

Respiratory Bulletin

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General

Articles

[Area under the expiratory flow-volume curve: predicted values by regression and deep learning methods and recommendations for clinical practice](#) - Ioachimescu OC, et al. *BMJ Open Respiratory Research* 2021;8:e000925.

Background: In spirometry, the area under expiratory flow-volume curve (AEX-FV) was found to perform well in diagnosing and stratifying physiologic impairments, potentially lessening the need for complex lung volume testing. Expanding on prior work, this study assesses the accuracy and the utility of several models of estimating AEX-FV based on forced vital capacity (FVC) and several instantaneous flows. These models could be incorporated in regular spirometry reports, especially when actual AEX-FV measurements are not available.

[Bearing witness to the challenges of breathlessness.](#) - Speakman L, Butcher D, Schutz S. *British Journal of Community Nursing* 2021;26(4):162-166.

Key Points: Community respiratory nurse specialists (CRNSs) support patients with complex symptom management throughout what is often a very long disease process; Witnessing the suffering of patients due to breathlessness can cause distress to the nurse, which may inadvertently influence the care given; Bearing witness to distress and vulnerability and caring and the consequent emotional labour are essential components of good nursing care.

[Comparative analysis between available challenge tests in the hyperventilation syndrome](#) - Tiotiu A, et al. *Respiratory Medicine*, 2021, 179, 106329.

Background: The hyperventilation syndrome (HVS) is characterized by somatic/ psychological symptoms due to sustained hypocapnia and respiratory alkalosis without any organic disease.

[Critical care trainees call for pulse oximetry reform](#) - Hidalgo DC, Olusanya O, Harlan E. *Lancet Respiratory Medicine*, 2021, 9(4), e.37.

Oxygen saturation via pulse oximetry is arguably the most relevant vital sign in pulmonary medicine.

Yet, decades of research assessing SpO₂ have consistently shown inconsistencies in its accuracy as an estimation of arterial haemoglobin oxygen saturation in Black patients. In the early 1990s, it was noted that Black patients often have falsely elevated SpO₂ readings, and that using pulse oximetry to target an SpO₂ of 92% in Black patients was associated with inaccurate oximetry readings and substantial hypoxaemia. ¹ Since the 1990s, additional analyses have found similar conclusions. ²³ Most recently, in a 2020 study of the accuracy of pulse oximetry in adult patients receiving supplemental oxygen, occult hypoxaemia was identified more frequently in Black patients compared with White patients. ⁴ Together, these studies show the differential inaccuracy and inconsistency of pulse oximetry in estimating SaO₂ in Black patients, suggesting that such patients might be at higher risk of adverse events due to inaccuracy of existing medical devices. The cumulative harm of inaccurate measurements via pulse oximetry remains



unquantified, but given the wide use of oxygen as a therapeutic intervention it is implausible that systemic hypoxaemia has not caused excess harm.

[Effects of aerobic, resistance, and mixed exercises on quality of life in patients with cancer: a systematic review and meta-analysis.](#) - Fukushima T. *Complementary Therapies in Clinical Practice* 2021;:doi.org/10.1016/j.ctcp.2020.101290.

This systematic review aimed to determine the effects of aerobic, resistance, and mixed exercise on multiple aspects of quality of life in patients with cancer through a meta-analysis. Conclusion: According to exercise type, aerobic and resistance exercises improved global, physical, and role quality of life, whereas aerobic exercise only improved emotional quality of life.

[Geography, generalisability, and susceptibility in clinical trials](#) - Clougherty JE, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.330-332.

Randomised clinical trials (RCTs) are generally considered the highest standard of evidence in medical research, as randomised treatment allocation promotes homogeneity in baseline characteristics between treatment groups, maximising internal validity and reducing both bias and confounding. RCTs, however, often enrol a convenience clinical sample, and can face challenges of external validity if that sample does not represent the full population at risk, or the full range of co-exposures and susceptibility factors likely to be encountered in clinical practice. 123 Many such biases can be geographical in nature; for example, proximity to clinical sites can influence recruitment and retention, 4 which is important because neighbourhoods differ in socioeconomic status and environmental exposures (ie, air pollution), both shown to affect respiratory health 5 and therefore potentially influencing observed treatment efficacy. In this moment, when clinical trials for COVID-19 vaccines are being run with unprecedented expediency to mitigate a virus that has disproportionately impacted minority populations and those with lower socioeconomic status, 6 thoughtful attention to representativeness, generalisability, and spatial co-exposures in RCT populations is of paramount importance.

[Highlights of the 11th International Cough Symposium](#) - Geraldes FO. *Lancet Respiratory Medicine*, 2021, 9(4), ee.40-41.

On Jan 21–22, 2021, clinicians and scientists gathered online for the Eleventh International Virtual Cough Symposium 2021, chaired by Prof Kian Fan Chung (Imperial College London, London, UK), to review and discuss the latest research advances regarding cough in clinical disease, pathophysiological mechanisms, and evolving treatments. Three of the many excellent talks are presented here.

[Inconsistent relationship between depth of sedation and intensive care outcome: systematic review and meta-analysis.](#) - Aitken LM, et al. *Thorax* 2021;:doi: 10.1136/thoraxjnl-2020-216098.

Evidence of benefit from lighter sedation is limited, with inconsistency between observational and randomised studies. Positive effects were mainly limited to low quality evidence from observational studies, which could be attributable to bias and confounding factors.



[Interleukin-6: obstacles to targeting a complex cytokine in critical illness.](#) - McElvaney OJ, et al. *The Lancet Respiratory Medicine* 2021

Review outlines the role of IL-6 in health and disease, describes the approaches to IL-6 inhibition that are currently available, and discuss implications for the future use of treatments such as tocilizumab in the critical care setting.

[Journal club](#) - Khaw CR. *Thorax* 2021;76:423.

[Moving towards a better identification and management of frailty in ICU survivors](#) - Louvaris Z, Langer D. *Thorax* 2021;76:322-323.

Frailty is a geriatric syndrome that is defined as 'a physiologic state of increased vulnerability to stressors due to decreased physiologic reserves, and dysregulation, of multiple physiologic systems'.¹ Frailty syndrome partly overlaps with sarcopenia, the latter encompass states of loss of muscle mass and function related to ageing alone.² Frail patients present with an increased burden of symptoms including muscle weakness, excessive muscle fatigue during daily activities and reduced tolerance to medical and surgical interventions.

[Multiple breath washout \(MBW\) testing using sulfur hexafluoride: reference values and influence of anthropometric parameters](#) - Trinkmann F, et al. *Thorax* 2021;76:380-386.

Background: Multiple breath washout (MBW) using sulfur hexafluoride (SF6) has the potential to reveal ventilation heterogeneity which is frequent in patients with obstructive lung disease and associated small airway dysfunction. However, reference data are scarce for this technique and mostly restricted to younger cohorts. We therefore set out to evaluate the influence of anthropometric parameters on SF6-MBW reference values in pulmonary healthy adults.

Guidelines

[Polyethylene glycol \(PEG\) laxatives and starch-based thickeners: potential interactive effect when mixed, leading to an increased risk of aspiration.](#) - Medicines and Healthcare Products Regulatory Agency (MHRA); 2021.

Drug Safety Update. Addition of a polyethylene glycol (PEG)-based laxative to a liquid that has been thickened with a starch-based thickener may counteract the thickening action, placing patients with dysphagia at a greater risk of aspiration.

Acute respiratory distress syndrome

Articles

[Bearing witness in the time of COVID](#) - Ramkumar M. *Lancet Respiratory Medicine*, 2021, 9(4), pp.347-348.

My patient was an octogenarian with numerous comorbidities. He had now been intubated for 10 days with acute respiratory distress syndrome from COVID-19. He had previously lived in a nursing home and



caught the virus at the facility. On arrival at the hospital, he reversed his previous status of “do not intubate” and agreed to a trial of intubation. As the oncoming intensive care unit (ICU) fellow in the COVID unit, I recognised he had developed multiorgan failure and was not going to leave the ICU, despite our aggressive interventions.

[Nebulised heparin for patients with or at risk of acute respiratory distress syndrome: a multicentre, randomised, double-blind, placebo-controlled phase 3 trial](#) - Dixon B, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.360-372.

Background: Mechanical ventilation in intensive care for 48 h or longer is associated with the acute respiratory distress syndrome (ARDS), which might be present at the time ventilatory support is instituted or develop afterwards, predominantly during the first 5 days. Survivors of prolonged mechanical ventilation and ARDS are at risk of considerably impaired physical function that can persist for years. An early pathogenic mechanism of lung injury in mechanically ventilated, critically ill patients is inflammation-induced pulmonary fibrin deposition, leading to thrombosis of the microvasculature and hyaline membrane formation in the air sacs. The main aim of this study was to determine if nebulised heparin, which targets fibrin deposition, would limit lung injury and thereby accelerate recovery of physical function in patients with or at risk of ARDS.

Acute respiratory failure

Articles

[Frailty subtypes and recovery in older survivors of acute respiratory failure: a pilot study](#) - Baldwin MR, et al. *Thorax* 2021;76:350-359.

Background: Identifying subtypes of acute respiratory failure survivors may facilitate patient selection for post-intensive care unit (ICU) follow-up clinics and trials.

Asthma

Articles

[Essential role of smooth muscle Rac1 in severe asthma-associated airway remodelling](#) - Dilasser F, et al. *Thorax* 2021;76:326-334.

Background: Severe asthma is a chronic lung disease characterised by inflammation, airway hyperresponsiveness (AHR) and airway remodelling. The molecular mechanisms underlying uncontrolled airway smooth muscle cell (aSMC) proliferation involved in pulmonary remodelling are still largely unknown. Small G proteins of the Rho family (RhoA, Rac1 and Cdc42) are key regulators of smooth muscle functions and we recently demonstrated that Rac1 is activated in aSMC from allergic mice. The objective of this study was to assess the role of Rac1 in severe asthma-associated airway remodelling.

[Trajectories of asthma and allergies from 7 years to 53 years and associations with lung function and extrapulmonary comorbidity profiles: a prospective cohort study](#) - Bui DS, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.387-396.



Background: Longitudinal trajectories of asthma and allergies from childhood to adulthood might be differentially associated with lung function and chronic obstructive pulmonary disease (COPD), but associations with extrapulmonary comorbidities have not been well investigated. We aimed to assess these trajectories and examine their associations with lung function outcomes and profiles of comorbidities.

[Using the Medication Adherence Reasons Scale \(MAR-Scale\) in asthma and chronic obstructive pulmonary disease to determine the extent and identify the reasons for non-adherence](#) - Unni EJ, Gupta S, Sternbach N. *Respiratory Medicine*, 2021, 179, 106337.

Introduction: Adherence to medications for asthma and COPD can reduce exacerbation rates, decrease healthcare costs, and improve health-related quality of life. In spite of the advantages to treatment adherence, individuals with asthma and COPD often fail to take medicines as prescribed. The objectives of this study were to determine the extent of non-adherence with asthma and COPD medicines and to describe the reasons for non-adherence in these conditions.

Bronchial diseases

Articles

[Ambient temperature, air pollution and childhood bronchiolitis](#) - Lam HCY, Hajat S. *Thorax* 2021;76:320-321.

Acute bronchiolitis is one of the main causes of lower respiratory infection-related hospitalisations among young children and is often attributed to infection with respiratory syncytial virus (RSV). Seasonality of RSV infection has been reported in different climatic regions, with a higher incidence in winter in temperate regions and in the rainy season in areas closer to the equator.¹ Ambient exposures, such as meteorological factors and air pollutants, that affect host susceptibility, survival of pathogen and transmission may partly drive the seasonality of acute bronchiolitis, but these have been less widely investigated when compared with other common childhood respiratory conditions such as asthma. In subtropical regions, seasonality in acute childhood bronchiolitis has been reported by a number of studies, but few investigated this in relation to environmental exposures.

[Cavity formation and its predictors in noncavitary nodular bronchiectatic Mycobacterium avium complex pulmonary disease](#) - Han DW, et al. *Respiratory Medicine*, 2021, 179, 106340.

Introduction: The temporal dynamics of cavity formation in patients with the noncavitary nodular bronchiectatic (NC-NB) form of Mycobacterium avium complex pulmonary disease (MAC-PD) have not yet been well described. We aimed to investigate the development of new cavities in the NC-NB form of MAC-PD.

[Living with bronchiectasis during the COVID-19 pandemic](#) - Williamson L. *Lancet Respiratory Medicine*, 2021, 9(4), pp.343-344.



When Kimberlee sat on a train as it rattled through the British countryside on her way to Edinburgh, UK, for a weekend away with friends, she wasn't to know that it would be a stranger's advice that would lead to an unexpected diagnosis. At the time, Kimberlee Cole was an active 40-year-old and had suffered with a persistent cough for some time but had taken no notice of it. As the train pulled into a station, a man got up from his seat to get off and came over to Kimberlee; "I think you need to go to the doctor about that cough you've got", he said. She had never seen the man before and has not seen him since. When Kimberlee got back to her hometown in Eastbourne, she took the man's advice and booked an appointment with her general practitioner. A few weeks later, she was diagnosed with idiopathic bronchiectasis.

COPD

Articles

[COPD prevalence in smokers with stable ischemic heart disease: A cross-sectional study in Tunisia](#) - Yangui F, et al. *Respiratory Medicine*, 2021, 179, 106335.

Background: Chronic obstructive pulmonary disease (COPD) and ischemic heart disease (IHD) are common causes of mortality worldwide, with shared risk factors. COPD continues to be largely underdiagnosed and undertreated, especially in patients with IHD.

[Cost-effectiveness of sustained-release morphine for refractory breathlessness in COPD: A randomized clinical trial](#) - Verberkt CA, et al. *Respiratory Medicine*, 2021, 179, 106330.

Background: Chronic breathlessness is a frequent symptom in advanced Chronic Obstructive Pulmonary Disease (COPD) and has major impact on quality of life, daily activities and healthcare utilization. Morphine is used as palliative treatment of chronic breathlessness. The aim is to analyze cost-effectiveness of regular, low-dose morphine in patients with advanced COPD from a healthcare and societal perspective.

[Elevated plasma level of Pentraxin 3 is associated with emphysema and mortality in smokers](#) - Zhang Y, et al. *Thorax* 2021;76:335-342.

Background: Pentraxin 3 (PTX3) influences innate immunity and inflammation, host defence, the complement cascade and angiogenesis. PTX3 expression in lung and blood of subjects with tobacco exposure, and its potential relationship with disease pattern and clinical outcome are poorly understood.

[Emergency department admission and hospitalization for COPD exacerbation and particulate matter short-term exposure in Brescia, a highly polluted town in northern Italy](#) - Pini L, et al. *Respiratory Medicine*, 2021, 179, 106334.

Background: Short-term exposure to high Particulate Matter (PM) concentrations worsens several respiratory conditions.

[Prehospital emergency medical technicians can perform ultrasonography and blood analysis in prehospital evaluation of patients with chronic obstructive pulmonary disease: a feasibility study.](#) - Nadim G, et al. *BMC*



Health Services Research 2021;21(1):290.

In a few selected patients with suspected acute exacerbations of COPD, it was technically and organisationally feasible for EMTs and PMs to perform prehospital POCT-ultrasound and laboratory testing and release the patients following treatment. None of the patients released at the scene requested a secondary ambulance within the first 48 h following the intervention.

[Rare cause of emphysema](#) - Benoit TM, et al. *Thorax* 2021;76:421-422.

A 52-year-old man with chronic obstructive pulmonary disease GOLD 4, group D, and severe, heterogeneous pulmonary emphysema (figure 1) and marked hyperinflation was treated with bronchoscopic lung volume reduction (LVR) using endobronchial valves (EBVs) and, 6 months thereafter, bilateral thoracoscopic lung volume reduction surgery (LVRS), both after multidisciplinary team consensus. The interventions individually resulted in a clear but only short-term success due to rapid progression of emphysema and hyperinflation.

[Structural airway imaging metrics are differentially associated with persistent chronic bronchitis](#) - Bhatt SP, et al. *Thorax* 2021;76:343-349.

Background: Chronic bronchitis (CB) is strongly associated with cigarette smoking, but not all smokers develop CB. We aimed to evaluate whether measures of structural airway disease on CT are differentially associated with CB.

[Using the Medication Adherence Reasons Scale \(MAR-Scale\) in asthma and chronic obstructive pulmonary disease to determine the extent and identify the reasons for non-adherence](#) - Unni EJ, Gupta S, Sternbach N. *Respiratory Medicine*, 2021, 179, 106337.

Introduction: Adherence to medications for asthma and COPD can reduce exacerbation rates, decrease healthcare costs, and improve health-related quality of life. In spite of the advantages to treatment adherence, individuals with asthma and COPD often fail to take medicines as prescribed. The objectives of this study were to determine the extent of non-adherence with asthma and COPD medicines and to describe the reasons for non-adherence in these conditions.

Emphysema

Article

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General

Articles

[Aspergillus isolation in nontuberculous mycobacterial pulmonary disease: Associated with antimycobacterial treatment initiation but not response](#) - Raats D, et al. *Respiratory Medicine*, 2021, 179, 106338.

Purpose: Chronic pulmonary aspergillosis is a serious complication of nontuberculous mycobacterial pulmonary disease (NTM-PD), and diagnosis remains challenging. The present study examined associations between the respiratory isolation of *Aspergillus* and the clinical characteristics and treatment outcomes of patients with NTM-PD.

[Predictors of starting antimicrobial treatment in patients with nontuberculous mycobacterial lung disease in the Italian scenario: A SITA GIOVANI-IRENE promoted web-survey](#) - Lombardi A, et al. *Respiratory Medicine*, 2021, 179, 106341.

The disease burden due to nontuberculous mycobacteria is growing worldwide, consequently to improved diagnostic abilities and an increase in the individuals at risk. Uncertainties exist about the right moment on which start treatment. We investigated the clinical features associated with starting an antimicrobial treatment in patients with nontuberculous mycobacterial lung disease among Italian physicians involved in the field. We found that in real life predictors of starting antimicrobial treatment are quite adherent to international guidelines, with some uncertainties regarding the implication of immunosuppressive drugs.

[Vitamin D supplementation to prevent acute respiratory infections: a systematic review and meta-analysis of aggregate data from randomised controlled trials.](#) - Jolliffe DA, et al. *The Lancet Diabetes & Endocrinology* 2021;:doi.org/10.1016/S2213-8587(21)00051-6.

Review of 46 RCTs (n=75,541) found a lower proportion of participants receiving vitamin D supplementation had acute respiratory tract infections vs placebo (61.3% vs 62.3%, OR 0.92, 95%CI 0.86-0.99). Authors highlight the relevance of these findings to COVID-19 is unknown.

COVID-19

Articles

[α1-Antitrypsin deficiency and the risk of COVID-19: an urgent call to action](#) - Yang C, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.337-339.

The COVID-19 pandemic is a global emergency. Identifying populations who are at risk of severe complications is crucial in developing special measures to prevent or reduce severe illness and mortality in vulnerable patients. 1 Emerging evidence indicates that alpha 1 -proteinase inhibitor might inhibit infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). α1-Antitrypsin also has anticoagulation effects and can protect against inflammation, cell death, and the formation of neutrophil extracellular traps, so this multifunctional protein has been considered as a candidate for COVID-19 treatment. 2



Several clinical trials of alpha 1 -proteinase inhibitor have been initiated. An urgent need exists to address the possibility that patients with α 1-antitrypsin deficiency (AATD) might be at increased risk of SARS-CoV-2 infection and development of severe COVID-19.

[Allocating scarce intensive care resources during the COVID-19 pandemic: practical challenges to theoretical frameworks](#) - Supady A, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.430-434.

The COVID-19 pandemic strained health-care systems throughout the world. For some, available medical resources could not meet the increased demand and rationing was ultimately required. Hospitals and governments often sought to establish triage committees to assist with allocation decisions. However, for institutions operating under crisis standards of care (during times when standards of care must be substantially lowered in the setting of crisis), relying on these committees for rationing decisions was impractical — circumstances were changing too rapidly, occurring in too many diverse locations within hospitals, and the available information for decision making was notably scarce. Furthermore, a utilitarian approach to decision making based on an analysis of outcomes is problematic due to uncertainty regarding outcomes of different therapeutic options. We propose that triage committees could be involved in providing policies and guidance for clinicians to help ensure equity in the application of rationing under crisis standards of care. An approach guided by egalitarian principles, integrated with utilitarian principles, can support physicians at the bedside when they must ration scarce resources.

[Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study.](#) - Aveyard P, et al. *The Lancet Respiratory Medicine* 2021

The risk of severe COVID-19 in people with asthma is relatively small. People with COPD and interstitial lung disease appear to have a modestly increased risk of severe disease, but their risk of death from COVID-19 at the height of the epidemic was mostly far lower than the ordinary risk of death from any cause. Use of inhaled steroids might be associated with a modestly increased risk of severe COVID-19.

[Bearing witness in the time of COVID](#) - Ramkumar M. *Lancet Respiratory Medicine*, 2021, 9(4), pp.347-348.

My patient was an octogenarian with numerous comorbidities. He had now been intubated for 10 days with acute respiratory distress syndrome from COVID-19. He had previously lived in a nursing home and caught the virus at the facility. On arrival at the hospital, he reversed his previous status of “do not intubate” and agreed to a trial of intubation. As the oncoming intensive care unit (ICU) fellow in the COVID unit, I recognised he had developed multiorgan failure and was not going to leave the ICU, despite our aggressive interventions.

[Challenges in the rollout of COVID-19 vaccines worldwide](#) - Burki TB. *Lancet Respiratory Medicine*, 2021, 9(4), ee.42-43.



On Feb 24, 2021, 600 000 doses of the Oxford–AstraZeneca COVID-19 vaccine arrived in Ghana. 2 days later, 500 000 doses of the same vaccine landed in the Ivory Coast. The west African nations are the first countries to receive the product as part of the COVAX initiative, a joint endeavour between WHO, Gavi, and the Coalition for Epidemic Preparedness Innovations, which aims to ensure that the COVID-19 vaccines are equitably distributed around the world. Demand for the vaccines will far exceed supply this year and there are growing concerns that poorer countries will get left behind.

[Characterisation of the first 250 000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data](#) - Ranzani OT, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.407-418.

Background: Most low-income and middle-income countries (LMICs) have little or no data integrated into a national surveillance system to identify characteristics or outcomes of COVID-19 hospital admissions and the impact of the COVID-19 pandemic on their national health systems. We aimed to analyse characteristics of patients admitted to hospital with COVID-19 in Brazil, and to examine the impact of COVID-19 on health-care resources and in-hospital mortality.

[COVID-19 and what comes after?](#) - Hopkinson NS, Jenkins G, Hart N. *Thorax* 2021;76:324-325.

At the end of January 2020, the WHO declared the SARS-CoV-2 outbreak a public health emergency of international concern, its highest level of alarm. Although measures in the UK to reduce spread and 'protect the NHS' did prevent a complete collapse of the acute healthcare system, delay in the implementation of a lockdown until 23 March led to tens of thousands of excess deaths and, by December, more than 220,000 COVID-19 hospital admissions, with effects for many individuals persisting beyond hospital discharge (<https://coronavirus.data.gov.uk/healthcare>).

[COVID-19, immunothrombosis and venous thromboembolism: biological mechanisms](#) - Loo J, Spittle DA, Newnham M. *Thorax* 2021;76:412-420.

Thrombotic events that frequently occur in COVID-19 are predominantly venous thromboemboli (VTE) and are associated with increasing disease severity and worse clinical outcomes. Distinctive microvascular abnormalities in COVID-19 include endothelial inflammation, disruption of intercellular junctions and microthrombi formation. A distinct COVID-19-associated coagulopathy along with increased cytokines and activation of platelets, endothelium and complement occur in COVID-19, which is more frequent with worsening disease severity. This proinflammatory milieu may result in immunothrombosis, a host defence mechanism that can become dysregulated, leading to excess formation of immunologically mediated thrombi which predominantly affect the microvasculature. The haemostatic and immune systems are intricately linked, and multifactorial processes are likely to contribute to VTE and immunothrombosis in COVID-19. This state-of-the-art review will explore the pathobiological mechanisms of immunothrombosis and VTE in COVID-19 focusing on: COVID-19-associated coagulopathy, pathology, endothelial dysfunction and haemostasis, the immune system and thrombosis, genetic associations and additional thrombotic mechanisms. An understanding of the complex interplay between these processes is necessary for developing and assessing how new treatments affect VTE and immunothrombosis in COVID-19.



[COVID-19 in the Caribbean](#) - Burki TK. *Lancet Respiratory Medicine*, 2021, 9(4), e.46.

It had looked as if Barbados might avoid a destructive COVID-19 pandemic. The Caribbean nation, home to around 287 000 people, registered fewer than 400 cases of the disease for the whole of 2020. But January, 2021, saw a surge. By the end of the month, Barbados had registered well over 1000 new cases of COVID-19. On Feb 3, 2021, it went into lockdown. On the same day, Saint Lucia declared a state of emergency. It has confirmed more than three times as many cases of COVID-19 this year as it did last year. Like Barbados, Saint Lucia has imposed a nightly curfew on its 180 000 or so residents. Community transmission of COVID-19 has also been established in other parts of the Caribbean, including Haiti, Jamaica, Saint Vincent and the Grenadines, and Trinidad and Tobago.

[Delayed-onset myocarditis following COVID-19](#) - Bajaj R, et al. *Lancet Respiratory Medicine*, 2021, 9(4), ee.32-34.

A multisystem inflammatory syndrome occurring several weeks after SARS-CoV-2 infection and that can include severe acute heart failure has been reported in children (MIS-C).¹² In adults with acute severe heart failure, we have identified a similar syndrome (MIS-A) and describe presenting characteristics, diagnostic features, and early outcomes. Our data also complement reports of MIS-A.

[Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: a prospective cohort study](#) - Gupta RK, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.349-359.

Background: Prognostic models to predict the risk of clinical deterioration in acute COVID-19 cases are urgently required to inform clinical management decisions.

[Ethics and evidence: learning lessons from pandemic triage](#) - Wilkinson DJC. *Lancet Respiratory Medicine*, 2021, 9(4), pp.328-330.

As the northern hemisphere winter comes to a close, and many are looking forward to what is hopefully the end of the COVID-19 pandemic, there is a need to look back at the lessons to be learned. One crucial ethical question has been how to allocate limited resources. 1 Alexander Supady and colleagues criticise two elements of the triage or rationing guidance offered in the first wave. 2 The authors suggest that practical experience should lead to rejection of the use of triage committees for allocation decisions and rejection of allocation based purely on the so-called utilitarian principles—they focus on preference for patients predicted to have higher survival, although in fact this is only part of a broader utilitarian approach. 3 Supady and colleagues argue that triage committees should be involved in policy and guidance for hospitals but not in individual patient decisions about allocation of resources. They further suggest that triage decisions should be based on both utilitarian and egalitarian principles.

[Extracorporeal membrane oxygenation network organisation and clinical outcomes during the COVID-19 pandemic in Greater Paris, France: a multicentre cohort study.](#) - Lebreton G, et al. *The Lancet Respiratory Medicine* 2021; [https://doi.org/10.1016/S2213-2600\(21\)00096-5](https://doi.org/10.1016/S2213-2600(21)00096-5).



Beyond associations with similar factors to those reported on ECMO for non-COVID-19 ARDS, 90-day survival among ECMO-assisted patients with COVID-19 was strongly associated with a centre's experience in venovenous ECMO during the previous year. Early ECMO management in centres with a high venovenous ECMO case volume should be advocated, by applying centralisation and regulation of ECMO indications, which should also help to prevent a shortage of resources.

[Face masks: all for one and one for all](#) - The Lancet Respiratory Medicine. *Lancet Respiratory Medicine*, 2021, 9(4), p.319.

On March 2, 2021, over a year into the pandemic, Texas Governor Greg Abbott joined 15 other states in the USA and lifted the mask mandate, stating that with vaccines being rolled out and case numbers falling it was time. It was met with grave concern from Federal health officials who feel it is too early to lift restrictions, with case numbers still worryingly high and new, potentially more contagious, variants emerging.

[Face masks in the post-COVID-19 era: a silver lining for the damaged tuberculosis public health response?](#) - Driessche KV, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.340-342.

Tuberculosis is the world's leading infectious cause of death, claiming at least 500 000 more lives than COVID-19 in 2020. 1 The COVID-19 pandemic has irrevocably damaged tuberculosis care and will cause an excess 6 million tuberculosis deaths by 2025. How can tuberculosis control possibly benefit from the varied and flawed public health response to COVID-19?

[Guidelines recommend measures to manage acute and chronic conditions during the COVID-19 pandemic: updated.](#) - BMJ Best Practice; 2021.

Further guidelines have been published to inform the management of patients with coexisting conditions during the COVID-19 pandemic. Updates within the following topics: Patients requiring anticoagulation; Mental health of children and adolescents; Acute kidney injury; Community-acquired pneumonia; Hospital-acquired pneumonia; Learning disability; Non-ST-elevation myocardial infarction (NSTEMI); Palliative care; ST-elevation myocardial infarction (STEMI); Tuberculosis.

[How could we forget?](#) - Ramchandran K. *Lancet Respiratory Medicine*, 2021, 9(4), pp.346-347.

My mother-in-law walked in a rush into my room at 3:13 am and shook me awake. "Your mom is trying to reach you. Derek is worried that Natalie is exhibiting symptoms of COVID." Even in the early blush of sleep—sleep had not come easy that night—I felt the cold rush of fear in my veins. I reached for the phone, over my now awake husband, and made a rushed call to my brother-in-law. "What's happening?", I asked. He explained clearly and deliberately that my sister had woken up in the middle of night with acute shortness of breath and chest tightness. I could hear her in the background saying tightly, "I can't breathe", panic in her voice.

[Identifying patients at risk of post-discharge complications related to COVID-19 infection](#) - Hall J, et al. *Thorax* 2021;76:408-411.



SARS-CoV-2 infection is a multisystem disease with post-discharge sequelae. We report early follow-up data from one UK hospital of the initial 200 hospital inpatients with slow recovery from the condition. At 4 weeks post-discharge, 321/957 survivors (34%) had persistent symptoms. A structured outpatient clinical assessment protocol was designed, and outcomes from the first 200 patients seen 4–6 weeks post-discharge are presented here. In 80/200 (40%), we identified at follow-up a cardiorespiratory cause of breathlessness, including persistent parenchymal abnormality (64 patients), pulmonary embolism (four patients) and cardiac complications (eight patients). These findings occurred both in patients who had intensive care unit (ICU) admissions and those who had been managed on the ward, although patients requiring ICU admissions were more likely to have a significant cardiorespiratory cause found for their breathlessness, risk ratio 2.8 (95% CI 1.5 to 5.1).

[Impact of corticosteroids in hospitalised COVID-19 patients](#) - Ho KS, et al. *BMJ Open Respiratory Research* 2021;8:e000766.

Background: Corticosteroids are a potential therapeutic agent for patients with COVID-19 pneumonia. The RECOVERY (Randomised Trials in COVID-19 Therapy) trial provided data on the mortality benefits of corticosteroids. The study aimed to determine the association between corticosteroid use on mortality and infection rates and to define subgroups who may benefit from corticosteroids in a real-world setting.

[Improving clinical management of COVID-19: the role of prediction models](#) - Wynants L, Sotgiu G. *Lancet Respiratory Medicine*, 2021, 9(4), pp.320-321.

A year after the identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its related disease, COVID-19, in the Chinese province of Hubei, one of the most difficult-to-manage modern health-care crises has unfolded worldwide. WHO declared COVID-19 a pandemic in March, 2020, and the epidemiological severity has since been shown by the high incidence of infections, critical cases, and deaths from the disease and, indirectly, by tragic socioeconomic disruption.

[Improving family access to dying patients during the COVID-19 pandemic](#) - Downar J, Kekewich M. *Lancet Respiratory Medicine*, 2021, 9(4), pp.335-337.

In response to the COVID-19 pandemic, most health-care organisations have implemented policies to restrict visitor access. Although there are exceptions to some of these policies, including limited visiting for patients nearing the end of life, they still have profound effects on the dying and their family members. We are still in the midst of the pandemic, but there are compelling reasons to expand access of family members to their loved ones as they near the end of life, despite the risk of infection.

[‘Long-COVID’: a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19](#) - Mandal S, et al. *Thorax* 2021;76:396-398.



Large numbers of people are being discharged from hospital following COVID-19 without assessment of recovery. In 384 patients (mean age 59.9 years; 62% male) followed a median 54 days post discharge, 53% reported persistent breathlessness, 34% cough and 69% fatigue. 14.6% had depression. In those discharged with elevated biomarkers, 30.1% and 9.5% had persistently elevated d-dimer and C reactive protein, respectively. 38% of chest radiographs remained abnormal with 9% deteriorating. Systematic follow-up after hospitalisation with COVID-19 identifies the trajectory of physical and psychological symptom burden, recovery of blood biomarkers and imaging which could be used to inform the need for rehabilitation and/or further investigation.

[Oxygen supplies and COVID-19 mortality in Africa](#) - Nakkazi E. *Lancet Respiratory Medicine*, 2021, 9(4), e.39.

Many countries are deploying COVID-19 vaccines under temporary authorisations (i.e., emergency use). Medical oxygen is becoming a critical need as the second wave of COVID-19 unfolds in Africa and health-care systems become overwhelmed with patients, the Africa Centres for Disease Control and Prevention (CDC) said. As of Feb 4, 2021, African Union member states reported 3 608 487 cases, accounting for 3.5% of total cases reported globally. 93 071 deaths have been recorded in the region, giving a case fatality rate of 2.6% versus the global average of 2.2%, and accounting for 4% of global deaths, according to the Africa CDC.

[Patient factors and temporal trends associated with COVID-19 in-hospital mortality in England: an observational study using administrative data](#) - Navaratnam AV, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.397-406.

Background: Analysis of the effect of COVID-19 on the complete hospital population in England has been lacking. Our aim was to provide a comprehensive account of all hospitalised patients with COVID-19 in England during the early phase of the pandemic and to identify the factors that influenced mortality as the pandemic evolved.

[Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: results from a prospective UK cohort](#) - Arnold DT, et al. *Thorax* 2021;76:399-401.

The longer-term consequences of SARS-CoV-2 infection are uncertain. Consecutive patients hospitalised with COVID-19 were prospectively recruited to this observational study (n=163). At 8–12 weeks postadmission, survivors were invited to a systematic clinical follow-up. Of 131 participants, 110 attended the follow-up clinic. Most (74%) had persistent symptoms (notably breathlessness and excessive fatigue) and limitations in reported physical ability. However, clinically significant abnormalities in chest radiograph, exercise tests, blood tests and spirometry were less frequent (35%), especially in patients not requiring supplementary oxygen during their acute infection (7%). Results suggest that a holistic approach focusing on rehabilitation and general well-being is paramount.

[Persistent symptoms 1.5–6 months after COVID-19 in non-hospitalised subjects: a population-based cohort study](#) - Stavem K, et al. *Thorax* 2021;76:405-407.



This study assessed symptoms and their determinants 1.5–6 months after symptom onset in non-hospitalised subjects with confirmed COVID-19 until 1 June 2020, in a geographically defined area. We invited 938 subjects; 451 (48%) responded. They reported less symptoms after 1.5–6 months than during COVID-19; median (IQR) 0 (0–2) versus 8 (6–11), respectively ($p < 0.001$); 53% of women and 67% of men were symptom free, while 16% reported dyspnoea, 12% loss/disturbance of smell, and 10% loss/disturbance of taste. In multivariable analysis, having persistent symptoms was associated with the number of comorbidities and number of symptoms during the acute COVID-19 phase.

[A prospective study of 12-week respiratory outcomes in COVID-19-related hospitalisations](#) - Shah AS, et al. *Thorax* 2021;76:402-404.

The long-term respiratory morbidity of COVID-19 remains unclear. We describe the clinical, radiological and pulmonary function abnormalities that persist in previously hospitalised patients assessed 12 weeks after COVID-19 symptom onset, and identify clinical predictors of respiratory outcomes. At least one pulmonary function variable was abnormal in 58% of patients and 88% had abnormal imaging on chest CT. There was strong association between days on oxygen supplementation during the acute phase of COVID-19 and both DLCO-% (diffusion capacity of the lung for carbon monoxide) predicted and total CT score. These findings highlight the need to develop treatment strategies and the importance of long-term respiratory follow-up after hospitalisation for COVID-19.

[SARS-CoV-2 evolution and vaccines: cause for concern?](#) - Williams TC, Burgers WA. *Lancet Respiratory Medicine*, 2021, 9(4), pp.333-335.

In little more than a year, the COVID-19 pandemic has reached every continent, causing 98 million confirmed cases and over 2 million deaths (as of Jan 25, 2021). Equally rapid has been the progress in vaccine development, with clinical trials commencing just months after the initial release of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genome on Jan 10, 2020. At present, a number of vaccines are already licenced or progressing through phase 3 trials. Most use a recombinant spike glycoprotein: either mRNA based (the Moderna and Pfizer–BioNTech vaccines), via an adenovirus vector (the Oxford–AstraZeneca, CanSino, and Johnson & Johnson vaccines), or via injection of the protein itself (the Novavax vaccine). In tandem with rapid vaccine development, widespread whole genome sequencing (WGS) efforts have provided more than 360 000 SARS-CoV-2 sequences on the Global Initiative on Sharing All Influenza Data platform. This sequencing has allowed researchers to track the spread of different lineages globally. Some mutations in the virus appear to provide fitness advantages and facilitate quicker spread of particular lineages, such as the globally dispersed variant with a Asp614Gly spike substitution, 1 and the recently described variant of concern 202012/01 (B.1.1.7) lineage in the UK. 2 A number of studies have yielded insight into the relationship between SARS-CoV-2 genomic variability and the host immune response; in this Comment, we discuss whether such variability has the potential to affect the efficacy of recently developed vaccines.

[SARS-CoV-2 infection and adverse outcomes in users of ACE inhibitors and angiotensin-receptor blockers: a nationwide case-control and cohort analysis](#) - Christiansen CF, et al. *Thorax* 2021;76:370-379.



Objective: To examine the impact of ACE inhibitor (ACE-I)/angiotensin receptor blocker (ARB) use on rate of SARS-CoV-2 infection and adverse outcomes.

[Symptomatic, biochemical and radiographic recovery in patients with COVID-19](#) - Mallia P, et al. *BMJ Open Respiratory Research* 2021;8:e000908.

Background: The symptoms, radiography, biochemistry and healthcare utilisation of patients with COVID-19 following discharge from hospital have not been well described.

[Trends in COVID-19-related in-hospital mortality: lessons learned from nationwide samples](#) - Madahar P, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.322-324.

SARS-CoV-2 infectivity remains widespread across the world, with the resulting disease, COVID-19, causing devastating sequelae. With disease-modifying therapy but no cure, and a long road to developing immunity through vaccination, understanding and identifying risk factors contributing to mortality must remain a priority. In *The Lancet Respiratory Medicine*, two Articles—one from England, 1 the other from Brazil 2 —offer insights into nationwide trends for inpatient mortality due to COVID-19.

[Trial participants' rights after authorisation of COVID-19 vaccines](#) - Dal-Ré R, Orenstein W, Caplan AL. *Lancet Respiratory Medicine*, 2021, 9(4), ee.30-31.

Many countries are deploying COVID-19 vaccines under temporary authorisations (i.e., emergency use authorisation in the USA, conditional approval in the EU, and emergency use listing by WHO). A WHO expert group provided ethical reasons supporting their proposal to maintain as long as possible large placebo-controlled randomised trials. 1 Although gathering long-term (≤ 27 months) safety and efficacy data is scientifically important, it will be impossible to achieve with the original trial designs. Once a vaccine is available, participants who received the placebo must have access to the available vaccine, as do all other citizens.

[A tribute to the gang](#) - Roman J. *Lancet Respiratory Medicine*, 2021, 9(4), pp.345-346.

“There goes my people. I must follow for I am their leader.” Mahatma Gandhi.

Ever since I learned those words, they have stuck with me. They emphasise the concept that great leaders are great because of the people that surround them, because they listen, and because, more often than not, they lead by following. For the past weeks of April, 2020, these words have come to mind every single morning as my faculty, trainees, and staff make themselves known just after 6:30 in the morning. “Good morning boss, 3ICU here. Full, seven COVID patients, and seven on the ventilator.” “Hi boss, 5ICU is almost full; 16 COVID patients and 12 on the ventilator.” “Sir, MTD ICU has two remaining beds. Ten COVID patients, eight on the ventilator.” “Yellow Team here boss. 18 patients, 15 COVID, and seven on high-flow oxygen.”



[When should the UK lift its lockdown?](#) - Kirby T. *Lancet Respiratory Medicine*, 2021, 9(4), ee.44-45.

By any reasonable measure, the UK has been one of the countries hardest hit by the COVID-19 pandemic. As of Feb 15, 2021, there have been more than 117 000 deaths and more than 4 million confirmed infections. The country is in the dark depths of a third national lockdown, which began on Jan 4, 2021, after a new SARS-CoV-2 variant (B1.1.7, also known as the UK or Kent variant) caused infections to soar nationwide. However, some good news has finally arrived. As of Feb 15, the UK has vaccinated more than 15 million people, mostly in vulnerable people aged 70 years and older, as well as health and social care workers. Lockdown, and now the rapid vaccine roll out, have combined to lower the daily death count and the number of patients hospitalised with COVID-19. The UK has now rapidly moved into vaccinating its next priority groups, with plans to vaccinate all adults 50 years and older by April. This would protect people who, prior to vaccination, represented 99% of the deaths and 80% of COVID-related hospitalisations.

[Yemen: Coronavirus in a War Zone](#) - Burki TK. *Lancet Respiratory Medicine*, 2021, 9(4), pp.343.

On average, the Saudi-led coalition bombs Yemen 12 times a day. They have been doing so since 2015. It amounts to more than 20 000 air strikes. The north of Yemen is controlled by the Iran-backed Houthis, who conquered the nation's capital Sana'a in September, 2014. The overthrown government, which Saudi Arabia is fighting to restore, has fled the country. It has established a temporary capital in Aden in southern Yemen, though various militias, including ones affiliated with Al Qaeda and Islamic State, are also vying for control. Caught in between are the people, 3-5 million of whom have been displaced. 2 million Yemeni children are starving.

Influenza

Articles

[Clinical impact of a routine, molecular, point-of-care, test-and-treat strategy for influenza in adults admitted to hospital \(FluPOC\): a multicentre, open-label, randomised controlled trial](#) - Clark TW, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.419-429.

Background: Diagnosis of influenza in patients admitted to hospital is delayed due to long turnaround times with laboratory testing, leading to inappropriate and late antiviral treatment and isolation facility use. Molecular point-of-care tests (mPOCTs) are highly accurate, easy to use, and generate results in less than 1 h, but high-quality evidence for their effect on management and clinical outcomes is needed. The aim of this study was to assess the clinical impact of an mPOCT on influenza detection, antiviral use, infection control measures, and clinical outcomes in adults admitted to hospital with acute respiratory illness.

[Use of point-of-care testing for respiratory viruses in hospital](#) - Hayward AC. *Lancet Respiratory Medicine*, 2021, 9(4), pp.324-326.

In The Lancet Respiratory Medicine , Tristan Clark and colleagues report the results of a randomised controlled trial of point-of-care testing for influenza in patients in two UK hospitals in Hampshire, UK. 1



Before the emergence of COVID-19, influenza was the most important cause of admission to hospital with a respiratory virus. In England, influenza is estimated to have caused an average of 11 300 deaths per year between the 2015–16 and 2019–20 influenza seasons. 2 Influenza often goes undiagnosed in hospital, in part because of an absence of routine testing of patients with respiratory illness in this setting. For example, a study from Canada found that only around a quarter of patients with hospital admissions due to influenza had a laboratory-confirmed diagnosis. 3 Standard PCR-based laboratory tests in hospital typically have a turnaround time of at least 24 h and sometimes longer, so cannot affect initial treatment decisions or early decisions about isolation for patients admitted as an emergency. 4 This long turnaround time might explain, in part, why widespread ordering of influenza tests does not occur in hospital. Given that early antiviral treatment in patients with influenza is more likely to reduce mortality than is later treatment, 5 these missed or delayed diagnoses could contribute to mortality. Data suggest that about 15% of influenza cases in hospital are due to nosocomial transmission, and around 9% of new influenza cases seed ongoing transmission in hospital; influenza outbreaks in hospital are thought to be common but under-recognised. 46 Hence, routine use of rapid diagnostics could contribute substantially to the prevention of influenza and influenza-related mortality among susceptible patients in hospital, but only if the diagnostics change clinical practice through earlier initiation of antivirals and appropriate isolation.

Interstitial lung diseases (pulmonary fibrosis)

Articles

[A comprehensive assessment of environmental exposures and the medical history guides multidisciplinary discussion in interstitial lung disease](#) - Dodia N, et al. *Respiratory Medicine*, 2021, 179, 106333.

Background: Multidisciplinary discussion (MDD) is widely recommended for patients with interstitial lung disease (ILD), but published primary data from MDD has been scarce, and factors influencing MDD other than chest computed tomography (CT) and lung histopathology interpretations have not been well-described.

[Feasibility of cardiopulmonary exercise testing in interstitial lung disease: the PETFIB study](#) - Tomlinson O, et al. *BMJ Open Respiratory Research* 2021;8:e000793.

Introduction: Cardiopulmonary exercise testing (CPET) provides a series of biomarkers, such as peak oxygen uptake, which could assess the development of disease status in interstitial lung disease (ILD). However, despite use in research and clinical settings, the feasibility of CPET in this patient group has yet to be established.

[Idiopathic pulmonary fibrosis: a more common condition than you may think.](#) - Tremayne P, Clark SJ. *British Journal of Nursing* 2021;30(6):359–366.

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive incurable lung disease that affects a significant amount of people in the UK. Many health professionals have a limited understanding of IPF, which can result in a delayed diagnosis and inadequate care for individuals and their families. This article aims to provide an overview of IPF and help to enhance health professionals' understanding of the disease, thus contributing towards improving the care that IPF sufferers receive. This article provides a definition of IPF and explores its pathophysiology. It discusses the causes and risk factors for developing the condition, examines how IPF is diagnosed and details the treatment options available for IPF patients.



Pleural effusion

Articles

[The role of nitric oxide in pleural disease](#) - Kotsiou OS, Gourgoulianis KI, Zarogiannis SG. *Respiratory Medicine*, 2021, 179, 106350.

Nitric oxide (NO) regulates various physiological and pathophysiological functions in the lungs. However, there is much less information about the effects of NO in the pleura. The present review aimed to explore the available evidence regarding the role of NO in pleural disease. NO, has a double-edged role in the pleural cavity. It is an essential signalling molecule mediating various physiological cell functions such as lymphatic drainage of the serous cavities, the immune response to intracellular multiplication of pathogens, and downregulation of neutrophil migration, but also induces genocytotoxic and mutagenic effects when present in excess. NO is implicated in the pathogenesis of asbestos-related or exudative pleural disease and mesothelioma. From a clinical point of view, the fraction of exhaled NO has been suggested as a potential non-invasive tool for the diagnosis of benign asbestos-related disorders. Under experimental conditions, NO-mimetics were found to attenuate hypoxia-induced therapy resistance in mesothelioma. Similarly, hybrid agents consisting of an NO donor coupled with a parent anti-inflammatory drug showed an enhancement of the anti-inflammatory activity of anti-inflammatory drugs. However, given the paucity of research work performed over the last years in this area, further research should be undertaken to establish reliable conclusions with respect to the feasibility of determining or targeting the NO signalling pathway for pleural disease diagnosis and therapeutic management.

Pneumonia

Articles

[Empiric antibiotics for community-acquired pneumonia in adult patients: a systematic review and a network meta-analysis](#). - Montes-Andujar L, et al. *Thorax* 2021

For cure rate, ceftaroline and piperacilone are the options with the highest probability of being the best (HPBB). However, for mortality rate, the options are ceftriaxone plus levofloxacin, ertapenem and amikacin plus clarithromycin. It seems necessary to conduct an RCT that compares treatments with the HPBB for each event (cure or mortality).

Pulmonary embolism

Articles

[Pulmonary embolism and thrombocytopenia following ChAdOx1 vaccination](#). - Muster V, et al. *The Lancet* 2021; [https://doi.org/10.1016/S0140-6736\(21\)00871-0](https://doi.org/10.1016/S0140-6736(21)00871-0).

A 51-year-old woman attended our emergency department with a 3-day history of dyspnoea, fatigue, and cough; 11 days earlier she had the ChAdOx1 nCoV-19 vaccination. Activation of the coagulation system producing thromboses in the context of thrombocytopenia and hypofibrinogenaemia—as occurred in our patient—is similar to heparin-induced thrombocytopenia and to that seen in critically ill COVID-19 patients.

Pulmonary hypertension

Articles

[Depression, anxiety and psychological distress in patients with pulmonary hypertension: a mixed-methods study](#) - Takita Y, et al. *BMJ Open Respiratory Research* 2021;8:e000876.



Introduction: Pulmonary hypertension (PH) is a chronic and progressive disease. While prognoses have improved, PH patients still experience side effects and activity restrictions. Accordingly, the key questions asked by this study are 'How many PH patients have depression/anxiety symptoms?' and 'Is there a difference in the symptoms and distress factors between pulmonary arterial hypertension (PAH) and chronic thromboembolic PH (CTEPH) patients, and how are they experiencing distress?'

[Exercise training for pulmonary hypertension: a systematic review and meta-analysis of randomized controlled trials.](#) - Albanaqi AL, Rahimi GRM, Smart NA. *Biological Research for Nursing* 2020

Pulmonary hypertension (PH) is a chronic disease with a notable health burden; regular exercise may improve specific health outcome measures. Conclusion: This meta-analysis demonstrates exercise training has a beneficial effect on fitness, walking performance, and self-reported QoL in PH patients.

[Intravenous prostacyclin-analogue therapy in pulmonary arterial hypertension – A review of the past, present and future](#) - Stubb B, et al. *Respiratory Medicine*, 2021, 179, 106336.

Therapy with intravenous prostacyclin analogues in patients with pulmonary arterial hypertension (PAH) has been established for decades and is an integral component of the current guidelines for the treatment of pulmonary hypertension. Initially, these drugs were infused by external pump systems via tunnelled right atrial catheters with the need for cooling and frequent exchange of drug reservoirs. Associated complications included, among others, catheter-related infections. More recently, fully implantable pump systems have been developed with drug reservoirs that are filled transcutaneously, allowing intervals between refills of several weeks. This technique results in a low rate of infections. Epoprostenol, iloprost and treprostinil have all been used intravenously in PAH, but titration, dosing and dose escalation in long-term therapy are not standardized. Intravenous prostacyclin analogues are still under-used, despite available data suggesting that early and broad application of these therapies as part of risk-oriented, guideline-directed combination therapy for patients with PAH may lead to a survival benefit. This review provides a detailed overview of the drugs, infusion systems and dosing strategies used for intravenous therapy in patients with PAH.

[Pulmonary Hypertension.](#) - Poch D, Mandel J. *Annals of Internal Medicine* 2021

In the Clinic' review. Pulmonary hypertension is often a feature of advanced common diseases, such as chronic obstructive pulmonary disease and left heart disease, and treatment is focused primarily on the underlying disease. More rarely, pulmonary hypertension results from chronic organized thromboemboli or a primary vasculopathy. The former requires evaluation for surgical intervention, and the latter is treated with advanced medical therapies.

[Sotatercept for the Treatment of Pulmonary Arterial Hypertension.](#) - Humbert M, et al. *National England Journal of Medicine* 2021;:1204-1215.

Treatment with sotatercept resulted in a reduction in pulmonary vascular resistance in patients receiving background therapy for pulmonary arterial hypertension.



What's New in Pulmonary Vascular Disease from UpToDate

[Sotatercept for pulmonary arterial hypertension \(April 2021\)](#)

Sotatercept is an investigational ligand trap for transforming growth factor-beta that was recently studied in patients with pulmonary arterial hypertension (PAH). In patients with PAH who were receiving standard therapy, the addition of sotatercept subcutaneously every three weeks improved pulmonary vascular resistance, exercise tolerance, and brain natriuretic peptide levels compared with placebo 32. Common adverse effects included headache, diarrhea, and peripheral edema; in addition, thrombocytopenia and increased hemoglobin were also noted. Further efficacy and safety studies are required before sotatercept can be routinely be used to treat patients with PAH.

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

Articles

[High oxygen flow rates with the UCL Ventura CPAP device](#) - Kempley S, Reeves J, Wilkins A. *Lancet Respiratory Medicine*, 2021, 9(4), e.35.

We wish to alert users of the University College London (UCL) Ventura continuous positive airway pressure (CPAP) device that, under certain conditions, it might draw high flows of 116 L/min from oxygen supplies.

[High oxygen flow rates with the UCL Ventura CPAP device – Authors' reply](#) - Singer M, et al. *Lancet Respiratory Medicine*, 2021, 9(4), e.36.

We thank Stephen Kempley and colleagues for highlighting the potential for high oxygen flow rates if the University College London (UCL) Ventura continuous positive airway pressure (CPAP) device 1 is either disconnected from a patient or there is a mask leak. On a bench test, they measured an outflow of 116 L/min when the device was delivering 97% oxygen with fully opened valves. These settings would not actually be tolerated by a patient, although we fully acknowledge—and highlighted in our clinical use guide 2—the importance of not wasting oxygen by avoiding leaks, excessive flow rates, and leaving the device switched on if not in patient use.

[Nebulised heparin for patients on ventilation: implications for COVID-19 pneumonia](#) - Ball L, Schultz MJ, Pelosi P. *Lancet Respiratory Medicine*, 2021, 9(4), pp.321-322.

Pulmonary coagulopathy is intrinsic to pulmonary inflammation, occurs in patients with different types of lung injury, and is one of the potential mediators of harm caused by mechanical ventilation. 1 Locally applied anticoagulants, such as heparin, could affect bronchoalveolar haemostasis, including fibrin deposition in the alveoli and possibly also in the vascular compartment. 1 Although several clinical studies have shown that nebulised heparin mitigates both onset and progression of lung injury, one meta-analysis 2 did not confirm any benefit.



[Should we ration extracorporeal membrane oxygenation during the COVID-19 pandemic?](#) - Supady A, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.326-328.

The COVID-19 pandemic has raised challenging questions about the rationing of intensive care unit (ICU) beds, mechanical ventilators, and extracorporeal membrane oxygenation (ECMO). 1 Experts have recommended that ECMO be curtailed or even halted when patient numbers surpass an ill-defined threshold, wherein demand for critical care outstrips available resources. 2 It might seem counterintuitive to reduce the provision of ECMO at precisely the time when demand increases, yet it could be deemed necessary. In this Comment, we argue that a decision to curtail or continue ECMO should be deliberate and reasoned, such that alternatives are actively rejected.

[Systematic early versus late mobilization or standard early mobilization in mechanically ventilated adult ICU patients: systematic review and meta-analysis.](#) - Menges D, et al. *Critical Care* 2021

This review aimed to determine the effectiveness of systematic early mobilization in improving muscle strength and physical function in mechanically ventilated intensive care unit (ICU) patients. Conclusion: The evidence regarding a benefit of systematic early mobilization remained inconclusive. However, our findings indicate that the larger the difference in the timing between the intervention and the comparator, the more likely an RCT is to find a benefit for early mobilization.

[The use of oxygen hoods in patients failing on conventional high-flow oxygen delivery systems, the effects on oxygenation, mechanical ventilation and mortality rates in hypoxic patients with COVID-19. A Prospective Controlled Cohort Study](#) - Dayya D, et al. *Respiratory Medicine*, 2021, 179, 106312.

Introduction: Efforts to meet increased oxygen demands in COVID-19 patients are a priority in averting mechanical ventilation (MV), associated with high mortality approaching 76.4–97.2%. Novel methods of oxygen delivery could mitigate that risk. Oxygen hoods/helmets may improve: O₂-saturation (SaO₂), reduce in-hospital mechanical ventilation and mortality rates, and reduce length of hospitalization in hypoxic Covid-19 patients failing on conventional high-flow oxygen delivery systems.

What's New in Critical Care from UpToDate

[Serious adverse events during emergency intubation \(April 2021\)](#)

Serious adverse events are common during emergency intubation. In a prospective, international study of approximately 3000 consecutive intubations in critically ill adults in the intensive care unit, emergency department, or ward, 45 percent had at least one major adverse event, most commonly cardiovascular instability [12]. Cardiac arrest occurred in 3 percent of patients, with an associated 50 percent mortality. Use of ketamine or etomidate for induction was associated with a lower risk of cardiovascular instability compared with propofol or midazolam.

[Weaning from mechanical ventilation in the ICU \(April 2021\)](#) - For ICU patients on mechanical ventilation for longer than 24 hours, there is no standard weaning practice. A recent international study of 1868



mechanically ventilated patients in 142 intensive care units (ICUs) in six geographic regions (Canada, United States, United Kingdom, Europe, India, Australia/New Zealand) best illustrates the variation in practice including wide ranges reported in written directives to screen for a spontaneous breathing trial (SBT; 5 to 83 percent) as well as the performance of and mode used to conduct an SBT [11]. ICUs in the United States were associated with greater odds of having SBT directives and using an SBT with low-level pressure support compared with ICUs in other regions. Compared with direct extubation, individuals undergoing SBT had higher ICU mortality (10 versus 5 percent), longer median duration of mechanical ventilation (4 versus 3 days), and longer median length of ICU stay (11 versus 8 days) although greater severity of illness likely explains these results given previous trials demonstrating that SBT is efficient, safe, and effective. The wide variation in weaning practices highlighted in this study indicates that further research is needed to determine the best approach and to support its wider implementation.

Tuberculosis

Articles

[The long term effect of pulmonary tuberculosis on income and employment in a low income, urban setting](#) - Meghji J, et al. *Thorax* 2021;76:387-395.

Background: Mitigating the socioeconomic impact of tuberculosis (TB) is key to the WHO End TB Strategy. However, little known about socioeconomic well-being beyond TB-treatment completion. In this mixed-methods study, we describe socioeconomic outcomes after TB-disease in urban Blantyre, Malawi, and explore pathways and barriers to financial recovery.

[Safety and immunogenicity of the adjunct therapeutic vaccine ID93 + GLA-SE in adults who have completed treatment for tuberculosis: a randomised, double-blind, placebo-controlled, phase 2a trial](#) - Day TA, et al. *Lancet Respiratory Medicine*, 2021, 9(4), pp.373-386.

Background: A therapeutic vaccine that prevents recurrent tuberculosis would be a major advance in the development of shorter treatment regimens. We aimed to assess the safety and immunogenicity of the ID93 + GLA-SE vaccine at various doses and injection schedules in patients with previously treated tuberculosis.

