ILD Collaborative

Project ECHO

Hypersensitivity Pneumonitis: Diagnostic Approach and Challenges

Robert Hallowell, MD

Disclosures

- Consulting fees from Boehringer Ingelheim, Vicore Pharma
- Research trials with Boehringer Ingelheim

70 y/o man with 9 months of malaise, dry cough, progressive dyspnea

- Worked in an office for 25 years
- No hobbies
- No farm exposure
- **No pets**
- **No birds in the home (ever)**
- **No bird exposure**
- **No down products in the home**
- No hot tub

The exposure history is critical but difficult to obtain

Standard HP panel was ***negative***

Symptoms improved after he retired

The exposure history is critical but difficult to obtain












Causes of hypersensitivity pneumonitis

Mold
Farmer's Lung (moldy hay)
Tobacco Grower's Lung
Mushroom Worker's Lung
Potato Riddler's Lung
Paprika Slicer's Lung
Wine Maker's Lung
Cheese Washer's Lung
Coffee Worker's Lung
Tea Grower's Lung
Malt worker's Disease

Bible Printer's Lung
Bagpipe Lung
Gardening/landscaping
Woodworker's lung

Mold or bacteria
Humidifier Fever
Hot Tub Lung
Lifeguard Lung
Shower Lung
Grain Measurer's Lung
Machinist Lung

Animal proteins
Bird Fancier's Lung
Pigeon Breeder's Lung
Furrier's Lung
Lab worker's Lung (rats, gerbils)
Bat Lung droppings
Fish Meal Worker's Lung
Mollusk Shell Lung
Oyster Shell Pneumonitis

Inorganic chemicals
Chemical Workers Lung
Detergent Worker's Lung
Vineyard Sprayer's Lung
Epoxy Resin Lung

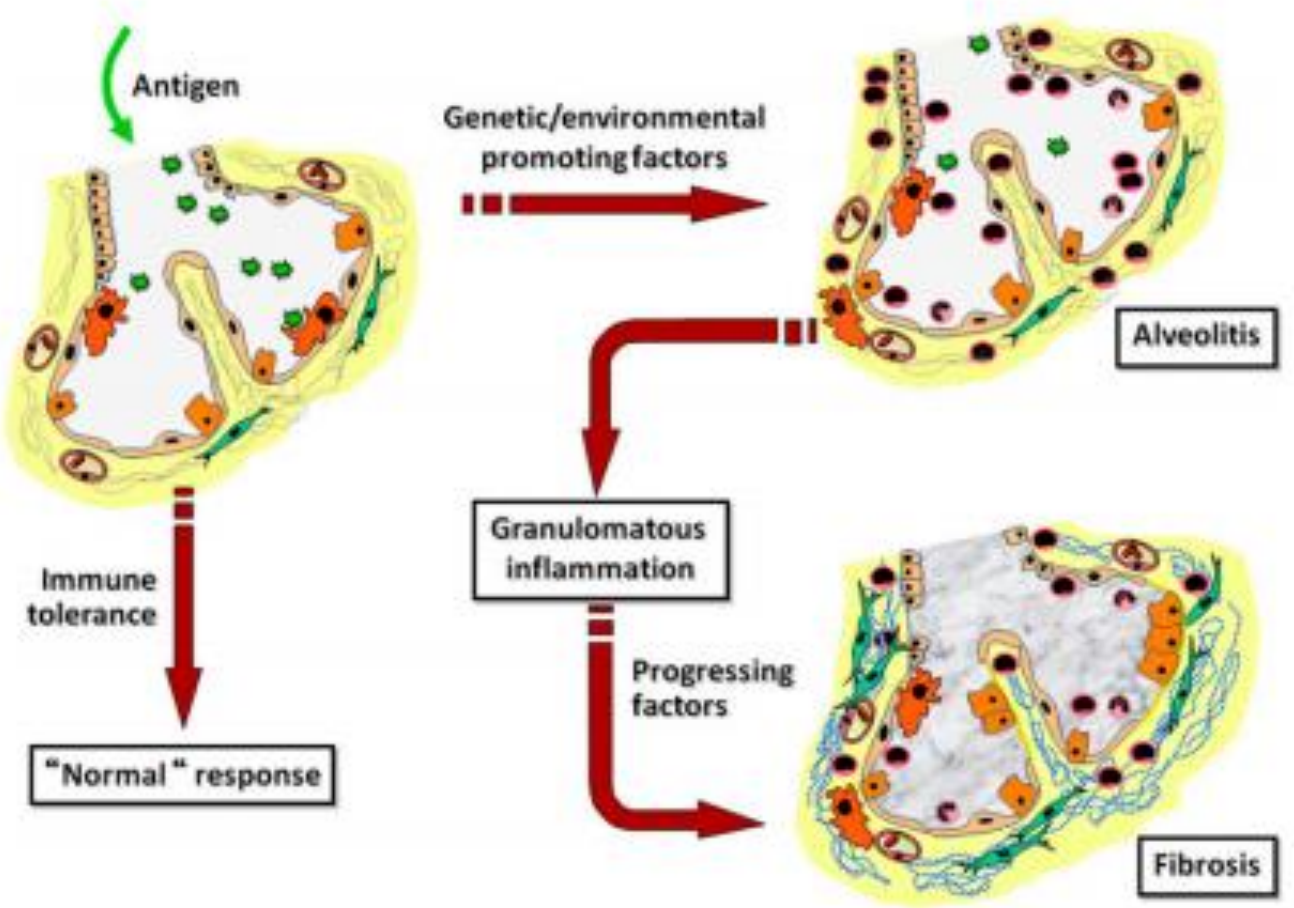
Down products alone can cause HP

Author	Total chronic HP patients, n	Down products as only known exposure, n (%)
Silva et al.	18	2 (11%)
Morell et al.	20*	10 (50%)
Tsutsui et al.	23	11 (48%)
Ishizuka et al.	28	11 (39%)
Morisset et al.	70	6 (8.6%)

*Initially diagnosed with IPF; others in cohort have no other known antigen exposure

Silva et al. Radiology: Volume 246: Number 1—January 2008
Morell et al. Lancet Respir Med 2013; 1: 685–94
Tsutsui et al. Ann Am Thorac Soc Vol 12, No 7, pp 1013–1021, Jul 2015
Ishizuka et al. Ann Am Thorac Soc Vol 12, No 2, pp 167–173, Feb 2015
Morisset et al. CHEST 2017; 151(3):619-625

The presumed pathogenesis of HP



Clinical presentation of HP

Acute:

Fever, chills, malaise, cough, dyspnea
Fine crackles common; wheezing is not typical
CT abnormalities: ground glass or normal
(RF may be positive)

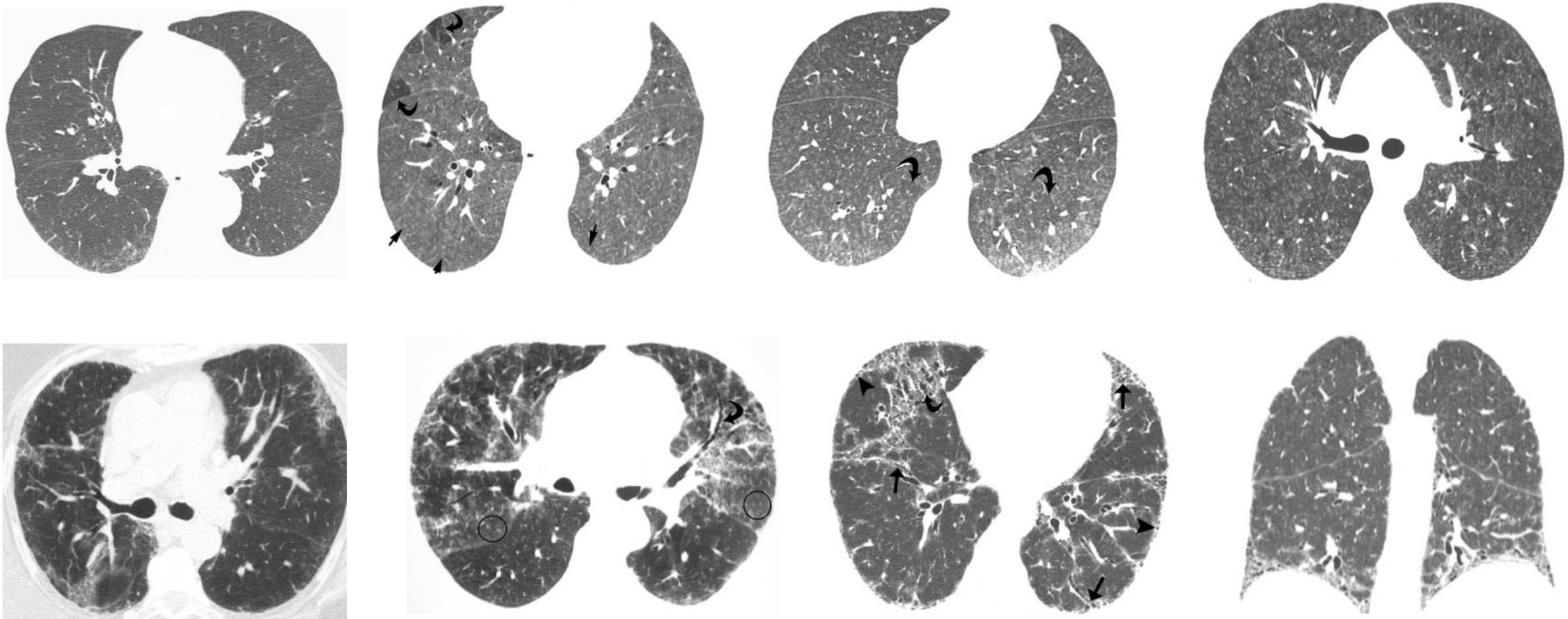
Subacute:

Productive cough, dyspnea, fatigue, anorexia, and weight loss
CT abnormalities: ground glass, diffuse micro-nodules,
patchy air trapping, early fibrotic changes

Chronic and progressive:

Cough, dyspnea, fatigue, anorexia, and weight loss
CT abnormalities: significant fibrotic changes, honeycombing,
micro-nodules may or may not be present

Characteristic CT findings in HP



Silva et al. *AJR* 2007; 188:334–344

CT findings in fibrotic HP are often non-specific

TABLE 2: CT Features of Patients with Chronic Hypersensitivity Pneumonitis (HP) and Usual Interstitial Pneumonia (UIP)

	No. (%) of Patients		
	Chronic HP (n = 19)	UIP (n = 33)	p
Honeycombing	3 (16)	29 (88)	<.0001
Traction bronchiectasis	10 (53)	28 (85)	.012
Micronodules	8 (42)	2 (6)	.002
Extensive ground-glass attenuation	6 (32)	4 (12)	.087
Irregular lines	16 (84)	32 (97)	.096
Parenchymal distortion	15 (79)	30 (91)	.224
Air-space opacity	2 (11)	6 (18)	.461
Overall extent of isolated ground-glass attenuation (mean ± standard error of the mean)	32 ± 5	26 ± 4	.350
Upper zone predominance	3 (16)	1 (3)	.096
Middle zone predominance	3 (16)	2 (6)	.252
Lower zone predominance	8 (42)	27 (81)	.003
No zone predominance	5 (26)	3 (9)	.097
Peripheral predominance	10 (53)	30 (91)	.002
Peripheral and lower zone predominance	5 (26)	25 (76)	.001
Relative sparing of lower half of lower zone	13 (48)	3 (8)	<.001

Common antigens on our local precipitins panels

Aspergillus fumigatus #1, #2, #3, #6

Aspergillus flavus

Thermoactinomyces candidus
Farmer's Lung

Thermoactinomyces vulgaris
Water contamination, humidifiers

Saccharomonospora viridis
Humidifiers and hay

Micropolyspora faeni
(*Saccharopolyspora rectivirgula*)
Farmer's Lung

Pigeon serum

Aureobasidium pullulans
Black fungus in soil and water

How useful is the HP precipitins panel?

78% of patients with HP had positive precipitins
31% of controls had positive precipitins

TABLE 4. PROBABILITY OF HAVING HYPERSENSITIVITY PNEUMONITIS

Exposure to a Known Offending Antigen	Recurrent Episodes of Symptoms	Symptoms 4–8 h After Exposure	Weight Loss	Crackles, %: + / Serum Precipitins: +	Crackles, %: + / Serum Precipitins: −	Crackles, %: − / Serum Precipitins: +	Crackles, %: − / Serum Precipitins: −
+	+	+	+	98	92	93	72
+	+	+	−	97	85	87	56
+	+	−	+	90	62	66	27
+	+	−	−	81	45	49	15
+	−	+	+	95	78	81	44
+	−	+	−	90	64	68	28
+	−	−	+	73	33	37	10
+	−	−	−	57	20	22	5
−	+	+	+	62	23	26	6
−	+	+	−	45	13	15	3
−	+	−	+	18	4	5	1
−	+	−	−	10	2	2	0
−	−	+	+	33	8	10	2
−	−	+	−	20	4	5	1
−	−	−	+	6	1	1	0
−	−	−	−	3	1	1	0

All the predictors are dichotomous variables: '−' indicates absent; '+' indicates present.

BAL patterns seen in HP

17 patients with HP,

9 with fibrosis on CT

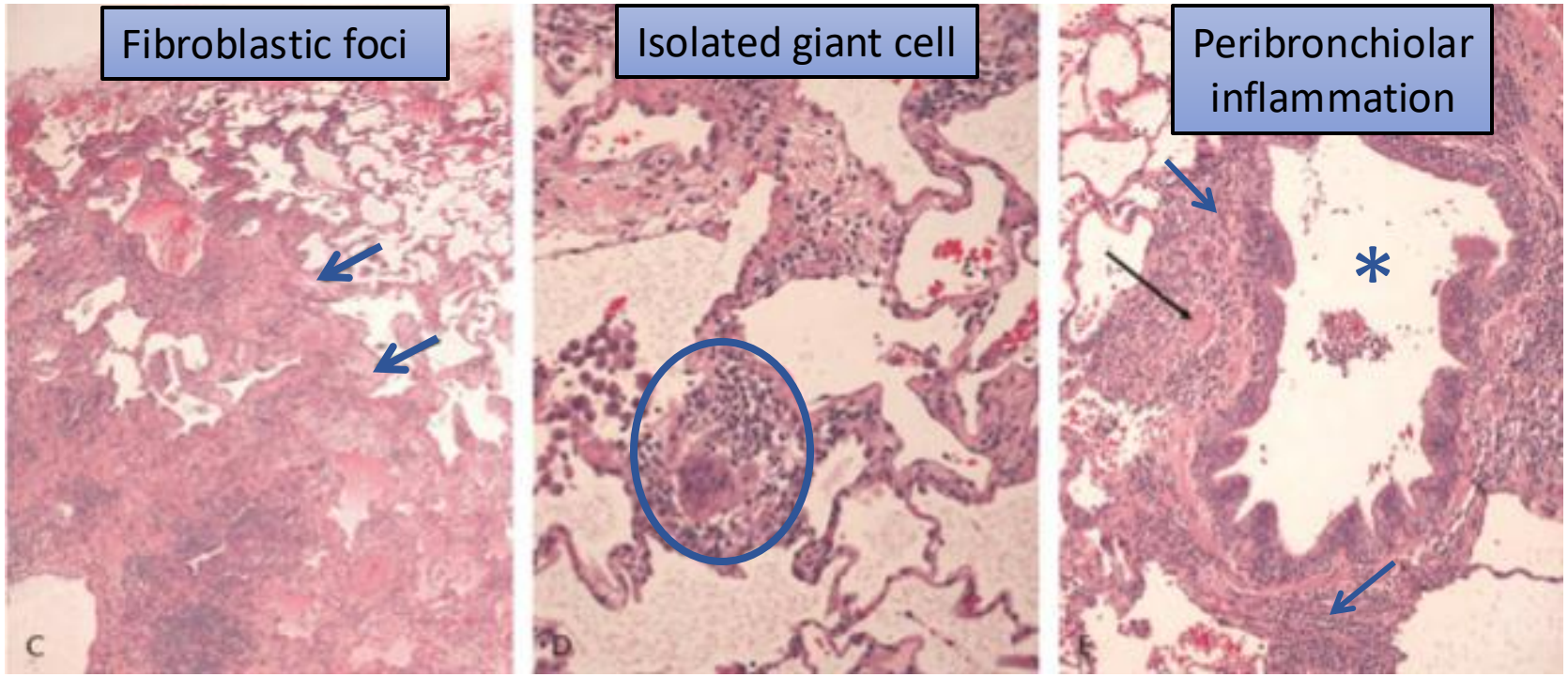
8 without fibrosis on CT

Table 3—*Comparison of Cellular Composition of BAL Fluids Between Nonfibrosis Group and Fibrosis Group

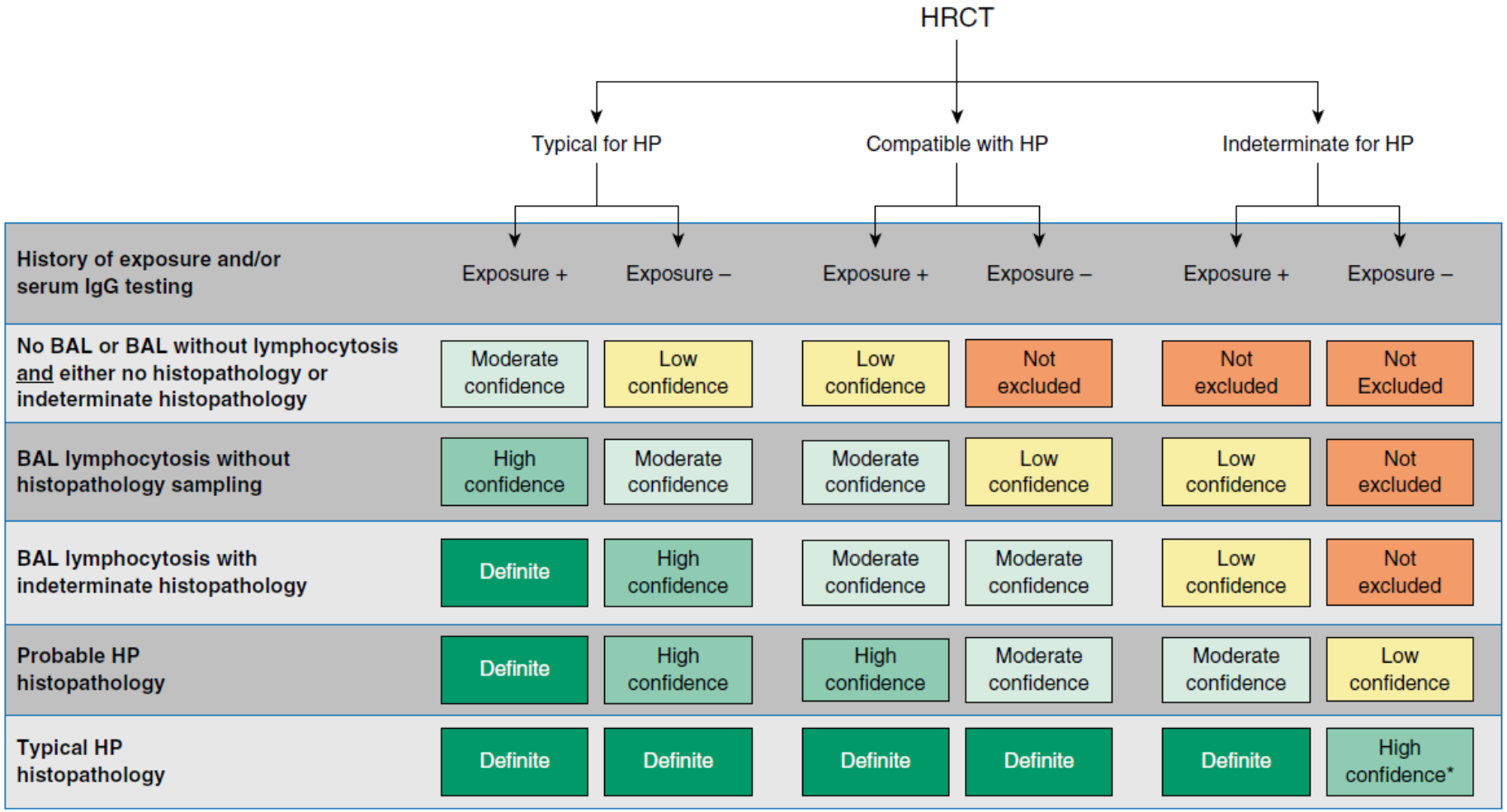
	Nonfibrosis Mean ± SD	Fibrosis Mean ± SD	p Value
Total cell	78.90 ± 25.77	36.39 ± 21.95	0.002†
Macrophages	14.49 ± 6.05	13.77 ± 12.95	NS
Neutrophils	2.60 ± 1.81	1.04 ± 1.04	0.043†
Eosinophils	0.80 ± 0.78	1.39 ± 3.21	NS
Mast cells	0.91 ± 2.01	0.04 ± 0.07	NS
Lymphocytes	59.79 ± 23.23	20.04 ± 17.85	0.001†
T cell	51.64 ± 21.20	17.36 ± 15.49	0.002†
B cell	1.95 ± 1.02	0.95 ± 0.92	NS
CD4	11.35 ± 4.96	9.94 ± 10.81	NS
CD8	37.00 ± 15.83	4.83 ± 4.19	0.000†
CD4/CD8	0.31 ± 0.13	2.59 ± 2.63	0.027†

Pathology in fibrotic HP

6/13 had only giant cells without any granulomas
9/13 patients had **UIP** on some areas of pathology
4/13 had areas of **NSIP**

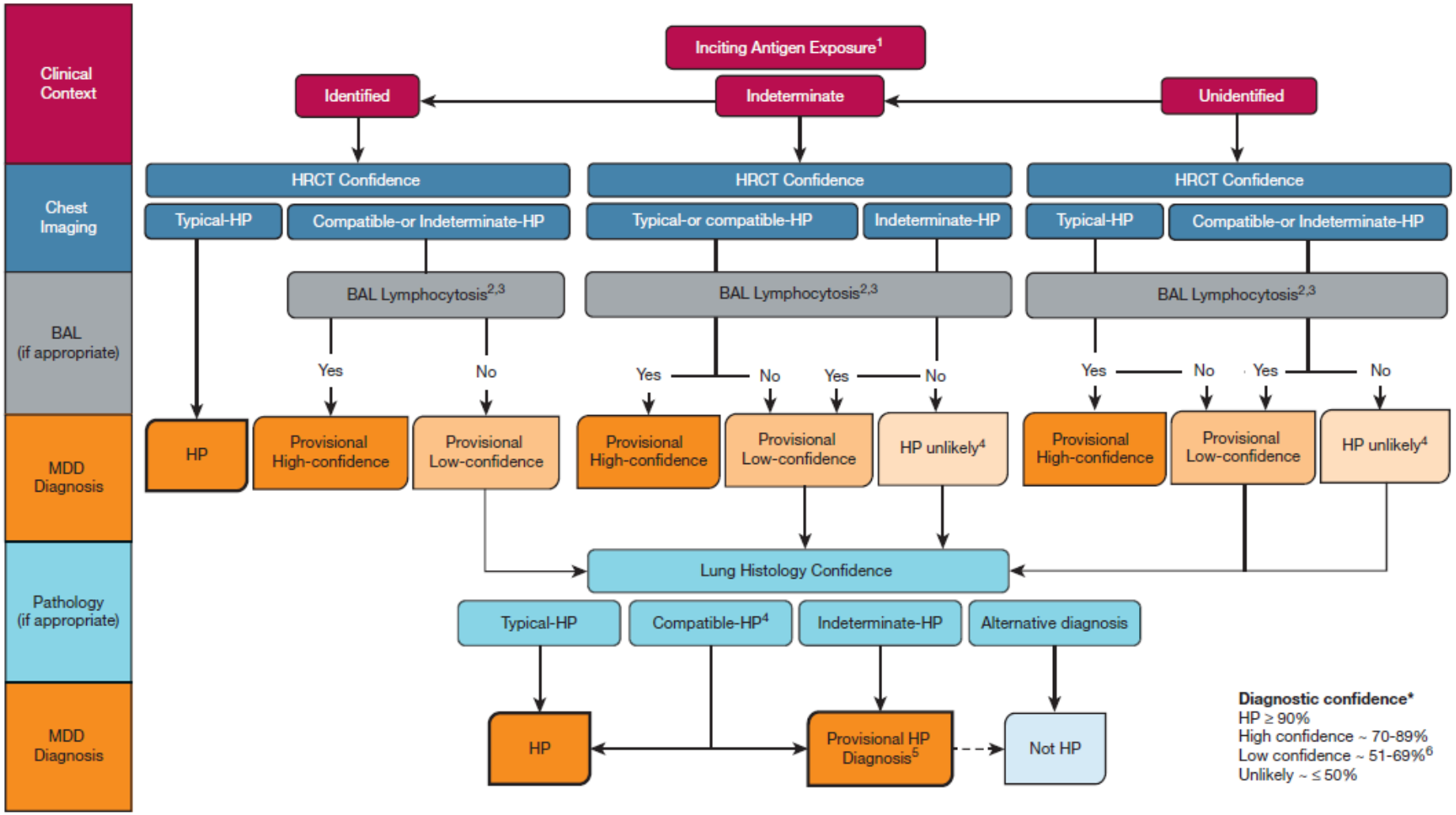


Diagnostic algorithm--ATS



History of exposure and/or serum IgG testing	Typical for HP: Exposure +	Typical for HP: Exposure –	Compatible with HP: Exposure +	Compatible with HP: Exposure –	Indeterminate for HP: Exposure +	Indeterminate for HP: Exposure –
No BAL or BAL without lymphocytosis and either no histopathology or indeterminate histopathology	Moderate confidence	Low confidence	Low confidence	Not excluded	Not excluded	Not Excluded
BAL lymphocytosis without histopathology sampling	High confidence	Moderate confidence	Moderate confidence	Low confidence	Low confidence	Not excluded
BAL lymphocytosis with indeterminate histopathology	Definite	High confidence	Moderate confidence	Moderate confidence	Low confidence	Not excluded
Probable HP histopathology	Definite	High confidence	High confidence	Moderate confidence	Moderate confidence	Low confidence
Typical HP histopathology	Definite	Definite	Definite	Definite	Definite	High confidence*

Diagnostic algorithm--ACCP



Fernandez Perez et al. CHEST 2021; 160(2):e97-e156

Mimics of HP

Inhalation Fever: "Metal fume fever," "Monday morning miseries"

Injury to pulmonary cells leads to cytokine release

Fevers, chills, malaise, dyspnea, cough 4-12 hours after exposure

Organic Dust Toxic Syndrome: "Pulmonary mycotoxicosis"

Mycotoxins and endotoxins from Fusarium (aflatoxin)

Intense exposure in a single day

Fevers, chills, myalgias, dyspnea

Get infiltrates, reduced DLCO

Path shows obliterative bronchiolitis or DAD

Asthma triggered by dust, mold, etc.

Rarely have wheezing with HP

International Pillow Fight Day
04/05/2025 (Saturday)

(Masks recommended)

Summary

- HP can be challenging to diagnose!
- The exposure history is critical and can be extremely difficult to elicit.
- Although “classic” features may exist, the radiographic and pathologic findings are frequently non-specific.