

## *FP Essentials*

### Call for Authors – October 2024

#### Topics in Lung Disease

We are seeking an author or author group to write an edition of *FP Essentials* on the topic of lung disease. This edition will cover four topics:

1. Pulmonary hypertension in adults
2. Pulmonary nodules
3. Obesity hypoventilation syndrome
4. Noninfectious pleural effusion

The main text of the manuscript should be approximately 10,000 words in length, divided into four sections of approximately 2,500 words each, plus an abstract of approximately 200 words for each section. In addition, there should be key practice recommendations, a maximum of 15 tables/figures total, additional resources, and up to 200 references to provide support for all recommendations and factual statements in the manuscript. References must be numbered sequentially by section, with section headers dividing the list and each new section starting over at “1.”

This edition should focus on what is new in each topic and should answer the key questions listed for each section. Each section should begin with an illustrative case, similar to the examples provided, with modifications to emphasize key points; each case should have a conclusion that demonstrates resolution of the clinical situation. The references provided here include information that should be considered in preparation of this edition of *FP Essentials*. However, these should be used only as a starting point in identifying the most current guidelines and references to include in the edition.

**Needs Assessment:** Family physicians often are responsible for evaluating and managing patients with complex lung diseases such as pulmonary hypertension, pulmonary nodules, obesity hypoventilation syndrome, and pleural effusion. Education about updated diagnostic criteria, evidence-based treatment guidelines, and strategies for appropriate specialist referral is needed to equip physicians with the knowledge and confidence to enhance diagnostic accuracy, streamline treatment decisions, and improve patient outcomes in their daily practice.

## Section 1: Pulmonary Hypertension in Adults

**Example case:** AC is a 54-year-old female with exertional dyspnea, fatigue, and lower extremity edema that has progressed over the past 6 months. She has a history of obstructive sleep apnea, and she wears her CPAP infrequently at night. Lungs are clear to auscultation, and CT-angiography of the chest is negative for pulmonary embolism. However, echocardiogram reveals pulmonary artery pressure of 25 mm Hg (normal  $\leq 20$  mm Hg) with associated right ventricular hypertrophy.

### Key questions to consider:

#### Presentation

- What are pulmonary hypertension (PH) and pulmonary arterial hypertension (PAH)?
- How do patients with PH present? How often is PH diagnosed clinically vs incidentally? How does prognosis vary based on symptoms?
- Describe the classification of PH according to etiology. What are the leading causes of each group? How common is each?
- What are the risk factors and comorbidities for PAH and PH? Can PH be prevented? If so, how?

#### Diagnostic Evaluation

- What is the recommended diagnostic evaluation for PH? What findings on echocardiography suggest PH? What is the role of right heart catheterization? What other laboratory and imaging tests should be obtained, both for diagnosing and for determining the etiology of PH?
- When a diagnosis of PH/PAH is made incidentally on an echocardiogram, when should the patient be referred to cardiology?
- How should risk calculators be used in the evaluation and management of PH?

#### Management

- What medications are recommended for treating PAH? Does combination therapy improve outcomes compared to monotherapy?
- What are the recommended treatments for various other types of PH? When should diuretics be used in PH?
- How effective are pulmonary rehabilitation and exercise training for patients with PH?
- What is the prognosis for patients with PAH and other types of PH?
- What are the potential complications of PH? Can these complications be prevented? If so, how? How should these complications be managed?
- What treatment options should be considered for patients with progressive or refractory symptoms? When should lung transplantation and shunt procedures be considered?
- What are the indications for referral to a pulmonologist or cardiologist?

### Initial references to consider:

- Bjork S, Jain D, Marliere MH, et al. Obstructive sleep apnea, obesity hypoventilation syndrome, and pulmonary hypertension: a state-of-the-art review. *Sleep Med Clin.* 2024;19(2):307-325.
- Johnson S, Sommer N, Cox-Flaherty K, et al. Pulmonary hypertension: a contemporary review. *Am J Respir Crit Care Med.* 2023;208(5):528-548.

- Virsinskaite R, Karia N, Kotecha T, et al. Pulmonary hypertension - the latest updates for physicians. *Clin Med (Lond)*. 2023;23(5):449-454.
- Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618-3731.
- Tsujimoto Y, Kumasawa J, Shimizu S, et al. Doppler trans-thoracic echocardiography for detection of pulmonary hypertension in adults. *Cochrane Database Syst Rev*. 2022;5(5):CD012809.
- Hendriks PM, van de Groep LD, Veen KM, et al. Prognostic value of brain natriuretic peptides in patients with pulmonary arterial hypertension: a systematic review and meta-analysis. *Am Heart J*. 2022;250:34-44.
- Correale M, Tricarico L, Bevere EML, et al. Circulating biomarkers in pulmonary arterial hypertension: an update. *Biomolecules*. 2024;14(5):552.
- Ahmed A, Ahmed S, Kempe D, et al. Evaluation of the European Society of Cardiology/European Respiratory Society derived three- and four-strata risk stratification models in pulmonary arterial hypertension: introducing an internet-based risk stratification calculator. *Eur Heart J Open*. 2023;3(2):oead012.
- Benza RL, Grünig E, Sandner P, et al. The nitric oxide-soluble guanylate cyclase-cGMP pathway in pulmonary hypertension: from PDE5 to soluble guanylate cyclase. *Eur Respir Rev*. 2024;33(171):230183.
- Moutchia J, McClelland RL, Al-Naamani N, et al. Pulmonary arterial hypertension treatment: an individual participant data network meta-analysis. *Eur Heart J*. 2024;45(21):1937-1952.
- Liu C, Chen J, Gao Y, et al. Endothelin receptor antagonists for pulmonary arterial hypertension. *Cochrane Database Syst Rev*. 2021;3(3):CD004434.
- Barnes H, Yeoh HL, Fothergill T, et al. Prostacyclin for pulmonary arterial hypertension. *Cochrane Database Syst Rev*. 2019;5(5):CD012785.
- Barnes H, Brown Z, Burns A, et al. Phosphodiesterase 5 inhibitors for pulmonary hypertension. *Cochrane Database Syst Rev*. 2019;1(1):CD012621.
- Mandras S, Kovacs G, Olschewski H, et al. Combination therapy in pulmonary arterial hypertension-targeting the nitric oxide and prostacyclin pathways. *J Cardiovasc Pharmacol Ther*. 2021;26(5):453-462.
- Morris NR, Kermeen FD, Jones AW, et al. Exercise-based rehabilitation programmes for pulmonary hypertension. *Cochrane Database Syst Rev*. 2023;3(3):CD011285.
- Provencher S, Mai V, Bonnet S. Managing pulmonary arterial hypertension with cardiopulmonary comorbidities. *Chest*. 2024;165(3):682-691.

## Section 2: Pulmonary Nodules

**Example case:** *JP is a 58-year-old male smoker with a 40 pack-year history who presents in follow up for low-dose CT chest that was performed for lung cancer screening. He has a history of mild COPD but currently is asymptomatic. CT showed a 6 mm, solid pulmonary nodule in the right lower lobe. According to the radiologist's report, repeat CT in 6 months is recommended. JP is concerned about waiting so long if the nodule might be malignant.*

### Key questions to consider:

#### Presentation

- What are the most common causes of benign and malignant pulmonary nodules? What patients are at greatest risk of development of these nodules?
- What are the current recommendations for lung cancer screening? What is the incidence of pulmonary nodules with lung cancer screening?
- What is the likelihood that an incidentally found pulmonary nodule is benign vs. malignant?

#### Diagnostic Evaluation

- What is the recommended diagnostic evaluation for pulmonary nodules, depending on the suspected etiology?
- What radiographic features of nodules suggest a benign vs. a malignant etiology?
- How well do artificial intelligence and deep learning models predict malignancy risk of pulmonary nodules?
- What is the potential role of biomarkers in the diagnostic evaluation of pulmonary nodules?
- What is the relationship between oral microbiota and pulmonary nodules? Does evidence support the role of salivary microbiome patterns as a biomarker for pulmonary nodules?

#### Management

- What is the recommended management for pulmonary nodules found during lung cancer screening? What is the recommended management of incidentally discovered pulmonary nodules?
- What is the recommended follow-up for pulmonary nodules based on the American College of Radiology's Lung Imaging Reporting and Data System (Lung-RADS) v2022?
- When should pulmonary nodules be biopsied? What methods of biopsy should be considered? What are the indications, advantages, and risks of each method? When is it reasonable to postpone or forego biopsy?
- What are the indications for referral to a pulmonologist or thoracic surgeon for evaluation and treatment of pulmonary nodules?

### Initial references to consider:

- Langan RC, Goodbred AJ. Pulmonary nodules: common questions and answers. *Am Fam Physician*. 2023;107(3):282-291.
- US Preventive Services Task Force. Screening for lung cancer: US Preventive Services Task Force recommendation statement. *JAMA*. 2021;325(10):962-970.

- Meza R, Jeon J, Toumazis I, et al. Evaluation of the benefits and harms of lung cancer screening with low-dose computed tomography: modeling study for the US Preventive Services Task Force. *JAMA*. 2021;325(10):988-997.
- Marcus MW, Duffy SW, Devaraj A, et al. Probability of cancer in lung nodules using sequential volumetric screening up to 12 months: the UKLS trial. *Thorax*. 2019;74(8):761-767.
- Mazzone PJ, Lam L. Evaluating the patient with a pulmonary nodule: a review. *JAMA*. 2022;327(3):264-273.
- Reid M, Choi HK, Han X, et al. Development of a risk prediction model to estimate the probability of malignancy in pulmonary nodules being considered for biopsy. *Chest*. 2019;156(2):367-375.
- Quanyang W, Yao H, Sicong W, et al. Artificial intelligence in lung cancer screening: detection, classification, prediction, and prognosis. *Cancer Med*. 2024;13(7):e7140.
- Wulaningsih W, Villamaria C, Akram A, et al. Deep learning models for predicting malignancy risk in CT-detected pulmonary nodules: a systematic review and meta-analysis. *Lung*. 2024.
- Wang Q, Song X, Zhao F, et al. Noninvasive diagnosis of pulmonary nodules using a circulating tsRNA-based nomogram. *Cancer Sci*. 2023;114(12):4607-4621.
- Ren Y, Ma Q, Zeng X, et al. Saliva-microbiome-derived signatures: expected to become a potential biomarker for pulmonary nodules (MCEPN-1). *BMC Microbiol*. 2024;24(1):132.
- Christensen J, Prosper AE, Wu CC, et al. ACR Lung-RADS v2022: assessment categories and management recommendations. *J Am Coll Radiol*. 2024;21(3):473-488.
- Rendle KA, Saia CA, Vachani A, et al. Rates of downstream procedures and complications associated with lung cancer screening in routine clinical practice: a retrospective cohort study. *Ann Intern Med*. 2024;177(1):18-28.
- Farjah F, Monsell SE, Smith-Bindman R, et al. Fleischner Society guideline recommendations for incidentally detected pulmonary nodules and the probability of lung cancer. *J Am Coll Radiol*. 2022;19(11):1226-1235.
- Fernandez-Bussy S, Yu Lee-Mateus A, Reisenauer J, et al. Shape-sensing robotic-assisted bronchoscopy versus computed tomography-guided transthoracic biopsy for the evaluation of subsolid pulmonary nodules. *Respiration*. 2024;103(5):280-288.
- Yu Lee-Mateus A, Reisenauer J, Garcia-Saucedo JC, et al. Robotic-assisted bronchoscopy versus CT-guided transthoracic biopsy for diagnosis of pulmonary nodules. *Respirology*. 2023;28(1):66-73.

### Section 3: Obesity Hypoventilation Syndrome

**Example case:** *PG is a 45-year-old female with a history of severe obstructive sleep apnea and obesity (BMI 41 kg/m<sup>2</sup>) who presents to the emergency department for progressive daytime dyspnea and lethargy. Her oxygen saturation is 85% while awake on room air. Arterial blood gas reveals a pH of 7.24, a pCO<sub>2</sub> of 75 mm Hg, and a pO<sub>2</sub> of 65 mm Hg. Her serum bicarbonate level is 28 mEq/L. Chest X-ray shows bilateral atelectasis without infiltrate or effusion. Following a dose of nebulized albuterol, she is placed on supplemental oxygen and BiPap and is admitted to intensive care.*

#### Key questions to consider:

##### Presentation

- What is obesity hypoventilation syndrome (OHS)? How common is it?
- How does BMI affect the risk of OHS? Other than obesity, what are the risk factors for OHS? Why are some people affected more severely than others? How can a patient's risk be estimated?
- Can OHS be prevented in at-risk patients? If so, how?
- How does OHS typically present? What are the clinical manifestations?

##### Diagnostic evaluation

- What are the diagnostic criteria for OHS? What is the recommended diagnostic evaluation?
- What complications are associated with OHS?

##### Management

- What is the recommended management of OHS and its complications, both in the clinic and in the hospital?
- How effective is weight loss, both for treatment and reversal of OHS and for preventing acute hypercapnic respiratory failure? What weight loss strategies are most effective? When is bariatric surgery indicated?
- What is the role of pulmonary rehabilitation for patients with OHS?
- What ventilation strategies are recommended for hospitalized patients with OHS? What is noninvasive ventilation (NIV), and how effective is it? What are the indications for intubation and invasive mechanical ventilation?
- What are the indications and criteria for home NIV? Is it cost effective compared to inpatient care?
- What strategies are effective for improving patient adherence to positive airway pressure at home?
- What are the indications for referral to a pulmonologist?

#### Initial references to consider:

- Mokhlesi B, Masa JF, Brozek JL, et al. Evaluation and management of obesity hypoventilation syndrome. an official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med.* 2019;200(3):e6-e24.
- Afshar M, Brozek JL, Soghier I, et al. The role of positive airway pressure therapy in adults with obesity hypoventilation syndrome. A systematic review and meta-analysis. *Ann Am Thorac Soc.* 2020;17(3):344-360.

- Kakazu MT, Soghier I, Afshar M, et al. Weight loss interventions as treatment of obesity hypoventilation syndrome. A systematic review. *Ann Am Thorac Soc.* 2020;17(4):492-502.
- Xu J, Wei Z, Li W, et al. Effect of different modes of positive airway pressure treatment on obesity hypoventilation syndrome: a systematic review and network meta-analysis. *Sleep Med.* 2022;91:51-58.
- Faqihi BM, Trethewey SP, Morlet J, et al. Bilevel positive airway pressure ventilation for non-COPD acute hypercapnic respiratory failure patients: a systematic review and meta-analysis. *Ann Thorac Med.* 2021;16(4):306-322.
- Soghier I, Brožek JL, Afshar M, et al. Noninvasive ventilation versus CPAP as initial treatment of obesity hypoventilation syndrome. *Ann Am Thorac Soc.* 2019;16(10):1295-1303.
- Brown LK. Targeting Hypercapnia in chronic lung disease and obesity hypoventilation: benefits and challenges. *Sleep Med Clin.* 2024;19(2):357-369.
- Kampelmacher MJ. Moving from inpatient to outpatient or home initiation of non-invasive home mechanical ventilation. *J Clin Med.* 2023;12(8):2981.
- Mokhlesi B, Masa JF, Afshar M, et al. The effect of hospital discharge with empiric non-invasive ventilation on mortality in hospitalized patients with obesity hypoventilation syndrome. An individual patient data meta-analysis. *Ann Am Thorac Soc.* 2020;17(5):627-637.
- Jimenez JV, Ackrivo J, Hsu JY, et al. Lowering PCO<sub>2</sub> with noninvasive ventilation is associated with improved survival in chronic hypercapnic respiratory failure. *Respir Care.* 2023;68(12):1613-1622.
- Wilson M, Wang Z, Dobler CC, et al. Noninvasive positive pressure ventilation in the home (with addendum) [internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2020.
- Murphy PB, Patout M, Arbane G, et al. Cost-effectiveness of outpatient versus inpatient non-invasive ventilation setup in obesity hypoventilation syndrome: the OPIP trial. *Thorax.* 2023;78(1):24-31.
- D'Cruz RF, Kaltsakas G, Suh ES, et al. Quality of life in patients with chronic respiratory failure on home mechanical ventilation. *Eur Respir Rev.* 2023;32(168):220237.
- Wearn J, Akpa B, Mokhlesi B. Adherence to positive airway pressure therapy in obesity hypoventilation syndrome. *Sleep Med Clin.* 2021;16(1):43-59.

## Section 4: Noninfectious Pleural Effusion

**Example case:** *EG is a 62-year-old male with cough, dyspnea, and right-sided pleuritic chest pain for 5 days. He has a history of non-small cell lung cancer (adenocarcinoma stage IA2) of the right lung, for which he completed primary surgical wedge resection without adjunctive chemotherapy one year ago. He is afebrile but tachypneic with mild respiratory distress. His complete blood cell count is normal. Chest X-ray shows scarring consistent with previous surgery and a new, moderate right-sided pleural effusion without mass, infiltrate, or tracheal deviation.*

*Note: Infectious causes of pleural effusions, parapneumonic effusion, and lung abscess were reviewed in a recent issue of FP Essentials (#550), so they do not need to be discussed here.*

### Key questions to consider:

#### Presentation

- What are pleural effusions? How are they classified?
- What are the leading noninfectious causes of pleural effusion? How common are they?
- What symptoms and physical exam findings are associated with noninfectious pleural effusions?

#### Diagnostic Evaluation and Thoracentesis

- What is the recommended diagnostic evaluation for a patient with a new pleural effusion?
- What are the roles of radiography, ultrasonography (including POCUS), and computed tomography? What imaging findings suggest a noninfectious vs an infectious etiology?
- Have any noninvasive criteria been shown to distinguish exudates from transudates reliably?
- What are the indications and contraindications for diagnostic thoracentesis? What are the potential risks of thoracentesis?
- How is thoracentesis performed? Describe the procedure, including patient positioning and anatomic approach. What is the role and benefit of ultrasound guidance, including POCUS?
- What tests are recommended for pleural fluid analysis? What are Light's criteria?

#### Management

- What is the recommended management of noninfectious pleural effusions, depending on the etiology?
- What are the indications for therapeutic thoracentesis? How much fluid can be removed safely at one time?
- When is it reasonable to treat patients empirically without thoracentesis?
- What are the indications for catheter or chest tube drainage, medical thoracoscopy, and video-assisted thoracoscopic surgery?
- What strategies are recommended for managing chronic and recurrent pleural effusions, including malignant pleural effusions?
- When should consultation with a pulmonologist or thoracic surgeon be considered?

### Initial references to consider:



- Shen-Wagner J, Gamble C, MacGilvray P. Pleural effusion: diagnostic approach in adults. *Am Fam Physician*. 2023;108(5):464-475.
- Gayen S. Malignant pleural effusion: presentation, diagnosis, and management. *Am J Med*. 2022;135(10):1188-1192.
- Roberts ME, Rahman NM, Maskell NA, et al. British Thoracic Society Guideline for pleural disease. *Thorax*. 2023;78(11):1143-1156.
- Gartlehner G, Wagner G, Affengruber L, et al. Point-of-care ultrasonography in patients with acute dyspnea: an evidence report for a clinical practice guideline by the American College of Physicians. *Ann Intern Med*. 2021;174(7):967-976.
- Porcel JM, Light RW. Pleural fluid analysis: are light's criteria still relevant after half a century? *Clin Chest Med*. 2021;42(4):599-609.
- Gardiner A, Ling R, Chan YH, et al. DUETS for Light's in separating exudate from transudate. *Respirology*. 2024. Epub ahead of print.
- Williams JG, Lerner AD. Managing complications of pleural procedures. *J Thorac Dis*. 2021;13(8):5242-5250.
- Gonnelli F, Hassan W, Bonifazi M, et al. Malignant pleural effusion: current understanding and therapeutic approach. *Respir Res*. 2024;25(1):47.
- Walker SP, Bintcliffe O, Keenan E, et al. Randomised trial of indwelling pleural catheters for refractory transudative pleural effusions. *Eur Respir J*. 2022;59(2):2101362.
- Wang S, Zhang R, Wan C, et al. Incidence of complications from indwelling pleural catheter for pleural effusion: a meta-analysis. *Clin Transl Sci*. 2023 Jan;16(1):104-117.
- Trindade AJ, Lentz RJ, Gannon WD, et al. Safety and utility of indwelling pleural catheters in lung transplant recipients. *Clin Transplant*. 2023;37(10):e15056.
- Dipper A, Jones HE, Bhatnagar R, et al. Interventions for the management of malignant pleural effusions: a network meta-analysis. *Cochrane Database Syst Rev*. 2020;4(4):CD010529.
- Yeung M, Loh EW, Tiong TY, et al. Indwelling pleural catheter versus talc pleurodesis for malignant pleural effusion: a meta-analysis. *Clin Exp Metastasis*. 2020;37(4):541-549.
- Walker S, Mercer R, Maskell N, et al. Malignant pleural effusion management: keeping the flood gates shut. *Lancet Respir Med*. 2020;8(6):609-618.