Hypersensitivity Pneumonitis Common Diagnostic and Treatment Dilemmas

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Conflict of Interest

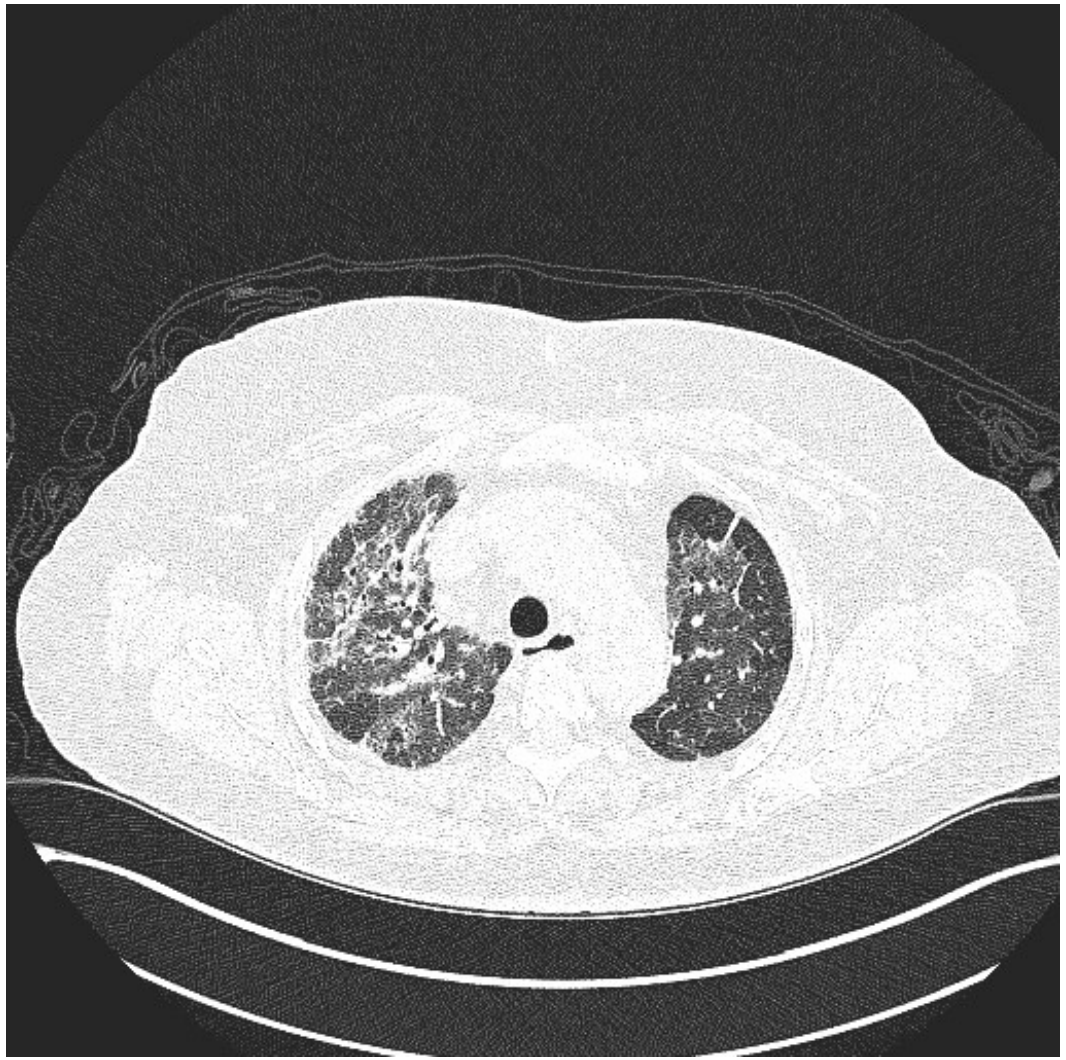
No conflicts of interest to declare for any materials presented in the current talk

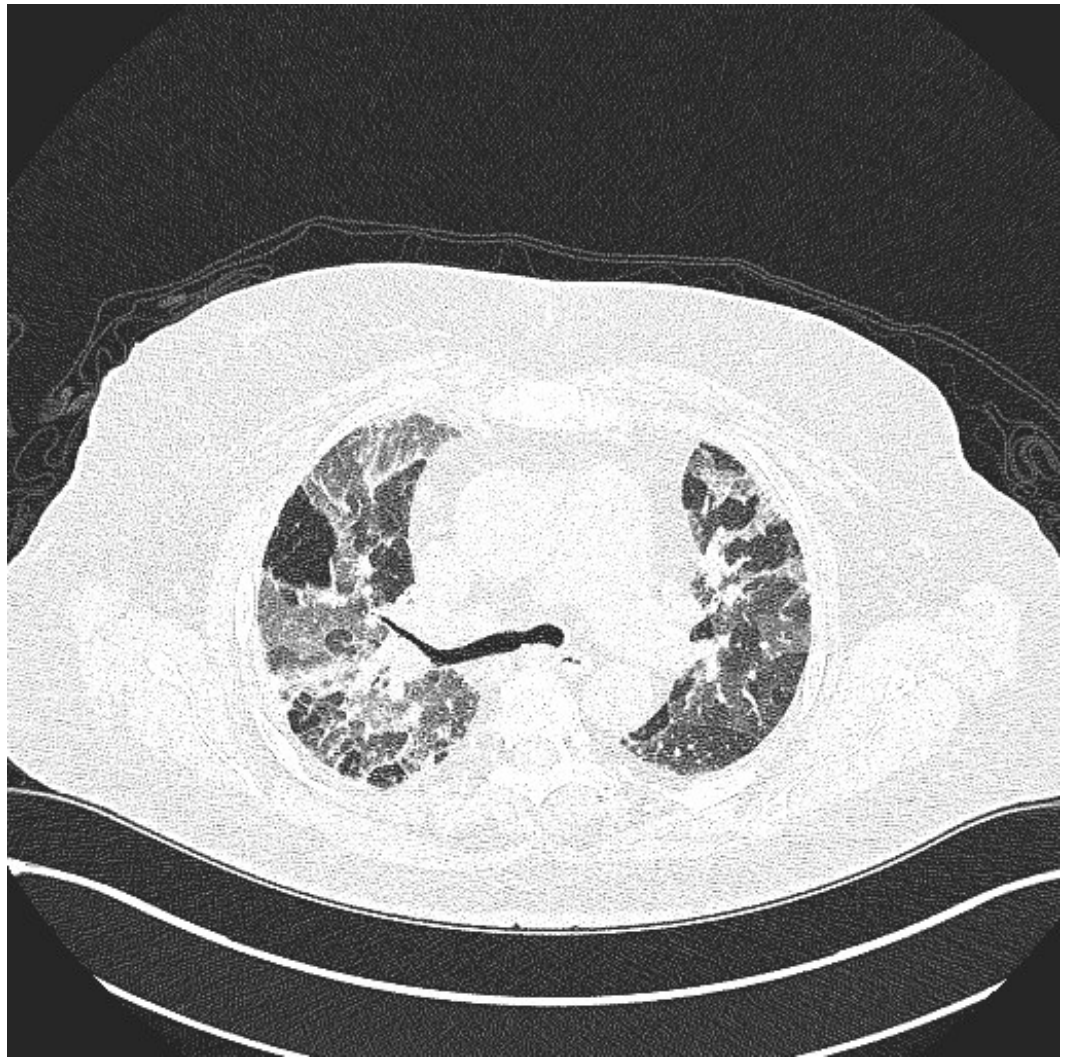
What is hypersensitivity pneumonitis ?

Patient BA

- 78 year man
- 18 months of cough and shortness of breath

Patient BA

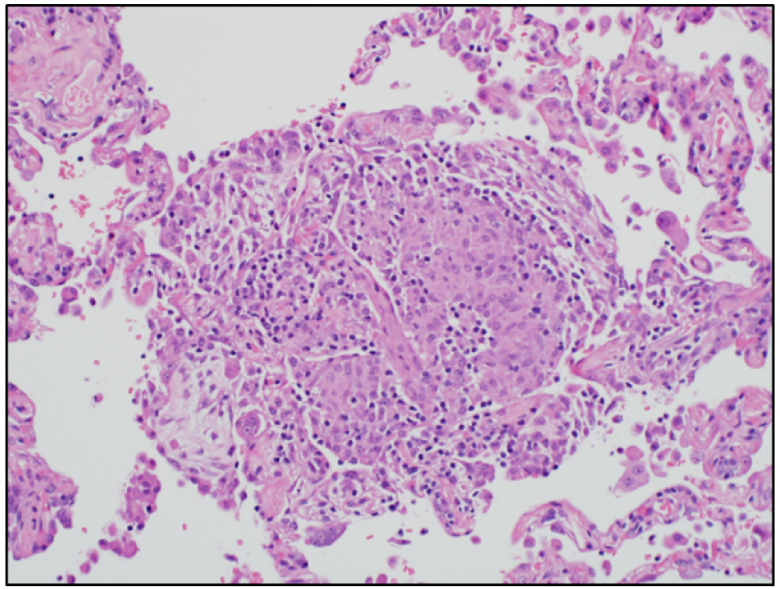




Patient BA

- Risk factors for HP
  - Is a bird lover
  - Has converted his garage into an aviary and has had 100+ pigeons for > 5 years

Patient BA



BAL

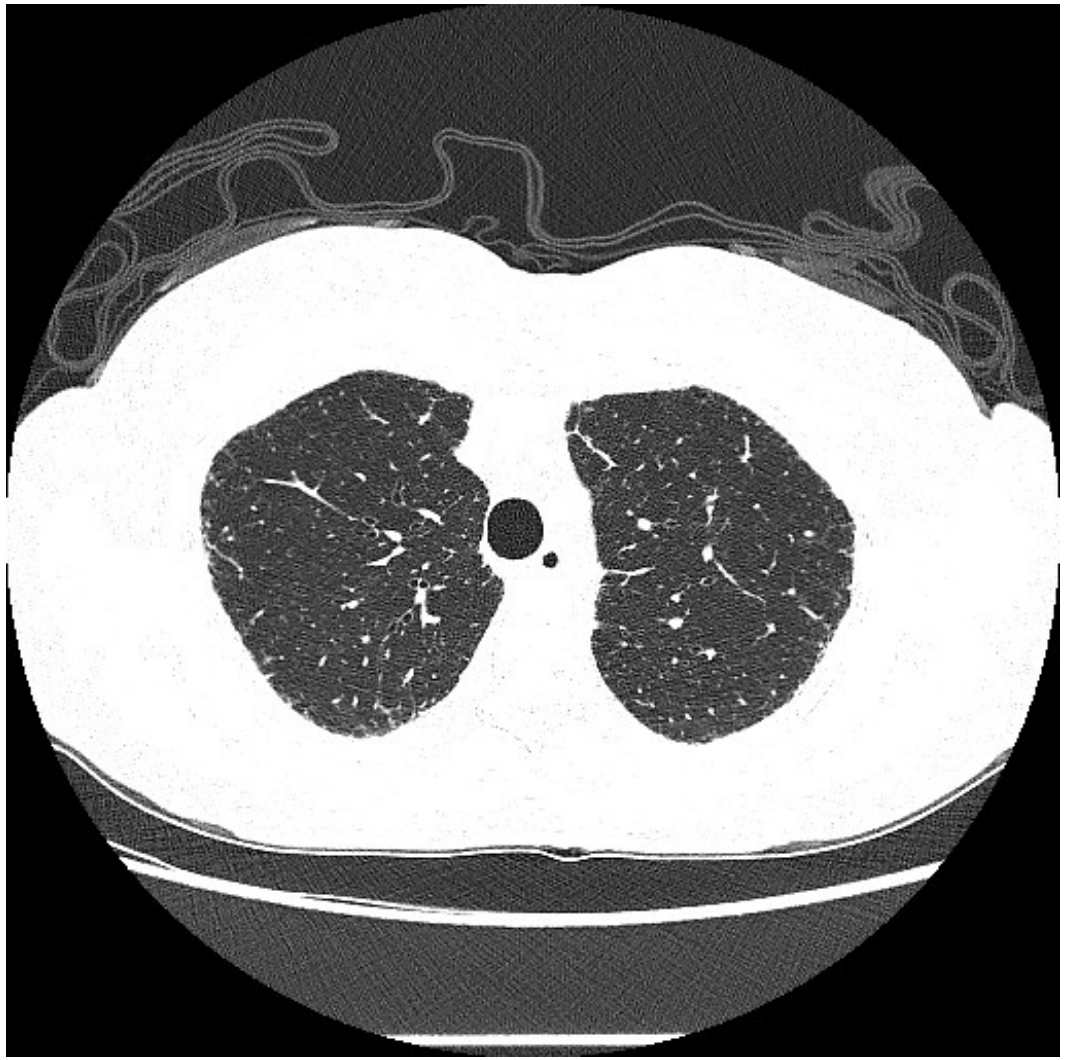
- 62% lymphocytes
- 10% eosinophils
- 12% neutrophils
- 16% monocytes and others

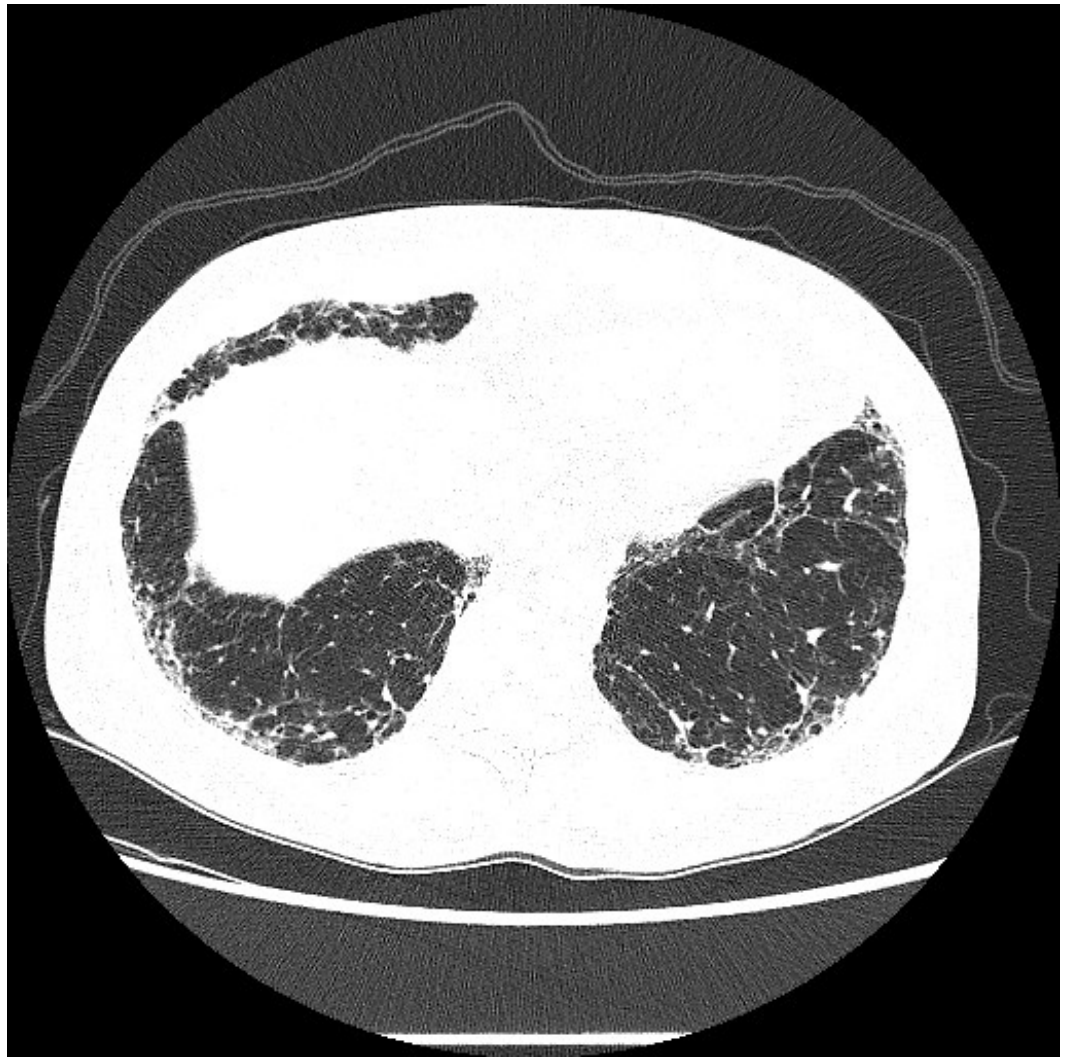
Does this patient have HP ?

Case CF

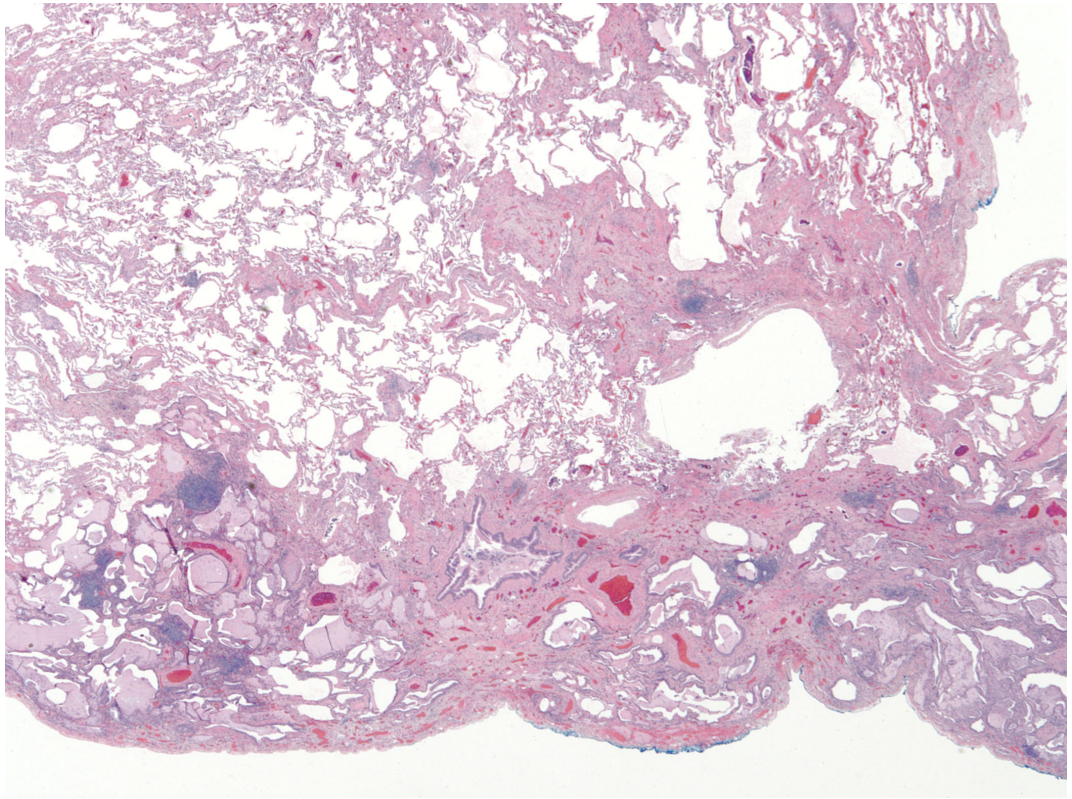
- 57 year old woman
- 10 months of cough and shortness of breath
- NO risk factors for HP on detailed questioning; even had a home inspection; negative for mold infestation, water leaks or any other risks for HP

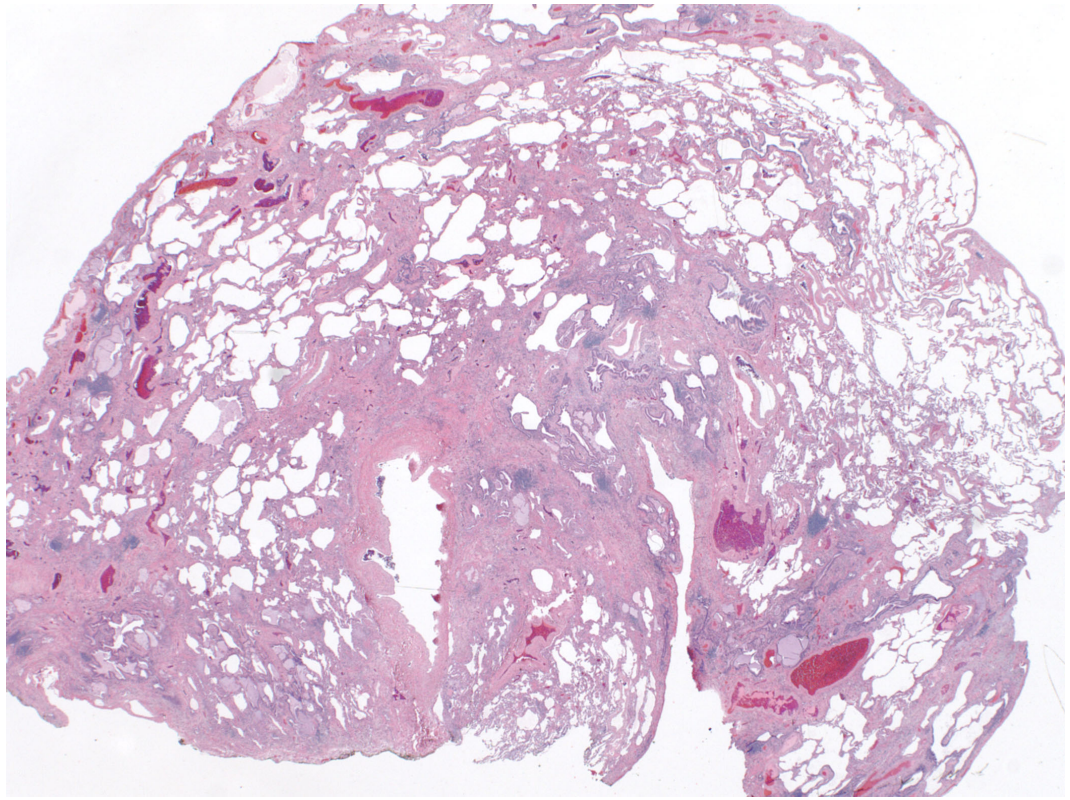
Patient CF





Patient CF



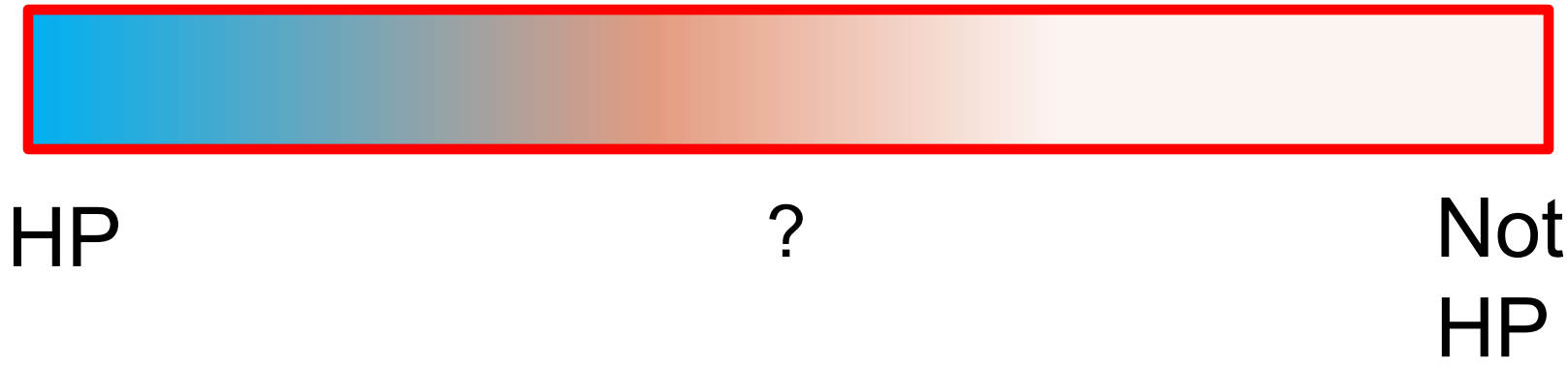


Does this patient have HP ?

Hypersensitivity Pneumonitis

No universally accepted definition of what constitutes Hypersensitivity Pneumonitis

HP vs Not HP



Practical problems with diagnosis and treatment of Hypersensitivity Pneumonitis

“Significant Exposure”

Exposure

Definitely significant exposure

?

No exposure

Role of Serologic testing in the diagnosis of HP

- Positive serology denotes past exposure to antigen, and not HP
- Not standardized
- HP serology is neither sensitive nor specific enough to be clinically useful
- ? High titer denotes disease ?
- Many centers including ours do not routinely test for HP serology even in cases with suspected HP

Role of HRCT in the diagnosis of HP

Most studies over-estimate the performance characteristics of HRCT in the diagnosis of HP

- "Confident diagnosis of HP"
  - 88-92% accurate; 44-61% sensitive
  - (Lynch et al AJR 1995; Silva et al. Rad 2008)
- Model incorporating clinical and radiologic features
  - 91% specific and 48% sensitive for HP diagnosis
  - (Johannson et al. Thorax 2016)

Results not generalizable because:

- Limited alternative diagnoses included
- Low "prevalence" of confident diagnoses (24-62%)

Role of bronchoscopy in the diagnosis of HP

CD4/CD8 ratio

- Can be low in HP
- Not sensitive or specific enough to be clinically relevant
- We do not measure this in our clinical practice

Lymphocytosis on BAL

- Most lymphocyte data on HP derives from relatively small case series, studies without proper description of extent/degree of radiologic or histopathologic fibrosis, and are subject to confirmation bias
- Can be seen in other ILDs such as NSIP, OP and sarcoidosis
- Highly suggestive of HP in the appropriate clinical and radiologic setting, but neither sensitive nor specific to be diagnostic of HP by itself

Role of bronchoscopy in the diagnosis of HP

Transbronchial forceps biopsy

- Poorly formed granulomas and giant cells in the right context highly suggestive of HP
- Seen in only 11-25% of cases (Lacasse et al. Chest 1997, Seth et al. Chest 2017)

We routinely perform BAL and TBBx for all patients suspected of HP, even in typical cases and highly suggestive histories

Surgical lung biopsy in the diagnosis of HP

Classic triad

- Chronic cellular bronchiolitis
- Cellular chronic interstitial pneumonia with bronchiolocentric distribution
- Small, loose non necrotizing granulomas and/or giant cells located within peribronchiolar interstitium

These findings are not present in all patients

Following factors are variably present

- Cellular NSIP
- Fibrotic NSIP
- Organizing pneumonia
- Nonspecific fibrosis and inflammation

Suggested algorithms

PULMONARY PERSPECTIVE

Hypersensitivity Pneumonitis: Perspectives in Diagnosis and Management

Martina Vasakova[1], Ferran Morell[2], Simon Walsh[3], Kevin Leslie[4], and Ganesh Raghu[5]

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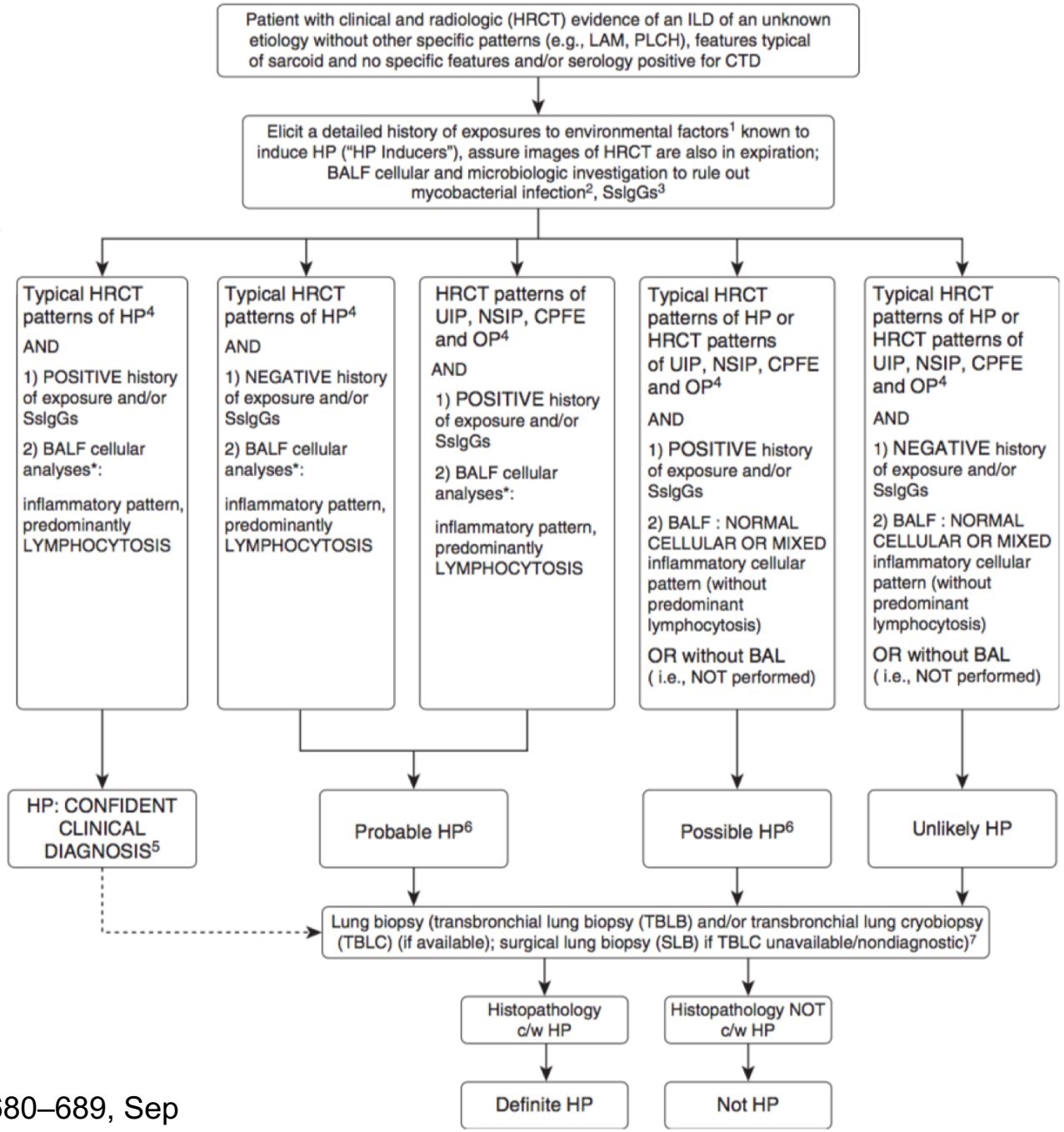

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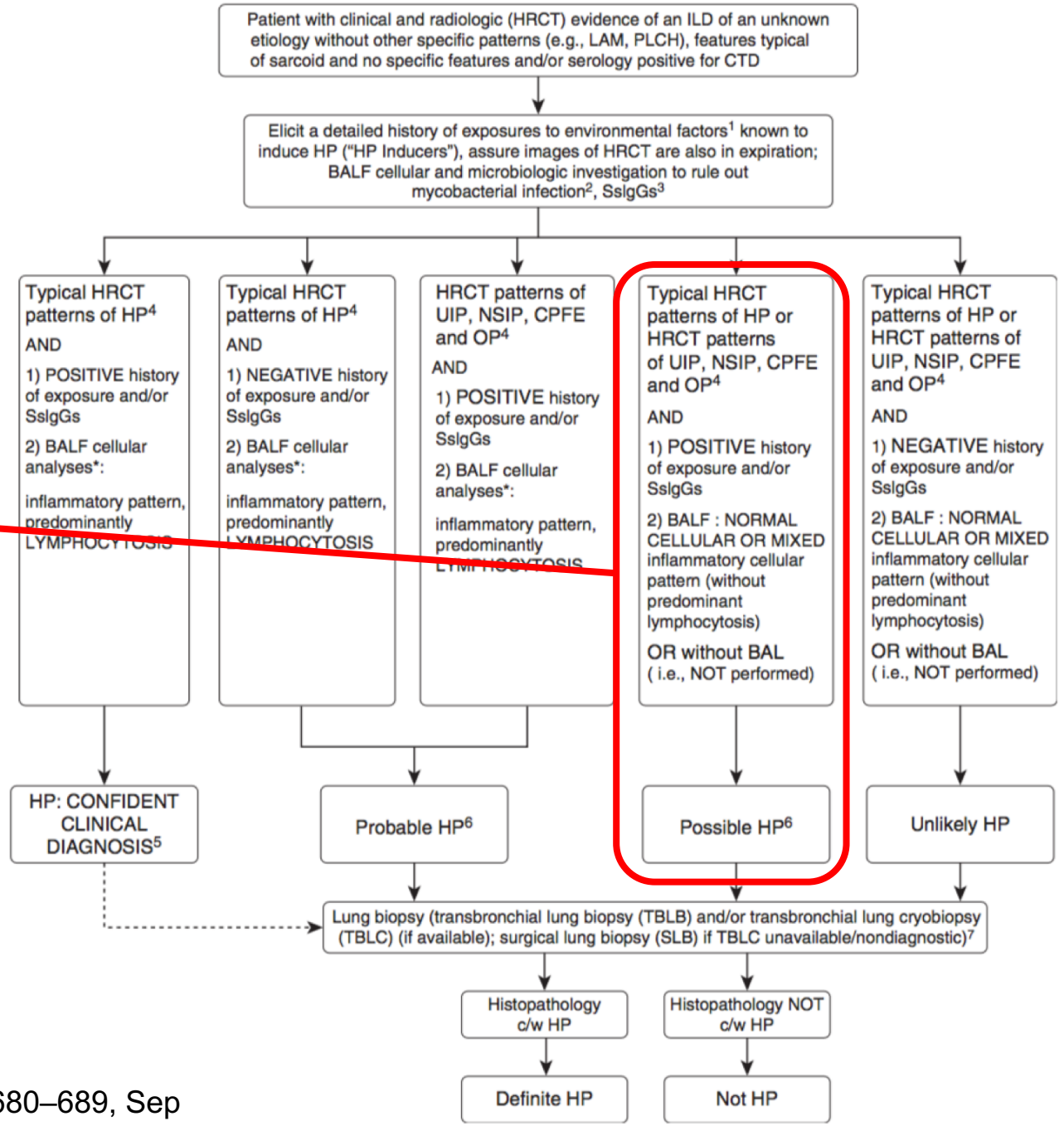
Typical HRCT patterns of HP or HRCT patterns of UIP, NSIP, CPFE and OP[4]

AND

1) POSITIVE history of exposure and/or SsIgGs

2) BALF : NORMAL CELLULAR OR MIXED inflammatory cellular pattern (without predominant lymphocytosis)

OR without BAL (i.e., NOT performed)



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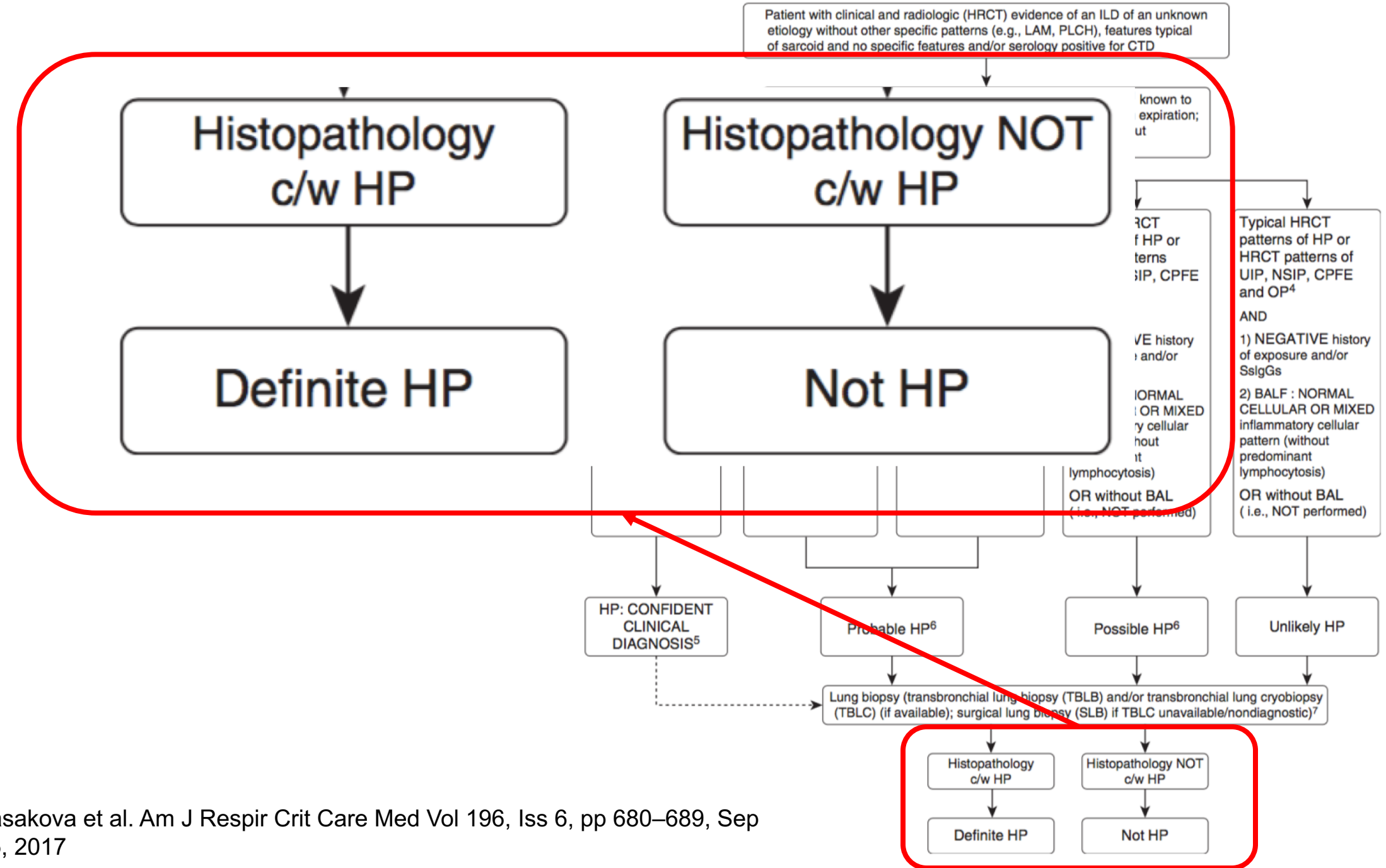

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Multidisciplinary Consensus: **The** Gold Standard

	Clinicians (κw)	Radiologists (κw)	Pathologists (κw)	MDTM (κw)
Idiopathic pulmonary fibrosis	0·72 (0·67–0·76)	0·60 (0·46–0·66)	0·58 (0·45–0·66)	0·71 (0·64–0·77)
Connective tissue disease-related interstitial lung disease	0·76 (0·70–0·78)	0·17 (0·08–0·31)	0·21 (0·06–0·36)	0·73 (0·68–0·78)
Non-specific interstitial pneumonia	0·31 (0·27–0·41)	0·32 (0·26–0·41)	0·30 (0·00–0·53)	0·42 (0·37–0·49)
Hypersensitivity pneumonitis	0·42 (0·30–0·47)	0·35 (0·29–0·43)	0·26 (0·10–0·45)	0·29 (0·24–0·40)

Data are median (IQR). MDTM=multidisciplinary team meeting.

Table 4: **Weighted kappa values (κw) for estimation of diagnostic likelihood for individual diagnoses of diffuse parenchymal lung disease**

Walsh et al. Lancet Respir Med 2016; 4: 557–65

Multidisciplinary Case Review: **The** Gold Standard

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Treatment of Hypersensitivity Pneumonitis

Only one randomized controlled trial

- 8 week tapering course of prednisone vs placebo in acute farmers lung
- Improvement noted in both groups
- No difference at 12 months
  - (Kokkarinen et al. ARRD 1992)

Virtually all data comes from relatively small non-randomized observational studies or expert opinion

Retrospective analysis of patients with fibrotic HP treated with mycophenolate or Azathioprine showed no change in FVC and improved DLCO after 1 year

- (Morriset et al. Chest 2017.)

Diagnosis of HP (Stanford)

- Detailed history including a modified HP questionnaire
- HRCT with exp views
- BAL/Transbronchial biopsy for all patients with suspected HP
  - Significant lymphocytosis
  - Giant cells and poorly formed granulomas
- Surgical lung biopsy if constellation of above does not give a confident diagnosis
- Weekly multidisciplinary ILD conference
- Other factors to consider
  - Presence or degree of inflammatory features
- Do not do the following
  - HP Serology
  - CD4/8 ratios
  - Specific antigen inhalational challenge

Pharmacologic treatment of HP (Stanford)

- Not everyone needs pharmacologic treatment
- Observation if
  - Stable symptoms, stable PFTs, and CT shows mostly fibrotic disease
- Withdraw therapy if
  - Slowly progressive mostly fibrotic disease unresponsive to therapy
- Corticosteroids
  - Prefer using lower doses of steroids (0.5 mg/kg/day equivalent of prednisone rather than 1mg/kg/day equivalent of prednisone)
  - Try to limit corticosteroid therapy to 3-4 months
- Steroid sparing agents
  - Mycophenolate (2000-3000 mg/day)
  - Azathioprine (up to 2 mg/kg/day)

Pharmacologic treatment of HP (Stanford)

Steroid monotherapy

- Relatively acute disease with little fibrosis
- No suggestion of fibrosis on CT

Addition of steroid sparing therapies

- Relapse after tapering steroids

Concomitant initiation of steroids and steroid sparing therapy

- Presence of fibrosis in addition to inflammation
- Relative contraindication to corticosteroids

Monotherapy, steroid sparing therapy

- Serious contraindication to corticosteroids
- Relatively chronic disease with progression

Future directions

- A clinically useful definition of what constitutes HP
- Role of anti-fibrotic IPF medications in HP

Questions ?

The mind is restless and difficult to restrain, but it is subdued by practice – The Gita.