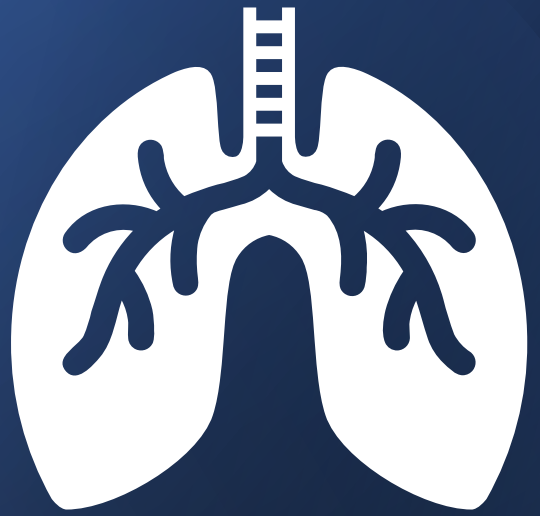

Pulmonary Medicine Board Questions

Selected topics

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HARVARD MEDICAL SCHOOL | Postgraduate Medical Education

Disclosures

- Associate Editor for Education at NEJM Group

ABIM Pulmonary Medicine Exam Blueprint

Medical Content Category	% of Exam
Obstructive Lung Disease	17.5%
Critical Care Medicine	15%
Diffuse Parenchymal Lung Disease (DPLD)	10%
Sleep Medicine, Neuromuscular and Skeletal	10%
Epidemiology	2%
Infections	12%
Neoplasia	9.5%
Pleural Disease	5%
Quality, Safety, and Complications	5%
Transplantation	2%
Vascular Diseases	6%
Respiratory Physiology and Pulmonary Symptoms	4%
Occupational and Environmental Diseases	2%
	100%

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Outline

- Case-based review of selected topics on the pulmonary medicine board exam:
  - Obstructive lung disease
  - Diffuse parenchymal lung disease
  - Pulmonary infections
  - Pulmonary vascular diseases

Case 1

A 45 year-old woman with asthma is referred for a second opinion. She has had asthma since she was a child. She has a history of seasonal allergies and has sensitivity to perennial allergens by blood testing as well. For the last year she has been on a high dose combination ICS/LABA inhaler, a LAMA inhaler, an as needed SABA inhaler, and a leukotriene receptor antagonist. Despite adherence to this regimen, in the last year she has had several exacerbations of her asthma requiring glucocorticoid bursts 4 times in the last 6 months, most recently 3 weeks ago. She has been to the ED for asthma symptoms but has never been hospitalized. Her FEV1 is moderately reduced. She reports improvement in respiratory symptoms with glucocorticoid treatment but feels like her symptoms are slowly starting to worsening again. What is the best next step in management of her asthma?

A. Make no change, this patient's asthma is currently controlled
B. Check total IgE and blood eosinophil count to determine eligibility for biologic therapy
C. Start standing daily glucocorticoid with PJP prophylaxis for uncontrolled asthma
D. Decrease ICS/LABA to moderate dose to minimize adverse effects of ICS

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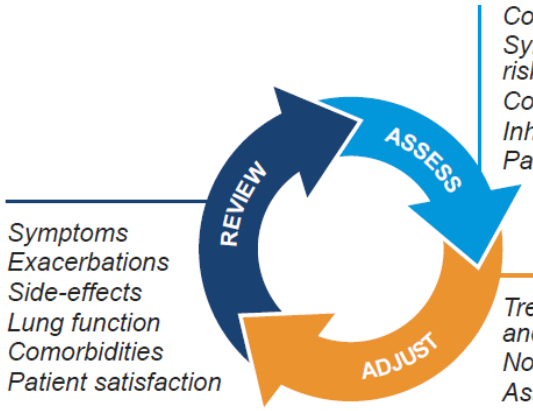
Asthma Definitions

- ATS/ERS definition of severe asthma (at least one)
  - treatment with GINA step 4-5 regimen for prior year
  - treatment with systemic glucocorticoid ≥50% of year

- ATS/ERS definition of uncontrolled asthma (at least one)
  - Poor symptom control
  - Frequent exacerbations (2 or more GC bursts)
  - Prior serious exacerbation (hospitalization, ICU stay, MV)
  - Airflow limitation (FEV < 80% predicted) despite appropriate bronchodilator therapy

GINA 2023 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP
RELIEVER: As-needed low-dose ICS-formoterol*			

See GINA severe asthma guide

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP
RELIEVER: as-needed ICS-SABA*, or as-needed SABA				

Other controller options (limited indications, or less evidence for efficacy or safety – see text)	*Low dose ICS whenever SABA taken*, or daily LTRA, or add HDM SLIT*	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects*

*Anti-inflammatory reliever (AIR)

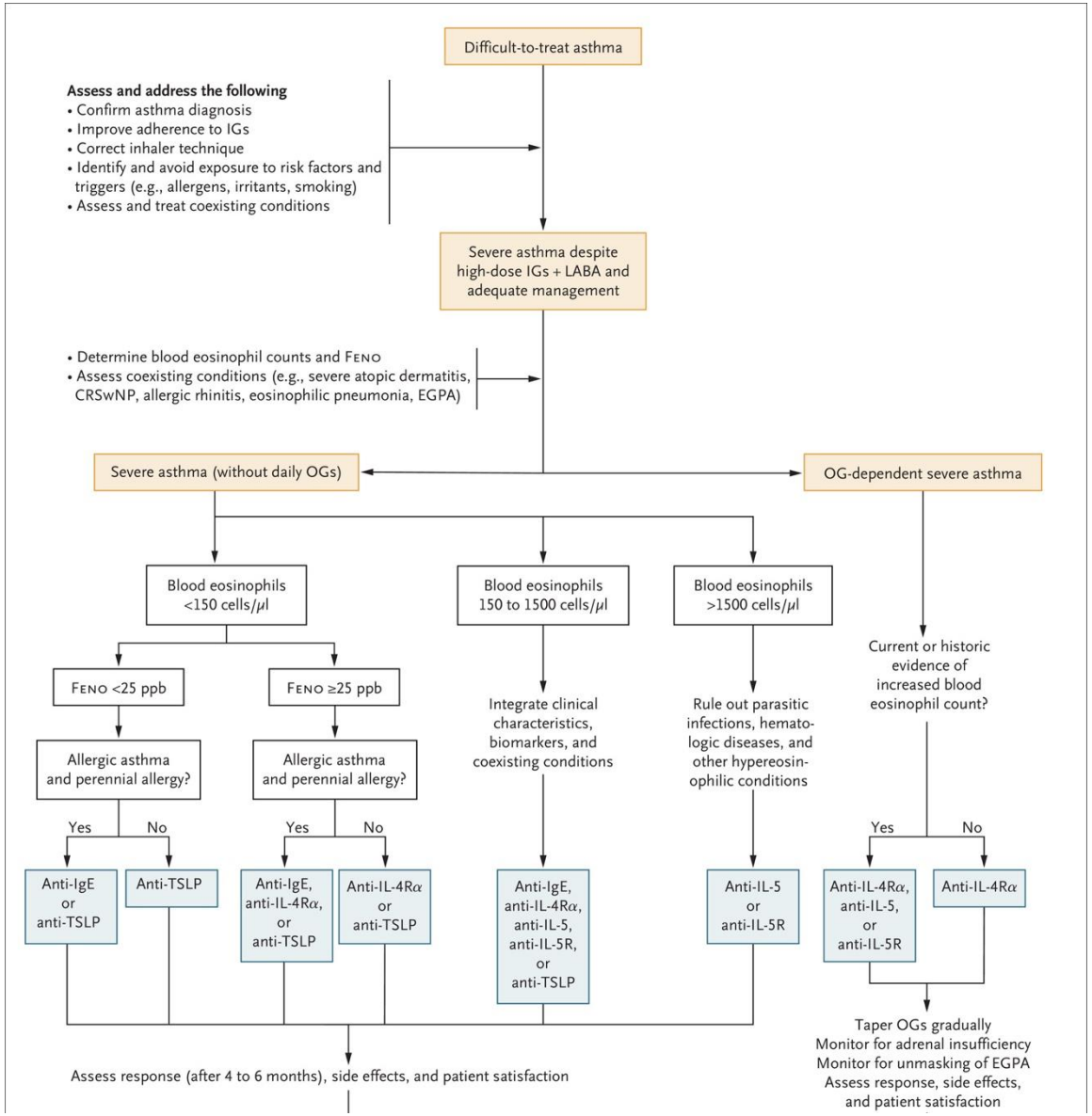
Choice of Biologic for Severe Asthma

Table 2. Choice of Monoclonal Antibody Treatment of Severe Asthma According to Patient Characteristics.*

Characteristic	Anti-IgE Antibody	Anti–Interleukin-4R Antibody	Anti–Interleukin-5 or Anti–Interleukin-5R Antibody
Indication	Severe allergic asthma	Severe type 2 asthma	Severe eosinophilic asthma
Age group	Children, adolescents, and young adults	Children, adolescents, and adults	Adults
Onset	Childhood	Childhood or adulthood	Adulthood
Allergy	Prerequisite: IgE sensitization to perennial allergen	Irrespective of allergy	Irrespective of allergy
Dominant biomarker	Serum total IgE (for dosing)	Increased FENO	Increased blood eosinophil count
Serum total IgE	Serum total IgE and weight within dose range, according to local eligibility criteria	Irrespective of total IgE	Irrespective of total IgE
Blood eosinophil count†	Slightly better response with increased count	>150 to <1500/μl†	Prerequisite: increased counts (according to local eligibility criteria), >150 to 300/μl†
FENO†	Slightly better response if increased FENO	Better response if FENO >25 ppb	Irrespective of FENO
Coexisting conditions	Allergic rhinitis, CRS with nasal polyposis, chronic urticaria	Atopic dermatitis, CRS with nasal polyposis	CRS with nasal polyposis
Exacerbations in previous yr	According to local criteria	According to local criteria	High frequency (≥2), as specified by local criteria

Brusselle, G. and G. Koppelman. *NEJM*, 2022.

Choice of Biologic for Severe Asthma



Brusselle, G. and G. Koppelman. *NEJM*, 2022.

Impact of Biologics

Table 2. Efficacy of the Biologics That Are U.S. Food and Drug Administration Approved for the Treatment of Moderate to Severe Persistent Asthma with Type 2–High Phenotype

Therapy	Asthma Exacerbation	Lung Function	Corticosteroid Weaning	Special Considerations
Omalizumab	Reduces by 25%	Minimal or equivocal improvement	Decreases use of ICS, but no data that it helps with OCS weaning	Only s.c. biologic approved for children 6–11 yr old
Mepolizumab	Reduces by ~50%	Inconsistent effect	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (14%)	Standard s.c. dosing has not been shown to decrease sputum eosinophilia; approved at higher dosing for EGPA
Reslizumab	Reduces by ~50–60%	Improved	Has not been specifically evaluated for this indication	Only weight-based dosing i.v. biologic approved for asthma
Benralizumab	Reduces by ~25–60%	Improved	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)	Only s.c. biologic that offers every-8-wk dosing
Dupilumab	Reduces by ~50–70%	Improved	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)	Only biologic that can be self-administered s.c.; showed benefit with $F_{ENO} \geqslant 25$ ppb regardless of eosinophil count

Definition of abbreviations: EGPA = eosinophilic granulomatosis with polyangiitis; F_{ENO} = fractional exhaled nitric oxide; ICS = inhaled corticosteroid; OCS = oral corticosteroid.

McGregor, M. et al. *AJRCCM*, 2019.

Asthma: learning points

- Biologic agents may be used for patients with poorly controlled severe asthma

- Anti-IL-5 therapy has been shown to improve clinical outcomes among patients with eosinophilic asthma including:
  - Reducing exacerbations
  - Reducing glucocorticoid use
  - Trend towards improving quality of life

(Bel, E. et al. *NEJM*, 2014.; Agache, I. et al. *Allergy*. 2020.; Farne, H. et al. *Cochrane*, 2022.)

Key Asthma References

- Agache I, et al. Efficacy and safety of treatment with biologicals (benralizumab, dupilumab, mepolizumab, omalizumab and reslizumab) for severe eosinophilic asthma. A systematic review for the EAACI Guidelines - recommendations on the use of biologicals in severe asthma. Allergy. 2020 May;75(5):1023-1042. doi: 10.1111/all.14221. Epub 2020 Feb 24. PMID: 32034960.

- Bel EH, et al; SIRIUS Investigators. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. N Engl J Med. 2014 Sep 25;371(13):1189-97. doi: 10.1056/NEJMoa1403291. Epub 2014 Sep 8. PMID: 25199060.

- Brusselle GG, Koppelman GH. Biologic Therapies for Severe Asthma. N Engl J Med. 2022 Jan 13;386(2):157-171. doi: 10.1056/NEJMra2032506. PMID: 35020986.

- Farne HA, et al. Anti-IL5 therapies for asthma. Cochrane Database Syst Rev. 2017 Sep 21;9(9):CD010834. doi: 10.1002/14651858.CD010834.pub3. Update in: Cochrane Database Syst Rev. 2022 Jul 12;7:CD010834. PMID: 28933516; PMCID: PMC6483800.

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Case 2

A 54-year-old woman presents with a history of mild intermittent asthma has had 3 episodes of fever, dyspnea, and sputum production (thick, brown, plugs) over the last 3 months. She has been using her inhaler regimen as usual. She has had CXRs during this time with infiltrates that resolve and then re-occur. A CT chest is significant for central bronchiectasis, mucus plugging, and high attenuation mucus. Her total IgE is elevated (1200 ng/mL). Her peripheral eosinophil count is normal. Her *Aspergillus fumigatus* IgG immunoassay is elevated. What is the most likely diagnosis, and what test is necessary to make the diagnosis?

A. Cystic fibrosis; sweat chloride test.
B. Cystic fibrosis; serum IgE level against *Aspergillus fumigatus*.
C. Loffler's syndrome; *Strongyloides stercoralis* ELISA test.
D. Lofgren syndrome; serum IgE level against *Aspergillus fumigatus*.
E. Allergic bronchopulmonary aspergillosis; *Strongyloides stercoralis* ELISA test.
F. Allergic bronchopulmonary aspergillosis; serum IgE level against *Aspergillus fumigatus*.

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F. Allergic bronchopulmonary aspergillosis; serum IgE level against *Aspergillus fumigatus*.

ABPA diagnosis

International Society for Human and Animal Mycology (ISHAM) working group diagnostic criteria for allergic bronchopulmonary aspergillosis

Predisposing conditions (one must be present)*:
Asthma
Cystic fibrosis
Obligatory criteria (both must be present):
Serum IgE levels against *Aspergillus fumigatus* (>0.35 kU/L) or *Aspergillus* skin test positivity.
Elevated total IgE concentration (typically >1000 IU/mL, but if the patient meets all other criteria, an IgE value <1000 IU/mL may be acceptable, especially if *A. fumigatus*-specific IgG levels are >27 mg/L)
Other criteria (at least two must be present):
Precipitating serum antibodies to *A. fumigatus* or elevated serum *Aspergillus* IgG by immunoassay (>27 mg/L)
Radiographic pulmonary opacities consistent with ABPA
Total eosinophil count >500 cells/microL in glucocorticoid-naïve patients (may be historical)

IgE: immunoglobulin E; ABPA: Allergic bronchopulmonary aspergillosis.

* Rarely, ABPA is identified in the absence of asthma or cystic fibrosis. COPD and post-tuberculous fibrocavitary disease may be predisposing conditions.

image source:
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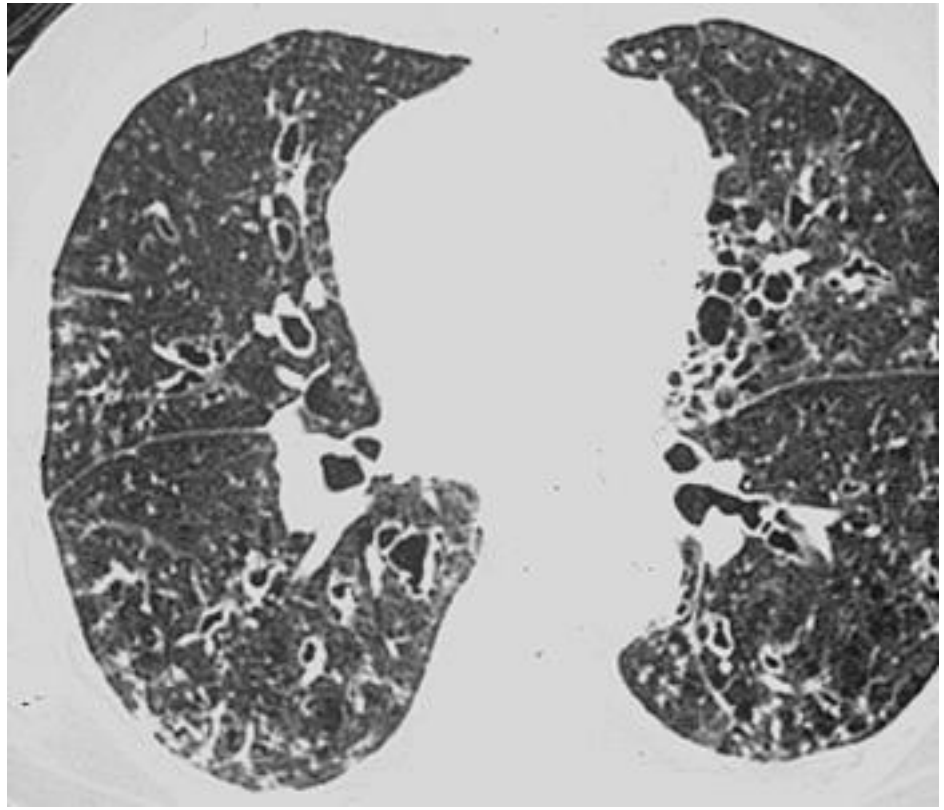
(Argarwal, C. et al. *Clinic Exp Allergy*, 2013.; Argarwal, C. et al. *Expert Rev Resp Med*, 2016.)

ABPA Imaging



Key features:

- Central bronchiectasis
- Tree-in-bud opacities
- Mucus plugging
- High-attenuation mucus

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Differential Diagnosis: elevated IgE

Infectious diseases

- Including parasites (ascaris, schisto, strongy), HIV, TB, CMV, EBV, Candida, Leprosy

Allergic diseases

- Including ABPA, allergic asthma, allergic rhinitis, atopic dermatitis

Inflammatory diseases

- Including EGPA, Kawasaki disease

Malignancy

- Including Hodgkin lymphoma, IgE myeloma

Immunodeficiency

- Including Hyper-IgE, Wiskott-Aldrich syndrome

Drugs

- Including Aztreonam, Penicillin G

Other

- Including CF, GVHD, BMT, tobacco smoking, nephrotic syndrome, bullous pemphigoid

Akuthota, P. et al. *Uptodate.com*, 2022.

ABPA: learning points

- An elevated total IgE concentration is **required** to make the diagnosis
- An elevated eosinophil count may be present but is **not** necessary
- Characteristic imaging features of ABPA include central bronchiectasis, mucus plugging, tree-in-bud opacities, and high attenuation mucus

(Kaur, M. et al. *JCDR*, 2014; Argawal, R. et al *CHEST*, 2007.)

Key ABPA References

- Agarwal R, et al. Clinical significance of hyperattenuating mucoid impaction in allergic bronchopulmonary aspergillosis: an analysis of 155 patients. Chest. 2007 Oct;132(4):1183-90. doi: 10.1378/chest.07-0808. Epub 2007 Jul 23. PMID: 17646221.

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- Kaur M, Sudan DS. Allergic Bronchopulmonary Aspergillosis (ABPA)-The High Resolution Computed Tomography (HRCT) Chest Imaging Scenario. J Clin Diagn Res. 2014 Jun;8(6):RC05-7. doi: 10.7860/JCDR/2014/8255.4423. Epub 2014 Jun 20. PMID: 25121041; PMCID: PMC4129294.

Case 3

A 21-year-old man has a history of frequent sinus infections as an adolescent who now has had a series of sinus infections that have not responded to antibiotic therapy is referred to ENT. He has laryngoscopy and the culture grows mucoid *Pseudomonas aeruginosa.* He has additional testing including a sweat chloride test which is abnormal (67mmol/L) and he is diagnosed with cystic fibrosis. What is the next best step in management?

A. Begin chronic antibiotics for suppression
B. Perform CFTR gene sequencing
C. Begin inhaled N-acetylcystine
D. Begin low dose daily oral glucocorticoids

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CF: chronic medications

- **CFTR modulators** (!)
- **Airway clearance therapies**
  - Inhaled dornase alpha and hypertonic saline
  - Chest physiotherapy
  - Exercise
- **Bronchodilators**
  - short-acting beta-2 adrenergic receptor agonists
- **Anti-inflammatory therapies**
  - Azithromycin
  - Ibuprofen
  - Inhaled glucocorticoids

- Chronic systemic glucocorticoids
- Sodium cromolyn
- Inhaled and oral N-acetylcystine

Mogayzel, P. et al. *AJRCCM*, 2013.

CFTR gene mutations approved for each type of CFTR modulator therapy

546insCTA	E403D	G628R	L346P	R117H	S912L
711+3A>G	E474K	G970D	L453S	R117L	S945L
2789+5G>A	E588V	G1061R	L967S	R117P	S977F
3141del9	E822K	G1069R	L997F	R170H	S1159F
3272-26A>G	E831X	G1244E	L1077P	R258G	S1159P
3849+10kbC>T	F191V	G1249R	L1324P	R334L	S1251N
A46D	F311del	G1349D	L1335P	R334Q	S1255P
A120T	F311L	H139R	L1480P	R347H	T338I
A234D	F508C	H199Y	M152V	R347L	T1036N
A349V	F508C;S1251N	H939R	M265R	R347P	T1053I
A455E	**F508del***	H1054D	M952I	R352Q	V201M
A554E	F575Y	H1085P	M952T	R352W	V232D
A1006E	F1016S	H1085R	M1101K	R553Q	V456A
A1067T	F1052V	H1375P	P5L	R668C	V456F
D110E	F1074L	I148T	P67L	R751L	V562I
D110H	F1099L	I175V	P205S	R792G	V754M
D192G	G27R	I336K	P574H	R933G	V1153E
D443Y	G85E	I502T	Q98R	R1066H	V1240G
D443Y;G576A;R668C	G126D	I601F	Q237E	R1070Q	V1293G
D579G	G178E	I618T	Q237H	R1070W	W361R
D614G	G178R	I807M	Q359R	R1162L	W1098C
D836Y	G194R	I980K	Q1291R	R1283M	W1282R
D924N	G194V	I1027T	R31L	R1283S	Y109N
D979V	G314E	I1139V	R74Q	S13F	Y161D
D1152H	G463V	I1269N	R74W	S341P	Y161S
D1270N	G480C	I1366N	R74W;D1270N	S364P	Y563N
E56K	G551D	K1060T	R74W;V201M	S492F	Y1014C
E60K	G551S	L15P	R74W;V201M;D1270N	S549N	Y1032C
E92K	G576A	L165S	R75Q	S549R	
E116K	G576A;R668C	L206W	R117C	S589N	
E193K	G622D	L320V	R117G	S737F	

Color key:

- Approved for ELX-TEZ-IVA, TEZ-IVA, and IVA
- Approved for ELX-TEZ-IVA and TEZ-IVA
- Approved for ELX-TEZ-IVA only
- Approved for IVA and TEZ-IVA but not ELX-TEZ-IVA¶

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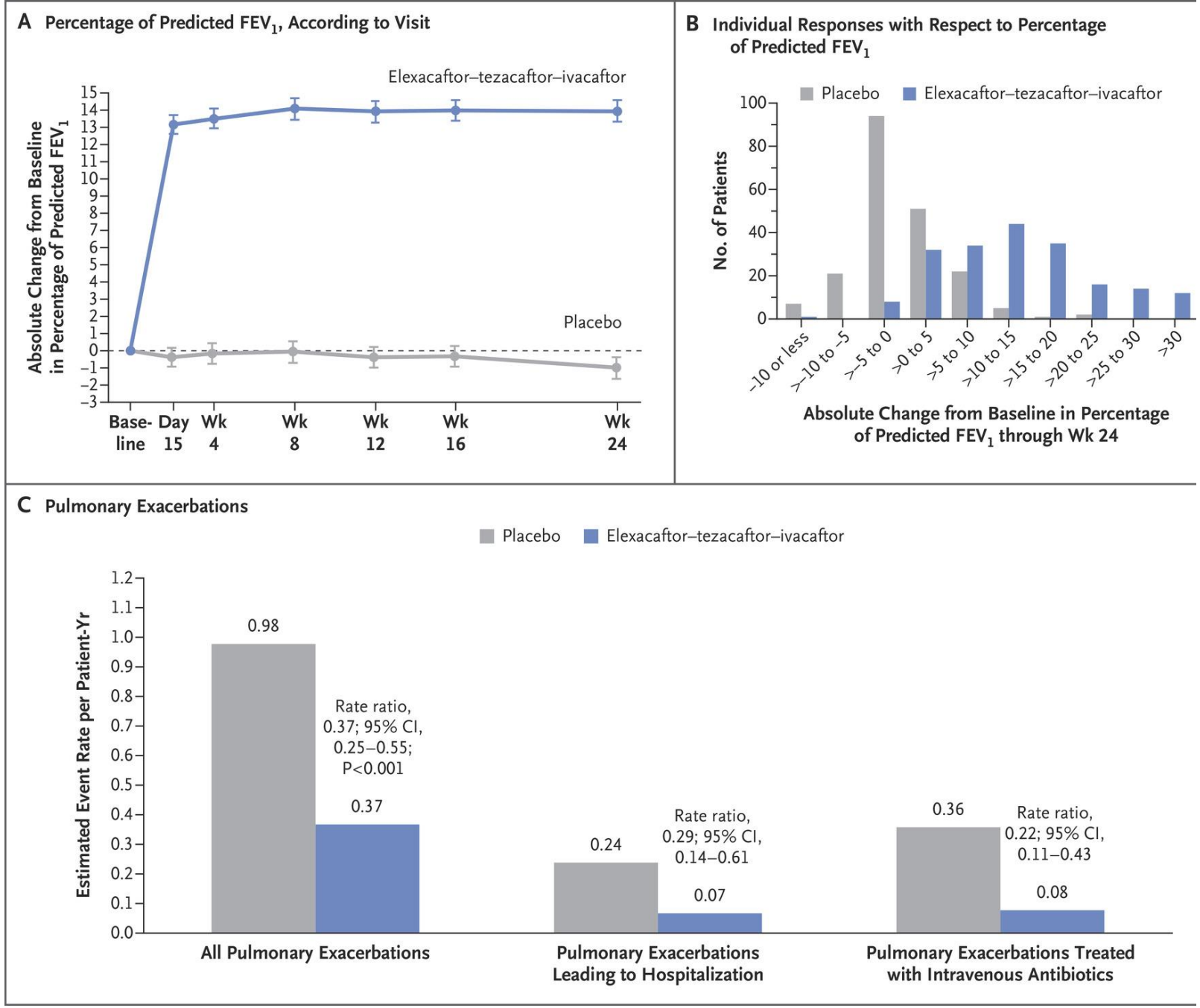
Clinical outcomes with triple CFTR therapy



Middleton, P. *NEJM*, 2019.

CF: learning points

- All patients with CF should be genotyped to determine whether they are eligible for treatment with CF transmembrane conductance regulator (CFTR) modulators

- Triple drug combination (elexacaftor-tezacaftor-ivacaftor) treatment among F508del homozygous patients has been shown to:
  - improve respiratory symptoms and FEV1
  - decrease sweat chloride levels
  - improve radiographic appearance of mucus plugging and airway thickening

(Bec, R et al. *EJR*, 2022; Heijerman, H et al. *Lancet*, 2020; Sutharsan, S. et al. *Lancet Resp Med*, 2022.)

Key CF References

- Bec R, et al. Chest computed tomography improvement in patients with cystic fibrosis treated with elexacaftor-tezacaftor-ivacaftor: Early report. Eur J Radiol. 2022 Sep;154:110421. doi: 10.1016/j.ejrad.2022.110421. Epub 2022 Jun 23. PMID: 35772339.
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- Sutharsan S, et al. Efficacy and safety of elexacaftor plus tezacaftor plus ivacaftor versus tezacaftor plus ivacaftor in people with cystic fibrosis homozygous for F508del-CFTR: a 24-week, multicentre, randomised, double-blind, active-controlled, phase 3b trial. Lancet Respir Med. 2022 Mar;10(3):267-277. doi: 10.1016/S2213-2600(21)00454-9. Epub 2021 Dec 20. PMID: 34942085.

Case 4

A 34-year-old woman presents with a history of cough for 4 months. She has a diagnosis of mild intermittent asthma for which she takes a low dose inhaled corticosteroid inhaler. She has a CXR which shows bilateral hilar lymphadenopathy but normal lung parenchyma. She has pulmonary function testing with normal spirometry, lung volumes, and DLCO. She undergoes bronchoscopy with endobronchial ultrasound and biopsy of her lymphadenopathy, which shows well-formed non-caseating granulomas. What are the next best steps in management?

A. ECG, eye exam, start oral corticosteroids.
B. ECG, eye exam, increase dose of inhaled corticosteroids.
C. ECG, eye exam, discuss treatment versus observation.
D. ECG, eye exam, start methotrexate.

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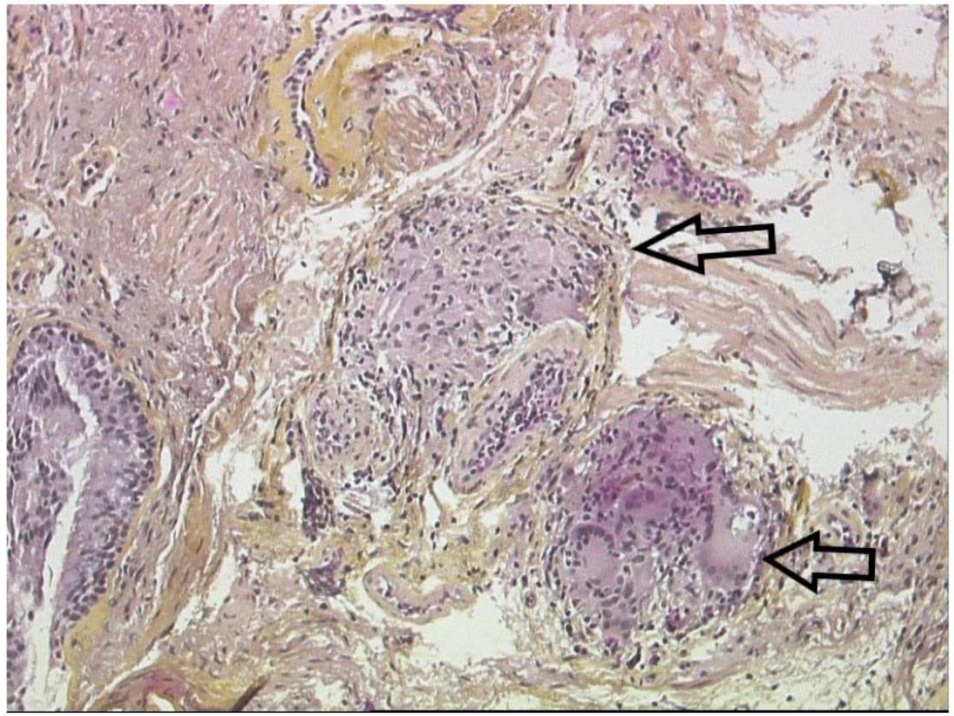
A. ECG, eye exam, start oral corticosteroids.

B. ECG, eye exam, increase dose of inhaled corticosteroids.

C. ECG, eye exam, discuss treatment versus observation.

D. ECG, eye exam, start methotrexate.

Sarcoidosis Diagnosis

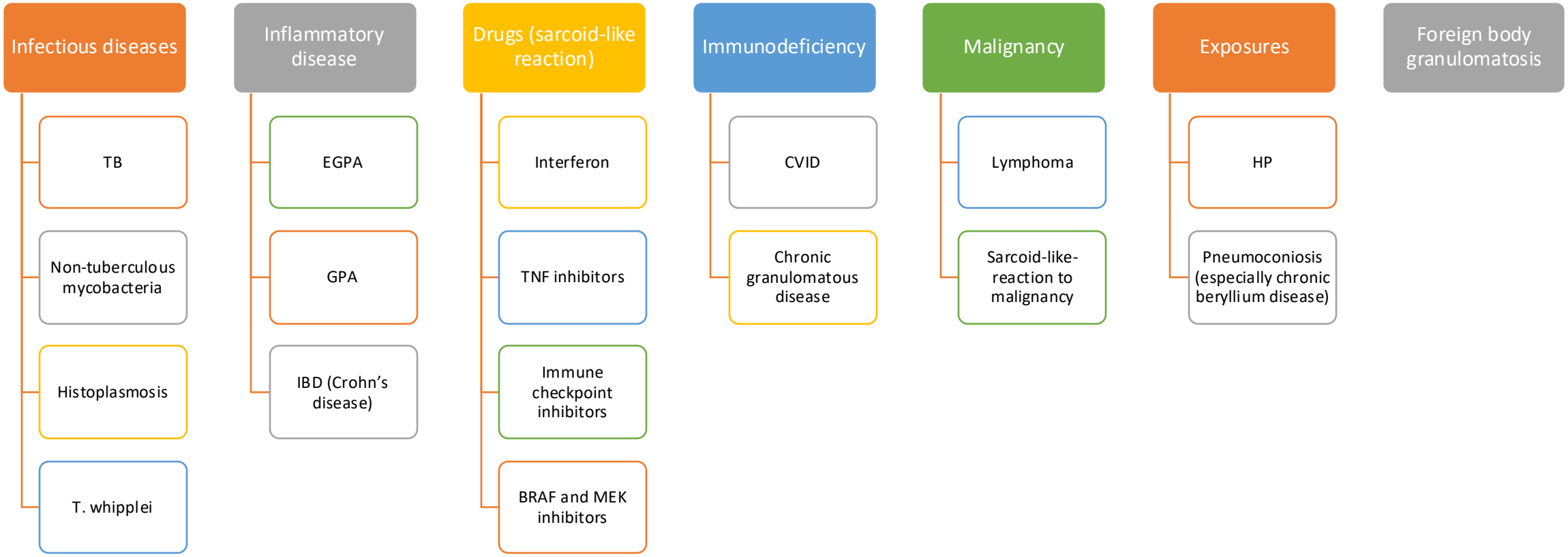


Lung biopsy with non-necrotizing epithelioid granulomas (arrows) with giant cells surrounding lymphocytes and fibrosis

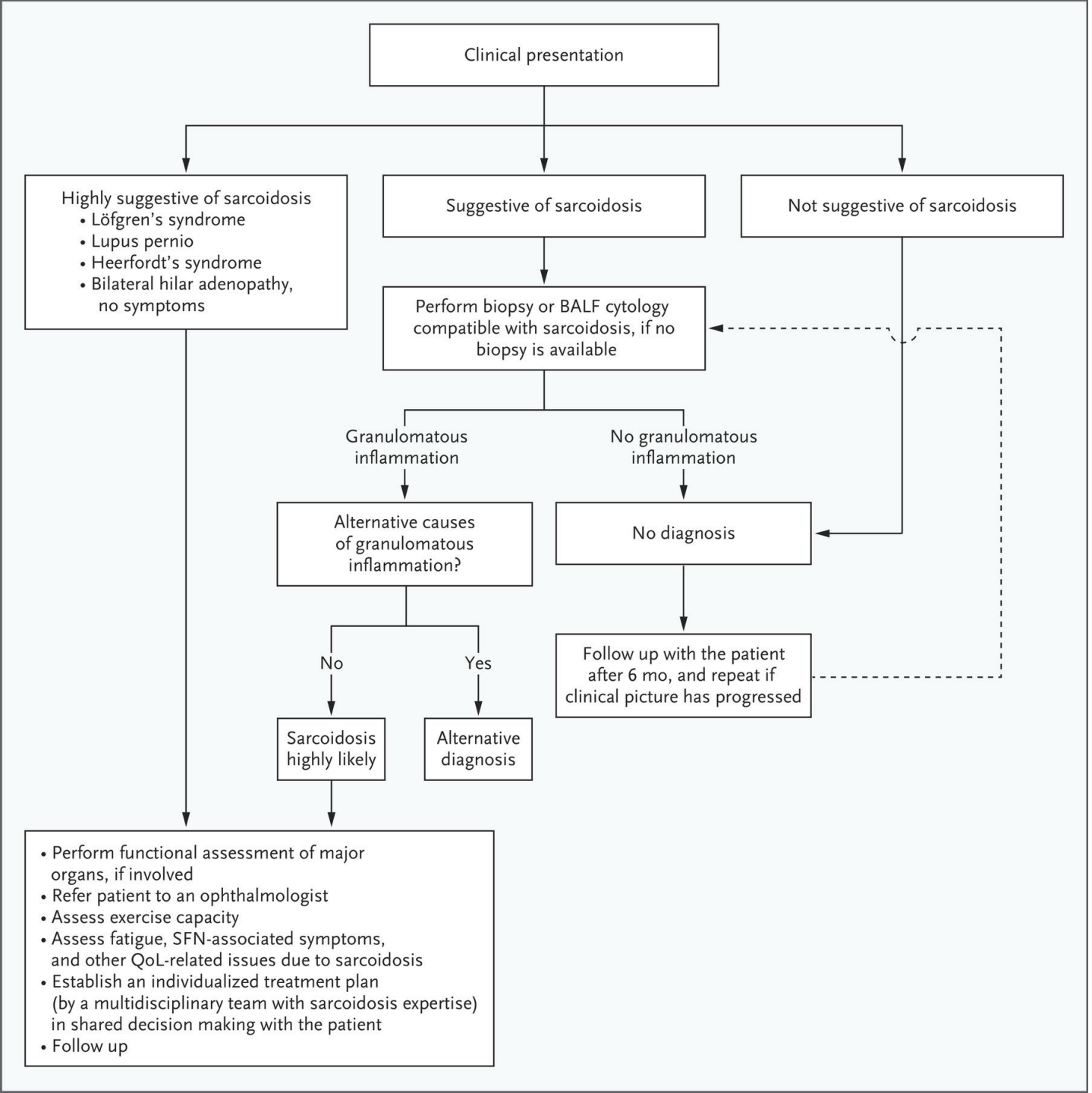
1. Characteristic **clinical presentation**
2. Presence of **non-caseating granulomas** on tissue biopsy
3. **Rule out** other granulomatous disorders

Sève, P. et al. *Cells*. 2021

Granulomatous Diseases Differential



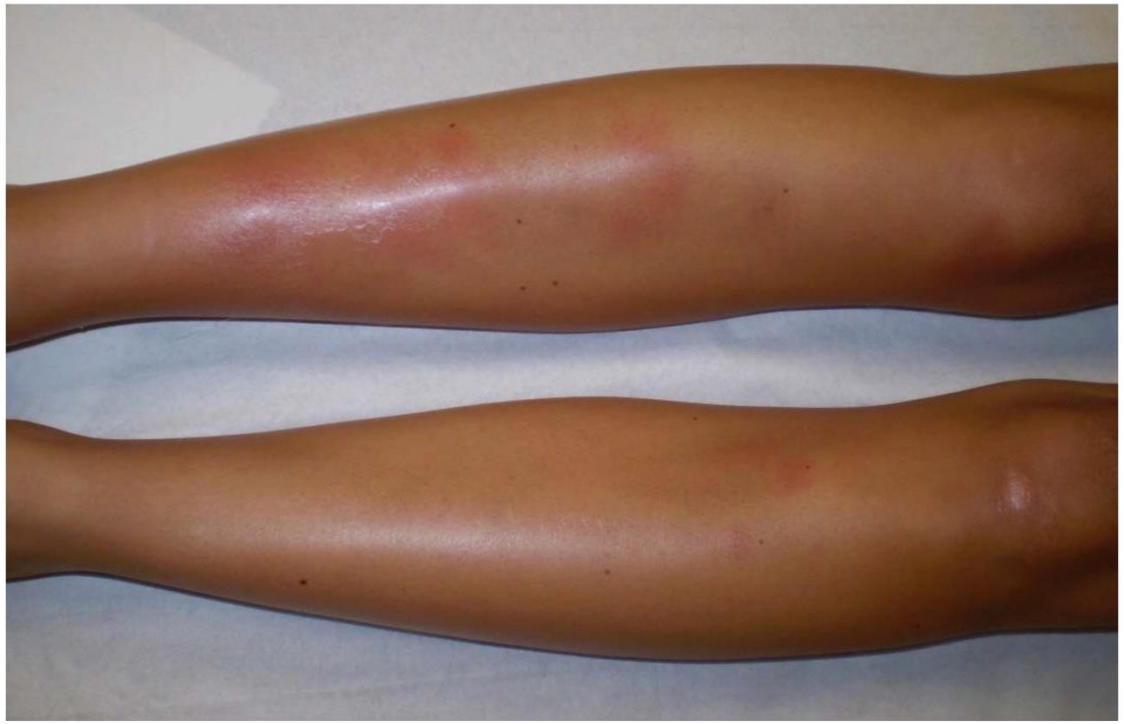
Diagnostic Algorithm



Drent, M et. Al. *NEJM*, 2021.

Löfgren's syndrome

- Acute onset with:
  - Bilateral hilar lymphadenopathy
  - Erythema nodosum
  - +/- Bilateral ankle arthritis or periarticular inflammation
- Often also have fever at presentation
- Good prognosis, usually benign course

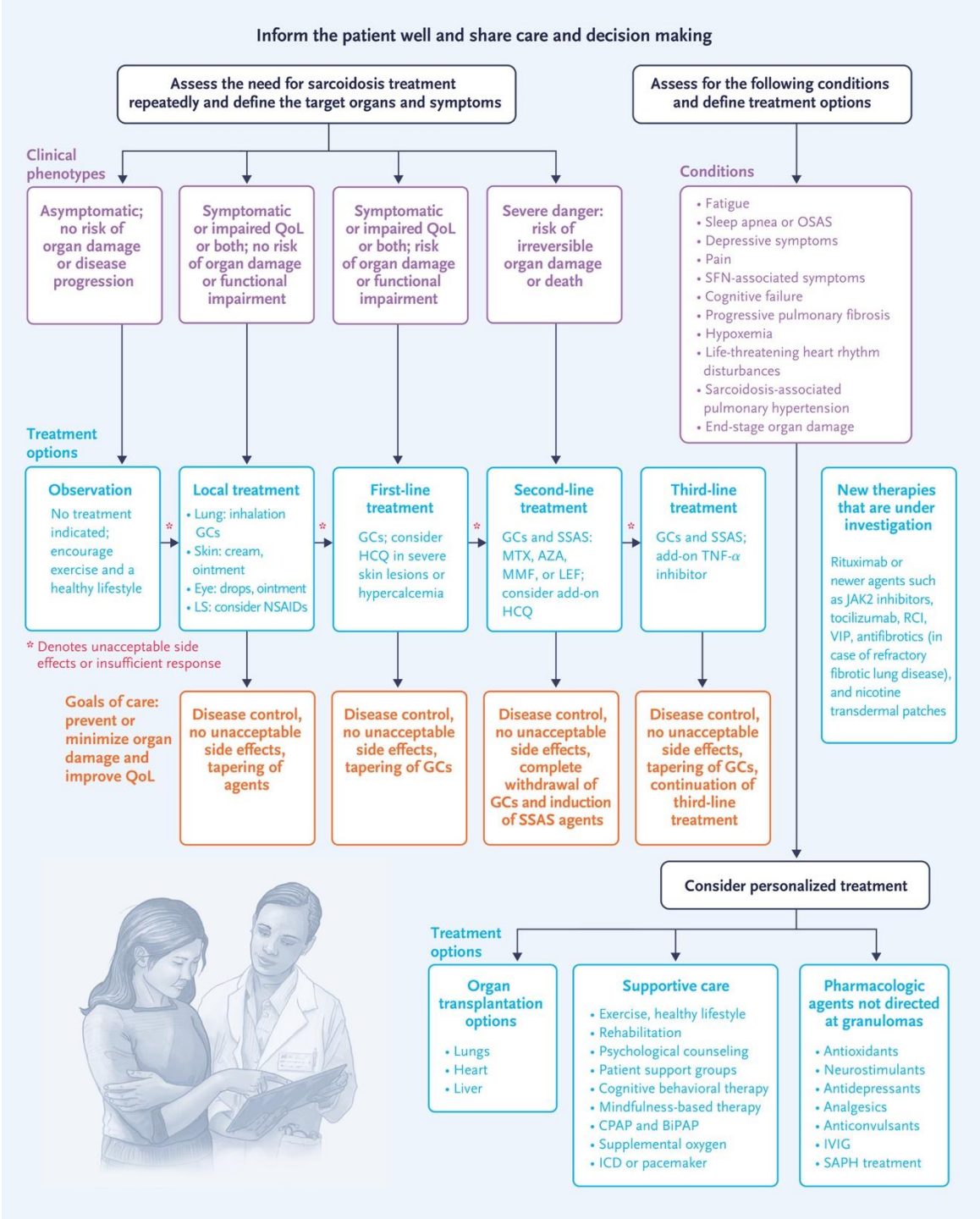


Erythema nodosum in a patient with Löfgren's syndrome.

Sève, P. et al. *Cells*. 2021

Sarcoidosis Management

- Patient-specific, no simple approach
- Consider:
  - Risk of organ failure or death
  - Symptom burden and quality of life
- If asymptomatic, always start with observation



Drent, M et. Al. *NEJM*, 2021.

Sarcoid: learning points

- Characteristic finding on tissue biopsy is non-caseating granuloma
- Treatment is complex and should start with a risk/benefit discussion for each patient
- All patients with a diagnosis of sarcoidosis should have annual ECG and eye exam to assess for cardiac and ocular sarcoid manifestations

Key Sarcoid References

- Drent M, Crouser ED, Grunewald J. Challenges of Sarcoidosis and Its Management. N Engl J Med. 2021 Sep 9;385(11):1018-1032. doi: 10.1056/NEJMra2101555. PMID: 34496176.

- Sève P, Pacheco Y, Durupt F, Jamilloux Y, Gerfaud-Valentin M, Isaac S, Boussel L, Calender A, Androdias G, Valeyre D, et al. Sarcoidosis: A Clinical Overview from Symptoms to Diagnosis. *Cells*. 2021; 10(4):766. https://doi.org/10.3390/cells10040766

Case 5

A 49-year-old man with severe rheumatoid arthritis refractory to multiple therapies now on methotrexate and rituximab, who presents with subacute onset of low-grade fevers, dyspnea on exertion, and productive cough. High resolution CT of the chest demonstrates multiple bilateral nodules, and one nodule in the right upper lobe with an area of cavitation. A bronchoscopy with bronchoalveolar lavage was performed. The gram stain demonstrated delicate, branching, filamentous, gram-positive rods. These were partially acid fast on modified acid-fast stain. What is the most likely diagnosis, and best treatment?

A. Actinomyces; start trimethoprim-sulfamethoxazole.
B. Actinomyces; start penicillin G.
C. Nocardia; start trimethoprim-sulfamethoxazole.
D. Nocardia; start penicillin G.

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Nocardia epidemiology

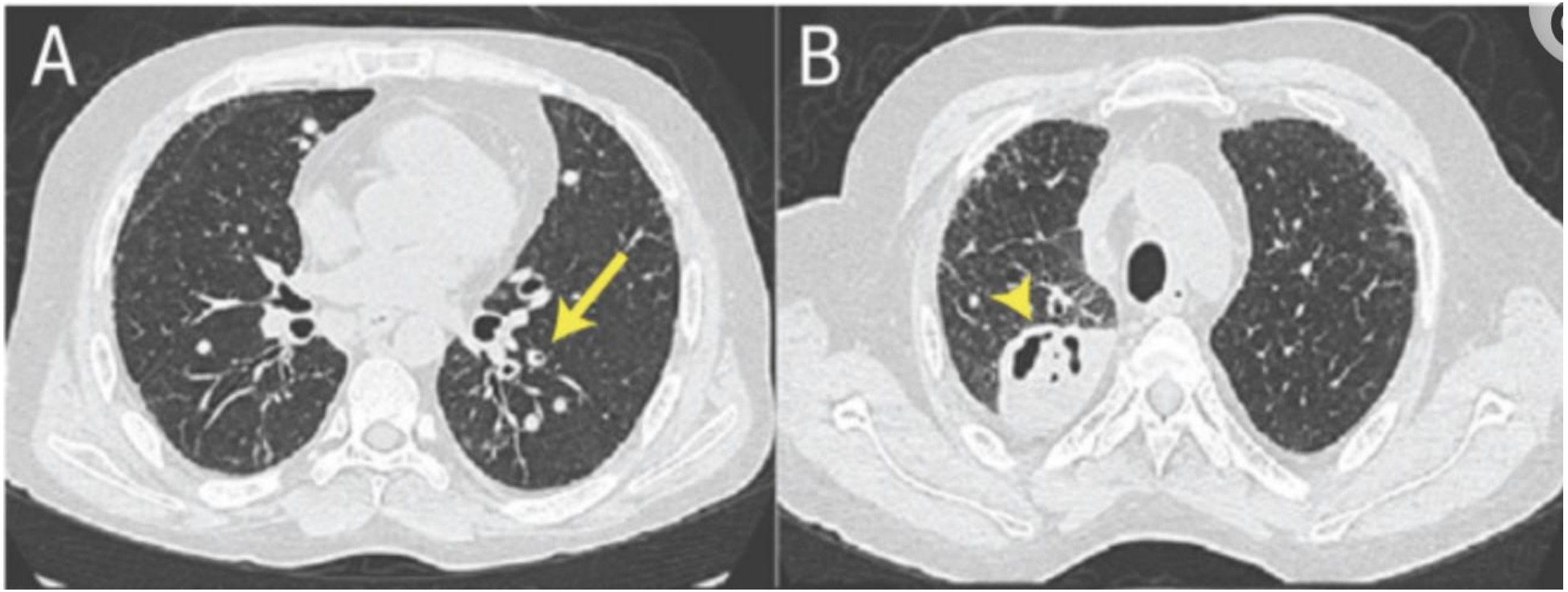
Reservoir

- Soil
- Decaying vegetation
- Water

Transmission

- Inhalation
- Inoculation via skin

Characteristic imaging



Multiple bilateral pulmonary nodules of variable size, some with ventral cavitation (arrow) and cavitary mass in the right upper lobe (arrow head) in patient with nocardiosis.

Image source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9423747/>

Al Umairi, RS. et al. *Sultan Qaboos Univ Med J*, 2022.

Nocardia learning points

- Nocardia infection occurs in immunocompromised patients, especially those on chronic steroids, and develops insidiously. Characteristic imaging findings are pulmonary nodules +/- cavitation.

- Nocardia is a branching, filamentous gram-positive rod that also stains partially acid fast and that can be identified from broncho-alveolar lavage

- Preferred treatment for nocardia is with trimethoprim-sulfamethoxazole.

Key nocardia references

- Lederman, Edith R. LCDR, USNR, MC; Crum, Nancy F. LCDR, USNR, MC. A Case Series and Focused Review of Nocardiosis: Clinical and Microbiologic Aspects. Medicine 83(5):p 300-313, September 2004. | DOI: 10.1097/01.md.0000141100.30871.39

- Liu B, et al. CT findings of pulmonary nocardiosis: a report of 9 cases. J Thorac Dis. 2017 Nov;9(11):4785-4790. doi: 10.21037/jtd.2017.09.122. PMID: 29268550; PMCID: PMC5720996.

- Minero, Maricela Valerio MD et al. Nocardiosis at the Turn of the Century. Medicine 88(4):p 250-261, July 2009. | DOI: 10.1097/MD.0b013e3181afa1c8

Case 6

A 65-year-old woman presents with subacute onset of cough and dyspnea on exertion and during her work-up she is found to have diffuse parenchymal infiltrates on chest imaging. High resolution CT shows upper lobe predominant small centrilobular nodules, ground glass opacities, and lobular areas of decreased attenuation and vascularity. She undergoes bronchoscopy with bronchoalveolar lavage (BAL) and the BAL fluid infectious studies are all negative, the cell count of the BAL fluid shows 30% lymphocytes. What is the most likely diagnosis and what testing is necessary to confirm this diagnosis?

A. Hypersensitivity pneumonitis; no additional testing necessary.
B. Hypersensitivity pneumonitis; serology for specific IgG antibodies.
C. Non-specific interstitial pneumonia; pulmonary function testing.
D. Non-specific interstitial pneumonia; serology for specific IgG antibodies.
E. Combined pulmonary fibrosis and emphysema; pulmonary function testing.
F. Combined pulmonary fibrosis and emphysema; transbronchial lung biopsy.

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D. Non-specific interstitial pneumonia; serology for specific IgG antibodies.
E. Combined pulmonary fibrosis and emphysema; pulmonary function testing.
F. Combined pulmonary fibrosis and emphysema; transbronchial lung biopsy.

Selected etiologies

Farmer's lung

- Antigen = Thermophilic actinomycetes (e.g. *Saccharopolyspora rectivirgula*) in hay or dust with high humidity

Hot tub lung

- Antigen = Mycobacterium avium complex (has granulomatous inflammation)

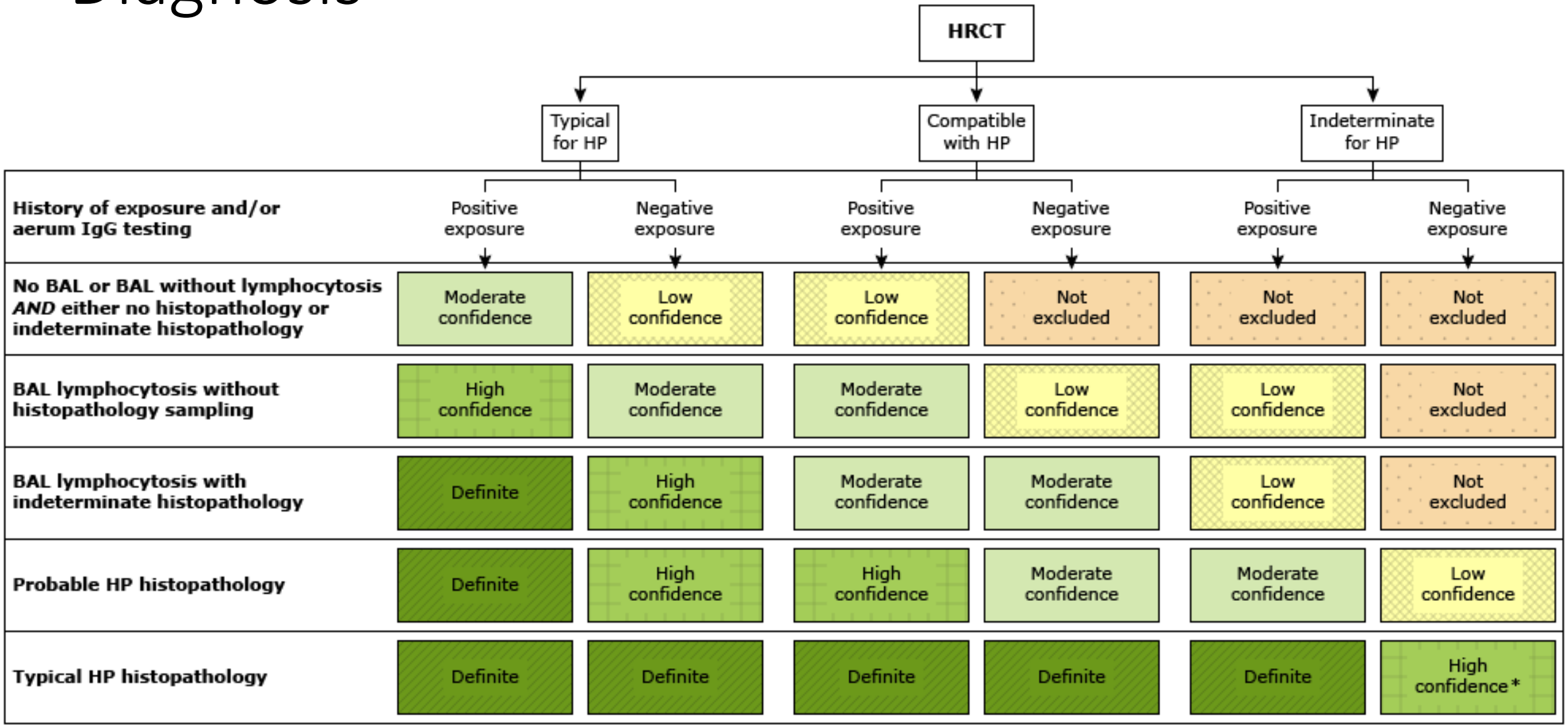
Ventilation/water

- Antigen = Fungi including *Penicillium spp* and *Aspergillus spp*

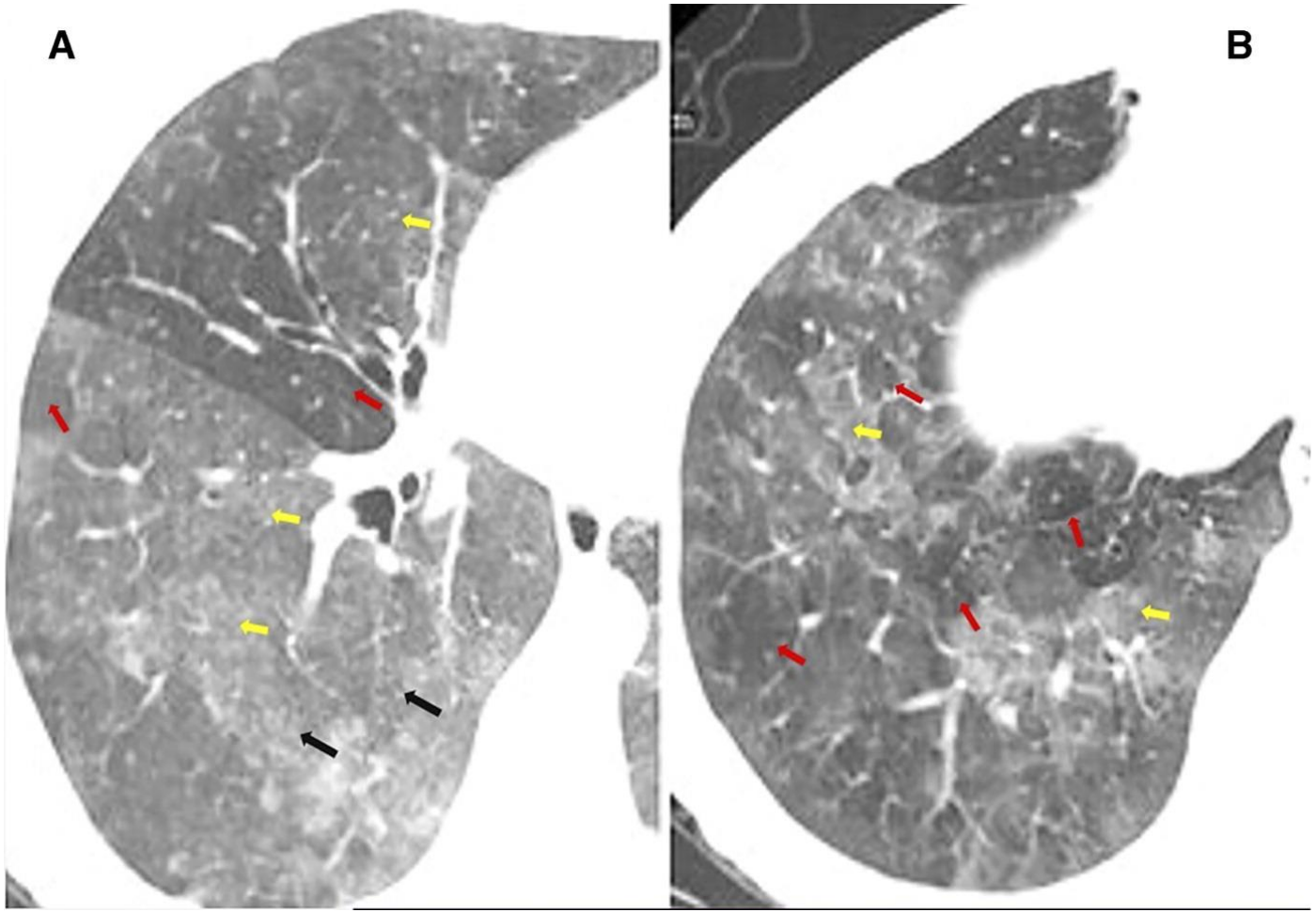
Bird fancier's lung

- Antigen = droppings, feathers, serum proteins

Diagnosis

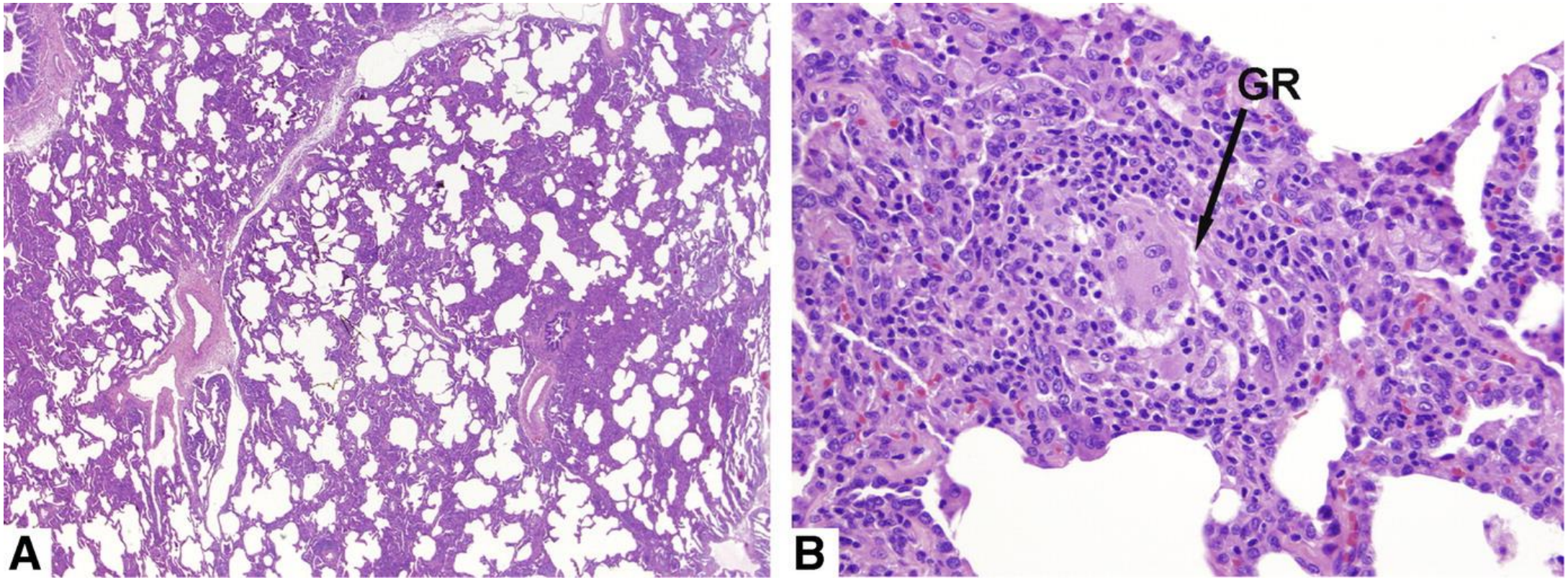


Raghu, G et al. *AJRCCM* 2021.



Acute HP with ground glass opacities (yellow arrows), small centrilobular nodules (black arrows) and mosaic attenuation (red arrows)

Vasakova, M et al. *AJRCCM*, 2017.



(A) Diffuse lymphohistiocytic infiltrate at very low magnification. (B) A characteristic poorly formed interstitial granuloma with giant cells containing calcified inclusions.

Vasakova, M et al. *AJRCCM*, 2017.

Treatment

- **Avoid exposure**
- Corticosteroids
- Immunomodulators
- Antifibrotics
- Lung transplantation

Vasakova, M. *AJRCCM*, 2017.

Hypersensitivity pneumonitis learning points

- Histopathology features of HP (presence of all three is not necessarily diagnostic)
  - Poorly formed non-caseating granulomas and multinucleated giant cells near respiratory or terminal bronchioles
  - Chronic cellular bronchiolitis
  - Chronic cellular pneumonitis with patchy lymphoplasmocytic infiltration

- Cornerstone of management is antigen avoidance

Key HP references

- Raghu G, et al. Diagnosis of Hypersensitivity Pneumonitis in Adults. An Official ATS/JRS/ALAT Clinical Practice Guideline. Am J Respir Crit Care Med. 2020 Aug 1;202(3):e36-e69. doi: 10.1164/rccm.202005-2032ST. Erratum in: Am J Respir Crit Care Med. 2021 Jan 1;203(1):150-151. Erratum in: Am J Respir Crit Care Med. 2022 Aug 15;206(4):518. PMID: 32706311; PMCID: PMC7397797.

- Vasakova M, Morell F, Walsh S, Leslie K, Raghu G. Hypersensitivity Pneumonitis: Perspectives in Diagnosis and Management. Am J Respir Crit Care Med. 2017 Sep 15;196(6):680-689. doi: 10.1164/rccm.201611-2201PP. PMID: 28598197.

Case 7

A 55 year old man with PMH of obesity and HTN presents for evaluation of dyspnea on exertion. He has normal lung parenchyma on imaging, no evidence of cardiac ischemia, and pulmonary function test which demonstrates mild restriction and a moderately reduced DLCO corrected for hemoglobin. He is referred for right heart catheterization with the following results:

Mean PA pressure 32 mmHg
Pulmonary capillary wedge pressure 22 mmHg
Pulmonary vascular resistance 2.8 Wood units

Based on these findings, what is the most accurate statement about this patient?

A. He meets criteria for pre-capillary pulmonary hypertension.
B. He meets criteria for isolated post-capillary pulmonary hypertension.
C. He does not have evidence of pulmonary hypertension.
D. More information needed to determine whether he has pulmonary hypertension.

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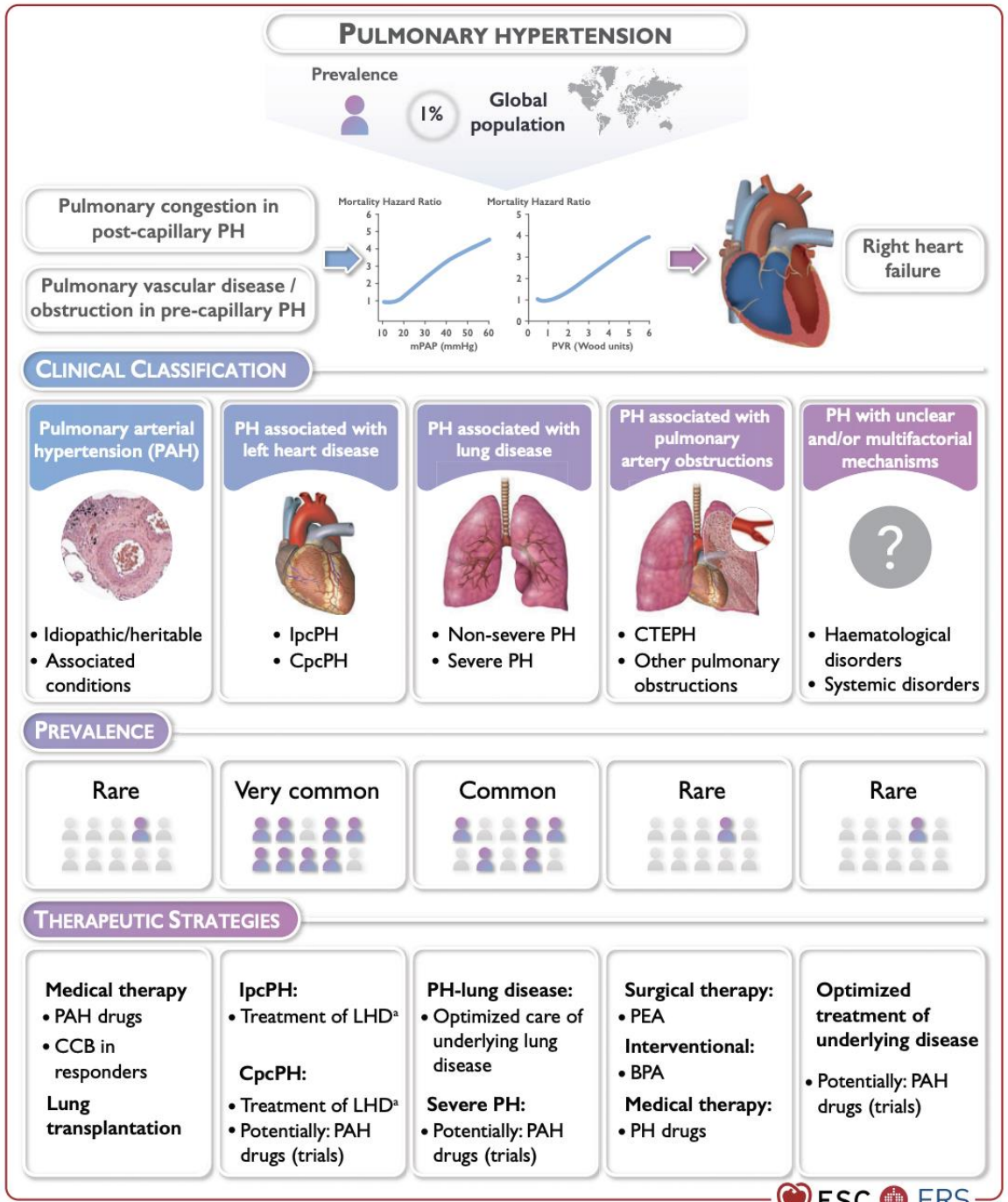
Hemodynamic definition of PH

Category	Hemodynamic features
PH	mPAP > 20mmHg
Pre-capillary PH	mPAP > 20mmHg PCWP ≤15 mmHg PVR >2 WU
Isolated post-capillary PH	mPAP > 20mmHg PCWP >15 mmHg PVR ≤2 WU
Combined pre- and post-capillary PH	mPAP > 20mmHg PCWP >15 mmHg PVR >2 WU

Clinical classification of PH

1. Pulmonary arterial hypertension (PAH)
2. Pulmonary hypertension due to left heart disease
3. Pulmonary hypertension due to lung disease and/or hypoxemia
4. Chronic thromboembolic pulmonary hypertension
5. Pulmonary hypertension of unclear and/or multifactorial mechanisms



Humbert et al. ESC/ERS Scientific Document Group , 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG)., *European Heart Journal*, Volume 43, Issue 38, 7 October 2022, Pages 3618–3731, https://doi.org/10.1093/eurheartj/ehac237

PH learning points

- 2019 ERS consensus recommendation for updated hemodynamic definition of pulmonary hypertension: mean PA over 20 mmHg and now also include pulmonary vascular resistance in the definition

- Clinical classification of pulmonary hypertension includes 5 groups

Key PH references

- Hassoun PM. Pulmonary Arterial Hypertension. N Engl J Med. 2021 Dec 16;385(25):2361-2376. doi: 10.1056/NEJMra2000348. PMID: 34910865.

- Humbert et al. ESC/ERS Scientific Document Group , 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG)., *European Heart Journal*, Volume 43, Issue 38, 7 October 2022, Pages 3618–3731, https://doi.org/10.1093/eurheartj/ehac237

- Johnson S. et al. Pulmonary Hypertension: A Contemporary Review. Am J Respir Crit Care Med. 2023 Sep 1;208(5):528-548. doi: 10.1164/rccm.202302-0327SO. PMID: 37450768; PMCID: PMC10492255.

- Maron BA, et al. Pulmonary Arterial Hypertension: Diagnosis, Treatment, and Novel Advances. Am J Respir Crit Care Med. 2021 Jun 15;203(12):1472-1487. doi: 10.1164/rccm.202012-4317SO. PMID: 33861689; PMCID: PMC8483220.

- Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, Williams PG, Souza R. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019 Jan 24;53(1):1801913. doi: 10.1183/13993003.01913-2018. PMID: 30545968; PMCID: PMC6351336.

Thank you for your time!