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General

Articles

[Idiopathic pulmonary hemosiderosis: A state of the art review](#) - Saha BK. *Respiratory Medicine*, 2021, 176, 106234.

Idiopathic pulmonary hemosiderosis (IPH) is an uncommon cause of diffuse alveolar hemorrhage (DAH). Patients with IPH usually present with hemoptysis, and the diagnosis is often delayed by years. Patients often present with intermittent episodes of hemoptysis interspersed between periods of relative normalcy. However, massive hemorrhage resulting in acute respiratory failure and non-remitting hemoptysis have also been described. The classic triad includes hemoptysis, radiologic lung infiltrate, and iron deficiency anemia. Several hypotheses regarding the pathogenesis of IPH have been proposed. These risk factors include an autoimmune, allergic or genetic predisposition, and possible environmental exposure. Since IPH appears to be responsive to corticosteroids, the autoimmune hypothesis is considered to play a crucial role. A diagnosis of IPH requires exclusion of other etiologies of DAH, including infection, medications, toxic inhalation, vasculitis, and anti-glomerular basement membrane disease, among others. Histologically, IPH is characterized by the presence of hemosiderin-laden macrophages in the alveolar space without any evidence of vasculitis or immunocomplex deposition. Corticosteroid therapy represents the primary modality of treatment. Other immunosuppressive medications have also been used with varying success, especially in the setting of steroid-refractory disease. The prognosis of IPH in adults is somewhat better compared to the pediatric population. The severity of the initial presentation does not predict future outcomes. Which risk factors and patient characteristics are associated with a poor outcome are also unknown. More research is necessary to elucidate the pathophysiology and appropriate treatment.

[Journal club](#) - Chapman R. *Thorax* 2021;76:104.

[Lung function is associated with tumour necrosis factor-related apoptosis-inducing ligand \(TRAIL\) levels in school-aged children](#) - Zaigham S. *Respiratory Medicine*, 2021, 176, 106235.

Background: Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) is a cytokine with inflammatory and apoptotic properties. A complex relationship exists between TRAIL and the lung where both elevated TRAIL and TRAIL deficiency are associated with lung impairment. In neonatal mice, TRAIL is thought to translate respiratory infections into chronic lung disease but the association between TRAIL and lung function in childhood has not been assessed.

[Plasma proteomics and lung function in four community-based cohorts](#) - Rydell A. *Respiratory Medicine*, 2021, 176, 106282.

Background: Underlying mechanism leading to impaired lung function are incompletely understood.

[Protocol for the Stather Canadian Outcomes Registry for Chest Procedures \(SCOPE\)](#) - Tremblay A. *BMJ Open Respiratory Research* 2021;8:e000834.



Introduction: The Stather Canadian Outcomes registry for chest Procedures (SCOPE registry) is a Canadian multicentre registry of chest procedures.

[The role of interferons in preschool wheeze](#) - Makrinioti H. *Lancet Respiratory Medicine*, 2021, 9(1), pp.9-11.

Recurrent wheeze is a common condition in early childhood years and has a significant effect on children, caregivers, and health-care services. Although most preschool children with recurrent wheeze have no further sequelae, nearly one-third will require regular asthma medications and clinical reviews thereafter. Preschool children with recurrent wheeze and multiple allergies, not just allergic sensitisation, are at higher risk of symptom persistence. Most allergen-sensitised children do not have multiple allergies. 1 Respiratory viruses are triggers of preschool wheeze exacerbations. However, it remains unclear whether viral infections directly drive the inception of airway allergic disease or whether respiratory viruses simply trigger wheeze exacerbations in children with multiple allergies.

[Role of unfolded proteins in lung disease](#) - Bradley KL. *Thorax* 2021;76:92-99.

The lungs are exposed to a range of environmental toxins (including cigarette smoke, air pollution, asbestos) and pathogens (bacterial, viral and fungal), and most respiratory diseases are associated with local or systemic hypoxia. All of these adverse factors can trigger endoplasmic reticulum (ER) stress. The ER is a key intracellular site for synthesis of secretory and membrane proteins, regulating their folding, assembly into complexes, transport and degradation. Accumulation of misfolded proteins within the lumen results in ER stress, which activates the unfolded protein response (UPR). Effectors of the UPR temporarily reduce protein synthesis, while enhancing degradation of misfolded proteins and increasing the folding capacity of the ER. If successful, homeostasis is restored and protein synthesis resumes, but if ER stress persists, cell death pathways are activated. ER stress and the resulting UPR occur in a range of pulmonary insults and the outcome plays an important role in many respiratory diseases. The UPR is triggered in the airway of patients with several respiratory diseases and in corresponding experimental models. ER stress has been implicated in the initiation and progression of pulmonary fibrosis, and evidence is accumulating suggesting that ER stress occurs in obstructive lung diseases (particularly in asthma), in pulmonary infections (some viral infections and in the setting of the cystic fibrosis airway) and in lung cancer. While a number of small molecule inhibitors have been used to interrogate the role of the UPR in disease models, many of these tools have complex and off-target effects, hence additional evidence (eg, from genetic manipulation) may be required to support conclusions based on the impact of such pharmacological agents. Aberrant activation of the UPR may be linked to disease pathogenesis and progression, but at present, our understanding of the context-specific and disease-specific mechanisms linking these processes is incomplete. Despite this, the ability of the UPR to defend against ER stress and influence a range of respiratory diseases is becoming increasingly evident, and the UPR is therefore attracting attention as a prospective target for therapeutic intervention strategies.



Acute respiratory distress syndrome

Articles

[Pathophysiology of COVID-19-associated acute respiratory distress syndrome](#) - Camporota L. *Lancet Respiratory Medicine*, 2021, 9(1), e.1.

We congratulate Giacomo Grasselli and colleagues for their important and informative work on the pathophysiology of COVID-19-associated acute respiratory distress syndrome (ARDS).¹ In particular, we appreciate the clarity with which the data show that respiratory system compliance was significantly higher in COVID-19-associated ARDS compared with classical aetiology ARDS, despite the former having more severe hypoxaemia. Along this line, we note their result that “static compliance decreased as the ratio of partial pressure of arterial oxygen to fractional concentration of oxygen in inspired air decreased in patients with classical ARDS and in a pneumonia subset of patients with ARDS, while it remained unchanged in patients with COVID-19 ARDS”.¹ The CT data also confirm more normally inflated and hyperinflated tissue in COVID-19 ARDS (measured at clinical positive end-expiratory pressure PEEP) compared with ARDS from classical aetiologies. This observation indicates that the clinically set PEEP might have been higher than necessary in COVID-19 ARDS, possibly contributing to increased dead space. Accordingly, the authors recommended—correctly, in our view—the use of lower PEEP in patients with COVID-19 ARDS with higher compliance.

[Pathophysiology of COVID-19-associated acute respiratory distress syndrome](#) - Dandel M. *Lancet Respiratory Medicine*, 2021, 9(1), e.4.

Compared with diseases from other coronaviruses (ie, severe acute respiratory syndrome and Middle East respiratory syndrome), COVID-19 has more adverse effects on the cardiovascular system, leading to a high incidence of cardiovascular events—most notably life-threatening pulmonary vessel injury and cardiac dysfunction, with and without severe myocardial injury.¹ Small pulmonary vessel injuries and thrombosis associated with pulmonary blood flow alterations followed by right heart dilation and right ventricular failure have been found among the major causes of death related to COVID-19.

[Pathophysiology of COVID-19-associated acute respiratory distress syndrome](#) - Narayan A. *Lancet Respiratory Medicine*, 2021, 9(1), e.3.

We congratulate Giacomo Grasselli and colleagues¹ on their work in comparing acute respiratory distress syndrome (ARDS) in COVID-19 with classical ARDS. They found that median compliance in COVID-19 ARDS was higher than in classical ARDS, even after stratified analysis. However, they finally concluded that this difference was not significant. There are multiple reasons why important differentiating information might have been lost in the analyses.

[Pathophysiology of COVID-19-associated acute respiratory distress syndrome](#) - Tsolaki V. *Lancet Respiratory Medicine*, 2021, 9(1), e.2.

We read with great interest Giacomo Grasselli and colleagues' study concerning the pathophysiology of COVID-19-associated acute respiratory distress syndrome (ARDS).¹ The authors conclude that COVID-19



ARDS presents lung mechanics that largely match those of classical ARDS. 1 However, we feel this conclusion is not supported by their findings.

[Pathophysiology of COVID-19-associated acute respiratory distress syndrome – Authors' reply](#) - Grasselli G. *Lancet Respiratory Medicine*, 2021, 9(1), ee.5-6.

Luigi Camporota and colleagues and Vasiliki Tsolaki and colleagues challenge our finding that suggests that patients with COVID-19 have a form of injury that is encompassed by the conceptual model of acute respiratory distress syndrome (ARDS). The argument used by Camporota and colleagues and Tsolaki and colleagues is that the median static compliance we observed in patients with COVID-19-associated ARDS (41 mL/cm H₂O) was significantly higher compared with patients with classical ARDS. However, they miss the point that the distribution of compliance in patients with COVID-19 ARDS was wide and only 17 (6%) of 297 patients had compliance greater than the 95th percentile of the classical ARDS cohort.

[Pulmonary pathology of ARDS in COVID-19: A pathological review for clinicians](#) - Batah SS. *Respiratory Medicine*, 2021, 176, 106239.

COVID-19 has quickly reached pandemic levels since it was first reported in December 2019. The virus responsible for the disease, named SARS-CoV-2, is enveloped positive-stranded RNA viruses. During its replication in the cytoplasm of host cells, the viral genome is transcribed into proteins, such as the structural protein spike domain S1, which is responsible for binding to the cell receptor of the host cells. Infected patients have initially flu-like symptoms, rapidly evolving to severe acute lung injury, known as acute respiratory distress syndrome (ARDS). ARDS is characterized by an acute and diffuse inflammatory damage into the alveolar-capillary barrier associated with a vascular permeability increase and reduced compliance, compromising gas exchange and causing hypoxemia. Histopathologically, this condition is known as diffuse alveolar damage which consists of permanent damage to the alveoli epithelial cells and capillary endothelial cells, with consequent hyaline membrane formation and eventually intracapillary thrombosis. All of these mechanisms associated with COVID-19 involve the phenotypic expression from different proteins transcription modulated by viral infection in specific pulmonary microenvironments. Therefore, this knowledge is fundamentally important for a better pathophysiological understanding and identification of the main molecular pathways associated with the disease evolution. Evidently, clinical findings, signs and symptoms of a patient are the phenotypic expression of these pathophysiological and molecular mechanisms of SARS-CoV-2 infection. Therefore, no findings alone, whether molecular, clinical, radiological or pathological axis are sufficient for an accurate diagnosis. However, their intersection and/or correlation are extremely critical for clinicians establish the diagnosis and new treatment perspectives.

Asthma

Articles

[Adherence to medication among adult asthma patients in the Middle East and North Africa: results from the ESMAA study](#) - Bassam M. *Respiratory Medicine*, 2021, 176, 106244.



Background: Low levels of adherence to asthma medication is reported in many countries worldwide. Improved knowledge of adherence in the Middle East and North Africa (MENA) is needed to address this major public healthcare burden.

[Asthma in a large COVID-19 cohort: Prevalence, features, and determinants of COVID-19 disease severity](#) - Caminati M. *Respiratory Medicine*, 2021, 176, 106261.

Background: Asthma prevalence among COVID-19 patients seems to be surprisingly low. However the clinical profile of COVID-19 asthmatic patients and potential determinants of higher susceptibility/worse outcome have been scarcely investigated. We aimed to describe the prevalence and features of asthmatic patients hospitalized for COVID-19 and to explore the association between their clinical asthma profile and COVID-19 severity.

[An asthma plan](#) - Wilson M. *Lancet Respiratory Medicine*, 2021, 9(1), pp.18-20.

I was first diagnosed with asthma in 1988; back then, I was a typical outgoing, sports-mad teenager. My asthma wasn't too bad at first, and like many people I was prescribed 2 inhalers: a "brown preventer" and a "blue reliever". They both helped, and my life continued as normal and without any concerns of how my asthma would impact upon my quality of life as I got older. I reached my 30s before my asthma became a real problem. Whereas previously I had only had a few visits to the emergency department (ED) and no hospital admissions, things started to become more serious, with more frequent ED visits, which turned into hospital admissions, and all of sudden my asthma was a significant part of my life.

[Composite type-2 biomarker strategy versus a symptom–risk-based algorithm to adjust corticosteroid dose in patients with severe asthma: a multicentre, single-blind, parallel group, randomised controlled trial](#) - Heaney LG. *Lancet Respiratory Medicine*, 2021, 9(1), pp.57-68.

Background: Asthma treatment guidelines recommend increasing corticosteroid dose to control symptoms and reduce exacerbations. This approach is potentially flawed because symptomatic asthma can occur without corticosteroid responsive type-2 (T2)-driven eosinophilic inflammation, and inappropriately high-dose corticosteroid treatment might have little therapeutic benefit with increased risk of side-effects. We compared a biomarker strategy to adjust corticosteroid dose using a composite score of T2 biomarkers (fractional exhaled nitric oxide FENO, blood eosinophils, and serum periostin) with a standardised symptom–risk-based algorithm (control).

[Dual-combination maintenance inhaler preferences in asthma and chronic obstructive pulmonary disease: A patient-centered benefit-risk assessment](#) - Tervonen T. *Respiratory Medicine*, 2021, 176, 106278.

Background: A variety of dual-combination maintenance inhalers are used to treat asthma and chronic obstructive pulmonary disease (COPD). Understanding patient preferences for treatment attributes may help select an optimal treatment from the patient perspective.



[Effectiveness of fevipiprant in reducing exacerbations in patients with severe asthma \(LUSTER-1 and LUSTER-2\): two phase 3 randomised controlled trials](#) - Brightling CE. *Lancet Respiratory Medicine*, 2021, 9(1), pp.43-56.

Background: Fevipiprant, an oral antagonist of the prostaglandin D₂ receptor 2, reduced sputum eosinophils and improved lung function in phase 2 trials of patients with asthma. We aimed to investigate whether fevipiprant reduces asthma exacerbations in patients with severe asthma.

[Effects of continuous aerobic exercise on lung function and quality of life with asthma: a systematic review and meta-analysis](#). - Wu X. *Journal of Thoracic Disease* 2020;12(9):doi: 10.21037/jtd-19-2813.

Our meta-analysis proved that regular continuous aerobic exercise benefits asthma patients on FEV₁, PEF, FVC, FVC%pred, FEF_{25–75%}, and quality of life, and was well tolerated, while there were no improvements in FEV₁%pred and FEV₁/FVC%. As such, swimming and treadmill training may be appropriate options.

[Efficacy and safety of once-daily single-inhaler triple therapy \(FF/UMEC/VI\) versus FF/VI in patients with inadequately controlled asthma \(CAPTAIN\): a double-blind, randomised, phase 3A trial](#) - Lee LA. *Lancet Respiratory Medicine*, 2021, 9(1), pp.69-84.

Background: Despite inhaled corticosteroid plus long-acting β 2 -agonist (ICS/LABA) therapy, 30–50% of patients with moderate or severe asthma remain inadequately controlled. We investigated the safety and efficacy of single-inhaler fluticasone furoate plus umeclidinium plus vilanterol (FF/UMEC/VI) compared with FF/VI.

[More options for managing severe asthma in adults](#) - Chang AB. *Lancet Respiratory Medicine*, 2021, 9(1), pp.3-5.

Personalised medicine for various diseases including asthma has been advocated for decades. Although the initial focus on β 2 -adrenoceptor genotypes proved to be impractical and largely failed, 1 the focus on type-2 (T2) airway inflammation biomarkers has had more success, particularly with high-cost biologics (eg, interleukinIL-4, IL-5, and IL-13 inhibitors); however, many questions remain. 2 Two novel, well-conducted, randomised controlled trials 34 have assessed whether incorporation of T2 biomarkers might provide clinicians with more options when managing adults with uncontrolled or severe asthma without the use of biologics.

[A new formulation of fluticasone propionate/salmeterol in a metered-dose inhaler \(MDI HFA\) allows for the reduction of a daily dose of corticosteroid and provides optimal asthma control - A randomized, multi-center, non-inferiority, phase IV clinical study](#) - Kupczyk M. *Respiratory Medicine*, 2021, 176, 106274.

Background: Improvement of the delivery method of inhaled corticosteroids and subsequent dose reduction can minimize the risk of unfavorable outcomes while providing optimal asthma control.



[Night shift work is associated with an increased risk of asthma](#) - Maidstone RJ. *Thorax* 2021;76:53-60.

Introduction: Shift work causes misalignment between internal circadian time and the external light/dark cycle and is associated with metabolic disorders and cancer. Approximately 20% of the working population in industrialised countries work permanent or rotating night shifts, exposing this large population to the risk of circadian misalignment-driven disease. Analysis of the impact of shift work on chronic inflammatory diseases is lacking. We investigated the association between shift work and asthma.

[Oral corticosteroid prescription for asthma by general practitioners: A three-year analysis in Germany](#) - Lommatzsch M. *Respiratory Medicine*, 2021, 176, 106242.

Background: Regular treatment of patients with asthma with oral corticosteroids (OCS) remains common despite potential severe side effects and alternative treatment options. However, there is limited data on the prevalence of OCS prescriptions for patients with asthma in Germany.

[Oral corticosteroid sparing effects of anti-IL5/ anti-IL5 receptor treatment after 2 years of treatment](#) - Bjerrum AS. *Respiratory Medicine*, 2021, 176, 106260.

Introduction: Clinical trials have shown oral corticosteroid (OCS) sparing effects of anti-IL5/anti-IL5-receptor treatments. The generalisability of these clinical trials may be limited, due to the rigid inclusion and exclusion criteria, and the short tapering duration. Real-world evidence is needed to bridge the gap between the clinical trials and the clinical practice. With this study we present real-life data on the OCS sparing effects of anti-IL5/anti-IL5-receptor treatments after 12 and 24 months of treatment.

[Personalised medicine for asthma in a post-pandemic world](#) - The Lancet Respiratory Medicine. *Lancet Respiratory Medicine*, 2021, 9(1), p.1.

At the time of writing, optimism is in the air as the Pfizer vaccine against SARS-CoV-2 is rolled out in the UK to essential health-care workers and in care homes. For many, this is the first big step along the pathway out of the COVID-19 pandemic. However, as the year draws to a close, the collective term “ long COVID ” is becoming commonplace in clinics globally and it is uncertain how COVID-19 will continue to affect those with respiratory comorbidities , with many vulnerable groups continuing to shield. Furthermore, as the world emerges from the pandemic, research efforts tailored to specific groups will be key; so-called personalised medicine.

[Prevalence and features of IOS-defined small airway disease across asthma severities](#) - Cottini M. *Respiratory Medicine*, 2021, 176, 106243.

Background: Impulse oscillometry (IOS) is a noninvasive method based on the forced oscillation technique able to detect small airway dysfunction (SAD) in asthma. We aimed to analyze the prevalence and the functional features of IOS-defined SAD across the different Global Initiative for Asthma (GINA) steps.



[Prostaglandin D 2: the end of a story or just the beginning?](#) - Kerstjens HAM. *Lancet Respiratory Medicine*, 2021, 9(1), pp.2-3.

Tremendous progress has been made in the treatment of asthma over the past decade. The development of monoclonal antibodies against IgE, interleukin-5 (IL-5) or its receptor, or the IL-4 receptor in particular has been a game changer, for a selected group of patients. These biologics all target the allergic or type 2 side of the spectrum of asthma, but even within the severe allergic or type 2 high asthma population these drugs do not completely prevent exacerbations, reducing their frequency by around 40–60%. Additionally, they must be administered intravenously or subcutaneously, and are costly. In short, there are multiple reasons for expanding the range of treatment options for patients with severe asthma.

[Risk of osteoporosis and fragility fractures in asthma due to oral and inhaled corticosteroids: two population-based nested case-control studies](#) - Chalitsios CV. *Thorax* 2021;76:21-28.

Background: Inhaled (ICS) and oral (OCS) corticosteroids are used widely in asthma; however, the risk of osteoporosis and fragility fracture (FF) due to corticosteroids in asthma is not well-established.

[The triad of current asthma, rhinitis and eczema is uncommon among adults: Prevalence, sensitization profiles, and risk factors](#) - Pullerits T. *Respiratory Medicine*, 2021, 176, 106250.

Background: Coexistence of asthma, rhinitis, and eczema has been studied in children, but data are lacking in adults. As new treatments emerge, epidemiological data on the coexistence are needed.

Bronchial diseases

Articles

[The detrimental qualitative and quantitative alterations of circulating endothelial progenitor cells in patients with bronchiectasis](#) - Liu Y. *Respiratory Medicine*, 2021, 176, 106270.

Background: Bronchiectasis is an independent risk factor for cardiovascular disease (CVD) and cardiac dysfunction. Endothelial progenitor cells (EPCs) play a crucial role in maintaining endothelial function, and is inversely correlated with cardiovascular risk factors or cardiac dysfunction. However, the relationship between EPCs and bronchiectasis is unknown.

[Inhaled tobramycin for chronic infection with pseudomonas aeruginosa in non-cystic fibrosis bronchiectasis: A systematic review and meta-analysis](#) - Sangiovanni S. *Respiratory Medicine*, 2021, 176, 106283.

Introduction: Non-cystic fibrosis bronchiectasis (NCFBE) is a chronic and progressive disease characterized by the permanent destruction of small and mid-sized airways. Many patients are chronically colonized by *Pseudomonas aeruginosa*, for which oral antibiotics are given. Evidence to support the use of inhaled antibiotics is contradictory.



Cancers of the respiratory tract

Articles

[Overdiagnosis in lung cancer screening](#) - Callister MEJ. *Lancet Respiratory Medicine*, 2021, 9(1), pp.7-9.

Overdiagnosis in cancer screening is the detection of cancers that would not have become clinically apparent if the person had not been screened. Diagnosis of cancer causes anxiety, and treatment often causes physical harm. For individuals with overdiagnosed cancer, these harms occur without any benefits. There are two major contributors to overdiagnosis: indolent cancers and competing causes of death. In practice, there is a spectrum of interaction between these two factors.

[Predicting survival in malignant pleural mesothelioma using routine clinical and laboratory characteristics](#) - Gunatilake S. *BMJ Open Respiratory Research* 2021;8:e000506.

Introduction: The prognosis of malignant pleural mesothelioma (MPM) is poor, with a median survival of 8–12 months. The ability to predict prognosis in MPM would help clinicians to make informed decisions regarding treatment and identify appropriate research opportunities for patients. The aims of this study were to examine associations between clinical and pathological information gathered during routine care, and prognosis of patients with MPM, and to develop a 6-month mortality risk prediction model.

Chest imaging

Articles

[Cardiac arrest in infant due to giant fetus-in-fetu](#) - Wu Y. *Thorax* 2021;76:100-101.

A 7-month-old boy was referred to our institution following a cardiac arrest which was treated by timely cardiopulmonary resuscitation at another hospital. Previously, he had a progressive cough with a low-grade fever despite the use of antibiotics for 4 days. He was transferred to our institution for further investigation. He had no other associated diseases, nor use of medication. His mother did not report any abnormal findings from ultrasonography during prenatal examinations. Auscultation revealed shallow respiration with moist rales in the left lung. The echocardiogram revealed a 3.8 mm atrial septal defect with the heart shifted to the right. CT scan indicated a giant tumour in the posterior mediastinum (figure 1A, B). Serum alpha-fetoprotein (AFP) and β -chorionic gonadotropin (HCG) were negative. To exclude malignant conditions where chemotherapy would be warranted, a mini-thoracotomy for biopsy was performed. However, the biopsy indicated tissues of fibre, fat and bone without evidence of malignancy. A definite pathological diagnosis could not be determined due to limited specimens.

[MRI of the upper airways in children and young adults: the MUSIC study](#) - Elders B. *Thorax* 2021;76:44-52.

Rationale: Paediatric laryngotracheal stenosis (LTS) is often successfully corrected with open airway surgery. However, respiratory and vocal sequelae frequently remain. Clinical care and surgical interventions could be improved with better understanding of these sequelae.



[Predictive value of chest CT scoring in COVID-19 patients in Wuhan, China: A retrospective cohort study](#) - Li S. *Respiratory Medicine*, 2021, 176, 106271.

Background: Computed tomography (CT) findings of COVID-19 patients were demonstrated by cases series and descriptive studies, but quantitative analysis performed by clinical doctors and studies on its predictive value were rarely seen. The aim of the study is to analyze CT score in COVID-19 patients and explore its predictive value.

[Utility of radial endobronchial ultrasonography combined with transbronchial lung cryobiopsy in patients with diffuse parenchymal lung diseases: a multicentre prospective study](#) - Inomata M. *BMJ Open Respiratory Research* 2021;8:e000826.

Background: Radial endobronchial ultrasonography (R-EBUS) has been used in conjunction with transbronchial lung cryobiopsy (TBLC) to diagnose diffuse parenchymal lung disease (DPLD) and to decrease the risk of bleeding complications. The diagnostic utility of different R-EBUS signs, however, remains unknown.

COPD

Articles

[Cognitive function following pulmonary rehabilitation and post-discharge recovery from exacerbation in people with COPD](#) - France G. *Respiratory Medicine*, 2021, 176, 106249.

Background: Cognitive impairment (CI) is prevalent in COPD and is associated with poor health-related quality of life. Recovery of cognition following an acute exacerbation of COPD (AECOPD), the impact of CI on pulmonary rehabilitation (PR) uptake and the effect of PR on CI are not fully understood.

[COPD in women – New results presented](#) - Backman H. *Respiratory Medicine*, 2021, 176, 106238.

In this issue a large international research collaboration on COPD 1, 2 highlights interesting differences in clinical characteristics in men and women with COPD 1. In this work Alonso Pérez et al. 1 pooled data from 22 cohorts from seven countries, and included results from 17,139 COPD patients among whom 5355 were women. Two of the cohorts are from well-known large scale populations studies, the Copenhagen City Heart Study 3 and the Norwegian HUNT study 4, while the others are health care based.

[Is the use of two versus one long-acting bronchodilator by patients with COPD associated with a higher risk of acute coronary syndrome in real-world clinical practice?](#) - Parkin L. *BMJ Open Respiratory Research* 2021;8:e000840.

Background: Cardiovascular comorbidity is common among patients with chronic obstructive pulmonary disease (COPD) and there is concern that long-acting bronchodilators (long-acting muscarinic antagonists (LAMAs) and long-acting beta2 agonists (LABAs)) may further increase the risk of acute coronary events. Information about the impact of treatment intensification on acute coronary syndrome (ACS) risk in real-



world settings is limited. We undertook a nationwide nested case–control study to estimate the risk of ACS in users of both a LAMA and a LABA relative to users of a LAMA.

[Falls prevalence and risk factors in people with chronic obstructive pulmonary disease: A systematic review](#) - Oliveira CC. *Respiratory Medicine*, 2021, 176, 106284.

Background: Falls are frequent in people with chronic obstructive pulmonary disease (COPD) and related to increased morbidity, mortality, and health care costs in older adults. This systematic review aims to synthesise the falls outcomes and to examine risk factors for falls in the COPD literature.

[A few more steps lead to improvements in endothelial function in severe and very severe COPD](#) - Kohlbrenner D. *Respiratory Medicine*, 2021, 176, 106246.

Introduction: Cardiovascular disease is among the most prevalent concomitant chronic diseases in COPD. Physical activity (PA) modifies endothelial function and is commonly impaired in COPD. However, studies directly investigating the effects of increased PA on endothelial function in COPD are lacking. We investigated the effect of changes in PA on endothelial function in patients with severe to very severe COPD. Furthermore, we determined which variables modify this effect.

[Impact of patients' perception of COPD and treatment on adherence and health-related quality of life in real-world: Study in 53 community pharmacies](#) - López-Pintor E. *Respiratory Medicine*, 2021, 176, 106280.

Background: Patient adherence to treatment in chronic obstructive pulmonary disease (COPD) is essential to optimize disease management. We aimed to assess the impact of patients' perception of their treatment and disease on adherence and Health-Related Quality of Life (HRQL) in patients attending a community pharmacy, where usually subjects have a better condition than those in clinical settings.

[Managing malnutrition in COPD: A review](#) - Keogh E. *Respiratory Medicine*, 2021, 176, 106248.

In the UK approximately 1.2 million people have COPD with around 25–40% being underweight and 35% have a severely low fat-free mass index. Measuring their body mass index is recommended and Health care professionals should endeavour to ensure that COPD patients are achieving their nutritional requirements. A narrative review summarizes evidence from 28 original articles identified through a systematic searches of databases, grey literature and hand searches covering 15 years, focusing on two themes, on the impact of malnutrition on COPD, and the management of malnutrition in COPD. Malnutrition causes negative effects on exercise and muscle function and lung function as well as increasing exacerbations, mortality and cost. Management options include nutritional supplementation which may increase weight and muscle function. Nutritional education has short-term improvements. Malnutrition affects multiple aspects of COPD, but treatment is of benefit. Clinical practice should include nutrition management.



[Morbidity and mortality associated with prescription cannabinoid drug use in COPD - Vozoris NT. *Thorax* 2021;76:29-36.](#)

Introduction: Respiratory-related morbidity and mortality were evaluated in relation to incident prescription oral synthetic cannabinoid (nabilone, dronabinol) use among older adults with chronic obstructive pulmonary disease (COPD).

[Physician's attitude against COPD guidelines and the choice of first-line treatment for COPD - Baha A. *Respiratory Medicine*, 2021, 176, 106273.](#)

Aim: Our aim was to evaluate changes in attitudes of pulmonologists in Turkey towards COPD guidelines and their choice of first-line treatments for COPD patients.

[Qualitative emphysema and risk of COPD hospitalization in a multicenter CT lung cancer screening cohort study - Gazourian L. *Respiratory Medicine*, 2021, 176, 106245.](#)

Background: In the United States, 9 to 10 million Americans are estimated to be eligible for computed tomographic lung cancer screening (CTLS). Those meeting criteria for CTLS are at high-risk for numerous cardio-pulmonary co-morbidities. The objective of this study was to determine the association between qualitative emphysema identified on screening CTs and risk for hospital admission.

[Specialty COPD care during COVID-19: patient and clinician perspectives on remote delivery - Wu F. *BMJ Open Respiratory Research* 2021;8:e000817.](#)

Introduction: The COVID-19 pandemic has impacted specialty chronic obstructive pulmonary disease (COPD) care. We examined the degree to which care has moved to remote approaches, eliciting clinician and patient perspectives on what is appropriate for ongoing remote delivery.

[Updated international guideline on the diagnosis and management of COPD. - BMJ Best Practice; 2020.](#)

Diagnosis and Monitoring

Articles

[Measuring vital capacity in amyotrophic lateral sclerosis: Effects of interfaces and reproducibility - Pellegrino GM. *Respiratory Medicine*, 2021, 176, 106277.](#)

Background: Deterioration of vital capacity (VC) in amyotrophic lateral sclerosis (ALS) signifies disease progression and indicates need for non-invasive ventilation. Weak facial muscles consequent to ALS, with resulting poor mouth seal, may interfere with the accuracy of VC measurements.



[Multiple breath washout: A noninvasive tool for identifying lung disease in symptomatic military deployers](#) - Zell-Baran LM. *Respiratory Medicine*, 2021, 176, 106281.

Rationale: Military deployments to austere environments since November 9, 2001 may put “deployers” at risk for respiratory disease. Sensitive, noninvasive tools for detecting large and small airways injury are needed to identify early disease and help inform management for this at-risk population.

[Nailing the diagnosis: severe nail involvement in adult pulmonary Langerhans cell histiocytosis](#) - Delaval L. *Thorax* 2021;76:102-103.

A 36-year-old male ex-smoker was referred for the management of pulmonary Langerhans cell histiocytosis (LCH) confirmed by surgical biopsy (figure 1A). He had been treated with desmopressin for 5 years for diabetes insipidus. One year before admission, dyspnoea on exertion had appeared. At the same time, the patient developed painful nail abnormalities on all 10 fingers with subungual hyperkeratosis, purpuric striae, paronychia erythema, longitudinal grooving, splinter haemorrhages, onycholysis, lunula deformation (figure 1B), with no underlying bone involvement on hand X-ray examination. Nail samples were negative for bacteria and fungi. Maculopapular and crusted lesions in the axillary fold, the scalp and the external auditory canal were also present. A nail biopsy showed hyperplastic epidermis, surmounted by thick parakeratosis. The upper dermis was infiltrated by pale histiocytes with eosinophilic cytoplasm and reniform nuclei that positively stained for CD1a antigen, consistent with LCH (figure 1C).

[Novel non-invasive particles in exhaled air method to explore the lining fluid of small airways—a European population-based cohort study](#) - Hussain-Alkhatieb L. *BMJ Open Respiratory Research* 2021;8:e000804.

Introduction: Respiratory tract lining fluid of small airways mainly consists of surfactant that can be investigated by collection of the particles of exhaled aerosol (PExA) method. This offers an exciting prospect to monitor small airway pathology, including subjects with asthma and smokers.

What's New in Critical Care from UpToDate

[Limitations of pulse oximetry and racial bias \(January 2021\)](#)

To date, weak data have suggested that skin pigmentation may affect pulse oximetry readings. In a recent analysis of over 48,000 paired measurements of pulse oximetry and arterial blood gas cooximetry (ABG-Co) taken from hospitalized adults receiving supplemental oxygen (75 percent intensive care unit patients), pulse oximetry overestimated true oxygen saturation by ABG-Co (gold standard) more frequently in Black than White individuals, and more Black patients had an ABG-Co <88 percent despite a pulse oximetry reading of 92 to 96 percent compared with White patients (12 to 17 percent versus 4 to 6 percent) 17. These findings suggest that overreliance on pulse oximetry to make clinical decisions may place Black individuals at an increased risk for occult hypoxemia. Clinicians should be aware of this discrepancy and have a low threshold to perform ABG analysis, particularly in Black patients.



Dyspnoea

Articles

[Facemasks as a COVID-19 barrier: a window into the overlooked experience of chronic dyspnoea?](#) - Similowski T. *Lancet Respiratory Medicine*, 2021, 9(1), pp.12-13.

The COVID-19 pandemic has resulted in the widespread use of facemasks globally. Facemasks contribute to the protection against contamination of the people wearing them and those in close proximity, and they also protect against the fear of contamination. Wearing facemasks is, however, associated with a series of material constraints: you have to think about the mask, to have it with you, to pay for it, to change it, or to wash it frequently. Facemasks are also associated with marked sociological inconveniences, obstructing verbal communication (eg, muffled voice, invisible lip movements) and hindering non-verbal communication by making facial expressions hard to read. Facemasks can also be uncomfortable to wear. Primarily, being slightly resistive to airflow and a possible source of carbon dioxide rebreathing, they change our relationship with our own breathing. We suddenly become consciously aware of our respirations, and many of us find this unsettling. What if there was a sociological upside to this particular consequence of wearing protective masks? What if this could make us more attentive to the predicament of patients with chronic breathing problems?

Emphysema

Articles

[Qualitative emphysema and risk of COPD hospitalization in a multicenter CT lung cancer screening cohort study](#) - Gazourian L. *Respiratory Medicine*, 2021, 176, 106245.

Background: In the United States, 9 to 10 million Americans are estimated to be eligible for computed tomographic lung cancer screening (CTLS). Those meeting criteria for CTLS are at high-risk for numerous cardio-pulmonary co-morbidities. The objective of this study was to determine the association between qualitative emphysema identified on screening CTs and risk for hospital admission.

Infections (including COVID-19)

Articles

[Disinfection of *Pseudomonas aeruginosa* from N95 respirators with ozone: a pilot study](#) - Manning EP. *BMJ Open Respiratory Research* 2021;8:e000781.

Introduction: Personal protective equipment shortages require the reuse of N95 respirators. We sought the necessary conditions for ozone to disinfect N95 respirators for reuse and the effects of multiple cycles of exposure.

COVID-19

Articles

[Association of inhaled and systemic corticosteroid use with Coronavirus Disease 2019 \(COVID-19\) test positivity in patients with chronic pulmonary diseases](#) - Liao SY. *Respiratory Medicine*, 2021, 176, 106275.



Background: The effects of chronic inhaled and systemic corticosteroids use on COVID-19 susceptibility and severity are unclear. Since many patients with chronic pulmonary diseases rely on corticosteroids to control disease, it is important to understand the risks of their use during the pandemic. We aim to study if the use of inhaled or systemic corticosteroids affects the likelihood of developing COVID-19 infection.

[Beyond the clot: perfusion imaging of the pulmonary vasculature after COVID-19](#) - Dhawan RT. *Lancet Respiratory Medicine*, 2021, 9(1), pp.107-116.

A compelling body of evidence points to pulmonary thrombosis and thromboembolism as a key feature of COVID-19. As the pandemic spread across the globe over the past few months, a timely call to arms was issued by a team of clinicians to consider the prospect of long-lasting pulmonary fibrotic damage and plan for structured follow-up. However, the component of post-thrombotic sequelae has been less widely considered. Although the long-term outcomes of COVID-19 are not known, should pulmonary vascular sequelae prove to be clinically significant, these have the potential to become a public health problem. In this Personal View, we propose a proactive follow-up strategy to evaluate residual clot burden, small vessel injury, and potential haemodynamic sequelae. A nuanced and physiological approach to follow-up imaging that looks beyond the clot, at the state of perfusion of lung tissue, is proposed as a key triage tool, with the potential to inform therapeutic strategies.

[Clinical status and lung function 10 weeks after severe SARS-CoV-2 infection](#) - Smet J. *Respiratory Medicine*, 2021, 176, 106276.

Introduction: Since studies about clinical status after COVID-19 are scarce, we conducted a cross sectional study with assessment of residual symptoms, lung function and chest CT.

[Corticosteroids for COVID-19: the search for an optimum duration of therapy](#) - Mishra GP. *Lancet Respiratory Medicine*, 2021, 9(1), e.8.

Michael A Matthay and B Taylor Thompson 1 have very nicely summarised the evidence-based role of dexamethasone in hospitalised patients with COVID-19. Their pertinent analysis is based on the background of the RECOVERY trial, 2 which concluded that therapy with dexamethasone at a dose of 6 mg once daily for up to 10 days decreased 28-day mortality in patients with COVID-19 on respiratory support. Patients not requiring oxygen showed no benefit but had a possibility of harm with corticosteroid therapy.

[Effect of anakinra versus usual care in adults in hospital with COVID-19 and mild-to-moderate pneumonia \(CORIMUNO-ANA-1\): a randomised controlled trial.](#) - The CORIMUNO-19 Collaborative group. *The Lancet Respiratory Medicine* 2021

Patients with COVID-19 pneumonia have an excess of inflammation and increased concentrations of cytokines including interleukin-1 (IL-1). Anakinra did not improve outcomes in patients with mild-to-moderate COVID-19 pneumonia. Further studies are needed to assess the efficacy of anakinra in other



selected groups of patients with more severe COVID-19.

[Guidance on nebulization during the current COVID-19 pandemic](#) - Cazzola M. *Respiratory Medicine*, 2021, 176, 106236.

Awareness of the risk of airborne transmission of SARS-CoV-2 makes patients hesitant about using inhaled medications that are considered as a potential source of viral transmission and immunosuppression. However, patients with asthma or COPD should continue all prescribed inhaled medications. Apparently, inhalers, including pMDIs, DPIs, or SMIs, have a low risk of contamination although characteristics of drug formulation can precipitate cough, whereas some researchers do not rule out the probability that nebulizer treatments may increase the risk of infection transmission via droplet nuclei and aerosols. Considering that aerosol therapy generates fugitive emissions that are not inhaled by the patient and are released from the device during expiration, several international professional bodies have provided recommendations for drug delivery via inhalers and in particular, nebulizers. Unfortunately, these recommendations are often in conflict with each other and do not clarify whether it is appropriate to use nebulizers during this COVID-19 pandemic. Considering what is available in literature, there are no known infection-related hazards to an uninfected patient and also a patient with COVID-19 that preclude the use of a nebulizer at home, but it is fundamental that all patients, regardless of whether or not suffering from COVID-19, always follow some practical advices.

[Implementing rapid diagnostics for COVID-19](#) - Nimmo C. *Lancet Respiratory Medicine*, 2021, 9(1), e.7.

We congratulate Nathan Brendish and colleagues for doing their trial during the first COVID-19 wave. 1 The reduction in turnaround time in the point-of-care testing group was impressive, especially considering 6 months later more than 10% of patients in English hospitals still have to wait more than 24 h for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) PCR test results. 2 We agree that rapid diagnostics offer numerous benefits, but a substantial challenge remains in optimal implementation. In our hospital (Homerton University Hospital, London, UK) we have had access to another rapid diagnostic PCR (Cepheid Xpert Xpress SARS-CoV-2; Cepheid, Sunnyvale, CA, USA) that similarly delivers results within 1 h. In comparison with the study of Brendish and colleagues, in which the point-of-care test was available to all patients at hospital admission, we have used rapid testing on clinician request, for example, to inform a specific patient cohorting decision or if there was a substantial diagnostic uncertainty.

[Levels of resilience, anxiety and depression in nurses working in respiratory clinical areas during the COVID pandemic](#) - Roberts NJ. *Respiratory Medicine*, 2021, 176, 106219.

Background: The delivery of healthcare during the COVID pandemic has had a significant impact on front line staff. Nurses who work with respiratory patients have been at the forefront of the pandemic response. Lessons can be learnt from these nurses' experiences in order to support these nurses during the existing pandemic and retain and mobilise this skilled workforce for future pandemics.



[Rationale for azithromycin in COVID-19: an overview of existing evidence](#) - Gyselinck I. *BMJ Open Respiratory Research* 2021;8:e000806.

Azithromycin has rapidly been adopted as a repurposed drug for the treatment of COVID-19, despite the lack of high-quality evidence. In this review, we critically appraise the current pharmacological, preclinical and clinical data of azithromycin for treating COVID-19. Interest in azithromycin has been fuelled by favourable treatment outcomes in other viral pneumonias, a documented antiviral effect on SARS-CoV-2 in vitro and uncontrolled case series early in the pandemic. Its antiviral effects presumably result from interfering with receptor mediated binding, viral lysosomal escape, intracellular cell-signalling pathways and enhancing type I and III interferon expression. Its immunomodulatory effects may mitigate excessive inflammation and benefit tissue repair. Currently, in vivo reports on azithromycin in COVID-19 are conflicting and do not endorse its widespread use outside of clinical trials. They are, however, mostly retrospective and therefore inherently biased. The effect size of azithromycin may depend on when it is started. Also, extended follow-up is needed to assess benefits in the recovery phase. Safety data warrant monitoring of drug–drug interactions and subsequent cardiac adverse events, especially with hydroxychloroquine. More prospective data of large randomised controlled studies are expected and much-needed. Uniform reporting of results should be strongly encouraged to facilitate data pooling with the many ongoing initiatives.

[Smoking and COVID-19: What we know so far](#) - Shastri MD. *Respiratory Medicine*, 2021, 176, 106237.

The ongoing COVID-19 pandemic has placed a spotlight on infectious diseases and their associations with host factors and underlying conditions. New data on the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus are entering the public domain at a rapid rate such that their distillation often lags behind. To minimise weak associations becoming perceived as established paradigms, it is imperative that methodologies and outputs from different studies are appropriately critiqued and compared. In this review, we examine recent data on a potential relationship between smoking and COVID-19. While the causal role of smoking has been firmly demonstrated in regard to lung cancer and chronic obstructive pulmonary disease, such associations have the benefit of decades' worth of multi-centre epidemiological and mechanistic data. From our analysis of the available studies to date, it appears that a relationship is emerging in regard to patients with a smoking history having a higher likelihood of developing more severe symptoms of COVID-19 disease than non-smokers. Data on whether COVID-19 has a greater incidence in smokers than non-smokers is thus far, contradictory and inconclusive. There is therefore a need for some caution to be exercised until further research has been conducted in a wider range of geographical settings with sufficient numbers of patients that have been carefully phenotyped in respect of smoking status and adequate statistical control for confounding factors.

[Tobacco use as a well-recognized cause of severe COVID-19 manifestations](#) - Gupta AK. *Respiratory Medicine*, 2021, 176, 106233.

Introduction: The Coronavirus disease (COVID-19) infection is caused by the novel Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) primarily affecting the lungs. All tobacco-related illnesses including asthma, chronic obstructive pulmonary disease (COPD), and coronary artery disease are known to reduce the lung capacity and impair the immune system of the body and can greatly influence



the ability to fight the novel coronavirus. The purpose of this state-of-the-art literature review is to summarize the evidence of the association of tobacco use with the severity of the COVID-19 manifestations.

[Upper respiratory viral load in asymptomatic individuals and mildly symptomatic patients with SARS-CoV-2 infection](#) - Ra SH. *Thorax* 2021;76:61-63.

Background: Asymptomatic individuals with SARS-CoV-2 infection have viable viral loads and have been linked to several transmission cases. However, data on the viral loads in such individuals are lacking. We assessed the viral loads in asymptomatic individuals with SARS-CoV-2 infection in comparison with those in symptomatic patients with COVID-19.

[Use of exhaled breath condensate \(EBC\) in the diagnosis of SARS-COV-2 \(COVID-19\)](#) - Ryan DJ. *Thorax* 2021;76:86-88.

False negatives from nasopharyngeal swabs (NPS) using reverse transcriptase PCR (RT-PCR) in SARS-CoV-2 are high. Exhaled breath condensate (EBC) contains lower respiratory droplets that may improve detection. We performed EBC RT-PCR for SARS-CoV-2 genes (E, S, N, ORF1ab) on NPS-positive (n=16) and NPS-negative/clinically positive COVID-19 patients (n=15) using two commercial assays. EBC detected SARS-CoV-2 in 93.5% (29/31) using the four genes. Pre-SARS-CoV-2 era controls (n=14) were negative. EBC was positive in NPS negative/clinically positive patients in 66.6% (10/15) using the identical E and S (E/S) gene assay used for NPS, 73.3% (11/15) using the N/ORF1ab assay and 14/15 (93.3%) combined.

What's New in Critical Care from UpToDate

[Decrease in COVID-19-associated mortality rates \(January 2021\)](#)

Several analyses have suggested that COVID-19-associated mortality may be decreasing as the pandemic progresses 12-15. As examples, two cohort studies of critically ill patients from the United States and Europe reported reductions in mortality rates from the beginning of the pandemic (42 to 44 percent) to the end of the first surge, 2.5 to 4 months later (19 to 25 percent) 13,15. The reasons for the decrease in mortality are unknown but may be related to reduced burden on institutions as the first surge waned, increased use of evidence-based therapies, and/or growing expertise with COVID-19 supportive care. Further data regarding mortality during subsequent surges are awaited.

What's New in Other Pulmonary Medicine from UpToDate

[Persistent symptoms following acute COVID-19 illness \(January 2021\)](#)

Two prospective studies provide additional information about persistent symptoms in patients with COVID-19:



●Of 143 Italian patients hospitalized for COVID-19, 83 percent continued to have at least 1 symptom at a mean of 60 days after discharge 35.

●Of 669 Swiss patients with positive tests for COVID-19 (mostly outpatients), 32 percent continued to have at least one symptom at a mean of 43 days after discharge 36.

Based on these and other studies, prolonged symptoms following acute COVID-19 illness are common and include fatigue, dyspnea, chest pain, cough, anxiety, depression, post-traumatic stress disorder, and cognitive deficits (eg, poor memory and concentration) (table 1). Persistent symptoms, which can last up to three months or longer, are more common in individuals who were hospitalized but are also reported by those with less severe disease who were never admitted. It is unclear whether the constellation of symptoms and persistent issues represent a new syndrome unique to COVID-19 or reflect a more nonspecific response that may be seen during recovery from other illnesses with similar acuity and pathophysiology.

Interstitial lung diseases (pulmonary fibrosis)

Articles

[Clinicoserological features of antisynthetase syndrome \(ASyS\)-associated interstitial lung disease presenting to respiratory services: comparison with idiopathic pulmonary fibrosis and ASyS diagnosed in rheumatology services](#) - Barratt SL. *BMJ Open Respiratory Research* 2021;8:e000829.

Introduction: Antisynthetase syndrome (ASyS) is a rare autoimmune connective tissue disease (CTD), associated with autoantibodies targeting tRNA synthetase enzymes, that can present to respiratory (interstitial lung disease (ILD)) or rheumatology (myositis, inflammatory arthritis and systemic features) services. The therapeutic management of CTD-associated ILD and idiopathic pulmonary fibrosis (IPF) differs widely, thus accurate diagnosis is essential.

[Efficacy and safety of nintedanib in patients with systemic sclerosis-associated interstitial lung disease treated with mycophenolate: a subgroup analysis of the SENSICIS trial](#) - Highland KB. *Lancet Respiratory Medicine*, 2021, 9(1), pp.96-106.

Background: In the Safety and Efficacy of Nintedanib in Systemic Sclerosis (SENSICIS) trial, nintedanib reduced the rate of decline in forced vital capacity (FVC) in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD). Patients on stable treatment with mycophenolate for at least 6 months before randomisation could participate. The aim of this subgroup analysis was to examine the efficacy and safety of nintedanib by mycophenolate use at baseline.

[Efficacy and safety of sildenafil added to pirfenidone in patients with advanced idiopathic pulmonary fibrosis and risk of pulmonary hypertension: a double-blind, randomised, placebo-controlled, phase 2b trial](#) - Behr J. *Lancet Respiratory Medicine*, 2021, 9(1), pp.85-95.

Background: The benefit of sildenafil in patients with advanced idiopathic pulmonary fibrosis (IPF) at risk of poor outcomes from pulmonary hypertension, whether already present or likely to develop, is uncertain. We aimed to assess the efficacy and safety of sildenafil added to pirfenidone versus placebo added to pirfenidone for 52 weeks in patients with advanced IPF and at risk of group 3 pulmonary hypertension.



[Minimum important difference of the EQ-5D-5L and EQ-VAS in fibrotic interstitial lung disease - Tsai APY. *Thorax* 2021;76:37-43.](#)

Rationale: The European Quality of Life 5-Dimensions 5-Levels questionnaire (EQ-5D-5L) is a multidimensional patient-reported questionnaire that supports calculation of quality-adjusted life-years. Our objectives were to demonstrate feasibility of use and to calculate the minimum important difference (MID) of the EQ-5D-5L and its associated visual analogue scale (EQ-VAS) in patients with fibrotic interstitial lung disease (ILD).

[Serum calprotectin as new biomarker for disease severity in idiopathic pulmonary fibrosis: a cross-sectional study in two independent cohorts - Machahua C. *BMJ Open Respiratory Research* 2021;8:e000827.](#)

Background: Non-invasive biomarkers for the assessment of disease severity in idiopathic pulmonary fibrosis (IPF) are urgently needed. Calprotectin belongs to the S-100 proteins produced by neutrophils, which likely contribute to IPF pathogenesis. Calprotectin is a well-established biomarker in inflammatory bowel diseases. In this cross-sectional study, we aimed to establish the potential role of calprotectin as a biomarker in IPF. Specifically, we hypothesised that patients with IPF have higher serum calprotectin levels compared with healthy controls, and that calprotectin levels are associated with disease severity.

[Statins: cause of fibrosis or the opposite? Effect of cardiovascular drugs in idiopathic pulmonary fibrosis - Lambert EM. *Respiratory Medicine*, 2021, 176, 106259.](#)

Background and objective: Idiopathic pulmonary fibrosis (IPF) is a progressive and irreversible interstitial lung disease with poor prognosis despite the recent availability of two antifibrotic drugs. Patients are more susceptible to cardiovascular comorbidities. In this study, we aimed to determine the impact of concomitant cardiovascular drugs on disease progression and survival in a modern IPF cohort.

[Transcriptome analysis of IPF fibroblastic foci identifies key pathways involved in fibrogenesis - Guillotin D. *Thorax* 2021;76:73-82.](#)

Introduction: Fibroblastic foci represent the cardinal pathogenic lesion in idiopathic pulmonary fibrosis (IPF) and comprise activated fibroblasts and myofibroblasts, the key effector cells responsible for dysregulated extracellular matrix deposition in multiple fibrotic conditions. The aim of this study was to define the major transcriptional programmes involved in fibrogenesis in IPF by profiling unmanipulated myofibroblasts within fibrotic foci in situ by laser capture microdissection.

[Treatment of systemic sclerosis-associated interstitial lung disease: a work in progress - Oldham JM. *Lancet Respiratory Medicine*, 2021, 9\(1\), pp.5-7.](#)

In 2014, two randomised controlled trials were published showing that nintedanib and pirfenidone can slow lung function decline in patients with idiopathic pulmonary fibrosis, 12 prompting an era of antifibrotic therapy for this devastating disease. Overlapping features between idiopathic pulmonary



fibrosis and other fibrosing interstitial lung diseases (ILDs) naturally led clinicians to wonder whether antifibrotic therapy could effectively treat a broad range of conditions that result in pulmonary fibrosis. The Safety and Efficacy of Nintedanib in Systemic Sclerosis (SENSCIS) trial suggested as much after nintedanib effectively slowed the decline in lung function in patients with systemic sclerosis-associated ILD (SSc-ILD).³ Despite a relatively small treatment effect compared with that reported in studies of idiopathic pulmonary fibrosis, nintedanib was approved for the treatment of SSc-ILD in several countries throughout Asia, North America, and Europe.

What's New in Pulmonary Vascular Disease from UpToDate

[Inhaled treprostinil for interstitial lung disease-related pulmonary hypertension \(January 2021\)](#)

Currently, pulmonary hypertension-specific therapies are of limited value and may be harmful in patients with interstitial lung disease-related pulmonary hypertension (ILD-PH). However, in a recent randomized trial of 326 patients with ILD-PH, 16 weeks of an inhaled prostanoid treprostinil, compared with placebo, was shown to improve exercise capacity (mean difference 31 meters on a six-minute walk), N-terminal pro-brain natriuretic peptide (15 percent reduction versus 46 percent increase), and proportion of patients who deteriorated during the trial (33 versus 23 percent)³³. Adverse effects were mild. These findings are encouraging but further studies are needed before use of inhaled treprostinil for ILD-PH becomes routine.

Obstructive sleep apnoea

Articles

[Sleep apnoea is a risk factor for severe COVID-19](#) - Strausz S. *BMJ Open Respiratory Research* 2021;8:e000845.

Background: Obstructive sleep apnoea (OSA) is associated with higher body mass index (BMI), diabetes, older age and male gender, which are all risk factors for severe COVID-19. We aimed to study if OSA is an independent risk factor for COVID-19 infection or for severe COVID-19.

Pneumonia

Articles

[Pulmonary function and health-related quality of life after COVID-19 pneumonia](#) - Van der Sar - van der Brugge S. *Respiratory Medicine*, 2021, 176, 106272.

Background: The COVID-19 pandemic has led to many cases of pneumonia with extensive lung abnormalities on CT-scans. The consequences of COVID-19 pneumonia on survivors' pulmonary function and quality of life are unknown. The purpose of this study is to examine the impact of COVID-19 pneumonia on pulmonary function, health-related quality of life (HRQoL) and perceived dyspnoea.

[Specific pathogens as predictors of poor long-term prognosis after hospital discharge for community-acquired pneumonia](#) - Akiyama Y. *Respiratory Medicine*, 2021, 176, 106279.



Background: Some studies have reported that long-term prognosis after pneumonia is poor. Our aim was to determine predictors of long-term outcomes with special attention to community-acquired pneumonia (CAP) etiology.

Pneumothorax

Articles

[Outpatient management of primary spontaneous pneumothorax](#) - Jouneau S. *Respiratory Medicine*, 2021, 176, 106240.

The outpatient management of primary spontaneous pneumothorax (PSP) is still debated. The risk of a tension pneumothorax is used to justify active treatment like chest-tube drainage, although outpatient management can reduce both the time in hospital and the cost of treatment. It is also likely to be the patient's choice. This report is a reappraisal of the situations for which outpatient management, by monitoring alone, or using minimally invasive techniques, can be considered.

Pulmonary embolism

Articles

[Age-sex specific pulmonary embolism-related mortality in the USA and Canada, 2000–18: an analysis of the WHO Mortality Database and of the CDC Multiple Cause of Death database](#) - Barco S. *Lancet Respiratory Medicine*, 2021, 9(1), pp.33-42.

Background: Pulmonary embolism (PE)-related mortality is decreasing in Europe. However, time trends in the USA and Canada remain uncertain because the most recent analyses of PE-related mortality were published in the early 2000s.

Respiratory interventions (aspiration, chest drain, drug therapy, mechanical ventilation, oxygen therapy)

Articles

[Modification of a domiciliary ventilator to increase FiO₂: an off-label modification which may be of value in COVID-19](#) - Mebrate Y. *Thorax* 2021;76:83-85.

Although nasal continuous positive airway pressure or non-invasive ventilation is used to manage some patients with acute lung injury due to COVID-19, such patients also demonstrate increased minute ventilation which makes it hard, if the device is used in line with the manufacturer's instructions, to achieve adequate oxygen delivery. In addition, if a hospital contains many such patients, then it is possible that the oxygen requirements will exceed infrastructure capacity. Here we describe a simple modification of two exemplar ventilators normally used for domiciliary ventilation, which substantially increased the fraction of inspired oxygen (FiO₂) delivered.

[Topical antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving mechanical ventilation](#). - Minozzi S. *Cochrane Database of Systematic Reviews* 2021;1:CD000022.

OBJECTIVES: To assess the effect of topical antibiotic regimens (SDD and SOD), given alone or in



combination with systemic antibiotics, to prevent mortality and respiratory infections in patients receiving mechanical ventilation for at least 48 hours in ICUs.

[Turbocharging NIV: how to increase oxygen delivery in home mechanical ventilators](#) - Kaltsakas G. *Thorax* 2021;76:3.

In patients with hypoxaemic respiratory failure, supplement oxygen is added to a non-invasive ventilator to increase the fraction of inspired oxygen (FiO₂). The FiO₂ delivered through these domiciliary, non-critical care ventilators is limited and it is determined by a number of factors, including mode of ventilation, location of the oxygen connection point, intentional and unintentional leak, oxygen flow rate, length of circuit and type of interface.^{1 2} In this issue of the Journal, Mebrate et al³ described a novel adaptation for two commercially available non-invasive ventilators, which increases FiO₂ delivery. The process of increasing oxygen mass in a motor engine is called turbocharging and the approach by Mebrate et al³ can be viewed as turbocharging non-invasive ventilation (NIV). The simple modifications described allowed capture of the gas mixture expelled by the ventilator during expiration so that in the subsequent inspiration the ventilator drew from an oxygen enriched gas mixture and mixed it with oxygen added in the usual manner.

[Use of proton pump inhibitors to treat persistent throat symptoms: multicentre, double blind, randomised, placebo controlled trial.](#) - O'Hara J. *BMJ* 2021;372:m4903.

No evidence was found of benefit from PPI treatment in patients with persistent throat symptoms. RSI scores were similar between the lansoprazole and placebo groups after 16 weeks of treatment and at the 12 month follow-up.

What's New in Critical Care from UpToDate

[High-flow oxygen for nonhypercapnic, hypoxemic respiratory failure \(January 2021\)](#)

The clinical benefit of heated and humidified high-flow oxygen delivered via nasal cannulae (HFNC) is unclear. In a recent meta-analysis of over 2000 individuals with severe nonhypercapnic, hypoxemic respiratory failure (none with COVID-19), HFNC decreased the need for both intubation and escalation of respiratory support, compared with conventional low-flow oxygen systems, but had no impact on mortality, length of stay, or patient dyspnea and comfort¹⁸. In patients with severe nonhypercapnic, hypoxemic respiratory failure, we continue to advocate for HFNC as an effective oxygenation strategy that can help avoid intubation.

[Optimal PEEP level in ventilated patients without ARDS \(January 2021\)](#)

In patients who are mechanically ventilated for conditions other than acute respiratory distress syndrome (ARDS), the optimal initial level of positive end-expiratory pressure (PEEP) is unknown. A recent randomized trial of 980 mostly surgical patients without ARDS reported no difference in any outcome measured (ventilator-free days, oxygenation, need for rescue therapy, or mortality) when a low PEEP



strategy (range 0 to 5 cm H₂O) was compared with a high PEEP strategy (PEEP 8 cm H₂O) 16. We continue to suggest an initial PEEP level of 3 to 5 cm H₂O in patients without ARDS who are mechanically ventilated.

[Oxygenation goals in acute hypoxemic respiratory failure \(January 2021\)](#)

Data suggest a possible increase in mortality among critically ill patients when a liberal oxygenation strategy is targeted compared with a conservative one. In a recent, randomized trial of over 2900 adults with acute hypoxemic respiratory failure, patients managed with a liberal oxygenation strategy (target PaO₂ 90 mmHg), compared with a conservative oxygenation strategy (target PaO₂ 60 mmHg), had similar 90 day mortality, number of ventilator-free days, and adverse effects 11. In patients with acute hypoxemic respiratory failure, we continue to suggest individualized goals for oxygenation, the avoidance of hyperoxia, and, if feasible, a target peripheral arterial saturation between 90 and 96 percent.

Respiratory syncytial virus (RSV)

Articles

[Nebulised ALX-0171 for respiratory syncytial virus lower respiratory tract infection in hospitalised children: a double-blind, randomised, placebo-controlled, phase 2b trial](#) - Cunningham S. *Lancet Respiratory Medicine*, 2021, 9(1), pp.21-32.

Background: Respiratory syncytial virus (RSV) is the most common cause of severe lower respiratory tract infection, with a high global health burden. There are no effective treatments available. ALX-0171 is a novel trivalent Nanobody with antiviral properties against RSV. We aimed to assess the safety and antiviral activity of nebulised ALX-0171 in children admitted to hospital with RSV lower respiratory tract infection.

[TMEM16A/ANO1 calcium-activated chloride channel as a novel target for the treatment of human respiratory syncytial virus infection](#) - Pearson H. *Thorax* 2021;76:64-72.

Introduction: Human respiratory syncytial virus (HRSV) is a common cause of respiratory tract infections (RTIs) globally and is one of the most fatal infectious diseases for infants in developing countries. Of those infected, 25%–40% aged ≤1 year develop severe lower RTIs leading to pneumonia and bronchiolitis, with ~10% requiring hospitalisation. Evidence also suggests that HRSV infection early in life is a major cause of adult asthma. There is no HRSV vaccine, and the only clinically approved treatment is immunoprophylaxis that is expensive and only moderately effective. New anti-HRSV therapeutic strategies are therefore urgently required.

