ILD

By

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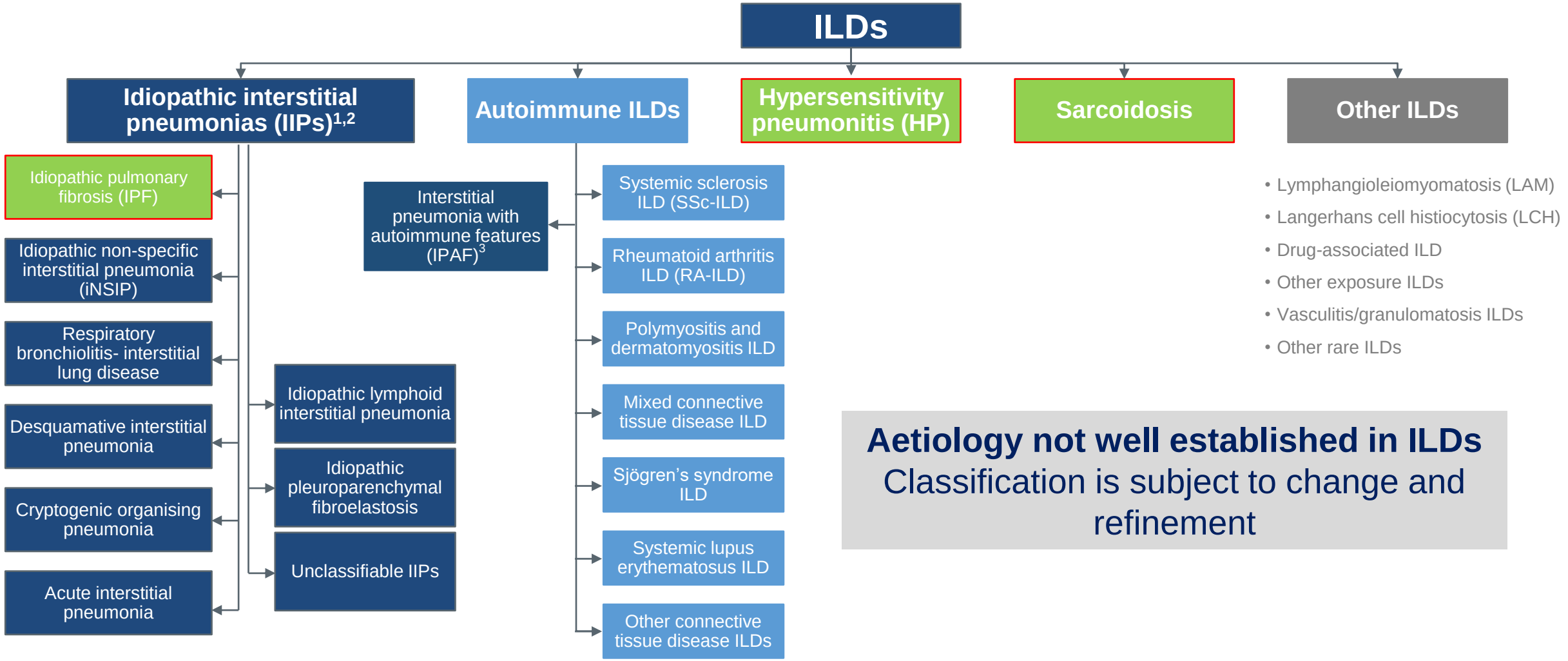
Content

- Classification of ILD
- Idiopathic pulmonary fibrosis (IPF)
- Sarcoidosis
- Hypersensitivity pneumonitis

Classification of ILDs based on disease etiology



Aetiology not well established in ILDs
Classification is subject to change and refinement

1. ATS/ERS. *Am J Respir Crit Care Med* 2002;165:277–304; 2. Travis WD *et al. Am J Respir Crit Care Med* 2013;188:733–48; 3. Fischer A *et al. Eur Respir J* 2015;46:976–87

Classification of ILDs based on disease behaviour

ATS/ERS classification for IIPs[1]

- Reversible and self-limited
- Reversible disease with risk of progression
- Stable with residual disease
- Progressive irreversible disease with potential for stabilisation
- Progressive irreversible disease despite therapy

IPF Consensus working group proposal for classification of **fibrosing ILDs**[2]

- Non-progressive
- Progressive but responds to immunomodulation, at least in short term*
- Progressive regardless of treatment considered appropriate for individual ILDs

Corresponds to progressive fibrosing phenotype[3]

* If fibrosing ILDs progress after perceived response to immunosuppressive treatment, this disease behavior also contributes to the progressive fibrosing phenotype

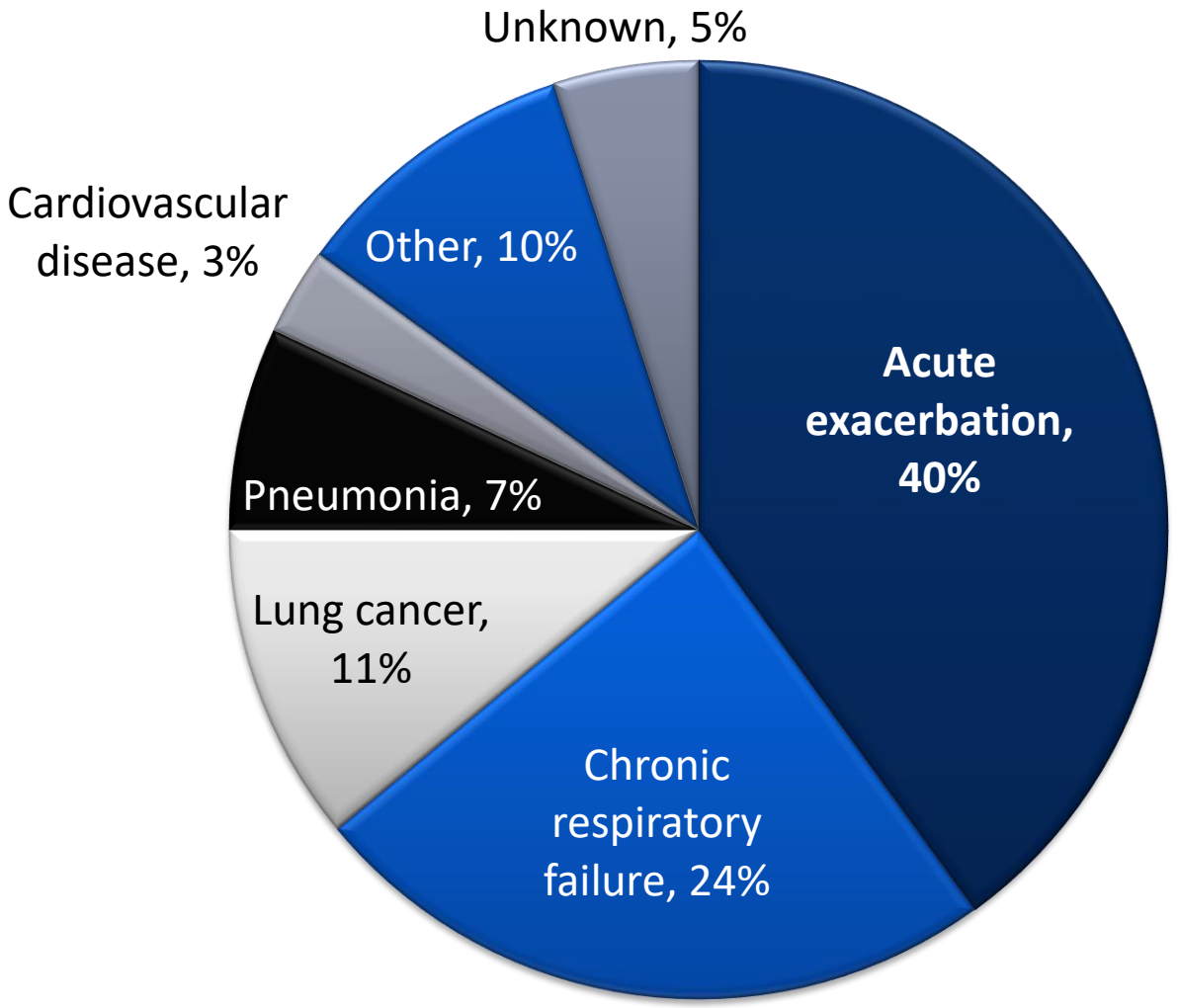
1. Travis WD *et al. Am J Respir Crit Care Med* 2013;188:733–48; 2. Wells AU *et al. Eur Respir J* 2018;51.pii: 1800692; 3. Flaherty KR *et al. BMJ Open Respir Res* 2017;4:e000212

What is IPF?

- IPF is a chronic disease characterised by worsening dyspnoea and progressive loss of lung function[1]
- The most common and debilitating symptoms of IPF are cough and dyspnoea, which negatively affect patients' quality of life[2]
- IPF is **rare**, occurs primarily in older adults, and is more common in **men** than women[3]
- Median survival time from diagnosis of IPF is **2–3 years**[1]
  (Before the era of antifibrotics)

1. Raghu G, et al. Am J Respir Crit Care Med 2011;183:788–824; 2. Swigris JJ, et al. Health Qual Life Outcomes 2005;3:61;
3. Nalysnyk L, et al. Eur Respir Rev 2012;21:355–361.

IPF: CAUSE OF DEATH



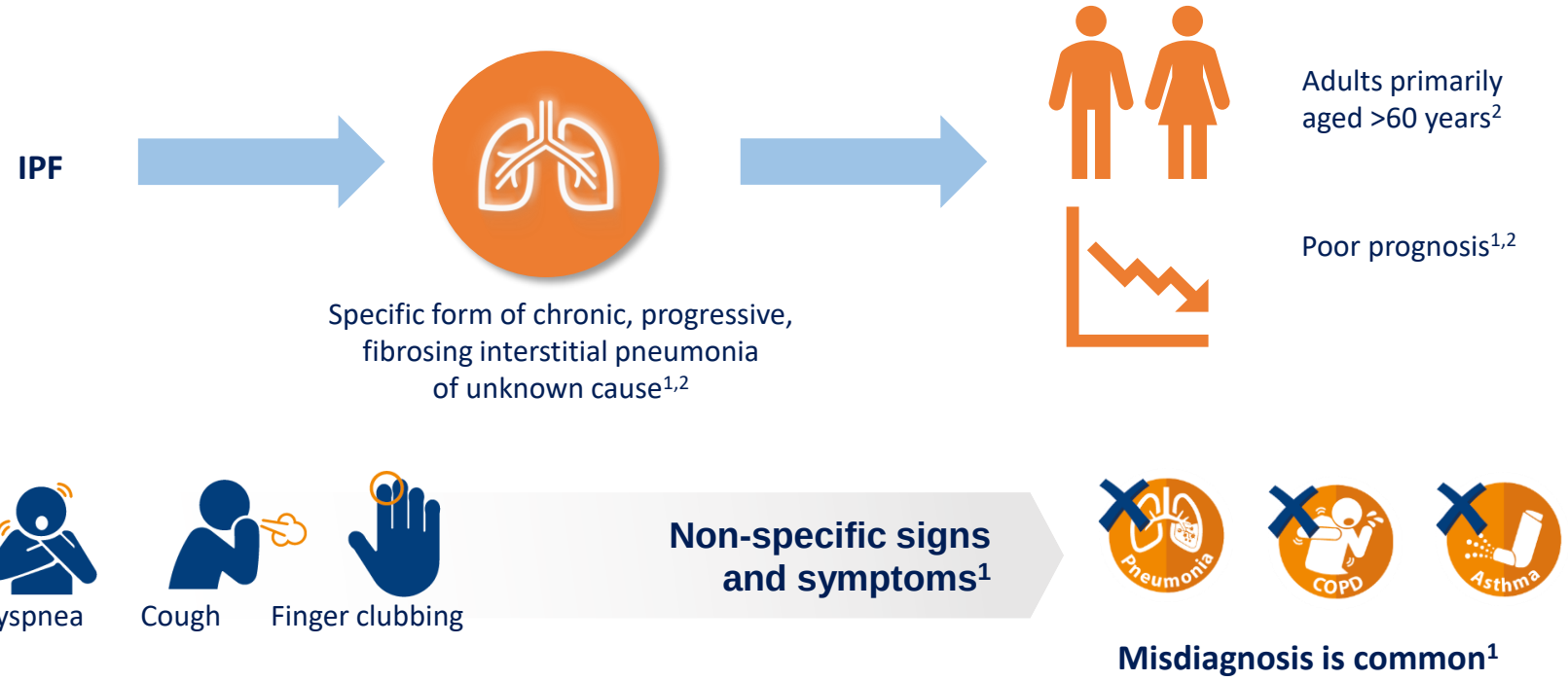
Modified from *AJRCCM* 2014;190:773

Comorbidities that may impact the course of IPF

- Pulmonary hypertension[1]
- Emphysema[2]
- Lung cancer[3]
- Gastroesophageal reflux disease[4,5]
- Coronary artery disease[6]
- Diastolic dysfunction[7]
- Sleep disorders[8]
- Psychiatric disturbances[9]
- Obesity[10]

1. Patel NM, et al. Chest 2007;132:998–1006; 2. Mejia M, et al. Chest 2009;136:10–15; 3. Daniels CE and Jett JR. Curr Opin Pulm Med 2005;11:431–437; 4. Raghu G. Eur Resp J 2006:27:136–142; 5. Patel S, at al. Am J Respir Crit Care Med 2009;179:A4063; 6. Kizer JR, et al. Arch Intern Med 2004;164:551–556; 7. Papadopoulos CE, et al. Eur Respir J 2008;31:701–706; 8. Lancaster LH, et al. Chest 2009;136:772–778; 9. Shanmugam G, et al. Psychiatr Clin North Am 2007;30:761–780; 10. Raghu G, et al. Am J Respir Crit Care Med 2011;183:788–824.

IPF is associated with a poor prognosis and is often misdiagnosed



IPF, idiopathic pulmonary fibrosis

1. Molina-Molina M *et al. Expert Rev Respir Med* 2018;12:537–539; 2. Raghu G *et al. Am J Respir Crit Care Med* 2018;198:e44–e68

Key diagnostic criteria for IPF

- Exclusion of other known causes of ILD

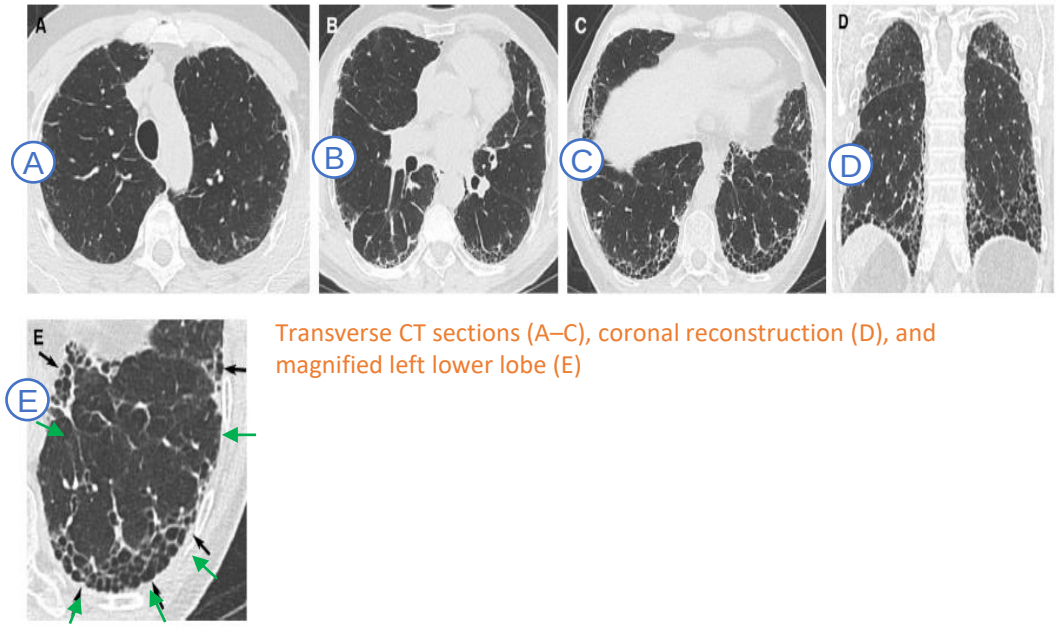
Presence of a UIP pattern on HRCT

Specific combinations of histopathology and HRCT patterns

HRCT, high-resolution computed tomography; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; UIP, usual interstitial pneumonia
Raghu G *et al. Am J Respir Crit Care Med* 2018;198:e44–e68

UIP

- Predominantly **subpleural and basal**[1]
- Distribution is often heterogeneous and occasionally diffuse or asymmetrical[1]
- **Honeycombing**, with or without peripheral **traction bronchiectasis or bronchiolectasis,** must be present for a definite HRCT diagnosis of UIP[1]
- Mild GGO, reticular pattern and pulmonary ossification may be present[1]



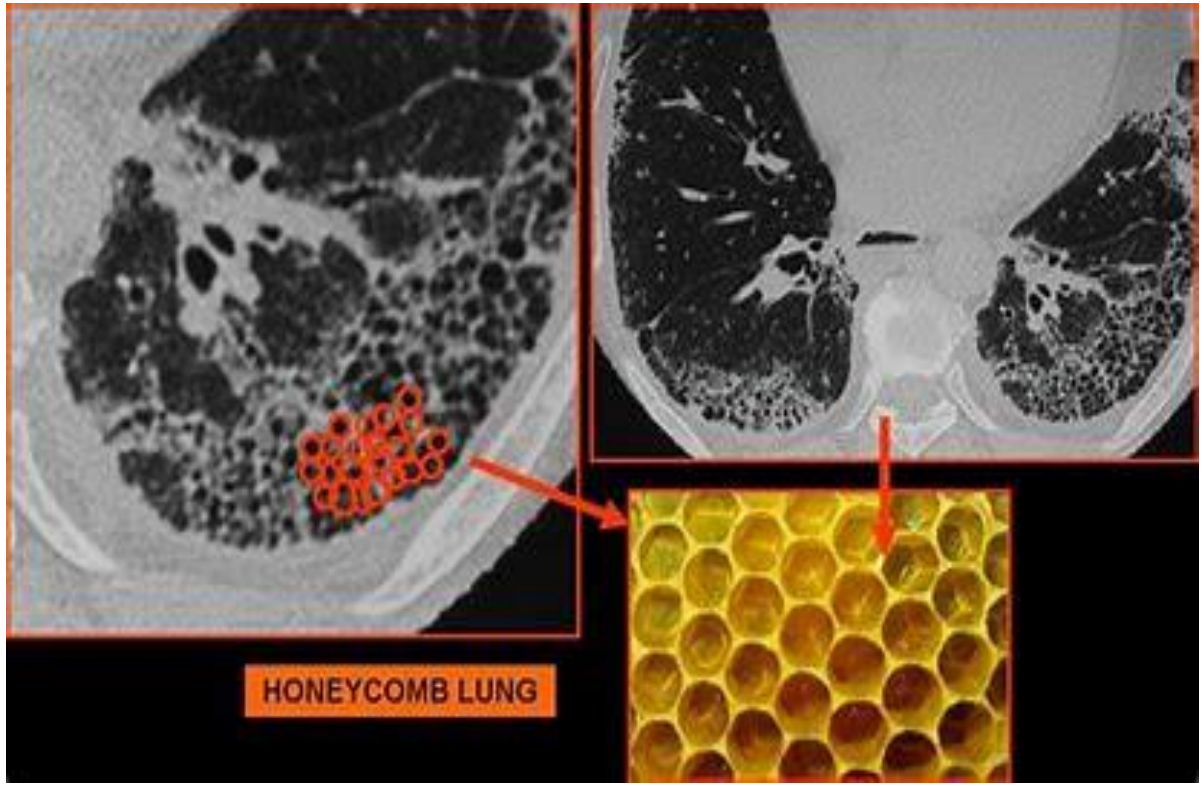
Transverse CT sections (A–C), coronal reconstruction (D), and magnified left lower lobe (E)

Fleischner Society[2]	The absence of honeycombing should not exclude a diagnosis of UIP if all other features are present (particularly subpleural and basal predominant and traction bronchiectasis)

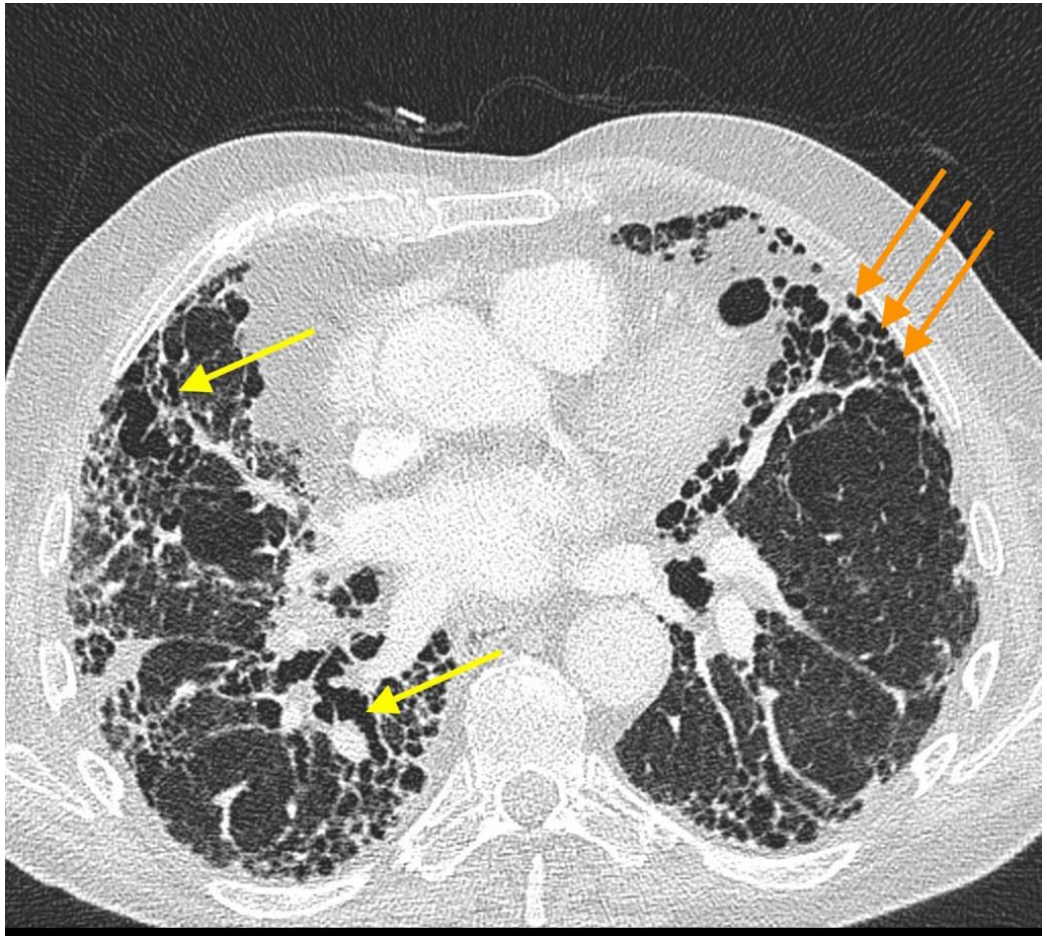
CT, computed tomography; GGO, ground-glass opacification; HRCT, high-resolution computed tomography; UIP, usual interstitial pneumonia

1. Raghu G *et al. Am J Respir Crit Care Med* 2018;198:e44–e68; 2. Lynch DA *et al. Lancet Respir Med* 2018;6:138–153

Honeycombing of the lung



Traction bronchiectasis vs honeycombing



Antifibrotics are the recommended pharmacological treatments for IPF

Agent	2015 guidelines
Nintedanib	Conditional recommendation **for** use*
Pirfenidone	Conditional recommendation **for** use*
Anticoagulation (warfarin)	Strong recommendation **against** use*
Combination prednisone + azathioprine + N-acetylcysteine	Strong recommendation **against** use†
Selective endothelin receptor antagonist (ambrisentan)	Strong recommendation **against** use†
Imatinib, a tyrosine kinase inhibitor with one target	Strong recommendation **against** use*
Dual endothelin receptor antagonists (macitentan, bosentan)	Conditional recommendation **against** use†
Phosphodiesterase-5 inhibitor (sildenafil)	Conditional recommendation **against** use*
Antiacid therapy	Conditional recommendation **for** use‡
N-acetylcysteine monotherapy	Conditional recommendation **against** use†
Antipulmonary hypertension therapy for idiopathic pulmonary fibrosis-associated pulmonary hypertension	Reassessment of the previous recommendation was deferred
Lung transplantation: single vs bilateral lung transplantation	Formulation of a recommendation for single vs bilateral lung transplantation was deferred

*Moderate confidence in effect estimates; †low confidence in effective estimates; ‡very low confidence in effect estimates. IPF, idiopathic pulmonary fibrosis

Raghu G *et al. Am J Respir Crit Care Med* 2015;192:238–248

Sarcoidosis

- Sarcoidosis is an **inflammatory disease** characterized by the formation of **granulomas** in one or more organs of the body, they can interfere with an organ's structure and function.

- Untreated , chronic inflammation **can lead to fibrosis**, which is the permanent scarring of organ tissue.

- This disorder affects lungs in approximately 90% of cases, but it can affect almost any organ in the body.

- Disease presentation and severity varies widely among patients.

- In some cases**, self limited**

- In others, the disease may not progress clinically, but individuals will still suffer from some symptoms that challenge their quality of life.

- The rest of patients—**up to a third** of people diagnosed with the disease—will require long-term treatment.

- Sarcoidosis is considered **chronic** in people whose disease remains active for **more than 2-5 years**; in this population sarcoidosis can be debilitating and life-threatening.

- Patients suffering from advanced sarcoidosis include those with **chronic** disease (active disease for **more than 2-5 years**) who:

  Have worsening disease symptoms despite treatment (usually more than 10 mg corticosteroids and other therapeutic options).

- Approximately **5-10%** of all patients diagnosed will suffer from **advanced sarcoidosis**.

Signs and symptoms of sarcoidosis **vary** widely depending on the organs affected

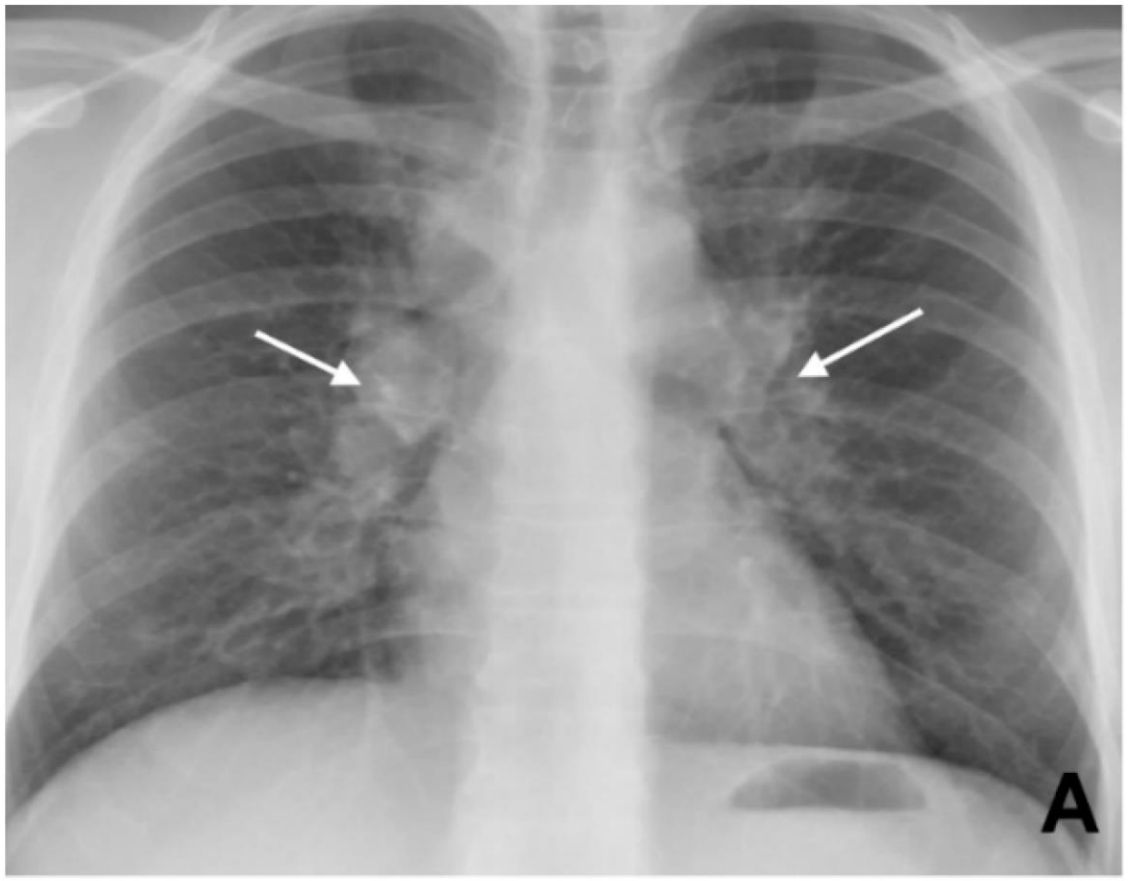
- classic set of signs described as **Lofgren's Syndrome**:

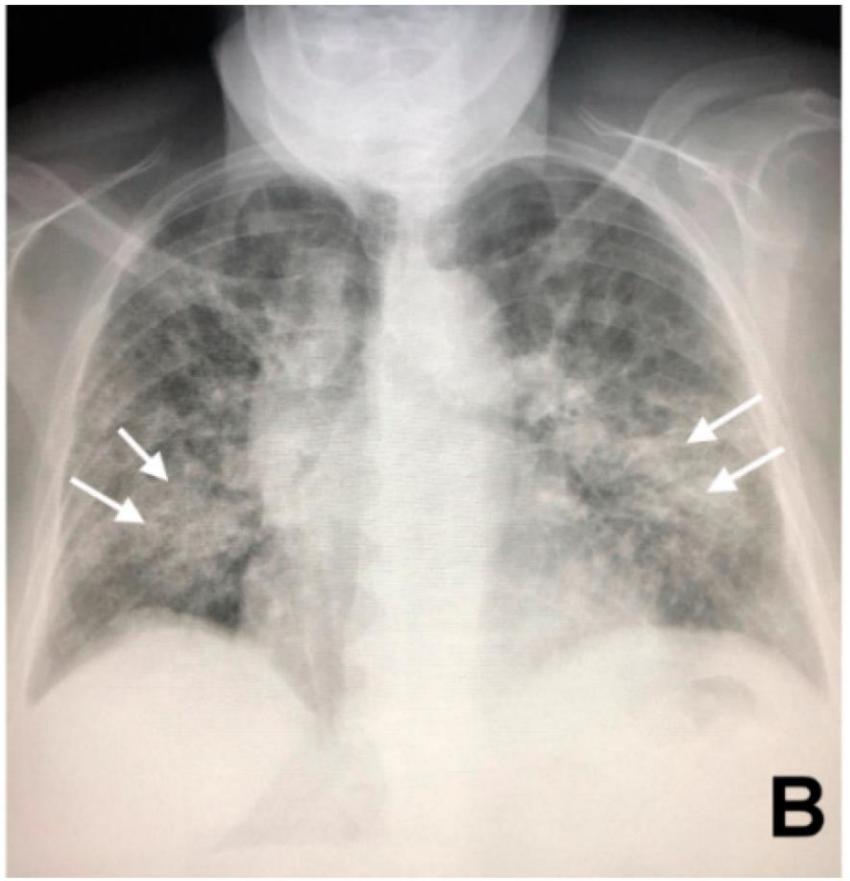
- Fever
- Enlarged lymph nodes
- Swollen and painful joints, arthritis
- Erythema nodosum, raised, red, and tender bumps to form on the skin, usually on the front of the legs. Nearby joints are often swollen and painful.
- Often, the presence of **erythema nodosum is a good sign**, indicating the type of sarcoidosis that also goes away on its own after a few months or years, often without treatment.

Because sarcoidosis can affect **any organ in the body**, a wide variety of symptoms can be seen, including:

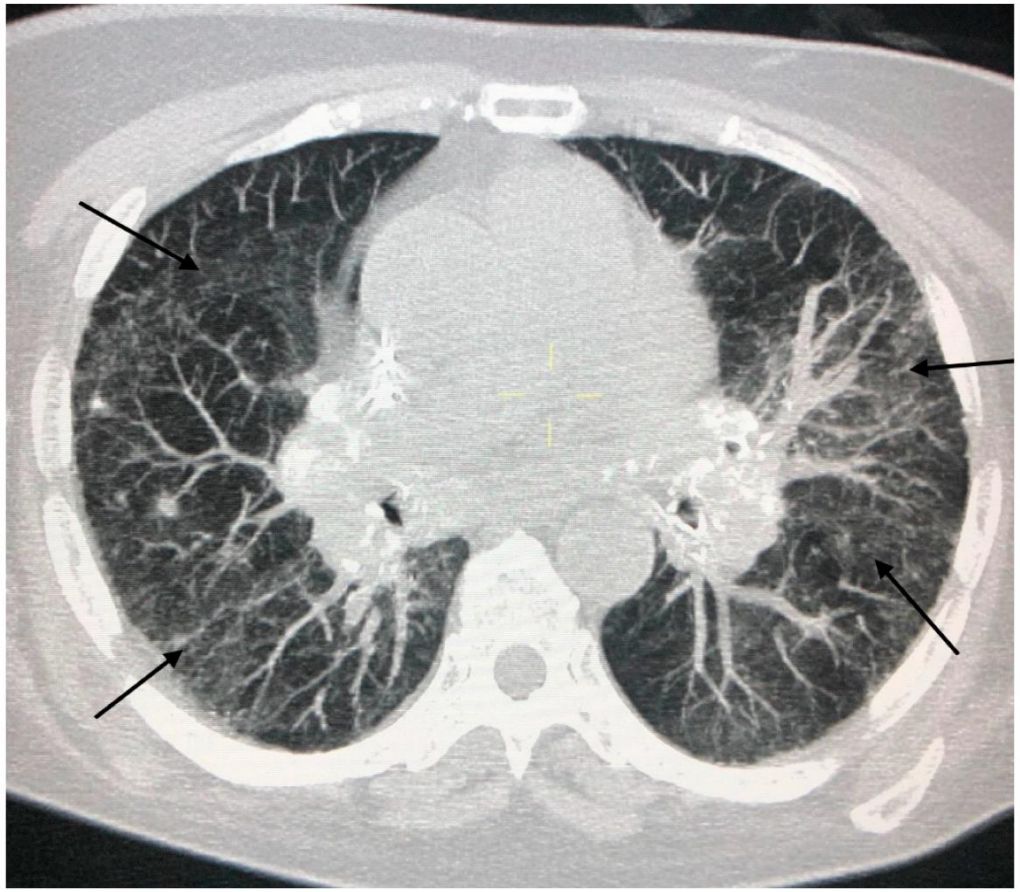
- Fatigue
- Unexplained weight loss
- Night sweats
- Overall feeling of sickness
- Irregular heart beat
- Swollen legs
- Headaches
- Visual problems
- Weakness or numbness of an arm, leg, or part of the face
- Discoloration of the nose, cheeks, lips, and ears
- Scaly-appearing skin rash
- Joint pain
- Muscle swelling and soreness
- Arthritis
- Burning, itching, tearing, or pain in the eyes
- Red eyes
- Sensitivity to light
- Blurred vision

Bilateral hilar lymphadenopathy ((**A**) arrows) and bilateral parenchymal infiltrations with a tendency to confluence ((**B**) arrows).

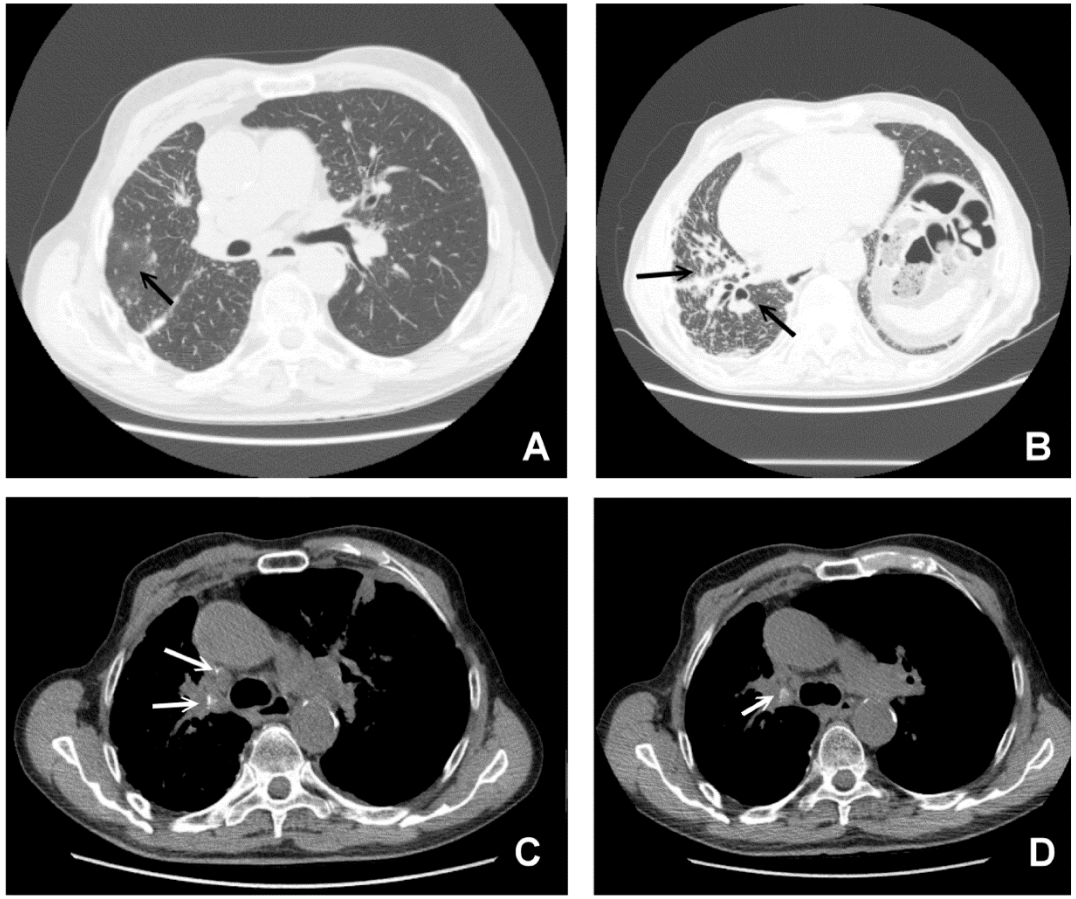




Bilateral parenchymal infiltrates that tend to merge into large pulmonary opacities (arrows).



CT findings in pulmonary sarcoidosis. Panel (**A**) large nodule surrounded by numerous tiny satellite nodules (the “Galaxy sign”, arrow). Panel (**B**) shows multiple traction bronchiectasis with architectural distortion of the parenchyma (black arrows). Panel (**C**,**D**) (white arrows) shows the presence of calcifications of enlarged lymph nodes.



Treatment

- None: supportive.
- **Steriod**: prednisone or prednisolone .
- **Immune suppressive** : methotrexate, azathioprine, and mycophenolate mofetil (CellCept). cyclophosphamide and biologic response modifiers (biologics or TNF-blockers).
- **Antimalarial drugs:** As a treatment for sarcoidosis, these drugs are most likely to be effective in people who have skin symptoms or a high level of calcium in their blood. Hydroxychloroquine (Plaquenil) and chloroquine (Aralen) .

Hypersensitivity pneumonitis

- **HP** is an **inflammatory and/or fibrotic** disease affecting the lung parenchyma and small airways. It typically results from an immune-mediated reaction provoked by an overt or occult **inhaled antigen** in susceptible individuals.

- HP as either **fibrotic** (i.e., mixed inflammatory plus fibrotic or purely fibrotic) or **nonfibrotic** (i.e., purely inflammatory).

- Common symptoms and signs of both nonfibrotic and fibrotic HP include dyspnea, cough, and mid-inspiratory squeaks (or chirping rales or squawks).

- Less frequently, there may be constitutional symptoms such as weight loss, flu-like symptoms (chills, low-grade fever, and malaise), chest tightness, and wheezing, as well as physical examination findings of rales and cyanosis

- Onset may **be acute** (developing over days to weeks, occasionally with pleural effusion) or may also **be insidious** (developing and worsening over months to years), may be recurrent.

- Although an **acute** presentation with or without constitutional symptoms seems more consistent with nonfibrotic HP and the **insidious** presentation seems more consistent with fibrotic HP.

- Prevalence of HP is highest among older individuals (i.e., 65 yr and older, with the average patient receiving a diagnosis in their fifth or sixth decade)

- It can also be diagnosed among younger adults and children. Patients with **fibrotic HP** are more likely to be **older**, have an unidentified inciting agent, and have a lower vital capacity (VC), diffusion capacity, and percentage of lymphocytes in their BAL fluid than patients with nonfibrotic HP.

- HP develops in susceptible individuals after repeated exposure to one or more inciting agents.

- These inciting agents are diverse, vary by geographic region, and are usually protein antigens derived from microorganisms, fungi, or animals (e.g., avian antigens).**very long list**

- They may also be polysaccharides or low-molecular-weight nonprotein chemicals (e.g., isocyanates) .

- The location of exposure can be occupational, household related, or recreational. In many cases, an exposure is not identified .

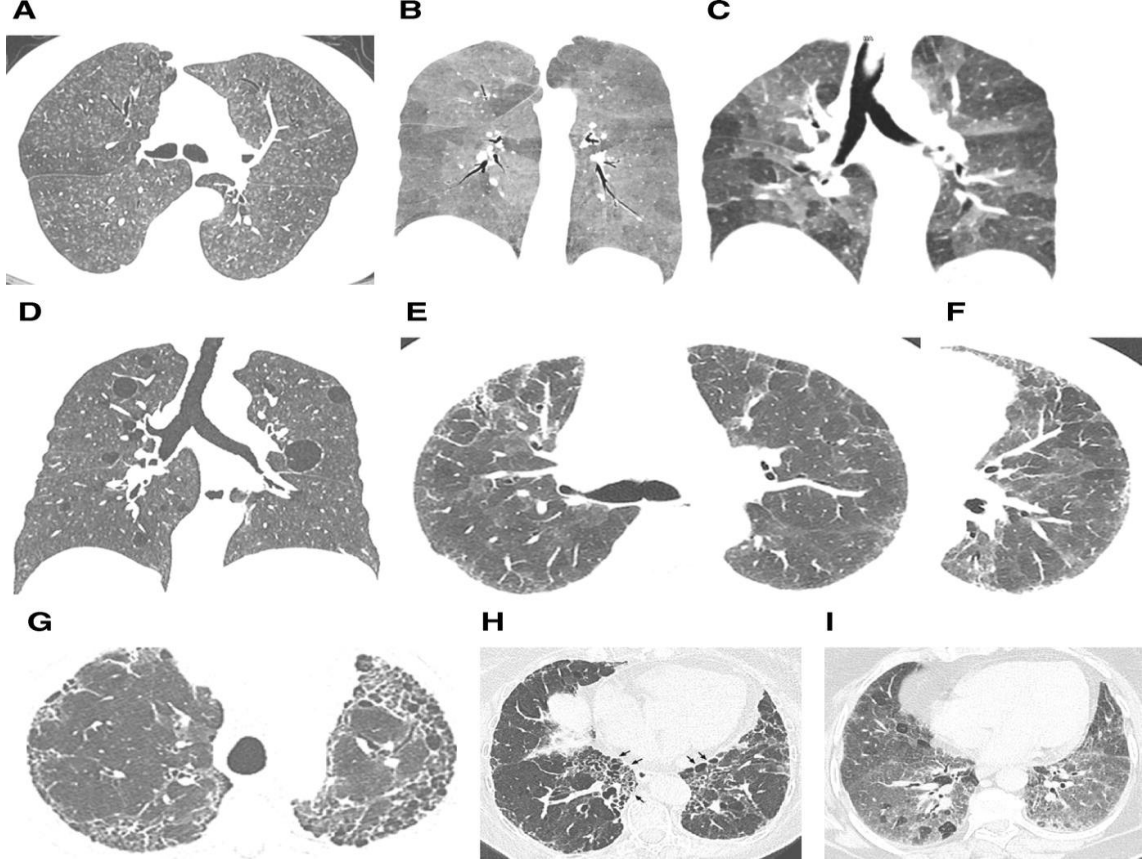


Figure 1. “Typical hypersensitivity pneumonitis (HP)” and “compatible-with-HP” high-resolution computed tomography patterns. The nonfibrotic typical HP pattern is characterized by (*A*) centrilobular nodules, (*B*) mosaic attenuation on an inspiratory scan, and (*C*) air trapping on an expiratory scan. (*D*) The nonfibrotic compatible-with-HP pattern is exemplified by uniform and subtle ground-glass opacity and cysts. The fibrotic typical HP pattern consists of (*E*) coarse reticulation and minimal honeycombing in a random axial distribution with no zonal predominance in association with (*F*) small airway disease. The fibrotic compatible-with-HP pattern varies in the patterns and/or distribution of lung fibrosis (e.g., basal and subpleural predominance, [*G*] upper-lung-zone predominance, [*H*] central [or peribronchovascular] predominance [arrows], or [*I*] fibrotic ground-glass attenuation seen alone or in association with small airway disease). The fibrotic indeterminate-for-HP pattern includes the usual interstitial pneumonia pattern, nonspecific interstitial pneumonia pattern, organizing pneumonia–like pattern, or truly indeterminate findings.

Am J Respir Crit Care Med, 2020
https://www.atsjournals.org/doi/abs/10.1164/rccm.202005-2032ST

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DOI: 10.1164/rccm.202005-2032ST

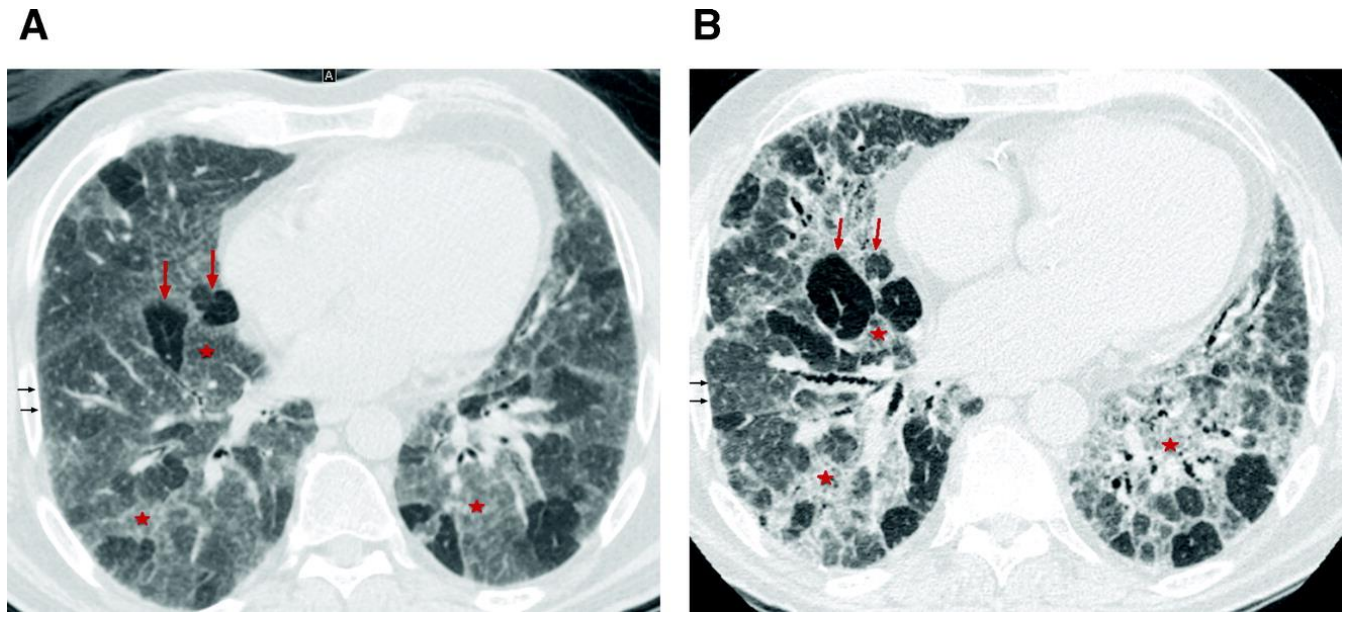

Figure 2. Three-density pattern. High-resolution computed tomography (*A*) inspiratory and (*B*) expiratory images from a patient with hypersensitivity pneumonitis demonstrating the three different densities: high attenuation (ground-glass opacity) (red stars), lucent lung (regions of decreased attenuation and decreased vascular sections) (red arrows), and normal lung (black arrows), which are sharply demarcated from each other.

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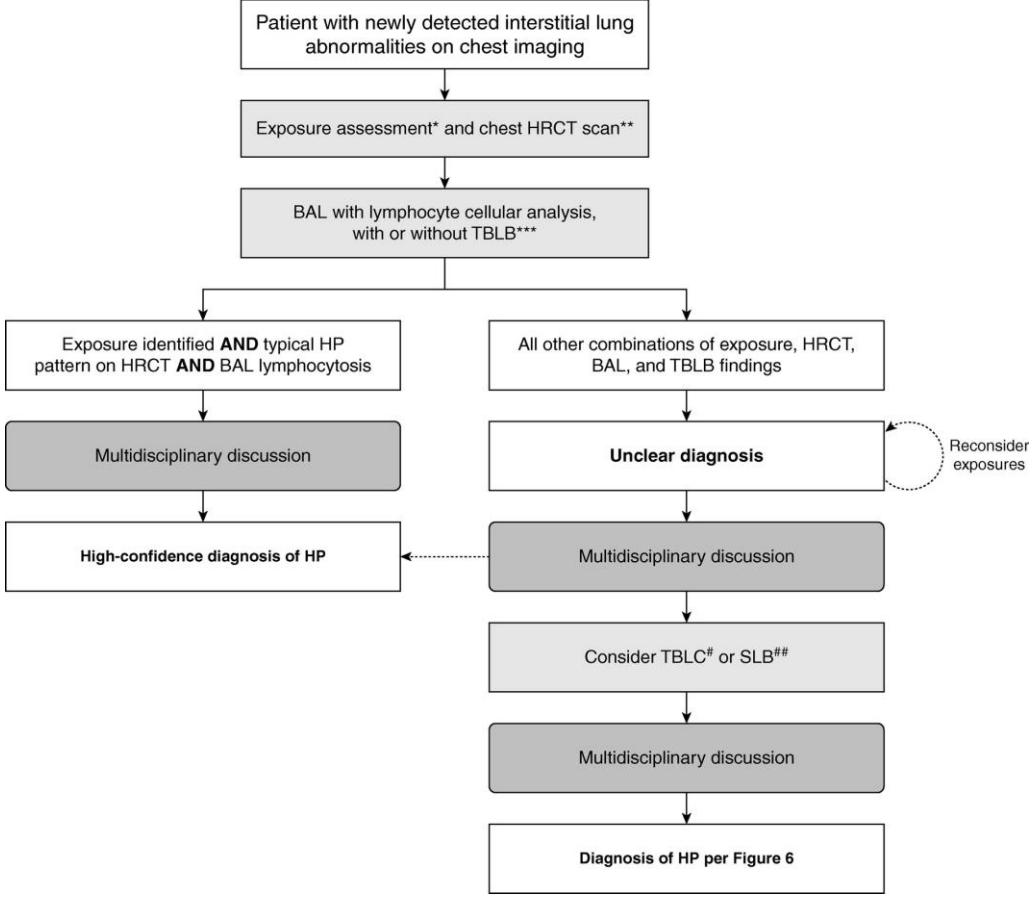

Figure 7. Algorithm for the diagnostic evaluation of possible hypersensitivity pneumonitis (HP). Specific features are described for all steps of the algorithm in the corresponding sections of the manuscript. A provisional diagnosis may be adequate in patients for whom the differential diagnosis has been sufficiently narrowed such that further investigations are unlikely to alter management, when invasive testing has unacceptable risks, or when such tests are declined by the patient. *Exposure assessment includes a thorough clinical history and/or serum IgG testing against potential antigens associated with HP and/or, in centers with the appropriate expertise and experience, specific inhalational challenge testing as described in References 9, 323, 324, and 325. **High-resolution computed tomography should be performed using the technique described in Table 3 and then reviewed with a thoracic radiologist. ***Transbronchial lung biopsy is suggested for patients with potential nonfibrotic HP (see question 4, recommendation 1). #TBLC is suggested for patients with potential nonfibrotic HP, depending on local expertise (see question 5, recommendation 2). ##SLB is infrequently considered in patients with nonfibrotic HP. HRCT = high-resolution computed tomography; SLB = surgical lung biopsy; TBLB = transbronchial lung biopsy; TBLC = transbronchial lung cryobiopsy.

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THANK YOU