Pulmonary and Critical Care Medicine

ACP Puerto Rico Chapter Meeting

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Pulmonary and Critical Care, ACP
Disclosures

- Relevant Financial Relationships
  - None

- Off-Label/Investigational Uses
  - None

MAYO CLINIC

Pulmonary and Critical Care
Objectives

- Pulmonary diseases
  - Obstructive Lung Disease
  - Neoplasia
  - Diffuse Parenchymal Lung Disease
  - Sleep
- Critical care
  - Sepsis
  - Shock
  - Hypoxic respiratory failure/ARDS
  - Hypercapnic respiratory failure

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Pulmonary
Clinical Pearls

- Things to think about in **every dyspnea** case:

1. **Duration:** days x months x years
2. **Exacerbating factors:** exercise, environment, position, none identifiable
3. **Alleviating factors**
4. **Exposures**
5. **Think:** GERD, OSA, Rhinosinusitis

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Question 1

- A 49 yo woman is evaluated in the office following recent hospitalization for asthma. She continues to have dyspnea and intermittent wheezing. She has had 2 other admissions in the past year. Other than asthma, her history is unremarkable. Current meds: mometasone/formoterol, montelukast, albuterol/tiotropium and prednisone. On physical exam, oxygen saturation is 95% on RA and she has expiratory wheezes.
- Labs: WBCs 10000, with 650 eosinophils. Serum IgE level is 12 U/mL (0-90U/mL).
- Fev1 is 56% predicted.

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Question 1

- Which of the following is the most appropriate treatment:
  A. Begin doxycycline
  B. Change mometasone/formoterol to fluticasone/salmeterol
  C. Initiate a trial of mepolizumab therapy
  D. Initiate a trial of omalizumab therapy

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Asthma

- Inflammatory disorder of the airways
  - Intermittent cough, wheezing, chest tightness, dyspnea and variable airflow obstruction
- Onset at any age
  - Two peaks (childhood and older than 65), women, blacks and persons below poverty levels
- Clinical groups: allergic, nonallergic, late-onset, adult onset eosinophilic and obesity-associated
- Confirmation of **reversible airflow obstruction** is essential for diagnosis
  - FEV1, FVC or ratio showing an increase from baseline of >12% and >200ml

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https://www.nhlbi.nih.gov/health-topics/guidelines-for-diagnosis-management-of-asthma

Asthma

- Careful history to determine if variant phenotype
- Remember common comorbidities
  - GERD
  - Sinus disease
  - OSA
  - Vocal cord dysfunction/paradoxical vocal cord movement

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Components of Severity		Classification of Asthma Severity ≥12 years of age			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment **Normal FEV_1/FVC:** **8–19 yr 85%** **20 –39 yr 80%** **40 –59 yr 75%** **60 –80 yr 70%**	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Treatment **(See figure 4–5 for treatment steps.)**		**Step 1**	**Step 2**	**Step 3** and consider short course of oral systemic corticosteroids	**Step 4 or 5** and consider short course of oral systemic corticosteroids
		In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

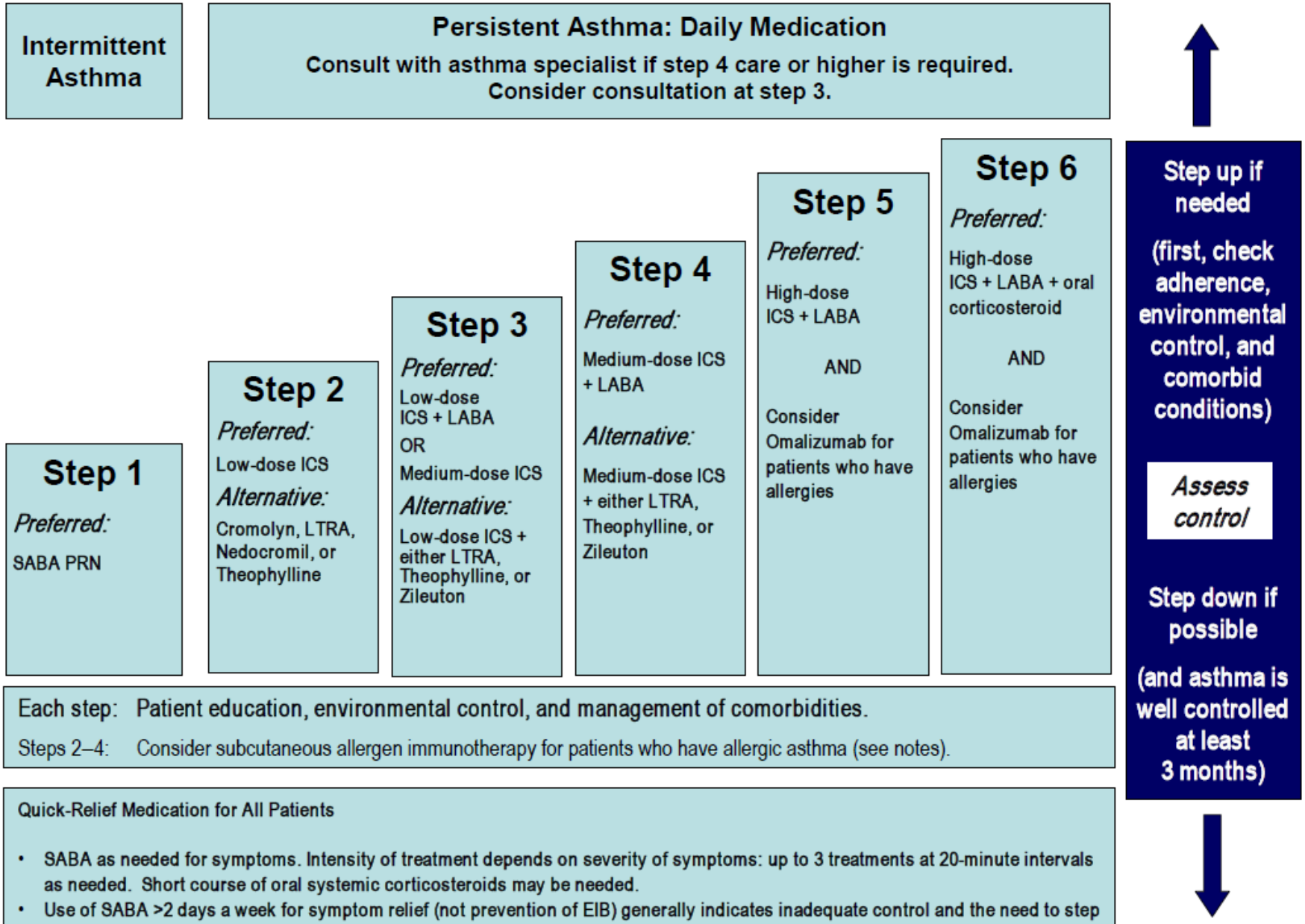
Intermittent Asthma
Persistent Asthma: Daily Medication
Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.
Step 1
Preferred:
SABA PRN
Step 2
Preferred:
Low-dose ICS
Alternative:
Cromolyn, LTRA, Nedocromil, or Theophylline
Step 3
Preferred:
Low-dose ICS + LABA
OR
Medium-dose ICS
Alternative:
Low-dose ICS + either LTRA, Theophylline, or Zileuton
Step 4
Preferred:
Medium-dose ICS + LABA
Alternative:
Medium-dose ICS + either LTRA, Theophylline, or Zileuton
Step 5
Preferred:
High-dose ICS + LABA
AND
Consider Omalizumab for patients who have allergies
Step 6
Preferred:
High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies
Step up if needed
(first, check adherence, environmental control, and comorbid conditions)
Assess control
Step down if possible
(and asthma is well controlled at least 3 months)
Each step: Patient education, environmental control, and management of comorbidities.
Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).
Quick-Relief Medication for All Patients
• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
• Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

FIGURE 4–8b. ESTIMATED COMPARATIVE DAILY DOSAGES FOR INHALED CORTICOSTEROIDS FOR YOUTHS ≥12 YEARS OF AGE AND ADULTS

Drug	Low Daily Dose Adult	Medium Daily Dose Adult	High Daily Dose Adult
Beclomethasone HFA 40 or 80 mcg/puff	80–240 mcg	>240–480 mcg	>480 mcg
Budesonide DPI 90, 180, or 200 mcg/inhalation	180–600 mcg	>600–1,200 mcg	>1,200 mcg
Flunisolide 250 mcg/puff	500–1,000 mcg	>1,000–2,000 mcg	>2,000 mcg
Flunisolide HFA 80 mcg/puff	320 mcg	>320–640 mcg	>640 mcg
Fluticasone			
HFA/MDI: 44, 110, or 220 mcg/puff	88–264 mcg	>264–440 mcg	>440 mcg
DPI: 50, 100, or 250 mcg/inhalation	100–300 mcg	>300–500 mcg	>500 mcg
Mometasone DPI 200 mcg/inhalation	200 mcg	400 mcg	>400 mcg
Triamcinolone acetonide 75 mcg/puff	300–750 mcg	>750–1,500 mcg	>1,500 mcg

Asthma – antibody therapies

- Anti-IL5
  - Mepolizumab (SC) and Reslizumab (IV)
  - Block the action of IL5, reducing eosinophils levels in sputum and airway
  - Indication: moderate/severe asthma and eos>150 cells
- Anti- IgE
  - Omalizumab (SC)
  - Monoclonal antibody directed at IgE
  - Indications: moderate/severe asthma, evidence of allergies and serum IgE levels 30-700U/mL

All: Reduce symptoms, need for oral steroids, and exacerbations

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Question 2

- 37 yo man is evaluated for a 1-month history of worsening cough and wheezing requiring use of rescue therapy several times/week, and increased nasal congestion/rhinorrhea. He has a hx of moderate persistent asthma and rhinorrhea since his 20s. For the past month he has been having knee pain. No GERD. Meds: albuterol, budesonide/formoterol and ibuprofen.
- Physical exam is normal with the exception of nasal polyps. Office spirometry →moderate airflow obstruction
- Labs: IgE 265; WBC of 4000 with 10% eos

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Question 2

- Which of the following is the most appropriate initial management?
  - A. 24h esophageal pH monitoring
  - B. Add montelukast
  - C. Discontinue ibuprofen
  - D. Nasal polypectomy

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All that wheezes is not asthma

- **Aspirin-Exacerbated Respiratory Disease (AERD)**
  - Asthma and rhisnosinusistis exacerbated by the use of aspirin and other NSAIDs (inhibition of cyclooxigenase = increase leukotriene synthesis)
  - Clues: adult onset, nasal polyps, triggered NSAIDs use
  - Treatment: usual asthma step-wise approach (emphasis on leukotriene-receptor antagonists) + discontinuing NSAIDs and desensitization to aspirin.

N Engl J Med 2018; 379:1060-1070

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All that wheezes is not asthma

- **Allergic Bronchopulmonary Aspergillosis (ABPA)**
  - Ongoing immunologic response to inhaled Aspergillus species
  - Clues: productive cough, brown mucus, bronchiectasis
  - Diagnosis: elevated IgE levels, positive skin test to aspergillus antigens, increased pulmonary Aspergillus-specific IgE and IgG levels
  - Treatment: oral steroids, antifungal

Allergy Asthma Immunol Res. 2016 Jul; 8(4): 282–297.

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All that wheezes is not asthma

Chart 1 – Causes of wheezing other than asthma.

Extrathoracic upper airway obstruction	Intrathoracic upper airway obstruction	Lower airway obstruction
Postnasal drip	Tracheal stenosis	COPD
Vocal cord dysfunction	Airway tumors	Bronchiectasis
Hypertrophied tonsils	Foreign body aspiration	Pulmonary edema
Upper airway tumors	Intrathoracic goiter	Gastric aspiration
Retropharyngeal abscess	Tracheobronchomegaly	Pulmonary embolism
Laryngeal edema or stenosis	Tracheomalacia	Bronchiolitis
Laryngocele	Vascular compression	Cystic fibrosis
Vocal cord paralysis		Carcinoid syndrome
Relapsing polychondritis		Lymphangitic carcinomatosis
Cricoarytenoid arthritis		Parasitic infections
Wegener's granulomatosis		Bronchospasm of various causes (anaphylaxis, toxic gas inhalation, post-viral infection, drug-induced cause, acute chest syndrome, etc.)

J Bras Pneumol. 2013 Jun-Aug; 39(4): 518–520.

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Question 3

- 58yo man with a 40 PPY smoking history complains of a 2-year history of slowly progressive exertional dyspnea with intermittent wheezing and a productive cough of clear sputum. He has no chest pain, palpitations or lower extremity edema. PMH of CAD. Meds: aspirin, metoprolol, rosuvastatin and lisinopril.
- Physical exam: SpO2 94% on RA, lung auscultation reveals prolonged expiratory phase but no wheezes.
- Chest Xray and ECG are normal.

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Question 3

- Which of the following is the most appropriate test to perform next?
  - A. Echocardiogram
  - B. Exercise stress test
  - C. High-resolution CT chest
  - ➡D. Spirometry

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COPD

- Persistent airflow limitation secondary to recurrent and significant exposure to noxious particles and gases.
- Dyspnea, chronic cough w/or w/o sputum production are the main symptoms
- Spirometry is required for diagnosis. FEV1/FVC<70 without reversibility after BD administration.
- Remember impact in overall health status and co-morbid illnesses

https://goldcopd.org/gold-reports/

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Table 2.4. Classification of airflow limitation severity in COPD (Based on post-bronchodilator FEV_1)		
In patients with $FEV_1/FVC < 0.70$:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

Table 2.5. Modified MRC dyspnea scale[a]	
PLEASE TICK IN THE BOX THAT APPLIES TO YOU (ONE BOX ONLY) (Grades 0–4)	
mMRC Grade 0. I only get breathless with strenuous exercise.	❑
mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill.	❑
mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	❑
mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level.	❑
mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing.	❑

https://goldcopd.org/gold-reports

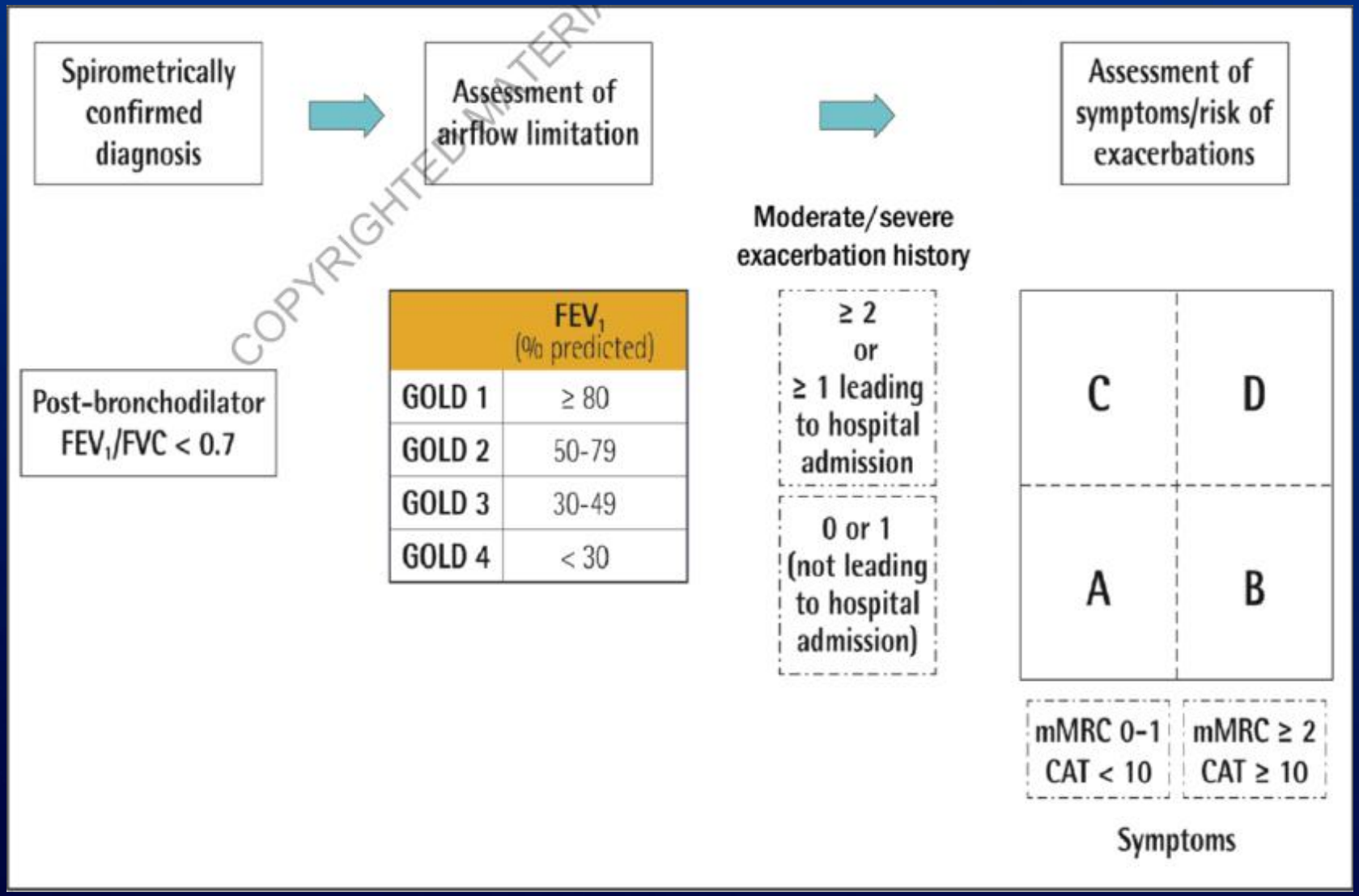
For each item below, place a mark (✗) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy (0) (✗) (2) (3) (4) (5) I am very sad

			SCORE
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	
		TOTAL SCORE	

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

https://goldcopd.org/gold-reports



https://goldcopd.org/gold-reports

COPD

- Management
  - Test for alpha1 deficiency if younger patient or atypical emphysema location
  - Smoking/exposure cessation
  - Inhalers/oral medications
  - Immunizations (flu, pneumococcal 13 and 23)
  - Oxygen
  - Suppressive antibiotics
  - Rehabilitation
  - Lung reduction surgery/endobronchial valves/lung transplant

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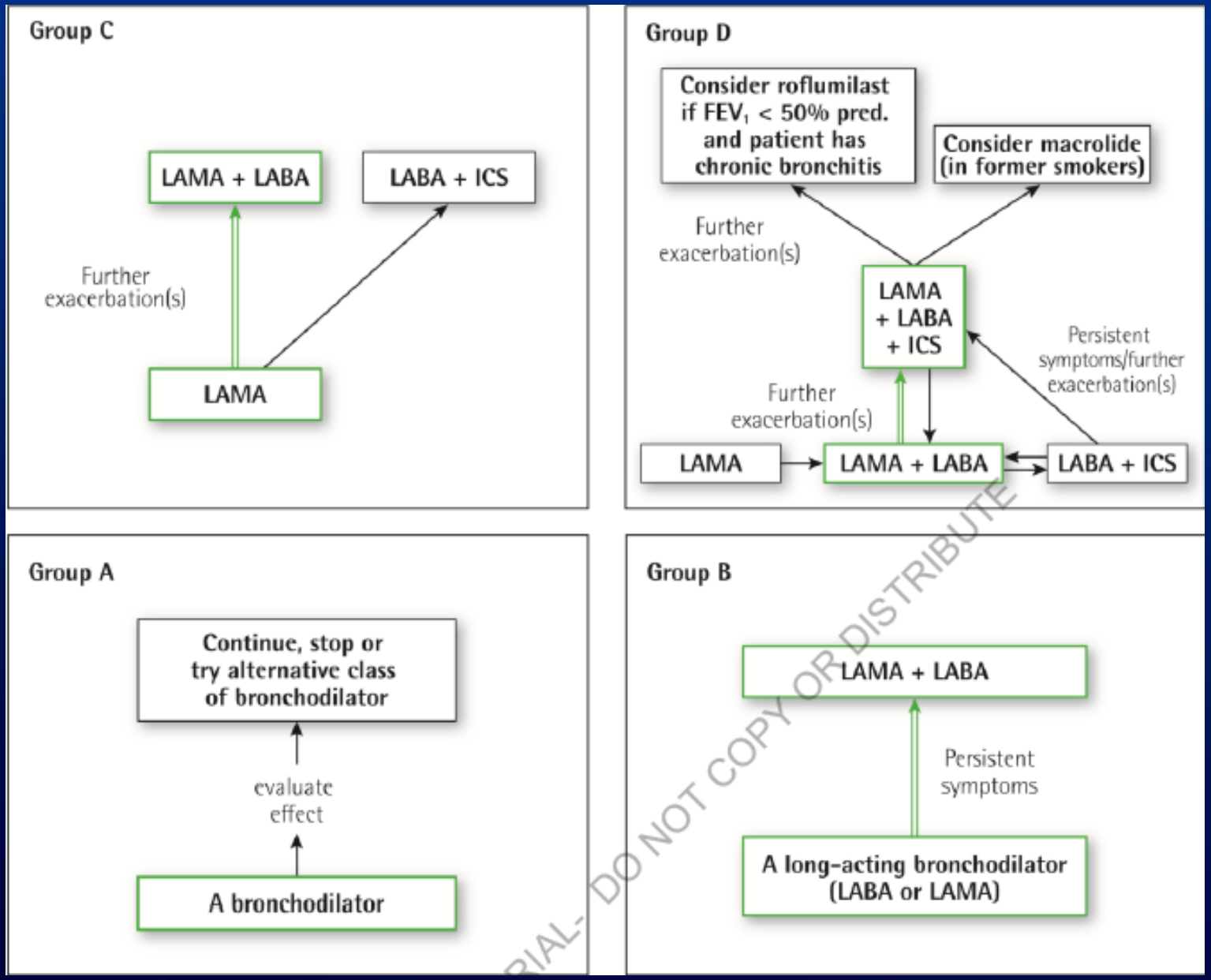

https://goldcopd.org/gold-reports

Table 4.9. Key points for the use of non-pharmacological treatments
Education, self-management and pulmonary rehabilitation
• Education is needed to change patient's knowledge but there is no evidence that used alone it will change patient behavior.
• Education self-management with the support of a case manager with or without the use of a written action plan is recommended for the prevention of exacerbation complications such as hospital admissions **(Evidence B)**.
• Rehabilitation is indicated in all patients with relevant symptoms and/or a high risk for exacerbation **(Evidence A)**.
• Physical activity is a strong predictor of mortality **(Evidence A)**. Patients should be encouraged to increase the level of physical activity although we still don't know how to best insure the likelihood of success.
Vaccination
• Influenza vaccination is recommended for all patients with COPD **(Evidence A)**.
• Pneumococcal vaccination: the PCV13 and PPSV23 are recommended for all patients > 65 years of age, and in younger patients with significant comorbid conditions including chronic heart or lung disease **(Evidence B)**.
Nutrition
• Nutritional supplementation should be considered in malnourished patients with COPD **(Evidence B)**.
End of life and palliative care
• All clinicians managing patients with COPD should be aware of the effectiveness of palliative approaches to symptom control and use these in their practice **(Evidence D)**.
• End of life care should include discussions with patients and their families about their views on resuscitation, advance directives and place of death preferences **(Evidence D)**.
Treatment of hypoxemia
• In patients with severe resting hypoxemia long-term oxygen therapy is indicated **(Evidence A)**.
• In patients with stable COPD and resting or exercise-induced moderate desaturation, long term oxygen treatment should not be routinely prescribed. However, individual patient factors may be considered when evaluating the patient's needs for supplemental oxygen **(Evidence A)**.
• Resting oxygenation at sea level does not exclude the development of severe hypoxemia when travelling by air **(Evidence C)**.
Treatment of hypercapnia
• In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long term non-invasive ventilation may be considered **(Evidence B)**.
Intervention bronchoscopy and surgery
• Lung volume reduction surgery should be considered in selected patients with upper-lobe emphysema **(Evidence A)**.
• Bronchoscopic lung volume reduction interventions may be considered in selected patients with advanced emphysema **(Evidence B)**.
• In selected patients with a large bulla surgical bullectomy may be considered **(Evidence C)**.
• In patients with very severe COPD (progressive disease, BODE score of 7 to 10, and not candidate for lung volume reduction) lung transplantation may be considered for referral with at least one of the following: (1) history of hospitalization for exacerbation associated with acute hypercapnia (Pco_2 > 50 mm Hg); (2) pulmonary hypertension and/or cor pulmonale, despite oxygen therapy; or (3) FEV_1 < 20% and either DLCO < 20% or homogenous distribution of emphysema **(Evidence C)**.

COPD

- Management of exacerbations
  - Assess severity of symptoms → inpatient x outpatient treatment
  - Oxygen therapy
  - Increase dose/frequency of SABAs/SAMAs
    - Consider patients' ability to use inhalers versus nebulizers
  - Systemic steroids
  - Treat the cause of the exacerbation
  - Evaluate volume status
  - Consider NIVPPV and IVM

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Question 4

- 62 yo man is evaluated during a general medical exam. He is a current smoker wit a 42 PPY history. He has a chronic cough, but no shortness of breath or chronic health conditions. Vital signs and physical exam are normal.
- Which of the follow interventions is most likely to improve this patient's long-term survival?
  - A. Annual chest radiograph
  - B. Annual low-dose chest CT
  - C. Annual sputum cytology
  - D. Smoking cessation

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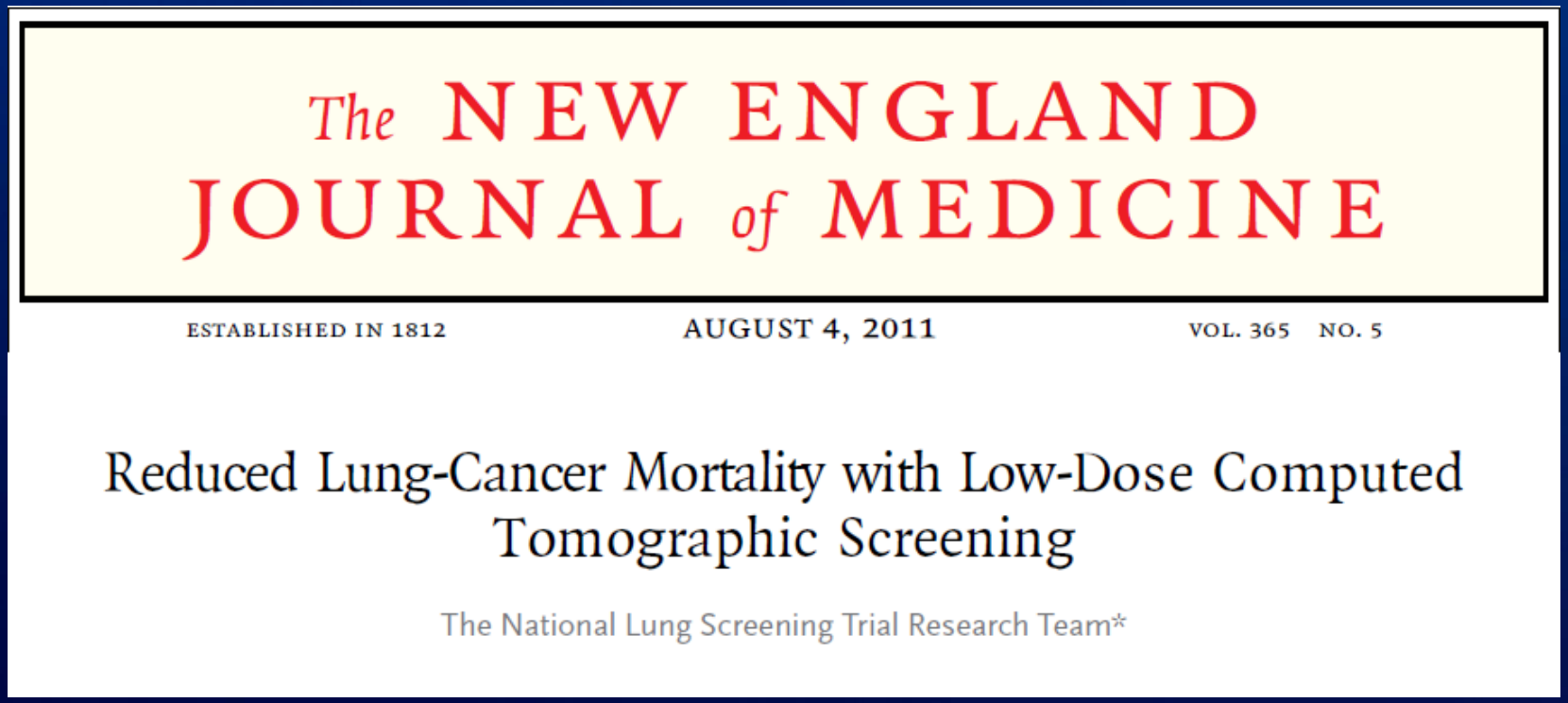
Lung Cancer Screening



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

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Lung Cancer Screening

- Patients who were 55-74 years of age, with a 30 PPY history of smoking or more
- Enrolled to undergo annual low dose CT chest or chest Xray
- Result: 20% of relative reduction in mortality from lung cancer in the low-dose CT group. No difference in false positive rates or rates if diagnosis

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Lung Cancer

- Leading cause of cancer death in the US and the world.
- Non-small cell lung cancer
  - Adeno→ most common, non smokers
    - Peripheral
    - Test for EGFR mutation, ALK and ROS1 translocations in advanced cases
  - Squamous → smokers, central
    - Usually symptomatic (cough, hemoptysis)

Siegel R, Naishadham D, Jemal A. Cancer statistics. 2013. CA Cancer J Clin. 2013;63(1):11–30

Lung Cancer

- Small cell lung cancer
  - 15% of all lung cancers
  - The most strongly associated with smoking
  - Central mass, with lymph node and airway involvement
  - Paraneoplastic syndromes most commonly associated with SCLC

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Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults

A: Solid Nodules*

Nodule Type	Size: <6 mm (<100 mm³)	Size: 6–8 mm (100–250 mm³)	Size: >8 mm (>250 mm³)	Comments
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).

B: Subsolid Nodules*

Nodule Type	Size: <6 mm (<100 mm³)	Size: ≥6 mm (>100 mm³)	Comments
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C)
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

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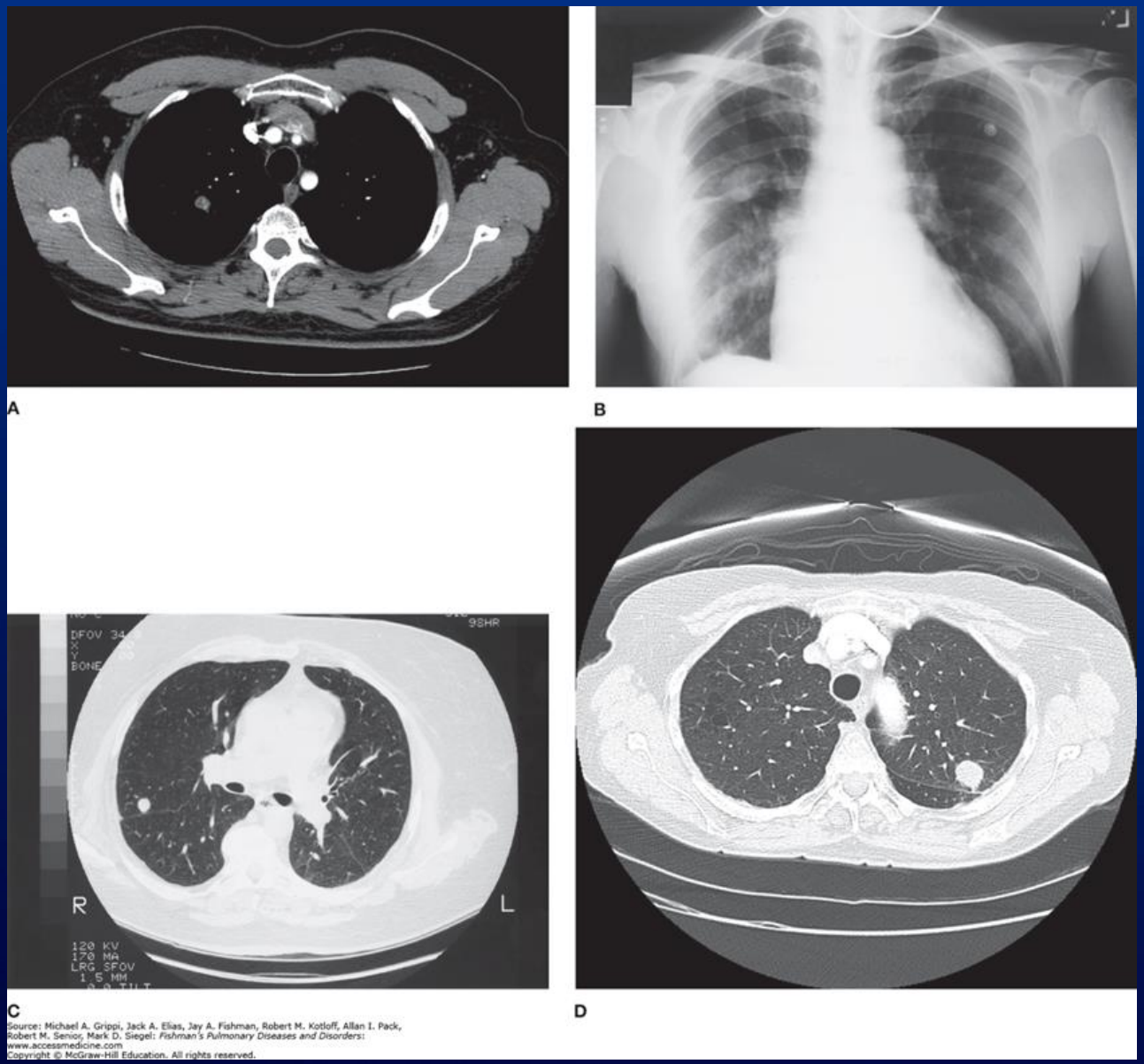
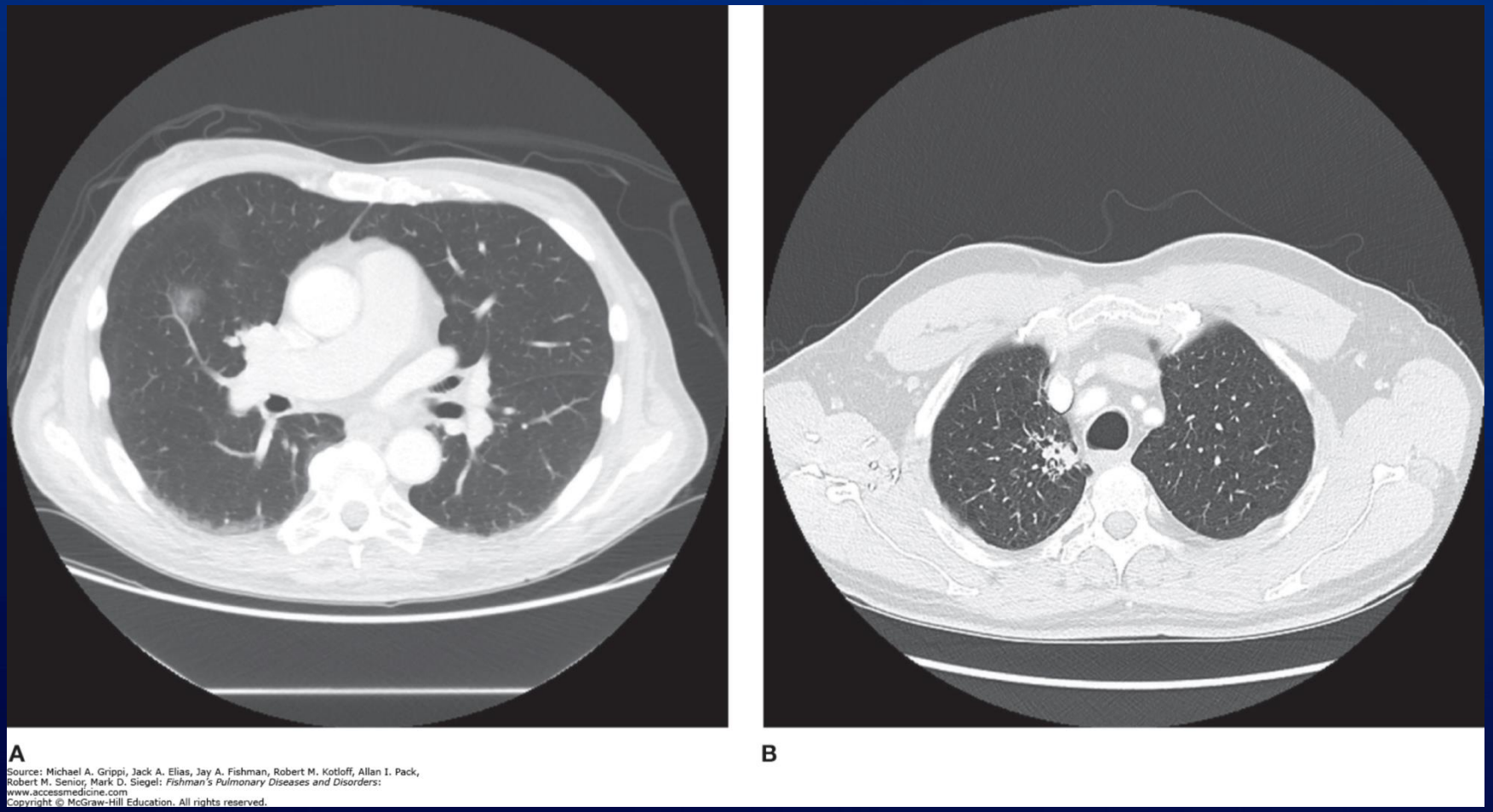
Radiology: Volume 284: Number 1—July 2017



Source: Michael A. Grippi, Jack A. Elias, Jay A. Fishman, Robert M. Kotloff, Allan I. Pack, Robert M. Senior, Mark D. Siegel: *Fishman's Pulmonary Diseases and Disorders*: www.accessmedicine.com

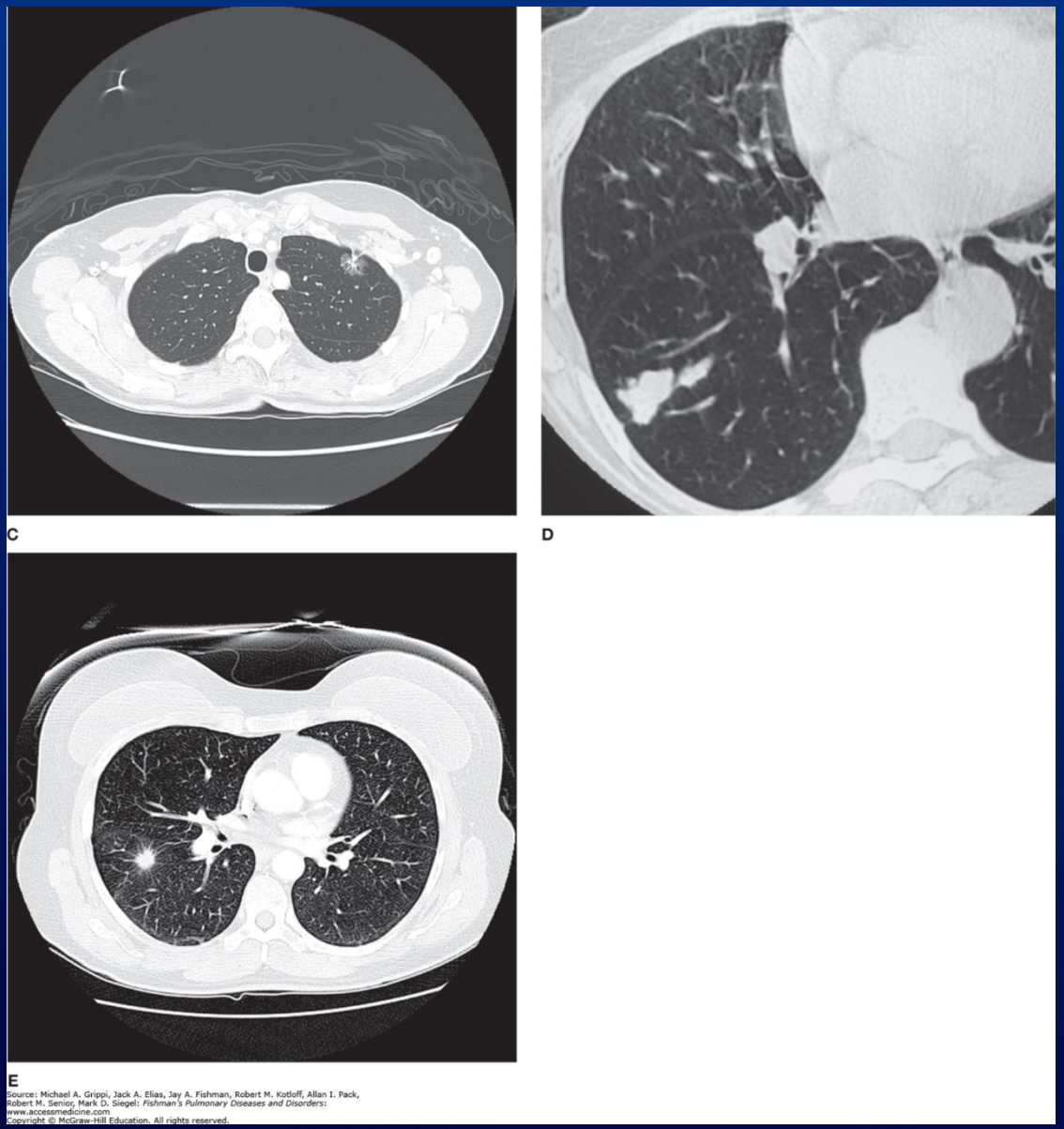
Approach to the Patient with Pulmonary Nodules, Grippi MA, Elias JA, Fishman JA, Kotloff RM, Pack AI, Senior RM, Siegel MD. Fishman's Pulmonary Diseases and Disorders, 5e; 2015



A

B

Approach to the Patient with Pulmonary Nodules, Grippi MA, Elias JA, Fishman JA, Kotloff RM, Pack AI, Senior RM, Siegel MD. Fishman's Pulmonary Diseases and Disorders, 5e; 2015



Approach to the Patient with Pulmonary Nodules, Grippi MA, Elias JA, Fishman JA, Kotloff RM, Pack AI, Senior RM, Siegel MD. Fishman's Pulmonary Diseases and Disorders, 5e; 2015

Lung Cancer

- Diagnostic approach
  - History and physical
  - CT chest →risk factors + concerning nodule > 0.8cm → PET scan
  - Tissue diagnosis
    - Modality depends on location of nodule/mass and distant disease

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Question 5

- 72yo man is evaluated during a follow up visit. He was evaluated in the ED 2 weeks ago for chest pain. CT angio was negative for PE but demonstrated an 8mm GG nodule in the RUL. Chest pain is resolved. PMH is significant for HTN, and he is on lisinopril.
- Vital signs and remainder of physical exam are normal.
- The patient undergoes follow-up CT scans of the chest at 12 and 24 months. The nodule is unchanged.

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Question 5

- Which of the following is the most appropriate management of the lung nodule?
  - A. Chest CT every 2 years for 5 years
  - B. PET/CT scan
  - C. Tissue Sampling
  - D. No further follow up

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Question 6

- 72 yo man complains of nonproductive cough and progressively worsening dyspnea on exertion during the past year. He has no history of dry eyes or mouth, raynaud's, arthralgia, myalgia or arthritis. He has a 30PPY smoking history, quit 15 years ago. He denies any environmental exposures.
- VS are normal SpO2 95% on RA. Auscultation reveals velcro crackles at the bases. Bilateral clubbing is also present.
- Spirometry was normal, DLCO was 65% of predicted. HRCT shows bilateral peripheral and basal predominant septal line thickening with honeycombing.

MAYO CLINIC

Question 6

- Which of the following is the most likely diagnosis?
  - A. Desquamative interstitial pneumonia
  - B. Hypersensitivity Pneumonitis
  - C. Idiopathic Pulmonary Fibrosis
  - D. Pulmonary langerhans cell histiocytosis
  - E. Respiratory bronchiolitis-associated interstitial lung disease

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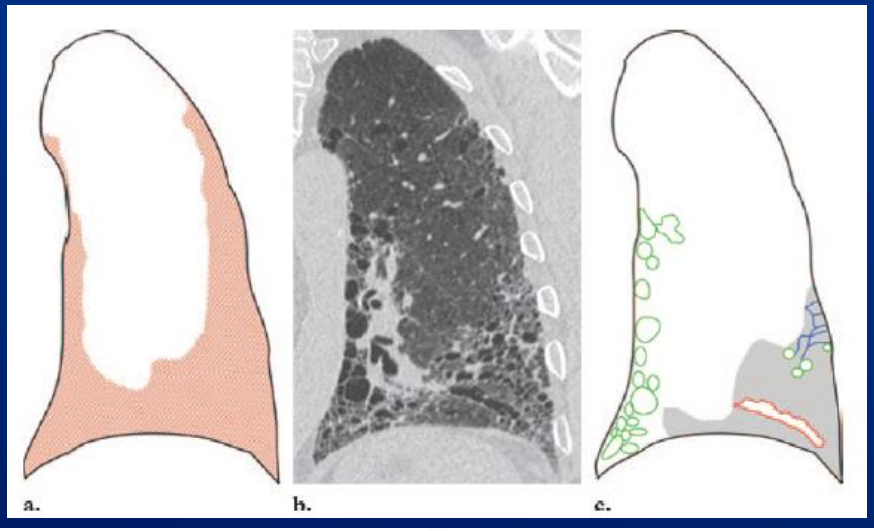
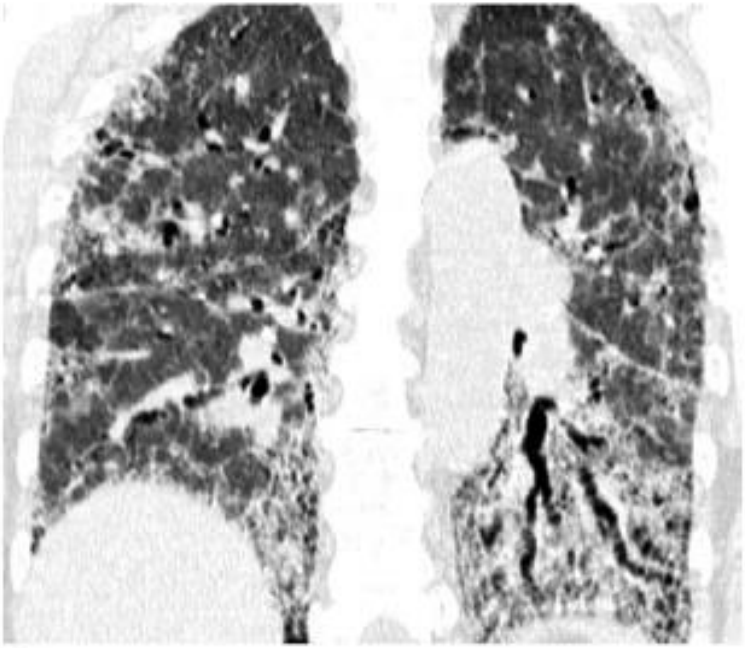


UIP Pattern



4b. 5b.

RadioGraphics 2007; 27:595–615 • Published online 10.1148/rg.273065130 • Content Code: CH

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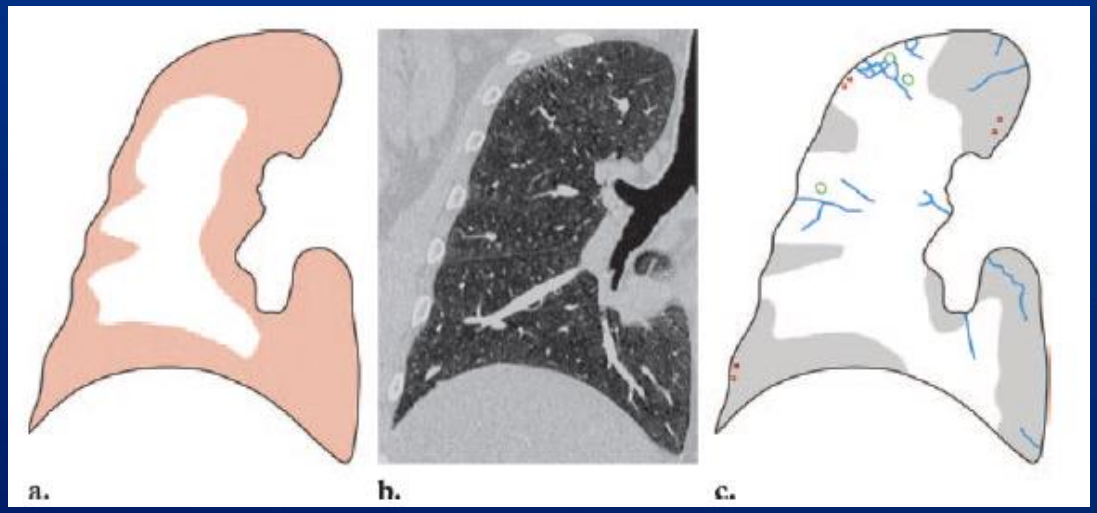
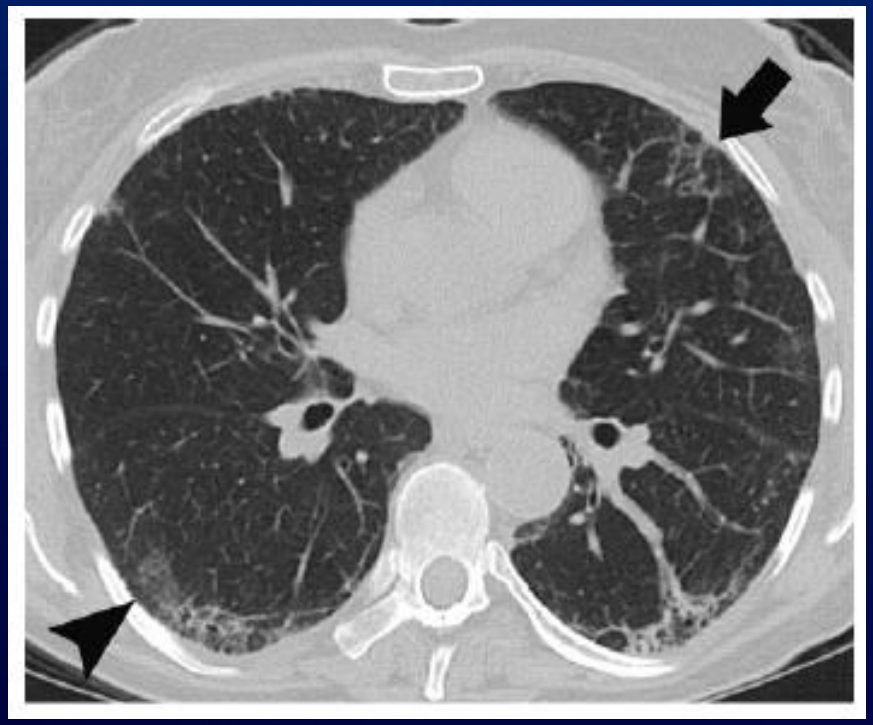


NSIP Pattern



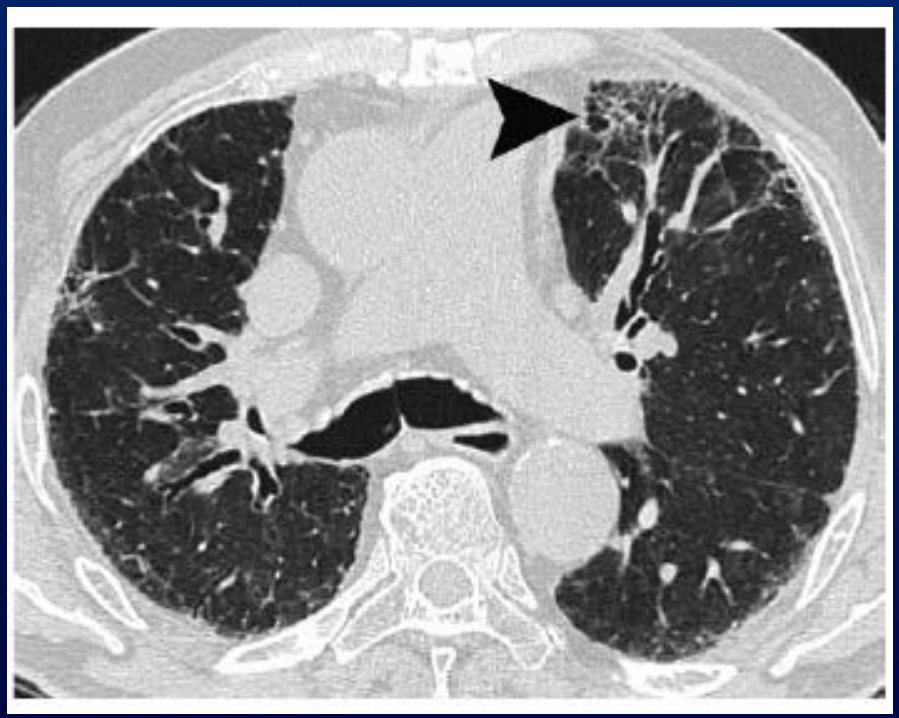


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TABLE 1. **Classification of ILDs***

- Known cause
  - Connective tissue disease–associated ILDs (eg, rheumatoid arthritis, polymyositis, scleroderma)
  - Hypersensitivity pneumonitis (eg, farmer's lung "hot tub lung," bird fancier's lung)
  - Pneumoconioses (eg, asbestosis, silicosis, coal worker's pneumoconiosis)
  - Drug-induced ILDs (eg, chemotherapeutic agents, amiodarone, nitrofurantoin)
  - Smoking-related ILDs
    - Pulmonary Langerhans cell histiocytosis
    - Respiratory bronchiolitis–associated ILD
    - Desquamative interstitial pneumonia
    - Acute eosinophilic pneumonia
  - Radiation-induced ILDs
  - Toxic inhalation–induced ILDs (eg, cocaine, zinc chloride [smoke bomb], ammonia)
- Unknown cause
  - Idiopathic pulmonary fibrosis
  - Sarcoidosis
  - Other idiopathic interstitial pneumonias
    - Cryptogenic organizing pneumonia
    - Nonspecific interstitial pneumonia
    - Lymphocytic interstitial pneumonia
    - Acute interstitial pneumonia
  - Eosinophilic pneumonias
  - Pulmonary vasculitides
  - Pulmonary lymphangioleiomyomatosis
  - Pulmonary alveolar proteinosis
  - Many other rare disorders

*ILDs = interstitial lung diseases.

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Mayo Clin Proc. 2007;82(8):976-986

TABLE 2. **Diagnosis of Interstitial Lung Disease***

- History
  - Demographics
  - Pulmonary and extrapulmonary manifestations
  - Temporal course of symptoms
  - Smoking
  - Environmental/occupational exposures
  - Drugs
  - Previous and concurrent illnesses
  - Familial disorders
- Physical examination
  - Lung auscultation
  - Digital clubbing
  - Extrapulmonary signs
- Laboratory tests
  - Complete blood cell count
  - Chemistry panel
  - Urinalysis
  - Hypersensitivity pneumonitis serologic tests†
  - Connective tissue disease serologic tests†
  - Antineutrophil cytoplasmic antibodies†
  - Brain natriuretic peptide level†
- Imaging studies
  - Chest radiography
  - CT of the chest with high resolution
  - Previous chest radiographs and chest CT studies
  - Echocardiography†
- Pulmonary function tests
  - Spirometry, lung volumes, diffusing capacity, and oximetry
  - Arterial blood gas study†
  - Cardiopulmonary exercise testing†
- Bronchoscopy†
- Surgical lung biopsy†

*CT = computed tomography.
†These tests are used in selected cases according to the clinical context.

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Mayo Clin Proc. 2007;82(8):976-986

TABLE 3. **Differential Diagnosis of ILDs Based on Radiologic Findings and Tempo***

Pattern

- Consolidation
  - Acute: diffuse alveolar hemorrhage syndromes, acute interstitial pneumonia, acute eosinophilic pneumonia, acute reactions to drug or inhalational exposure, cryptogenic organizing pneumonia (also consider infections, pulmonary edema, aspiration)
  - Chronic: chronic eosinophilic pneumonia, cryptogenic organizing pneumonia, lymphoproliferative diseases, pulmonary alveolar proteinosis, sarcoidosis (also consider chronic infections, chronic aspiration, lymphoma, bronchoalveolar cell carcinoma)
- Reticular pattern
  - Acute: consider infections, pulmonary edema
  - Chronic: IPF, connective tissue disease–associated ILD, asbestosis, sarcoidosis, hypersensitivity pneumonitis, drug-induced lung disease
- Nodular pattern (nodules <1 cm in diameter)
  - Acute: hypersensitivity pneumonitis, sarcoidosis (also consider infections, eg, tuberculosis, fungal infections)
  - Chronic: sarcoidosis, hypersensitivity pneumonitis, silicosis, coal worker's pneumoconiosis, respiratory bronchiolitis, alveolar microlithiasis (also consider metastatic disease)
- Cystic airspaces
  - Acute: consider *Pneumocystis* pneumonia, septic embolism
  - Chronic: pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, lymphocytic interstitial pneumonia, honeycomb lung caused by IPF
- Ground-glass opacities
  - Acute: diffuse alveolar hemorrhage, hypersensitivity pneumonitis, acute inhalational exposures, drug-induced lung diseases, acute interstitial pneumonia (also consider infections, pulmonary edema)
  - Chronic: nonspecific interstitial pneumonia, hypersensitivity pneumonitis, respiratory bronchiolitis–associated ILD, desquamative interstitial pneumonia, drug-induced lung diseases, pulmonary alveolar proteinosis
- Thickened interlobular septa
  - Acute: consider congestive heart failure, pulmonary edema
  - Chronic: pulmonary alveolar proteinosis, sarcoidosis

Distribution

- Upper lung predominance: sarcoidosis, pulmonary Langerhans cell histiocytosis, silicosis, coal worker's pneumoconiosis, carmustine-related pulmonary fibrosis (also consider tuberculosis, *Pneumocystis* pneumonia)
- Lower lung predominance: IPF, connective tissue disease–associated ILD, asbestosis (also consider chronic aspiration)
- Central predominance: sarcoidosis, berylliosis, pulmonary alveolar proteinosis
- Peripheral predominance: IPF, nonspecific interstitial pneumonia, chronic eosinophilic pneumonia, cryptogenic organizing pneumonia (also consider pulmonary infarctions, septic pulmonary embolism)

Associated findings

- Traction bronchiectasis: IPF, asbestosis, other chronic fibrotic disorders
- Lymphadenopathy: sarcoidosis, silicosis, berylliosis (also consider infections, lymphangitic carcinomatosis or metastases, lymphoma)
- Air trapping: hypersensitivity pneumonitis, respiratory bronchiolitis–associated ILD, desquamative interstitial pneumonia, sarcoidosis
- Pleural effusion or thickening: drug-induced ILDs, connective tissue disease–associated ILDs, asbestosis, lymphangioleiomyomatosis (also consider lymphangitic carcinomatosis, lymphoma)

*ILD = interstitial lung disease; IPF = idiopathic pulmonary fibrosis.
Adapted from *Mayo Clin Proc.*[4]

Mayo Clin Proc. 2007;82(8):976-986

Question 7

- 72yo man hospitalized for progressive dyspnea and cough following a sore throat 3 weeks ago. PMH is significant for IPF on 2L of O2.He is disabled because of lung disease and is homebound. His only medication is pirfenidone.
- On physical exam he is tachycardic, tachypneic, and hypoxic (89% on RA). He has diffuse inspiratory crackles, worse at the bases. He has clubbing and trace edema, but no JVD.
- BAL is positive for rhinovirus, BNP is 20. HRCT shows new bilateral GGOs on a background of basal-predominant septal line thickening with traction bronchiectasis and honeycombing. CTA was negative for PE.

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Question 7

- Which of the following is the most likely diagnosis?
  - A. Acute exacerbation of IPF
  - B. Acute heart failure
  - C. Acute hypersensitivity pneumonitis
  - D. Nonspecific interstitial pneumonia

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Question 8

- A 57-year-old male presents to your clinic due excessive sleepiness and difficulty functioning at his work. His wife had complained of long history of loud snoring and had witnessed frequent apneic episodes. His body mass index is 42 kg/m^2. His blood pressure is 155/85. His neck size is 48 cm.

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Question 8

- Which of the following tests should be performed next to confirm your suspicion?
  - A. Electroencephalogram.
  - B. 24-hour ambulatory blood pressure monitor.
  - C. Overnight polysomnogram.
  - D. Carotid duplex ultrasound.
  - E. Adrenal imaging with CT scan.

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Sleep-related Breathing Disorder

- Encompasses spectrum of disordered breathing during sleep
- Condition of repetitive upper airway collapse/narrowing associated with daytime somnolence
- At least 4% middle-aged men, 2% women
- Diagnosis by overnight polysomnogram

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Sleep-related Breathing Disorder

- Clinical presentation
  - Overweight, daytime somnolence, snoring
- Suggestive examination:
  - HTN
  - Obese
  - Large neck
  - Retro- or micrognathia
  - Deviation/congestion of nasal passage
  - Tonsillar hypertrophy

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Endocrine dysfunction:
- Thyroid
- Cortisol
- Growth hormone
- Testosterone

Nocturia
Proteinuria

Immune dysfunction
Cytokine dysregulation

Hypersomnia
CVA/TIA
Cognitive dysfunction
Memory impairment
Mood disorders
Seizures
Chronic pain syndromes
Headache

HTN
MI
CHF
Arrhythmia
Pulmonary HTN
Atherosclerosis

GERD
Irritable bowel syndrome

Courtesy of Dr. Kannan Ramar

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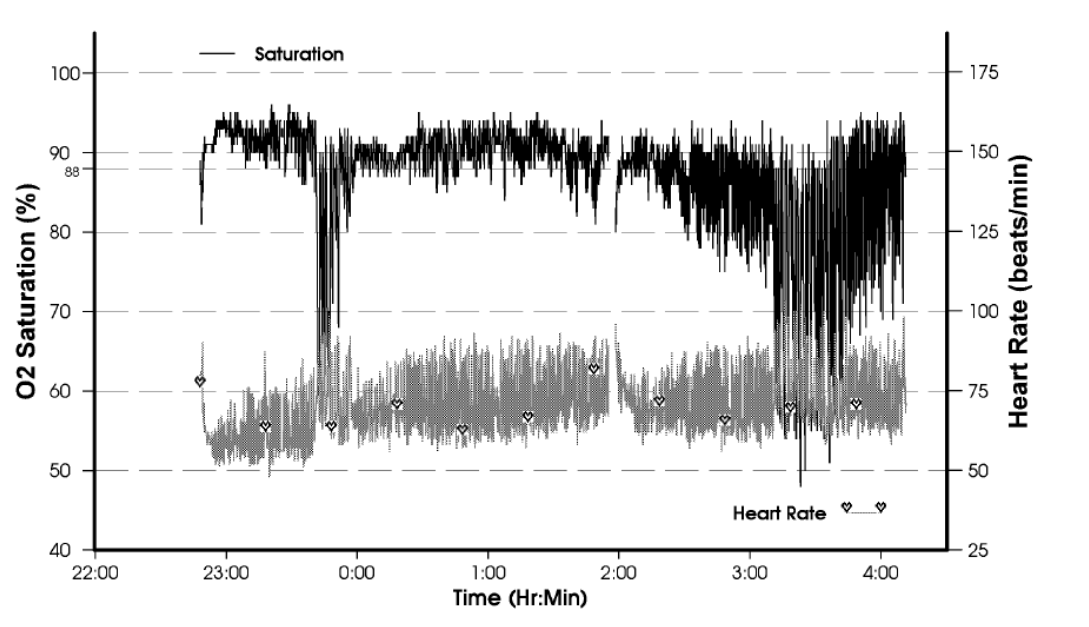
Sleep-related Breathing Disorder

- Screening: Overnight oximetry



- Diagnosis: Polysomnogram

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Sleep-related Breathing Disorder

- Treatment:
  - Weight loss
  - Positional therapy
  - Minimize alcohol or sedative exposure
  - Continuous positive airway pressure (CPAP)
  - Oral appliance
  - Uvulopalatopharyngoplasty (UPPP)
  - Maxillomandibular advancement (MMA)
  - Tracheostomy

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Question 9

- 53 yo man presents with 4 days of cough, fever, chills, myalgia and poor appetite. Currently, he has increased dyspnea and lightheadedness.
- On exam he is febrile, BP 82/40mmHg, HR 128 bpm, sat 92% RA. Otherwise, physical examination is normal.
- Labs: Hb:10, Lactate 4.6, WBCs 18000, ABG 7.32/CO2 32/PO2 79/Bicarb 16
- Chest xray shows a RLL consolidation. ECG shows sinus tachycardia.

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Question 9

- Which of the following is the most appropriate initial treatment?
  - A. 0.9 saline bolus
  - B. Intravenous furosemide
  - C. Norepinephrine
  - D. PRBCs

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Sepsis

Box 3. New Terms and Definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection.
  - The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
  - A SOFA score ≥2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.
- In lay terms, sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs.
- Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA, ie, alteration in mental status, systolic blood pressure ≤100 mm Hg, or respiratory rate ≥22/min.
- Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
- Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%.

Abbreviations: MAP, mean arterial pressure; qSOFA, quick SOFA; SOFA: Sequential [Sepsis-related] Organ Failure Assessment.

Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥22/min

Altered mentation

Systolic blood pressure ≤100 mm Hg

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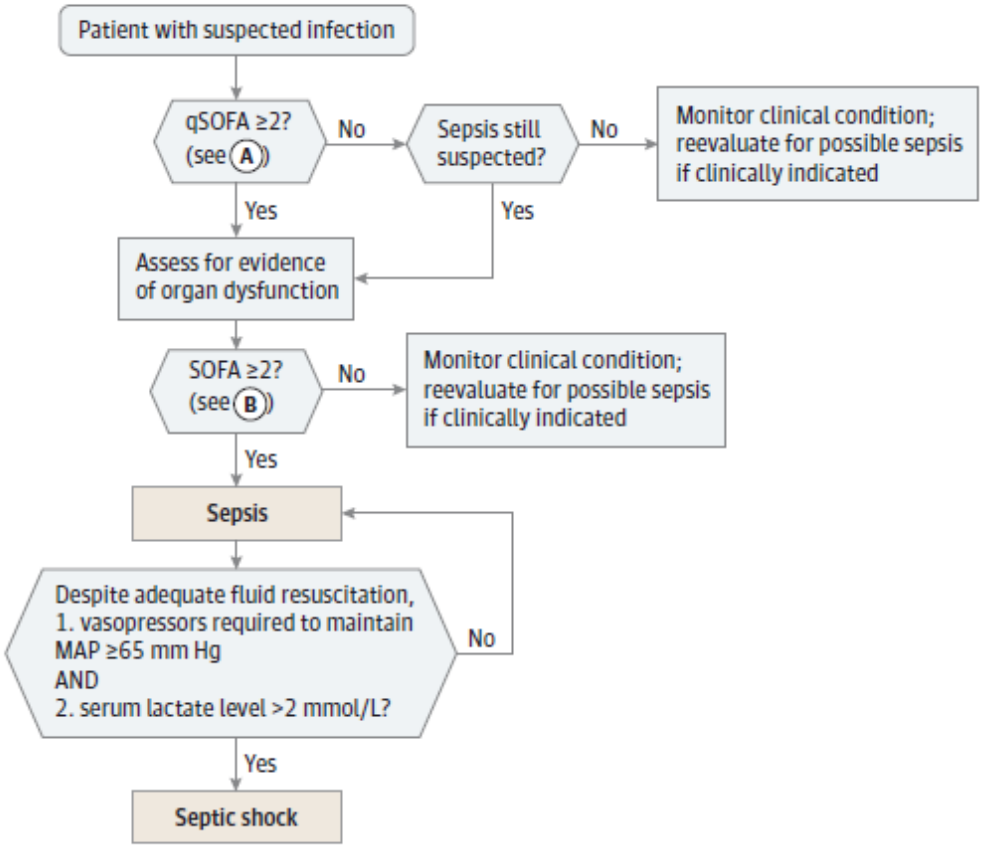
Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



A qSOFA Variables
- Respiratory rate
- Mental status
- Systolic blood pressure

B SOFA Variables
- PaO_2/FiO_2 ratio
- Glasgow Coma Scale score
- Mean arterial pressure
- Administration of vasopressors with type and dose rate of infusion
- Serum creatinine or urine output
- Bilirubin
- Platelet count

The baseline Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score should be assumed to be zero unless the patient is known to have preexisting (acute or chronic) organ dysfunction before the onset of infection. qSOFA indicates quick SOFA; MAP, mean arterial pressure.

Table 1.2 Flow Characteristics in Peripheral Vascular Catheters

Gauge Size	Length	Flow Rate	
		mL/min	L/hr
16	30 mm (1.2 in)	220	13.2
18	30 mm (1.2 in)	105	6.0
	50 mm (2 in)	60	3.6
20	30 mm (1.2 in)	60	3.6

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Table 1.3 Selected Features of Triple-Lumen Central Venous Catheters

Size	Length	Lumens	Lumen Size	Flow Rate (L/hr)[1]
7 Fr	16 cm	Distal	16 ga	3.4
	(6 in)	Medial	18 ga	1.8
		Proximal	18 ga	1.9
7 Fr	20 cm	Distal	16 ga	3.1
	(8 in)	Medial	18 ga	1.5
		Proximal	18 ga	1.6
7 Fr	30 cm	Distal	16 ga	2.3
	(12 in)	Medial	18 ga	1.0
		Proximal	18 ga	1.1

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Table 1.4 Selected Features of Peripherally Inserted Central Catheters

Size	Length	Lumens	Lumen Size	Flow Rate (L/hr)[1]
5 Fr	50 cm (195 in)	Single	16 ga	1.75
5 Fr	70 cm (27.5 in)	Single	16 ga	1.30
5 Fr	50 cm	Distal	18 ga	0.58
	(19.5 in)	Proximal	20 ga	0.16
5 Fr	70 cm	Distal	18 ga	0.44
	(27.5 in)	Proximal	20 ga	0.12

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Question 10

- 74 y/o with severe diarrhea presents to the ED with fever and hypotension. He was given 5 L of 0.9 normal saline (NS) and once stabilized, was admitted to the floor.
- In the ED, his bicarbonate was 21 and lactate was 2.1. Upon arrival, his blood pressure started to drop. You order 2 more liters of 0.9 NS. While his blood pressure normalized, follow up blood tests revealed: sodium - 132, chloride – 115, bicarbonate – 10, lactate - 1.0.

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Question 10

- What is the most likely reason for his worsening acidosis?
  - A. Bowel ischemia
  - B. Fluid resuscitation with 0.9 normal saline
  - C. Septic shock
  - D. Laboratory error

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Fluid Resuscitation

	NS	LR	5% Alb
Na	154	130	130-160
Cl	154	109	130-160
Osm	310	275	310
Lactate	0	28	0
Potassium	0	4	0
Calcium	0	3	0
pH	5	6.5	6.9
Cost	0.6	0.75	80

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Fluid Resuscitation

- Watch out for hyperchloremic metabolic acidosis with too much 0.9 normal saline
- Use lactated ringers with caution in those with hyperkalemia
- 5% albumin is iso-oncotic, whereas 25% albumin is hyper-oncotic
- With respect to electrolytes in the fluid, consider albumin and 0.9% normal saline to be equivalent

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Vasopressors

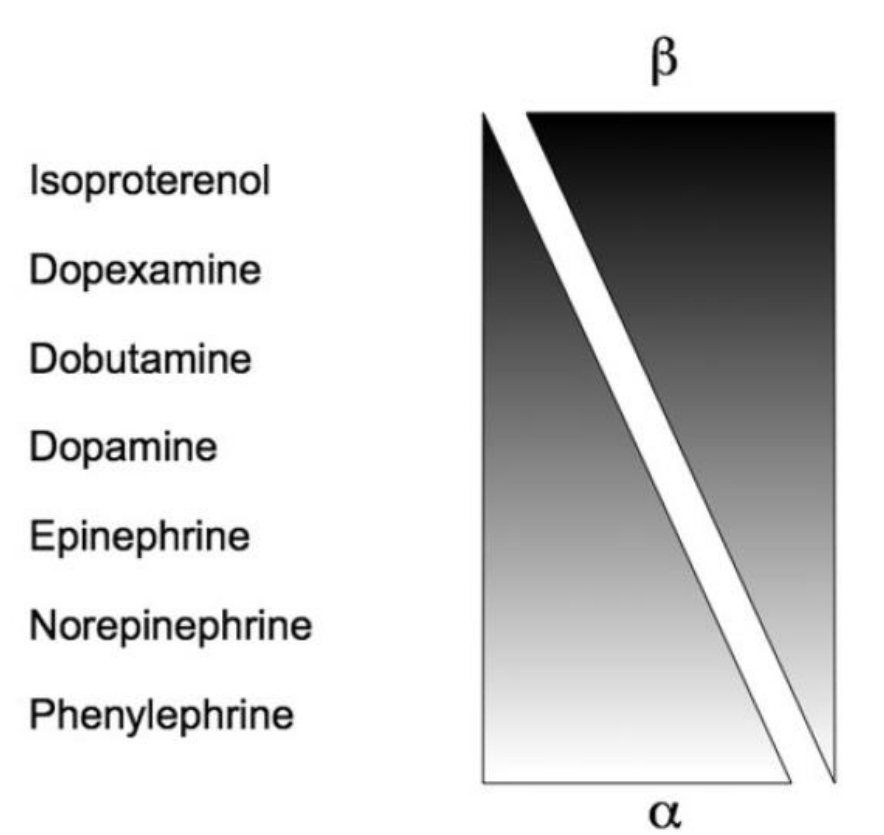

FIGURE 1. α-adrenergic and β-adrenergic effects of vasoactive catecholamines.

- Alpha adrenergic → vasoconstriction
- Beta 1 adrenergic → increase heart rate and myocardial contractility
- Beta 2 adrenergic → peripheral vasodilation

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Vasopressors

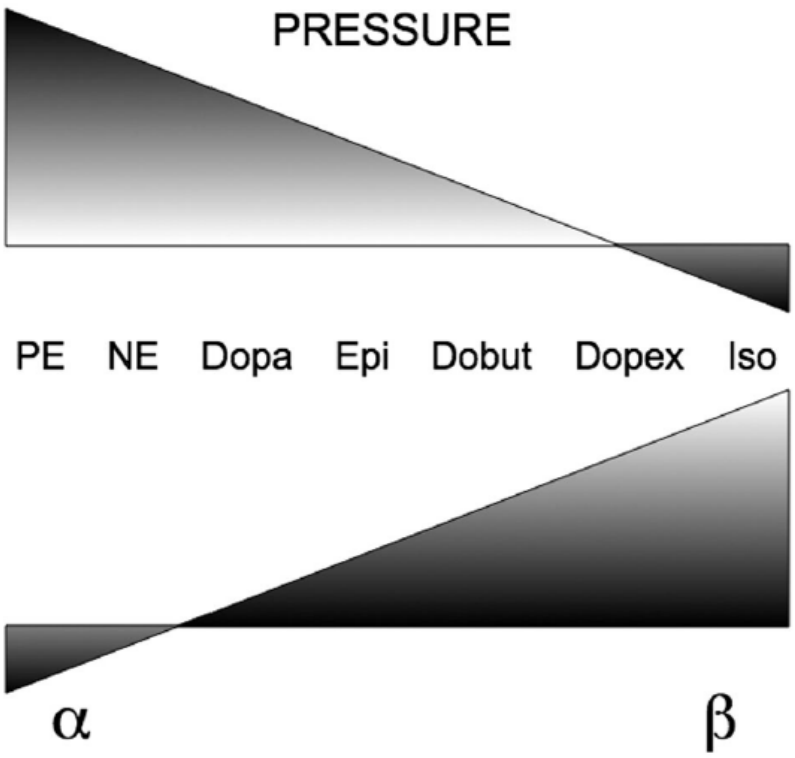

FIGURE 2. Effects of vasoactive catecholamines on pressure and blood flow. PE = phenylephrine; NE = norepinephrine; Dopa = dopamine; Epi = epinephrine; Dobut = dobutamine; Dopex = dopexamine; Iso = isoproterenol.

- Dopamine
  - <5 mcg/kg/min →dopaminergic effects with vasodilation in renal and mesenteric beds
  - >5 and <10 → beta 1
  - >10 → alpha 1
- Vasopressin → constricts vascular muscle via V1 receptors

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Hemodynamic findings in shock

	CO	PCWP	SVR	SvO2
Hypovolemic	Down	Down	Up	Down
Cardiogenic	Down	Up	Up	Down
Distributive	Up	Up or Down	Down	Up

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Question 10

- 43 year old with history of asthma and OSA (never-smoker) presents with worsening dyspnea, cough, and fevers. He recently had a flu-like illness and thought he was recovering, until symptoms worsened.
- His oxygen saturation is 88% on RA and progressed to 88% on CPAP of 7 cm H_2O and 8 L/min O_2. His temperature was 37.0°C.
- His subsequent CXR is shown. At the time of this CXR, his ABG was pH 7.35, PaO_2 239 on 100% FiO_2 on BiPAP (with EPAP of 7 cm H_2O).

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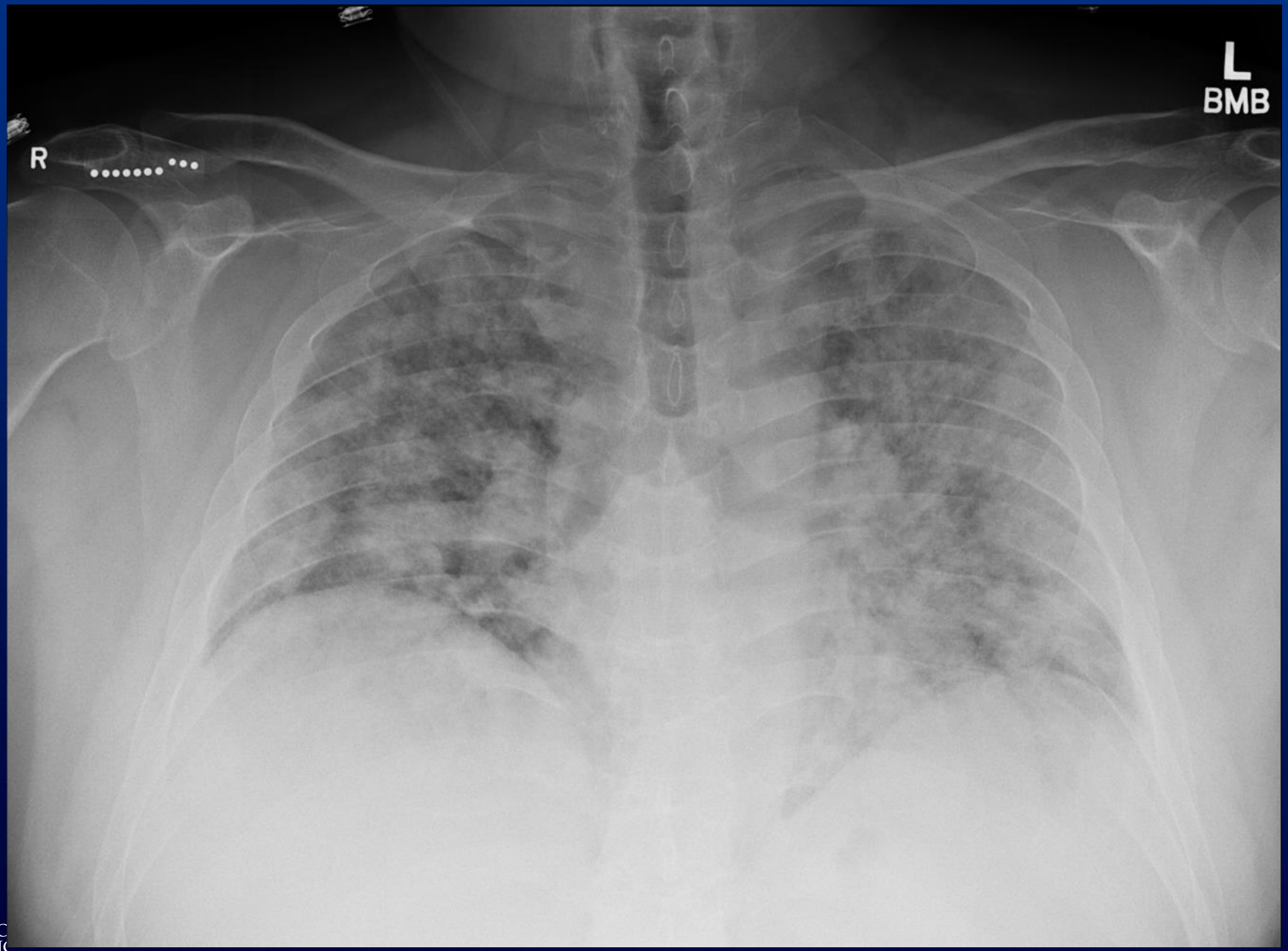
L
BMB
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Question 10

- What condition does this patient have?
  A. Congestive heart failure (CHF)
  B. Acute lung injury (ALI)
  C. Acute respiratory distress syndrome (ARDS)
  D. Need more information (NMI, not TMI)

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ARDS definition

Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

	Acute Respiratory Distress Syndrome
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mm Hg $<$ PaO_2/FIO_2 $\leq$ 300 mm Hg with PEEP or CPAP $\geq$5 cm H_2O[c]
Moderate	100 mm Hg $<$ PaO_2/FIO_2 $\leq$ 200 mm Hg with PEEP $\geq$5 cm H_2O
Severe	PaO_2/FIO_2 $\leq$ 100 mm Hg with PEEP $\geq$5 cm H_2O

JAMA 2012;307:2526

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Question 11

- As he is failing BiPAP, you decide to intubate and initiate mechanical ventilation. His ideal body weight is 70 kg.
- What is the most appropriate initial ventilator setting?

A. Tidal volume 700 mL, PEEP 10 cm H_2O, RR 12, FiO_2 100%

B. Tidal volume 420 mL, PEEP 10 cm H_2O, RR 12, FiO_2 100%

C. Tidal volume 320 mL, PEEP 10 cm H_2O, RR 12, FiO_2 100%

D. Tidal volume 840 mL, PEEP 10 cm H_2O, RR 12, FiO_2 100%

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Hypoxemia – Lung Protective Ventilation

- Start with tidal volumes of 6 ml/kg IBW
- Limit plateau and driving pressures
- Can carefully change tidal volume to improve ventilator synchrony
  - As long as P_{plat} <30 and drivingP <15
- Tolerate some degree of hypercapnia
  - “Permissive hypercapnia”
- Tolerate some degree of hypoxemia
  - “Permissive hypoxemia”
- High PEEP

NEJM 2000;342:1301

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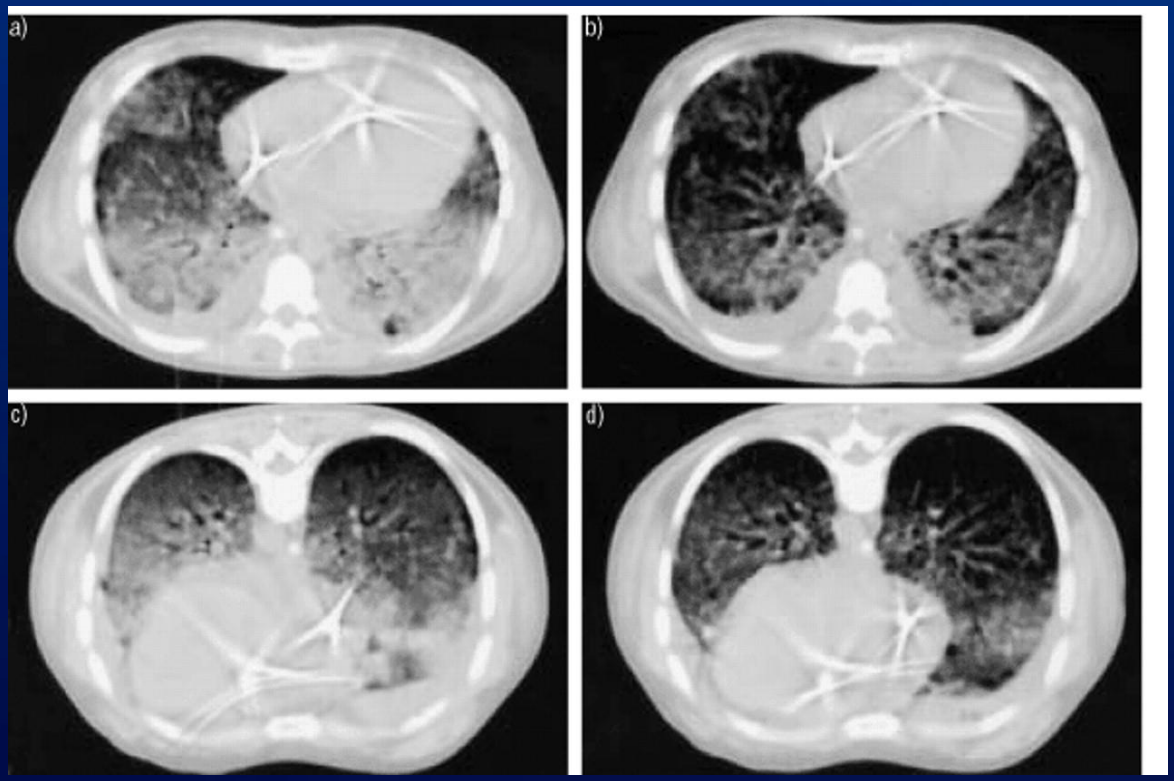
Refractory Hypoxemia

- Prone position



- ECMO
- Pulmonary Vasodilators → controversial

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Question 12

- 68 yo man with PMH of severe COPD, presents with productive cough, fever and worsening dyspnea for 4 days.
- On physical exam he is tachycardic, tachypneic, febrile and has diffuse respiratory wheezes.
- Chest xray shows hyperinflation, but no clear consolidation.
- ABG pH 7.21/CO2 70/O2 80/Bicarb 24

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Question 12

- Which of the following is the most appropriate treatment?
  - A. Continuous positive pressure
  - B. Bilevel positive pressure
  - C. High flow nasal cannula
  - D. Endotraqueal intubation

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Question 13

- After 30 minutes of BiPAP, ABG shows the following: pH 7.28/CO2 65/O2 95/Bicarb 24.
- Patient is clinically the same.
- Which of the following is the most appropriate next step?
  - A. Increase EPAP
  - B. Increase IPAP
  - C. Endotraqueal intubation

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Hypercapnic Respiratory Failure

- Decreased Drive
  - Anesthesia/Drugs
  - Central apnea
  - Obesity Hypoventilation Syndrome
  - CNS process
  - Hypothyroidism
- Decreased Vt
  - Chest wall/respiratory muscles abnormalities
  - Asthma/COPD exacerbations
  - Electrolyte disorder
  - Flail chest
  - Nerve damage
  - Airway obstruction

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Hypercapnic Respiratory Failure

- Increased Dead Space
  - PE
  - Pulmonary Vascular Disease
  - End stage ILD
- Increased CO_2 production
  - Fever
  - Thyrotoxicosis
  - Increased catabolism
  - Overfeeding
  - Metabolic acidosis
  - Exercise

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Questions & Discussion