Case Part 1

A 44-year-old woman presents to the emergency department with a chief complaint of dyspnea and fever which developed over the course of 3 days. Associated symptoms include rhinorrhea, sore throat, nonproductive cough, noisy breathing, and sensation of chest tightness. On presentation she is most anxious about her breathing which she describes as “difficult.” Her past medical history is notable for obesity, HTN, type 2 diabetes, and seasonal allergies. She works in a printing shop, smokes 1/2 PPD of cigarettes, reports occasional social alcohol consumption, and denies any history of drug use. Her family history is notable for breast cancer in her mother and childhood asthma in a sister. Current medications include lisinopril, metformin, atorvastatin, and Tylenol. Vitals show T 39.2 C, HR 116, BP 132/84, RR 28, and SpO2 92%. On exam, she is moderately dyspneic with conversation and appears tired but is alert, with yellow nasal congestion, erythematous posterior OP, 2+ tender cervical LAD bilaterally, tachypneic with decreased air movement bilaterally, diffuse expiratory
wheezing and prolonged exhalation, tachycardic with regular rhythm without murmur, warm and well perfused with flushed appearance, with no peripheral edema. Initial labs are notable for BUN 32, Cr 1.5, WBC 17 with 70% neutrophils, and PLT 480. A VBG shows 72.4/58/40/18, with a lactate of 1.3. PA, and lateral chest X-ray shows mild bilateral perihilar cuffing without focal infiltrate.

Respiratory failure is a common reason for critical care evaluation and ICU admission and invokes a broad differential. Respiratory failure is commonly categorized into four “types” – hypoxemic, hypercapnic, postoperative, and respiratory failure due to shock [1]. There is frequently overlap among the various types of respiratory failure, but it is important to recognize all the contributing etiologies to respiratory failure in each case in order to identify and reverse all pathologies.

This patient presents with dyspnea associated with abnormal ventilation, including wheezing with diminished air movement on exam and acute hypercapnia on venous blood gas: this is a case of type 2 (hypercapnic/ventilatory) respiratory failure. In this case, the clinical exam suggests impaired ventilation, occurring at the level of the small airways. Similar hypercapnic respiratory failure can develop due to impairment in ventilation at any level within the respiratory tract and in some cases can develop in the setting of normal ventilation due instead to an acute ventilation-perfusion (VQ) mismatch such as with acute pulmonary artery obstruction associated with a pulmonary embolism.

The most common causes of type 2 respiratory failure are asthma exacerbation and COPD. In this case, the exam findings indicate a process of diffuse airway narrowing leading to wheezing, most consistent with lower airway bronchoconstriction. Without a prior diagnosis of asthma or COPD and in the setting of risk factors for both (allergies and family history of asthma being risk factors for asthma and tobacco exposure being the major risk factor for COPD), it may be difficult to immediately distinguish between an acute asthma and COPD exacerbation. Her response to therapy and clinical course, and
ultimately pulmonary function testing after she has returned to her respiratory baseline, will assist with distinguishing between an underlying diagnosis of asthma and COPD.

If the patient did not have exam findings consistent with diffuse small airway airflow obstruction, the level of concern for alternative diagnoses would rise. Hypoventilation secondary to narcotic substance abuse is an increasingly common etiology of type 2 respiratory failure presenting to the ED as well as onset of type 2 respiratory failure during a hospitalization, and it should be suspected in the setting of decreased respiratory effort and somnolence on exam. This diagnosis is often confirmed by response to a trial of narcan therapy, with improvement in respiratory effort and mental status after narcan often significant enough to avoid intubation for their respiratory failure. Obtundation from other ingestion, injury, or syndrome may present similarly but would be unresponsive to narcan and require additional evaluation for determination of diagnosis and effective management.

Additional life-threatening causes of acute ventilatory dysfunction including pulmonary embolism, acute airway obstruction such as from a foreign body aspiration, acute diaphragm or respiratory muscle weakness, and pneumothorax. For an alert patient with diminished respiratory capability despite apparent good effort, diaphragm injury such as from spinal cord injury and viral or idiopathic phrenic nerve dysfunction can all present with type 2 respiratory failure in the setting of additional associated exam findings. Although many patients presenting with pneumothorax have a clinical history of trauma or predisposing factor such as Marfan syndrome or history of prior spontaneous pneumothorax, an asymmetric pulmonary exam with absent breath sounds on one side of the chest in any patient with acute respiratory changes should raise concern for the possibility of a pneumothorax. In cognitively intact adults, a history of a foreign body aspiration is typically available at the time of presentation; however in a patient with altered cognition, particularly if there is clinical suspicion for risk for aspiration, an asymmetric respiratory exam, upper airway stridor,
and occasionally central airway or asymmetric wheezing could be concerning for foreign body aspiration with airway obstruction. If there is clinical uncertainty regarding obstructed airway vs pneumothorax contributing to absent breath sounds on exam, a chest X-ray demonstrating air within the thoracic cavity or hyper-expansion of one side or portion of the lung with or without a radiopaque foreign body can be confirmatory for pneumothorax or foreign body airway obstruction, respectively; if there is a high suspicion for either of these diagnoses in a clinically unstable patient, it is advisable to intervene clinically without waiting for confirmatory imaging, as this may be lifesaving particularly in the case of a tension pneumothorax. Often in the absence of focal exam findings to explain dyspnea with hypercapnia, and especially if a patient reports sudden onset or accompanying chest pain, pulmonary embolism should be considered. If considering pulmonary embolism in your differential, it is helpful to use the Wells criteria to assist with risk-stratifying your patient before choosing to proceed with a diagnostic evaluation for possible PE.

The broad differential for hypercapnic/ventilatory respiratory failure is often narrowed by clinical history and exam, and management may be focused once a thorough clinical evaluation has been completed and the diagnosis is determined. Asthma and COPD exacerbations are clinical diagnoses, and while chest imaging with chest X-ray is often obtained in the evaluation of acute dyspnea, clinical imaging is neither required nor confirmatory for these diagnoses. Chest imaging including chest X-ray, chest CT, or CT angiogram is often obtained in order to exclude an alternative cause for the patient’s presentation and is frequently pursued in the absence of clinical history or findings consistent with asthma or COPD. Regardless of the etiology, a blood gas may differentiate between respiratory distress due to difficulty with work of breathing and type 2 respiratory failure associated with insufficient ventilation which would be identified based on respiratory acidosis with elevated PCO₂ and associated acidosis on blood gas. A venous blood sample, preferably
a central venous blood sample, is sufficient for the assessment of ventilation, although an arterial blood gas may alternatively be used in a patient with no central access.

Once identified, management of type 2 respiratory failure should be tailored both to the etiology of hypercapnic/hypoventilatory respiratory failure, with, for instance, albuterol, ipratropium, steroids, and magnesium for an asthma exacerbation and to support of the ventilatory distress or impairment associated with the presentation. Respiratory support of ventilation in an alert patient is commonly provided with noninvasive positive pressure ventilation (NIPPV), specifically bi-level positive airway pressure (BIPAP), which provides mechanical assistance with effort of ventilation and which has the benefit of being easy to wean or interrupt in addition to being much more tolerable for many patients than traditional invasive ventilation. In the case of contraindications to NIPPV including a high risk for aspiration (particularly due to altered mental status), physical inability to wear a BIPAP mask due to abnormal facial structure, recent surgery or some overlying skin conditions, patient anxiety or intolerance to BIPAP, or inability to maintain effective ventilation while on BIPAP, the more traditional invasive ventilation with endotracheal intubation and mechanical ventilation may be required. A variety of modes of mechanical ventilation may be successfully used to treat hypercapnic/ventilatory respiratory failure which will not be outlined in depth here, but it is worth recalling that ventilation is determined primarily by tidal volume and respiratory rate [2]. The mainstay of ventilatory support for respiratory failure is volume-cycled, assist-control ventilation, in which providers can optimize expiratory time and enhance patient synchrony with the ventilator. In particular, modes which minimize exhalation such as APRV should be avoided for respiratory failure due to air trapping such as respiratory failure from asthma or COPD.

High-flow nasal cannula has recently come into vogue as a method of providing respiratory support and may be helpful for a patient experiencing type 2 respiratory distress associated
with increased work of breathing; however it does not provide as much support as NIPPV with BIPAP, and ventilation cannot be adequately measured or ensured while on HFNC; therefore HFNC is not a preferred method of assisting ventilation in a patient with hypercapnic/hypoventilatory respiratory failure in the acute setting but may be better used as a method for weaning ventilatory support once their acute respiratory failure has been addressed. It is important to note that methods of respiratory support targeting oxygenation, specifically including nasal cannula, ventimask, non-rebreathers, and continuous positive airway pressure (CPAP), are ineffective alone in the management of type 2 respiratory failure as they do not support ventilation and may mask a patient’s respiratory decline.

Long-term management for patients experiencing type 2 respiratory failure should include risk-factor modification to minimize the risk of recurrent respiratory failure. This may include intensified medical management of asthma with emphasis on implementation of an effective asthma action plan early in any future asthma exacerbations, or tobacco cessation counseling, medical management of nicotine addiction, and pulmonary rehab for patients with COPD. In some cases patients presenting with apparent acute type 2 respiratory failure may have some degree of untreated chronic hypercapnic respiratory failure to address particularly those with severe COPD or neuromuscular weakness. This should be assessed after they have returned to their previous baseline function but before they are discharged from the hospital, with additional blood gas testing demonstrating chronic hypercapnia. In these cases management with chronic noninvasive ventilatory support such as nocturnal BIPAP, or in severe cases and if maximal support is desired by the patient, tracheostomy, and home chronic ventilation in the case of neuromuscular disease, may be considered. Pulmonary consultation during their hospitalization and outpatient pulmonary clinic follow-up is important for patients who have experienced hypercapnic/hypoventilatory respiratory failure to help modify their
disease course and optimize outpatient management in order to avoid recurrence of respiratory failure.

Case Part 2

AD, our 44-year-old patient, does well with BIPAP support and responds to treatment with prednisone and bronchodilator therapy for suspected asthma exacerbation associated with a viral respiratory tract infection and is weaned off of respiratory support and discharged home within a few days. She re-presents to the ED 1 week later complaining of worsening cough productive of thick yellow sputum, dyspnea with minimal exertion, pleuritic chest pain, fatigue, and recurrent fevers. Her medical history and exposures are unchanged. This time, vitals show T 40.3 C, HR 135, BP 92/45, RR 30, and SpO₂ 78% on room air which improves to 90% on 50% ventimask. On exam, she is ill appearing, flushed and fatigued, oriented to person and place but not date, with tacky mucous membranes, clear nares, tachypneic and speaking in short sentences with decreased breath sounds in the right lower lung field, diffuse inspiratory crackles and no wheezing, tachycardia with regular rhythm and no murmur, with a soft and non-tender abdomen, and no peripheral edema or extremity tenderness. Labs are notable for BUN 45, Cr 2.7, WBC 17 with 86% neutrophils and 12% bands, and PLT 130. An ABG shows 7.45/24/50/16, with arterial lactate of 2.8. PA, and lateral chest X-ray shows a dense, focal consolidation in the right lower lobe and diffuse fluffy infiltrates scattered throughout all lobes.

Although AD’s chief complaint of dyspnea and fever is the same as with her first presentation, her second presentation differs significantly from her prior illness. Her respiratory distress is now associated with hypoxia, and her arterial blood gas demonstrates significant hypoxia, particularly notable as it was obtained while she was on a 50% ventimask, as well as a respiratory alkalosis developing in the setting of increased work of breathing and elevated minute ventilation. In con-
trast to her first presentation, this is hypoxic, or type 1, respiratory failure. As you will recall, type 2 respiratory failure is hypercapnic/ventilatory respiratory failure and may present with normal or only mild abnormalities in oxygenation, type 3 respiratory failure may be hypoxic but is secondary to postoperative atelectasis, and type 4 respiratory failure is secondary to shock (which is not present here). If she had a concurrent asthma exacerbation leading to hypercapnic respiratory failure in addition to her hypoxic respiratory failure, as many patients with underlying obstructive lung disease do, that could be referred to as a mixed (type 1 and type 2) respiratory failure.

The differential for type 1 or hypoxic respiratory failure is quite broad and includes many infectious and noninfectious processes. AD presents with many symptoms of acute infection including fever, tachycardia, leukocytosis, bandemia, ill appearance, and purulent mucus production with a focal infiltrate on her chest imaging concerning for infectious process including bacterial pneumonia. AD has risk factors for bacterial pneumonia as her recent viral illness places her at risk for development of a secondary bacterial pneumonia during the 1–2 weeks after a viral respiratory illness, as do her recent hospitalization and her suspected underlying lung disease (either asthma or COPD.) In the setting of presentation with sepsis and acute respiratory failure, pneumonia must remain high on the differential until there is diagnostic certainty in a noninfectious source for the respiratory disease. Additional infectious concerns for acute type 1 respiratory failure include viral pneumonia, which can mimic a bacterial process with a focal infiltrate on chest imaging or present with more diffuse interstitial or inflammatory changes, and atypical pneumonias including legionella and mycoplasma which can also present with sepsis, rapid progression, and consolidative lung findings. In cases of more indolent development or the presence of an immunocompromised host, fungal infections including invasive aspergillus, histoplasma and cryptococcal infection, and mycobacterial infections including *Mycobacterium avium complex* and tuberculosis
should also be considered. A common pneumonia mimic is aspiration pneumonitis, which may or may not be followed by development of true bacterial aspiration pneumonia and in either case may lead to prolonged and recurrent respiratory distress. There are rare, noninfectious pulmonary processes which may also present in a similar fashion to acute bacterial pneumonia including hypersensitivity pneumonitis and eosinophilic pneumonia; however infectious processes should be comprehensively excluded prior to proceeding with evaluation or treatment for these pulmonary zebras.

Patients presenting with hypoxic respiratory failure without symptoms of acute infection, often with chest imaging concerning for alternative explanations for hypoxia or with illness refractory to treatment for initially suspected infectious process, may exhibit a variety of other structural, obstructive, infiltrative, or alveolar filling processes, or increasingly significantly, inflammatory lung diseases including acute respiratory distress syndrome. Unlike in the case of hypercapnic respiratory failure, chest imaging may be particularly useful in their evaluation and is often necessary in order to prioritize a differential and decide on a rational management approach. Lung masses may be suspected based on chest X-ray imaging and are often best clarified on chest CT imaging, with hypoxic respiratory failure often resulting from post-obstructive pneumonia or atelectasis distal to a solid lung mass associated with airway compression from the mass and/or due to a large volume of lung destroyed by a mass or masses. Absence of lung aeration due to a pleural effusion(s) significant enough to cause hypoxia can be easily visualized with chest X-ray or bedside ultrasound, typically presenting without mediastinal shift, while mucous plugging of medium to large airways leading to hypoxia from associated atelectasis will demonstrate collapsed lobar or peripheral lung regions with absence of aeration and mediastinal shift toward the affected side of the chest. Diagnosis of many less common infiltrative processes such as sarcoidosis, bronchiolitis obliterans, vasculitic lung diseases, or bronchoalveolar carcinoma will rely heavily on unusual imaging findings such
as tissue infiltration along airways and diffuse pulmonary nodules as well as clinical suspicion based on the presence of specific risk factors for disease or associated clinical findings, and patients will carry a heavy burden of disease before developing hypoxic respiratory failure. More chronic inflammatory lung diseases are often known based on prior chest imaging, although acute flares of ILD can present with acute inflammatory changes on a background of chronic fibrotic disease. Alveolar filling processes may be focal such as from focal pulmonary bleeding often presenting as hemoptysis with hypoxia, perhaps from a lung mass or a pulmonary AVM or infectious irritation of the airways, or diffuse such as from diffuse alveolar hemorrhage, pulmonary edema including from CHF exacerbations, pulmonary contusions, or drowning injury, or in the case of another pulmonary zebra, pulmonary alveolar proteinosis.

Management of hypoxic respiratory failure relies on treatment or reversal of the underlying process, as well as respiratory support during the course of illness. In the case of a suspected infectious process, early antibiotics targeted to the identified infectious process are a mainstay of therapy. Testing including sputum bacterial culture and gram stain, evaluation for viral respiratory pathogens, and frequently urine antigens for legionella and pneumonia may confirm an infectious etiology although they are often less than 100% sensitive due to sampling error and limitations in detecting all relevant infectious pathogens. Unfortunately, the serum biomarker procalcitonin has not been validated in the diagnosis of infection in the critically ill patient and should not be independently used to guide decisions regarding treatment of possible infectious process, although some data suggest that in a recuperating patient, a declining procalcitonin may be used to assist with decisions regarding completion of shorter rather than longer antibiotic courses. In cases of suspected unusual pulmonary infections where a pathogen has not been identified, additional diagnostic testing may be pursued with bronchoscopy for biologic specimens through bronchoalveolar lavage, bronchial brushings, or transbronchial biopsy.
Diagnostic bronchoscopy, which may be performed by a pulmonary trained physician and by many critical care trained physicians, is typically reserved for cases involving a high suspicion for fungal or other unusual infections, complicated infections occurring in immunocompromised patients, or when there is a high suspicion for a noninfectious process, and it is deemed important to exclude infection before proceeding with immunosuppressive or other involved treatment. Bronchoalveolar lavage may also be diagnostic for diffuse alveolar hemorrhage. Therapeutic bronchoscopy by an interventional pulmonologist may be considered in cases where a pulmonary lesion such as a mass or foreign body is causing respiratory failure due to airway obstruction or for evaluation and treatment of focal airway bleeding contributing to respiratory failure.

The initial goals of respiratory support include both alleviation of hypoxia and support for increased or inadequate work of breathing. In an awake patient without severe distress, CPAP therapy provides a quantifiable and titratable amount of positive end-expiratory pressure which serves to both recruit additional alveolar lung capacity and improve oxygen delivery across the pulmonary alveolar space, while allowing for escalation of the inspired fraction of oxygen up to 100%, and is often used first in the setting of escalating respiratory support in an ICU patient with hypoxic respiratory distress. Many patients requiring some lower levels of positive pressure support may benefit from high-flow nasal cannula which can be delivered at flow rates of up to 50 LPM with FiO₂ approaching 80–90%, and many patients feel less claustrophobic and experience less skin irritation and improved communication with care teams while on HFNC compared with CPAP. HFNC is limited in its ability to deliver PEEP relative to CPAP, and PEEP cannot be quantified while on HFNC. For patients whose oxygen requirement remains high (such as greater than 60%) while on CPAP at escalated levels despite initial treatment to stabilize disease who have unable to tolerate coming off of CPAP even briefly such as for medication administration, who have worsening
mental status. Who are at risk for aspiration or emesis, or who have persistent hypoxia or are developing hypercapnic respiratory failure despite addition of BIPAP to support ventilation while receiving PAP therapy, intubation and full mechanical ventilation for definitive control of their respiratory status and high levels of respiratory support should be considered.

Benefits of intubation and full mechanical ventilation include definitive control of oxygenation without periods of interruption of PEEP; definitive control over minute ventilation and airway pressures, often allowing for escalation of PEEP beyond levels at which CPAP may be tolerable; and ability to provide sedation, minimize oxygen consumption by alleviating work of breathing, and if necessary proceed to paralysis for refractory hypoxia. With this approach, the toxicities associated with persistent lung and systemic hyperoxia including lung scarring and chronic respiratory insufficiency and increased mortality may be minimized [3]. Generally acceptable oxygenation goals for an acutely ill patient vary based on the presence of known chronic lung disease such as COPD or interstitial lung disease as well as the severity of illness and relative risk of increased oxygenation support. Goal peripheral oxygen saturations in a patient with COPD are typically >88%, while we often target a goal peripheral saturation of 94–96% corresponding with PaO₂ on ABGs between 70 and 90 in a patient with presumably healthy lung function at baseline. In respiratory failure requiring intubation, arterial blood gas PaO₂ in the 60s may be tolerated if there is increased concern for long-term harm in maintaining FiO₂ greater than 60% or in increasing airway pressures due to risk of barotrauma. Intubation also allows for improved airway clearance compared with CPAP therapy where PEEP is applied without access for endotracheal suctioning of secretions. An important benefit of intubation includes more accurate monitoring and improved control over air flow and airway pressures, beneficial data for which is best established in the setting of ARDS as detailed below.
The most common inflammatory lung disease confounding acute respiratory failure stemming from many sources and independently responsible for acute hypoxic respiratory failure in patients with many initially non-pulmonary ailments, which is a significant contributor to morbidity and mortality in the ICU, is most certainly ARDS, or acute respiratory distress syndrome. ARDS was first described in 1967 [4]; however increasingly robust data has been published on best practices for management of ARDS with a goal of minimizing mortality and pulmonary morbidity for survivors, and it is important for any provider taking care of critically ill patients to be well versed in diagnosis and best-practice management of this process. ARDS is best defined by the Berlin criteria as acute onset (within 7 days) of respiratory inflammatory disease with impaired oxygenation and bilateral pulmonary opacities on chest imaging not better explained by heart failure, attributable to an inflammatory response triggered by an acute medical condition [5]. Specific diagnostic criteria include a calculated ratio of pulmonary arterial oxygen concentration from an arterial blood gas to inspired fraction of oxygen (PaO₂/FiO₂) of less than 300, measured while on a PEEP of 5 or greater. While ARDS can be stratified to mild, moderate, or severe based on PaO₂/FiO₂ ratios of 200–300, 100–200, and <100, practically, consideration for possible ARDS should be given early in any significant acute respiratory illness with respiratory insufficiency or failure. Given the long-term ramifications of lung damage associated with ARDS, any patient suspected to be developing ARDS can be managed under the general principles of ARDS care until ARDS has been excluded. These principles include minimization of barotrauma utilizing sedation combined with low tidal volume ventilation when intubated, avoidance of oxygen toxicity as outlined above, utilization of paralysis and prone positioning to optimize oxygenation while providing supportive care, and adherence to evidence-based limitations on the use of late steroid therapy and benefits of early ECMO in refractory ARDS.
The best data supporting the use of low tidal volume ventilation (LTVV) stems from a study demonstrating dramatically improved mortality and a shorter duration of respiratory failure performed by The Acute Respiratory Distress Syndrome Network and published in the New England Journal of Medicine in 2000 [6]. In this study a tidal volume of 6 ml/kg of ideal body weight or lower was targeted in order to minimize plateau pressures on the ventilator, with a goal of maintaining them below 30. As plateau pressures reflect pressure experienced at the level of the alveoli, this approach acts through reducing repetitive elevation of pressure in the inflamed alveolar and interstitial space. It is important to recognize that plateau pressures can only be adequately measured in a patient who is breathing passively on the ventilator and may be inaccurately measuring low in a patient with very stiff, non-complaint lungs who continues to actively breathe in with a negative inspiratory force while on the ventilator. Plateau pressures should be followed closely after intubation when intubation medications create a window of time with respiratory paralysis, with escalation of sedation as compliance with the ventilator is achieved, and with initiation of paralysis if that is indicated. Given the ability to minimize barotrauma by lowering tidal volumes while maintaining adequate ventilation by concurrently increasing the respiratory rate and accepting permissive hypercapnia and recently published data demonstrating no benefit for high-frequency oscillatory ventilation compared with conventional ventilation in ARDS, there is no longer a role for implementing oscillator-based ventilation for most severe hypoxic respiratory failure in the adult ICU [7].

There are two roles for instituting medical paralysis in the setting of ARDS, and this tool is most effective if implemented early in the course of ARDS. In a patient with profound hypoxia and high oxygen requirements, paralysis with continuous neuromuscular blockade such as with atracurium or cisatracurium infusions can decrease oxygen consumption, thereby improving sustained oxygenation of vital organs while allowing providers to avoid oxygen toxicity (again, with a goal of maintaining an FiO$_2$ of less than 60%
in the setting of acute lung inflammation). The second, and perhaps most important reason for paralyzing a patient with ARDS for long-term outcomes, is the ability to adequately control ventilation with dedicated attention to maintaining ventilatory compliance and achieving low tidal volume ventilation in an effort to minimize airway pressures and subsequently avoid barotrauma. Best practice is to optimize all other approaches to ARDS ventilatory management including escalated sedation in the first 12–24 h of respiratory failure and then move to paralysis if you are unable to achieve adequate supportive care within 24 h. After implementation, most patients benefit from remaining paralyzed for 2–3 days or longer while allowing time for ARDS to peak, with paralysis lifted when signs of improvement in oxygenation and lung compliance are seen [8].

After paralysis, two additional steps may be helpful for refractory hypoxia. Prone positioning can substantially improve oxygenation in ARDS by shifting the gradient of blood delivery. It should be approached in a methodical manner to minimize risk for extubation or dislodgment of lines during proning and requires adequate staffing to assist with the physical turning of the patient but is otherwise a low-tech intervention with a significant return. To be most effective, the prone position should be maintained for 16 h of the day, with a daily return to supine positioning to allow for attention to skin care and other patient needs. ECMO may also be employed in the setting of ARDS to provide adequate oxygenation and ventilation if a patient fails conventional ventilation strategies; however this should be considered as a bridge through an acute illness, or in rare cases of complex lung disease, a bridge to transplantation, and should not be used in the setting of irreversible lung disease unless transplantation is being actively pursued. In the CESAR study, investigators demonstrated that transfer of patients with severe but potentially reversible respiratory failure despite optimal conventional management to a center with ECMO capabilities improved survival without severe disability [9]. This study did exclude patients who required very high FiO₂
or PEEP for more than 7 days, and given this we would recommend starting discussions regarding potential need for ECMO early in cases of severe ARDS.

There are two strategies for treating ARDS for which there is limited or conflicting data. Flolan, a nebulized form of the vasodilator epoprostenol, can be effectively used to improve oxygen delivery in some patients with ARDS through focused vasodilatation of the pulmonary vasculature. It has a good safety profile and is worth trying in the setting of refractory hypoxia or high oxygen requirements, but there is as yet no evidence that it improves clinically significant outcomes for patients with ARDS. Contrastingly, there is evidence that initiation of intravenous steroid therapy in ARDS, which had been hypothesized to reduce inflammation and improve long-term pulmonary recovery, significantly increases mortality, risk for infection, and recurrent respiratory failure in patients with ARDS [10]. The evidence of harm is most compelling when steroids were started more than 14 days into an ARDS course, and we therefore strongly advise against the use of steroid therapy for late ARDS and do not recommend routine empiric therapy with steroids for ARDS at any stage based on the current literature.

In cases of type 1 or hypoxic respiratory failure, the importance of attentive supportive care while treating the underlying process cannot be overstated. Although respiratory support with mechanical ventilation can be lifesaving for many of our critical care patients, the downstream complications of positive pressure mechanical ventilation can lead to long-lasting pulmonary dysfunction including weakness and lung scarring. Many patients require substantial time for pulmonary recuperation following cases of severe respiratory failure or prolonged ventilation. Transition from traditional endotracheal intubation to tracheostomy can be considered early for patients who are likely to require a lengthy period of respiratory support and/or prolonged wean off of the ventilator and may help with active rehabilitation. Many patients’ oxygen requirement may persist after cases of severe ARDS due to lung scarring, although with time a substantial number
of patients discharged on home oxygen may also be able to wean off of this. Patients with any residual pulmonary disease such as an oxygen requirement will also benefit from outpatient pulmonary follow-up after discharge.

AD’s second presentation is clinically concerning by history and exam for secondary bacterial pneumonia after a recent viral illness, with severity of illness, degree of hypoxia, and bilateral infiltrates all concerning for development of ARDS in the setting of pneumonia. In her case, she would likely benefit from a lung protective strategy starting with intubation and low tidal volume ventilation with minimization of barotrauma and oxygen toxicity as outlined above.

Summary

Respiratory failure is a heterogeneous diagnosis, and a structured approach involving differentiation into type 1 vs type 2 respiratory failure, a broad differential narrowed based on a thorough clinical evaluation and history as well as response to treatment, and close attention to changes in your patient in response to respiratory support are all critical to successful management of respiratory failure in the ICU. Differentiating between a need for ventilatory support versus enhanced oxygen support can assist with triaging patients in need of critical care evaluation or treatment to the timely support they need. In many cases, the foundation of management of respiratory failure is supportive care while allowing time for treatment or resolution of an underlying pulmonary insult, and this is a critical period during which adherence to best practices in respiratory support can minimize mortality and optimize long-term pulmonary outcomes. There have been many unexpected findings in research into respiratory failure including ARDS, and the importance of following evidence-based recommendations in order to avoid iatrogenic harm while treating respiratory failure cannot be overstated. Exciting new research continues to expand our capabilities in this field and enhance respiratory outcomes for our critically ill patients each year.
References