Radiological Approach to Interstitial Lung Disease: A Guide for the Nonradiologist

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The term interstitial lung disease (ILD) comprises more than 200 separate disease entities, each having its separate and often unique radiological manifestations. Because the clinical presentation of most of these diseases is similar (dyspnea and cough) high-resolution computed tomography (HRCT) becomes a valuable tool in narrowing the differential diagnosis. The importance of HRCT is further underlined by the fact that there is no gold-standard diagnostic test for ILD; rather, a multidisciplinary approach, with integration of radiological, pathologic, and clinical data, is generally the best approach.

Multiple studies have described the HRCT patterns of specific ILDs; however, these have generally been written for the radiologist who already has a strong background in imaging. The purpose of this review is to introduce pulmonologists and clinicians to the imaging appearances of ILDs on HRCT, using a pattern approach in addition to focused discussion of the common ILDs.

**BASIC ARCHITECTURE OF THE LUNG INTERSTITIUM**

The lung interstitium is made up of 3 components, as described originally by Weibel\(^1\); these include the axial interstitium, the peripheral interstitium, and the septal interstitium. The axial interstitium is the connective tissue surrounding bronchovascular bundles as they emerge from the pulmonary hila and extend peripherally to the level of respiratory bronchioles. The septal interstitium consists of a fine network of connective tissue inside the secondary pulmonary lobule that supports the structure of the entire lobule. The peripheral interstitium originates from the undersurface of the visceral pleura, extending into the lung parenchyma; the venules and lymphatics that drain the visceral pleura and peripheral parts of the lung traverse the peripheral interstitium.

Lung tissue has a limited and predictable response to injury; therefore, a variety of disease processes may lead to similar alterations in the pulmonary anatomy, resulting in overlapping imaging findings. The pattern and distribution of these lung findings are what may suggest a specific diagnosis.

**APPROACH TO HRCT**

Having an organized approach is essential for efficient and accurate interpretation of HRCT studies. An example of this approach is a sequential analysis of the airways (the main bronchi as well as the smaller bronchioles), followed by the lung parenchyma (with separate attention to each lobe), the pleura itself, and the mediastinum. Each finding should be further described concerning size, shape, location within the lungs, and relationship to any normal surrounding structures. This approach is a sample approach describing the

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components that need to be addressed and can be tailored and reorganized according to one’s own style.

Lung parenchymal abnormalities can be grossly divided into those with increased attenuation or decreased attenuation. It is important to take note of both lobar and individual lung volumes because as a general trend (not absolute) the lung volumes are increased with processes that produce decreased attenuation, like air trapping and emphysema, and are decreased with processes that produce reticulations and honeycombing. The most common abnormal findings seen on HRCT are described later.

**INCREASED ATTENUATION**

**Reticulation/Reticular Opacities**

Reticulation refers to a netlike pattern. This pattern is most commonly the result of thickened interlobular and intralobular septa, connecting and interbridging with one another at different angles. On HRCT, this pattern is most frequently seen in the peripheral and basal lung zones (Fig. 1). The diseases that can cause this pattern are summarized in Table 1.

**Ground-glass Pattern**

Ground-glass opacities are defined as areas of increased attenuation that are not dense enough to obscure the underlying bronchovascular markings (Fig. 2). A wide variety of pathologic mechanisms can give rise to a ground-glass pattern on HRCT, including airspace disease, alveolar collapse, interstitial thickening, and increased vascularity of the alveoli. In cases of pulmonary fibrosis, ground-glass opacity can also represent very fine interstitial fibrosis beyond the spatial resolution of the scan obtained. The common ILDs that can present with ground-glass opacities on HRCT are summarized in Table 1.

Ground-glass opacities often signify a reversible disease process. However, about one-third of these cases may be associated with fibrosis. In the absence of any signs of fibrosis such as traction bronchiectasis and honeycombing, ground-glass opacity should be presumed to represent a reversible disease process.3

**Consolidation**

Consolidation appears as an area of increased attenuation, but it can be differentiated from ground-glass opacities by the inability to visualize bronchovascular markings in the affected areas. Air bronchograms are a common finding because of the resultant interface between the consolidated (high attenuation) lung parenchyma and the air-filled airways (low attenuation). This situation typically results from filling of the airspaces with fluid such as edema, blood, or pus. A large list of ILDs that can produce consolidation on HRCT is summarized in Table 1.

**Nodules**

Nodules are focal areas of increased attenuation, usually with discrete borders. They can vary in size from a few millimeters to up to 3 cm. Greater than 3 cm is referred to as a mass. Once shown on computed tomography (CT), they need to be further analyzed with respect to their size, density, borders, number, and location. The initial approach should focus on categorizing them into 1 of 3 categories (based on their relation with the secondary pulmonary lobule): centrilobular, perilymphatic, and random (Table 2).

Centrilobular nodules are characterized by their central location in the secondary pulmonary lobules; their base of origin can be either the pulmonary artery or the bronchiole, both of which traverse the center of the secondary pulmonary lobule. On HRCT, the features that can help in their recognition include their even-spaced distribution with respect to one another, central location in the secondary pulmonary lobule, lung parenchyma surrounding the nodule, and the absence of contact with the visceral pleural surface. Centrilobular nodules can be further subcategorized based on presence or absence of an associated tree-in-bud pattern, which appears as centrilobular nodules with a V-shaped or Y-shaped configuration. The tree-in-bud pattern is believed to be secondary to pus or mucus impaction within the centrilobular bronchioles, resulting in bronchial impaction and perilobular inflammation. Tree-in-bud opacities are most often caused by...
infection or aspiration. In the absence of tree-in-bud, the differential diagnosis is broad.

Perilymphatic nodules are found where the lymphatics are most concentrated, including the areas adjacent to the visceral pleura, interlobular septa, and adjacent to the bronchovascular bundles. The diseases that can present with perilymphatic nodular pattern are presented in Table 2.

Random nodules are found diffusely throughout the lung parenchyma and do not show a predominant distribution within either the secondary pulmonary lobules or the lymphatics. There is the additional finding that random nodules may be seen at the termination of small pulmonary arterial vessels. These nodules (Fig. 3) usually imply a hematogenous route of entry into the lungs; hematogenous spread of infection and metastases are the most common conditions that produce randomly distributed nodules. The conditions that can present with such a pattern are listed in Table 2.

An established algorithm for nodule characterization on HRCT is presented in Fig. 4.

### Linear Opacities

There are several different patterns of linear opacities on the HRCT scan. The common ones include interlobular septal thickening, parenchymal bands, subpleural curvilinear densities, and intralobular septal thickening or irregular linear opacities.

The normal nonthickened interlobular septa are generally too fine to be detected on standard HRCT, but when abnormally thickened they are detectable on HRCT. They appear as linear opacities extending from and perpendicular to the pleura (Fig. 5A). It is common to find a few of them in normal cases; however, the presence of diffuse, multiple thickened interlobular septa should raise the suspicion of an underlying interstitial disease process. They can be classified as either smooth (eg, from hydrostatic edema, lymphatic congestion), irregular (eg, from fibrosis, lymphoma, secondary solid tumor), or nodular (eg, from sarcoid, lymphoma, secondary tumor).

Parenchymal bands are linear opacities in contact with the pleura and generally greater in length compared with interlobular septa (see Fig. 5B). These bands usually represent fibrosis or a component of atelectasis. Subpleural lines are curvilinear densities seen adjacent and parallel to the visceral pleura. Like parenchymal bands, these also represent fibrosis or atelectasis and are seen frequently in asbestosis. Intralobular septal thickening or irregular linear opacities are linear densities that cannot be categorized into any of the above 3 categories; they are relatively nonspecific.

### DECREASED ATTENUATION

#### Honeycombing

Honeycombing can be identified on HRCT as subpleural regions of clustered cysts, usually stacked...
together in 1 or more layers (Fig. 6). The cysts are generally 3 to 10 mm thick and have a uniform size. Honeycomb cysts can be differentiated from emphysema by their thick, well-defined walls, usually but not always lower lobe predominance, and noncentrilobular distribution. Honeycombing represents areas of destroyed and fibrotic lung tissue on histology, where the architecture has been lost; therefore, it is not uncommon to find associated coarse reticulation, architectural distortion, and traction bronchiectasis on imaging. The diseases that may present with honeycomb ing on HRCT are shown in Table 3.

### Cysts

On HRCT, cysts are rounded areas of low attenuation that are well demarcated from normal lung parenchyma by a thin wall; the walls of a cyst are usually less than 2 mm thick. The most common conditions associated with cystic lung changes are listed in Table 3.

### SPECIFIC DISEASES

#### Langerhans Cell Histiocytosis

Langerhans cell histiocytosis (LCH) is a granulomatous disease of unknown cause. It has a strong association with smoking, and usually affects young adults. In later stages of the disease process, the granulomas are replaced by fibrosis and may cavitate, leading to cyst formation; however, the mechanism of the disease still remains unknown. The prominent findings on HRCT consist of multiple irregular cysts and nodules (Fig. 7). In

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**Table 2**

<table>
<thead>
<tr>
<th>Types of Nodules</th>
<th>Centrilobular Nodularity</th>
<th>Perilymphatic Nodules</th>
<th>Random Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subacute hypersensitivity pneumonitis</td>
<td>Sarcoïdosis</td>
<td>Hematogenous metastases</td>
</tr>
<tr>
<td></td>
<td>Respiratory bronchiolitis-ILD</td>
<td>Silicosis</td>
<td>Miliary fungal infection</td>
</tr>
<tr>
<td></td>
<td>Langerhans cell histiocytosis</td>
<td>Coal worker pneumoconiosis</td>
<td>Miliary tuberculosis</td>
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<td></td>
<td>Berylliosis</td>
<td>Silicosis (mimic)</td>
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<tr>
<td></td>
<td></td>
<td>Lymphoid interstitial pneumonia</td>
<td>Coal worker pneumoconiosis (mimic)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Sarcoidosis (mimic)</td>
</tr>
</tbody>
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**Fig. 3.** Axial maximum intensity projection image shows random nodules throughout the left lower lobe in this patient with disseminated mycobacterial infection; nodules are uniformly distributed throughout the lobe without sparing of fissures or subpleural lung.

**Fig. 4.** This flowchart shows an effective approach to recognizing the 3 different patterns of nodules on HRCT.
contrast to lymphangioleiomyomatosis (LAM), the cysts of LCH are irregularly shaped; they may have either thick or thin walls. The disease process classically affects the upper lung zones, with sparing of the costophrenic angles.\(^5\,\,\!^7\) Nodules may be the only abnormality in early disease, with cysts developing in the area of the nodules later in the disease course.\(^5\)

**LAM**

LAM can be an idiopathic disease, but is more commonly seen secondary to tuberous sclerosis.\(^8\) The cystic changes are believed to be a direct result of peribronchial atypical smooth muscle cell proliferation, with resultant air trapping.\(^9\) The cysts of LAM are generally thin-walled, multiple, uniform, and diffuse, without any specific regional distribution or sparing: they are typically 2 to 5 mm in size with a rounded or ovoid shape (Fig. 8). The remaining lung parenchyma is generally normal, but rarely there can a few scattered centrilobular nodules; however, they are not so prominent and diffuse as those seen in LCH. Associated findings that may support the diagnosis of LAM include the presence of pleural effusions (usually chylous as a result of lymphatic obstruction by smooth muscle cells) and pneumothorax.\(^10\) There is some degree of overlap in the appearance of LAM and LCH.

**Lymphoid Interstitial Pneumonia**

Lymphoid interstitial pneumonia (LIP) is a rare disease. It can be idiopathic, or secondary to lymphoproliferative disorders and immunodeficiency states such as Sjögren syndrome, common variable immune deficiency, and human immunodeficiency virus syndrome. HRCT shows a diffuse or lower lobe predominant involvement, including ground-glass abnormality, septal thickening, centrilobular nodules, and perivascular or subpleural cysts (Fig. 9).\(^11\,\,\!^{12}\) Cysts are the only finding that may be irreversible, and characteristically form in the areas of previous centrilobular nodules.\(^13\) The combination of small bronchovascular and subpleural cysts along with widespread ground-glass abnormality and centrilobular nodules is highly suggestive of LIP.

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**Fig. 5.** Linear opacities. (A) interlobular (axial image from noncontrast chest CT shows diffuse interlobular septal thickening (arrows), which highlights the margins of secondary pulmonary lobules). (B) Parenchymal bands (axial image from noncontrast chest CT shows a focal linear opacity (arrow) extending orthogonally from the subpleural aspect of the right lower lobe consistent with a focal parenchymal band).

**Fig. 6.** Usual interstitial pneumonia (UIP). Axial (A) and coronal (B) images from HRCT show stacked thin-walled cysts that extend to the subpleural portion of the lungs. As in most typical cases of UIP, lung fibrosis is most severe in the basilar and peripheral portions of the lungs.
Light-chain Deposition Disease

Light-chain deposition disease is a rare form of cystic ILD; only a few case series and case reports on the pulmonary manifestations of this disease have been reported. It is most commonly seen in patients with underlying plasma cell dyscrasias, such as multiple myeloma and Waldenström macroglobulinemia, but has also been associated with B-cell lymphomas. The pathogenesis involves deposition of monoclonal immunoglobulin light chains in the lung parenchyma, resulting in parenchymal destruction. The HRCT findings include cystic and, rarely, nodular changes. The nodules can vary in size from 2 mm to 5 cm. The cysts are believed to be a result of small airway dilation.14

Birt-Hogg-Dubé Syndrome

Birt-Hogg-Dubé (BHD) syndrome is a rare autosomal-dominant disorder with multisystemic involvement; typical findings include facial fibrofolliculomas, malignant renal tumors, and pulmonary cystic changes. On HRCT, the predominant finding is multiple thin-walled cysts. The size of these cysts can vary from a few millimeters to 2 cm. These cysts can have multiple septations.15 Differentiation from LAM can be difficult because the cysts are similar in appearance and both conditions can have an associated pneumothorax; however, the cysts of BHD syndrome are characteristically more concentrated in the lower and medial lung zones, whereas those of LAM are more diffuse.16–18 Cysts along the proximal lower lung pulmonary arteries and veins suggest the diagnosis.17

IDIOPATHIC INTERSTITIAL PNEUMONIAS

Idiopathic Pulmonary Fibrosis

Idiopathic pulmonary fibrosis (IPF) is the most common entity in the spectrum of interstitial
idiopathic pneumonias (IIPs), accounting for 50% to 60% of cases. The prognosis is usually worse compared with other IIPs, with a median survival time of 2 to 4 years. These patients are also at a higher risk of bronchogenic carcinoma than the general population, there is a predilection for the lower lobes as opposed to smoking-related bronchogenic carcinoma, which most often affects the upper lobes. IPF is characterized by the radiological pattern of usual interstitial pneumonia (UIP). UIP is most often seen in IPF; however, it can occasionally be caused by a multitude of other diseases including collagen vascular disease, chronic hypersensitivity pneumonitis (HP), drugs (eg, bleomycin, amiodarone), and asbestosis. A definite UIP pattern on HRCT in a patient without clinical evidence of an alternative diagnosis is sufficient for a confident diagnosis of IPF and carries an accuracy of 79% to 90%. Biopsy is generally reserved for atypical or uncertain cases. HRCT findings of UIP pattern include a predominantly subpleural disease pattern, with an apical-basal gradient. The specific features include honeycombing, peripheral reticular opacities, and minimal ground-glass abnormality. Honeycombing, if present, is shown to be the strongest predictor of the diagnosis of IPF, although it may be present in other causes of pulmonary fibrosis. Traction bronchiectasis is commonly associated with the reticular pattern and signifies advanced fibrosis with architectural distortion. Lower lobe volume loss is also a common finding. Ground-glass abnormality is minimal or absent, never being the predominant pattern. Many patients with IPF may show atypical features of UIP on HRCT, with overlapping features of nonspecific interstitial pneumonia (NSIP), chronic HP, or sarcoidosis; in these patients open lung biopsy is usually necessary to establish a confident diagnosis.

**NSIP**

NSIP is a common, albeit less prevalent entity than IPF. NSIP can be caused by many different disorders, including connective tissue diseases, HP, and drugs. When no associated process can be found in a patient with histologic or radiologic pattern of NSIP, the diagnosis of idiopathic NSIP is established.

On HRCT the predominant abnormality includes widespread, bilateral ground-glass opacities, which may be associated with peripheral irregular linear or reticular opacities. The degree of reticulation and traction bronchiectasis has been shown to correlate with the amount of fibrosis present. The disease distribution is mainly peripheral and basal. Subpleural sparing, if present, is a highly specific feature of NSIP, although seen in only a few cases. In a few cases, there may be additional findings such as micronodules, foci of consolidation, or mild honeycombing. Honeycombing, when present, is usually mild, as opposed to UIP, in which honeycombing tends to be more severe. Differentiation between fibrotic NSIP and UIP requires surgical lung biopsy.

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**Fig. 9.** LIP. Coronal reformation from chest CT shows subpleural and bronchovascular thin-walled lung cysts (arrows) consistent with LIP in this patient with Sjögren syndrome.

**Fig. 10.** NSIP. Coronal image from HRCT shows basilar predominant ground-glass opacity, reticulation, and traction bronchiectasis (arrows) consistent with fibrotic NSIP.
Cryptogenic organizing pneumonia
Cryptogenic organizing pneumonia (COP), previously known as bronchiolitis obliterans organizing pneumonia, is the idiopathic form of organizing pneumonia. On HRCT, the 2 most frequently seen features include bilateral, multifocal, patchy consolidation (present in up to 90% of cases) and ground-glass abnormalities (Fig. 11A). The lung volumes are generally preserved. COP tends to preferentially involve the subpleural and bronchovascular regions of the lung parenchyma. There may also be bronchial dilation and air bronchograms associated with regions of consolidation. The imaging findings in these cases can often be mistaken for pneumonic consolidation. The foci of consolidation generally involve the lower lung zones and have a tendency to migrate, especially after therapy. A perilobular pattern of increased attenuation has also been described in COP, which can resemble, and be confused with, interlobular septal thickening. Other less common findings that may be present in a subset of patients include irregular linear or reticular opacities and large nodules (<20% of cases) that may simulate lung cancer. In some cases, HRCT may also reveal the classic reverse halo/atoll sign, which is defined as a central focus of ground-glass opacity with a surrounding rim of consolidation (see Fig. 11B).

Respiratory bronchiolitis-ILD
Respiratory bronchiolitis (RB)-ILD (RB-ILD) is part of the spectrum of smoking-related lung diseases. It is possible that RB-ILD and desquamative interstitial pneumonia (DIP) are similar processes but at the opposite ends of the disease spectrum. RB-ILD is differentiated from simple RB on a clinical basis.

The predominant finding on HRCT is ground-glass abnormality, this is generally more patchy and less extensive than that seen in DIP and preferentially involves the upper lobes. The ground-glass abnormality of RB-ILD has been shown to represent areas of macrophage accumulation in the distal airspaces. An important finding that may help to distinguish RB-ILD form DIP is the presence of centrilobular nodules in the former (Fig. 12). Small cyst formation is unusual in RB-ILD. Bronchial wall thickening is another feature that can be present in RB-ILD or DIP. A large proportion of patients with either RB-ILD or DIP may also have concomitant upper lobe emphysema as a result of long smoking history.

DIP
DIP is a rare form of ILD. The usual age of presentation is 40 to 50 years, with men affected more than women (male/female >2:1). The disease predominantly affects smokers (90% cases), but can also be seen secondary to lung infections, organic dust exposure, and marijuana smoke inhalation.

HRCT typically shows a ground-glass pattern, which is caused by diffuse macrophage infiltration of the alveoli along with interstitial septal thickening; this is generally present in all cases of DIP. The ground-glass pattern can either be patchy or diffuse, with a predilection for peripheral and basal lung zones. Some cases may also show fine linear or reticular opacities, also concentrated in the peripheral and basal lung zones. In some cases HRCT may reveal small lung cysts that are generally thin-walled and less than 2 cm (Fig. 13); these cysts are believed to represent dilated bronchioles and alveolar ducts distal to the sites of obstruction; some of them may resolve over time. Severe honeycombing is unusual.

Acute interstitial pneumonia
Acute interstitial pneumonia (AIP) is notable for its acute presentation. On HRCT, the most common

Fig. 11. COP. (A) Axial image from chest CT shows bronchovascular consolidation and ground-glass opacity consistent with organizing pneumonia. (B) More superiorly in the thorax, there is an example of reversed halo sign in the right upper lobe (central ground-glass focus surrounded by a thin rim of consolidation), which is suggestive of organizing pneumonia.
findings include ground-glass abnormalities, traction bronchiectasis, and architectural distortion (Fig. 14). The ground-glass pattern is patchy in most cases, with areas of lobular sparing; however, some cases may show a more diffuse distribution. Consolidation can be present in some cases and preferentially affects the lower lobes. Traction bronchiectasis can be observed within areas of ground-glass or consolidation and represents fibrotic changes. Although a considerable overlap exists between AIP and acute respiratory distress syndrome (ARDS) in terms of HRCT findings, the presence of symmetric lower lobe abnormalities with honeycombing may be more suggestive of AIP. Among survivors with AIP, most experience marked improvement of the disease. Some may progress to a chronic, fibrotic phase. Fibrosis in AIP and ARDS typically manifests as reticular abnormalities and traction bronchiectasis in the nondependent portions of the lung (in portions of the lungs more exposed to the deleterious effects of long-term positive pressure ventilation).

**Occupational Lung Disease**

**Asbestosis**

Asbestosis refers to interstitial fibrosis caused by inhalation of asbestos fibers. The average latent period for the appearance of ILD is 20 years. Asbestosis must be differentiated from asbestos-related lung disease, which includes noninterstitial manifestation such as pleural plaques, pleural thickening, pleural effusions, bronchogenic carcinoma, and malignant mesothelioma.

In the early stages of the disease, HRCT scans typically reveal multiple subpleural nodules, patchy ground-glass opacities, and mild septal thickening along with reticular abnormalities (mostly in the subpleural and basal aspects of the lungs). Parenchymal bands may be noted in a few cases as well. Another early finding is subpleural curvilinear lines, representing peribronchial fibrosis. In advanced disease, asbestosis most closely resembles UIP (Fig. 15). However, a basal and subpleural-dominant disease pattern coupled with the presence of pleural plaques favors the diagnosis of asbestosis over UIP.

**Silicosis**

Silicosis is one of the more common occupational ILDs encountered; pathogenesis involves inhalational lung injury secondary to silica
dust exposure. Associated occupations include rock mining, sandblasting, drilling, quarrying, foundry working, and ceramic manufacturing.

Silicosis can have an acute as well as a chronic form, the latter being the more common ILD pattern. Chronic silicosis can be further subclassified into a simple and a complicated type based on HRCT findings.

Simple silicosis, on HRCT, is characterized by the presence of multiple nodules, which can either be diffuse or concentrated in the centrilobular and subpleural portions of the lungs (Fig. 16A). The nodules are generally small, ranging from 2 to 5 mm. Calcifications may be seen within some of the nodules as well. With disease progression, the initial subpleural nodules may coalesce and result in a pseudoplaque appearance, a finding that should not be confused with asbestos-related plaques. Mediastinal lymphadenopathy is a common feature of silicosis, usually showing intra-nodal calcifications; these may have either a punctate, diffuse, or a peripheral (egg-shell) pattern.

Complicated silicosis, also termed progressive massive fibrosis, results from the confluence of the earlier nodules. This lesion manifests as large, soft tissue masses with ill-defined borders; these conglomerate masses are mainly seen in the upper lung zones, and often show areas of calcification and cavitation (see Fig. 16B).

**Coal worker pneumoconiosis**

Coal worker pneumoconiosis is caused by inhalation of washed coal that leads to interstitial lung inflammation and fibrosis. A simple and a complicated form of coal worker pneumoconiosis can be recognized on imaging. The imaging appearance of coal worker pneumoconiosis is identical to that of silicosis.

**HP**

HP is a granulomatous disease with an immunologic basis. It can occur in response to a variety of environmental antigens. Classically, it can be separated into 3 phases: an acute, subacute, and a chronic phase, depending on the temporality relative to initial exposure. All 3 stages have a significant overlap, and a large number of patients may present with findings representative of more than 1 stage.

Acute HP generally presents within a few hours of antigen exposure, and is characterized by widespread homogeneous or heterogeneous opacities; these may mimic acute pulmonary edema. Subacute HP occurs in response to intermittent or low-dose antigen exposure, and is characterized by poorly defined widespread centrilobular nodularity and patchy ground-glass opacity (Fig. 17A). The ground-glass pattern is generally

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**Fig. 15.** Asbestosis. Axial image from contrast-enhanced chest CT shows peripheral reticulation and honeycombing (*thin arrows*) as well as calcified pleural plaques (*thick arrows*) consistent with asbestosis. Histologically, the pulmonary fibrosis pattern in asbestosis most often shows a UIP pattern.

**Fig. 16.** Silicosis. (A) Axial images from HRCT show centrilobular nodules (*arrows*) in the upper lobes and superior segments of the lower lobes; there is mediastinal lymphadenopathy, which is common in silicosis. (B) Nodules have coalesced into progressive massive fibrosis in the upper lung zones.
symmetric and diffuse but can be asymmetric in some cases. There may be concomitant reticulation and bronchiectasis in some cases, which may resemble NSIP. Some cases may show cystic changes as well. Expiratory images generally show mosaic attenuation, corresponding with areas of air trapping. This finding is believed to represent bronchiolitis and the resultant bronchiolar obstruction. Chronic HP classically occurs after a long-term antigen exposure, and usually shows a fibrotic pattern resembling UIP or fibrotic NSIP (see Fig. 17B). The imaging findings of chronic HP may be superimposed on a background of subacute HP pattern in some cases. Centrilobular nodules, if present, favor chronic HP over UIP. Also, the fibrosis in chronic HP generally involves the mid and upper lung zones, with sparing of the bases, whereas UIP and fibrotic NSIP tend to affect the lung bases more severely. Open lung biopsy is required to make a confident diagnosis in borderline cases.

Sarcoidosis Sarcoidosis is a multisystem inflammatory disease of unknown cause, characterized histologically by the formation of multiple noncaseating granulomas. The disease is 3 times more prevalent in African Americans than in Whites. Pulmonary involvement is the most common cause of morbidity and mortality in these patients, with up to 90% patients affected, and 20% developing chronic fibrotic lung disease. Based on the findings on standard chest radiograph, the disease is categorized into 5 stages, with increasing stage implying a worse prognosis. The stages of sarcoidosis are summarized in Table 4.

Sarcoidosis preferentially involves the upper lung zones; however, it can also have a more diffuse distribution in advanced stages of the disease. The most commonly observed finding on standard HRCT is multiple nodular opacities in a perilymphatic distribution (Fig. 18), which correlate with sites of granulomatous inflammation on histology. HRCT becomes indispensable in the management of sarcoidosis when there is a need for differentiating reversible granulomatous inflammation from fibrosis (a direct determinant of patient staging). Early findings, which may improve with treatment, include interstitial septal thickening, reticular or linear opacities, alveolar opacities, ground-glass opacities, foci of consolidation, and nodules. Of these findings, the presence of ground-glass abnormality and consolidation portend a worse prognosis compared with the rest. On the other hand, honeycombing, traction bronchiectasis, architectural distortion, upper lobe volume loss, and hilar retraction suggest an irreversible fibrotic component to the lung disease. Expiratory CT images can show focal air trapping in any stage of the disease.

Berylliosis Berylliosis is an uncommon occupational ILD, caused by exposure to beryllium dust or fumes. It is most frequently seen in people working in the nuclear industry, ceramic manufacture plants, or the aerospace industry. Like most

| Table 4: Chest radiographic stages of sarcoidosis |
|-----------------|------------------|
| **Stage** | **Chest Radiograph** |
| 0 | Normal |
| 1 | Hilar adenopathy alone |
| 2 | Hilar adenopathy with lung parenchymal abnormalities |
| 3 | Lung parenchymal abnormalities alone |
| 4 | Lung fibrosis |
occupational diseases, berylliosis has an acute and a chronic stage. The ILD pattern encountered in clinical practice is most often the chronic form. Chronic beryllium disease requires initial sensitization to beryllium before development of overt disease. This sensitivity to beryllium can be easily detected on a lymphocyte transformation test using blood or bronchoalveolar lavage fluid.

On HRCT, chronic berylliosis closely mimics sarcoidosis, with the most common finding being perilymphatic nodules along the bronchovascular bundles and interstitial septa (Fig. 19). Other common findings include interstitial septal thickening, ground-glass opacities, and bronchial wall thickening. Mediastinal and hilar lymphadenopathy can be present as well. Ground-glass opacities, believed to be related to granulomatous changes, are more commonly seen in chronic berylliosis than in sarcoidosis, and therefore, may help in differentiation between the two. With disease progression, a fibrotic pattern may emerge with development of peripheral reticular or linear opacities; honeycombing may be present in some of these cases as well.

**COLLAGEN VASCULAR DISEASES**

**Rheumatoid Arthritis**

Rheumatoid arthritis can be associated with a wide variety of possible pulmonary complications, including nodules, fibrosis, airway disease, and pleural disease. The most common findings on HRCT include bronchial wall thickening, bronchiectasis, and nodules; other less common findings are nonseptal thickening, ground-glass opacities, reticular abnormality, honeycombing, and consolidation (Fig. 20). The most common pattern of ILD in rheumatoid arthritis is UIP, followed by NSIP, and COP. The HRCT findings in early rheumatoid disease (<1 year) include expiratory air trapping, bronchiectasis, and a ground-glass pattern.

**Systemic sclerosis**

Systemic sclerosis is a type of multisystemic connective tissue disease. The lungs are one of the most commonly affected organs in the diffuse form of the disease, but can be present in more limited forms as well.

The predominant HRCT pattern consists of widespread, confluent ground-glass opacities along with associated reticular abnormalities (Fig. 21).
These findings predominantly involve the basal and posterior-lateral lung zones, as well as the subpleural regions. Airways are also commonly affected, showing traction bronchiectasis and bronchiolectasis. Mild honeycombing can be present in up to one-third of cases. The CT findings can be similar to those of idiopathic NSIP in many cases; this is not surprising, because 75% of scleroderma cases show a histologic NSIP pattern.

**Systemic lupus erythematosus**

Systemic lupus erythematosus (SLE) can present with a variety of different patterns on HRCT, including airway disease, pleuritis, lymphadenopathy, and pulmonary hemorrhage. ILD is present in up to one-third of SLE cases. The most common pattern seen is UIP or NSIP, usually mild. Diaphragmatic dysfunction in these patients may lead to low lung volumes (also known as shrinking lung syndrome).

**Mixed connective tissue disease**

Mixed connective tissue disease (MCTD) is a connective disorder with overlapping features of other connective tissue diseases such as SLE, PM, diabetes mellitus, rheumatoid arthritis and others. The lungs are commonly affected; in 1 study, up to 67% patients with MCTD had evidence of infiltrative lung disease. The most common HRCT findings include ground-glass opacity, along with subpleural nodules, and reticular or linear opacities, often resulting in an NSIP pattern (Fig. 22).

**Drug-related ILD**

Drugs can cause a wide variety of pulmonary manifestations, which may be nonspecific in most cases and can overlap with the disease pattern described earlier (Fig. 23). Some of the more common drugs and their HRCT manifestations are shown in Table 5.
SUMMARY

ILD is a broad category of diseases that may present with different but overlapping findings on HRCT. It is important for physicians taking care of patients with ILD to know the important HRCT findings of the lung that are representative of ILD. The different HRCT findings and the location of these findings in the lung often enable a specific diagnosis of ILD to be made in a given patient.

REFERENCES


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### Table 5
**Drug-induced ILD**

<table>
<thead>
<tr>
<th>Drug</th>
<th>HRCT Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>NSIP; diffuse ground-glass; multiple areas of organizing pneumonia; diffuse reticular opacities</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Early: reticular or nodular opacities involving the bases and costophrenic angles</td>
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<td></td>
<td>Late: diffuse fibrosis</td>
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<tr>
<td>Cyclophosphamide</td>
<td>Basal reticular or nodular opacities; pleural thickening</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Hilar lymphadenopathy; basal reticular or nodular opacities</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Early: basal opacities; diffuse ground-glass</td>
</tr>
<tr>
<td></td>
<td>Late: basal reticular or nodular opacities along with fibrosis</td>
</tr>
<tr>
<td>Nitrosoureas</td>
<td>Patchy or diffuse ground-glass abnormalities</td>
</tr>
</tbody>
</table>