made by community clinicians remained essentially unchanged; community clinicians were more likely to assign a final diagnosis of IPF compared with their academic counterpart. These results highlight the significant disagreement that currently exists between academic and community clinicians in the diagnosis of the IIPs and raises concerns that some patients will be misdiagnosed as having IPF with potentially deleterious consequences. This is especially important when it comes to the selection of patients for clinical trials of new drug therapies for IIPs. Indeed, the ATS/ERS guidelines emphasise that trials of therapy for IIPs should be discouraged until a concerted multidisciplinary effort has been made to establish a firm diagnosis based on currently recognised criteria.

CONCLUSIONS

The current classification of the idiopathic interstitial pneumonias recognises seven separate clinicopathological diagnoses, each of which has a corresponding histopathological pattern. Of the procedures used for the diagnosis of idiopathic interstitial

pneumonias, lung high-resolution computed tomography is amongst the most valuable. This is especially true for idiopathic pulmonary fibrosis, where the high-resolution computed tomography will typically reveal irregular reticular opacities, traction bronchiestasis and, most importantly, peripheral honeycombing. If usual interstitial pneumonia is not evident on a high-resolution computed tomography, then surgical lung biopsy is necessary to differentiate between usual interstitial pneumonia and nonspecific interstitial pneumonia and other nonidiopathic pulmonary fibrosis idiopathic interstitial pneumonias. Surgical lung biopsy is also indicated in patients with an atypical clinical presentation, in whom it can help distinguish between the different interstitial lung diseases. Because the clinical presentation of idiopathic pulmonary fibrosis is fairly nonspecific, idiopathic pulmonary fibrosis may be misdiagnosed or diagnosed when the disease is at an advanced stage. Differences in diagnosis may also arise between academic and community clinicians. This has important ramifications for the selection of patients for clinical trials of new treatments for idiopathic interstitial pneumonias and requires greater interaction between academic and community clinicians together with improved education to bridge this gap.

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