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Early View

Review

ERS International Congress 2021: highlights from the Respiratory Infections Assembly

Oliver W. Meldrum, Kylie B. R. Belchamber, Kiarina D. Chichirelo-Konstantynovych, Katie L. Horton, Tetyana V. Konstantynovych, Merete B. Long, Melissa J. McDonnell, Lidia Perea, Alberto L. Garcia-Basteiro, Michael R. Loebinger, Raquel Duarte, Holly R. Keir

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ERS International Congress 2021: highlights from the Respiratory Infections Assembly

Oliver W. Meldrum[1], Kylie BR. Belchamber[2], Kiarina D. Chichirelo-Konstantynovych[3], Katie L. Horton[4,5], Tetyana V. Konstantynovych[3], Merete B. Long[6], Melissa J. McDonnell[7], Lidia Perea[8], Alberto L. Garcia-Basteiro[9-10], Michael R. Loebinger[11-12], Raquel Duarte[13-15], Holly R. Keir[6]

1) Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore
2) Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK
3) National Pirogov Memorial Medical University, Vinnytsya, Ukraine
4) Primary Ciliary Dyskinesia Centre, NIHR Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, Southampton, UK
5) University of Southampton Faculty of Medicine, Academic Unit of Clinical and Experimental Medicine, Southampton, UK
6) Division of Molecular and Clinical Medicine, Medical School, University of Dundee, Dundee , UK
7) Galway University Hospitals and National University of Ireland (NUIG, Ireland
8) IDIBAPS, Hospital Clínic, Barcelona, Spain
9) ISGlobal, Hospital Clínic - Universitat de Barcelona, Barcelona, Spain
10) Centro de Investigação em Saude de Manhiça, Maputo, Mozambique.
11) Host Defence Unit, Royal Brompton Hospital, London, UK
12) National Heart and Lung Institute, Imperial College, London, UK
13) Pulmonology Unit, Centro Hospitalar de Vila Nova de Gaia/Espinho EPE, Vila Nova de Gaia, Portugal
14) ICBAS-UP, Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto
15) ISPUP, Instituto de Saúde Pública da Universidade do Porto

Abstract

The European Respiratory Society Annual Congress 2021 took place virtually for the second year running due to the coronavirus pandemic. The congress programme featured more than 400 sessions and 3000 abstract presentations, covering the entire respiratory science and medicine field. In this article, Early Career Members of the Respiratory Infections Assembly summarise a selection of sessions across a broad range of topics, including presentations on bronchiectasis, non-tuberculosis mycobacteria, tuberculosis, cystic fibrosis and COVID-19.

Introduction

Due to the on-going coronavirus pandemic, the 2021 European Respiratory Society (ERS) Annual Congress was held virtually for a second consecutive year. As the largest scientific and medical conference for respiratory research, ERS 2021 provides an excellent opportunity to hear about new and exciting developments in the field. This article shares some highlights from the Respiratory Infections Assembly across a broad range of clinical and scientific topics, randomized controlled trials, laboratory-based research and new guidelines.

State-of-the-Art Session: Respiratory Infections

Ranging across pneumonia, bronchiectasis, tuberculosis (TB), and antibiotic resistance, this session focused on the key challenges and future perspectives in respiratory infection for improving patient outcomes, with personalised medicine identified as a significant theme throughout.

First, noting the failure of many clinical trials in bronchiectasis to meet their specified end-points (1), Amelia Shoemark (Dundee, UK) talked about advances in disease profiling and endotyping to guide personalised therapy, presenting recent work from the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC)-BRIDGE study indicating that mucociliary dysfunction in bronchiectasis may be rescued by targeting the specific type of airway infection and inflammation. Promising examples of personalised strategies in bronchiectasis included utilising 16S rRNA sequencing rather than sputum cultures for integrative microbiomics and therapy selection (2), as well as a recent phase-2 clinical trial of the neutrophil protease inhibitor Brensocatib (3), and treatment of bronchiectasis patients with eosinophilia using inhaled corticosteroids (4).

Transitioning to antimicrobial resistance (AMR) in chronic respiratory infection, Michal Schteinberg (Haifa, Israel) next highlighted the prevalence of AMR, which may emerge due to factors including increased macrolide use (5) and long-term antibiotic treatment (6), which correlate with poor clinical outcomes, including reduced lung function and increased exacerbation frequency across respiratory diseases (7). Schteinberg summarised that better detection and monitoring of AMR genes is required where traditional culture methods fall short, utilising techniques like metagenomics, and AMR prevention should be targeted through antibiotic stewardship and alternative therapeutics focused on individual drivers of disease exacerbations. Finally, treatments should be developed for multiple drug resistant infections, including optimised dosing strategies (8) and non-antimicrobials (9).

With the 6-month antibiotic treatment protocol for TB initially established three decades ago, Cecile Magis-Escurra (Nijmegen, Netherlands) next described current drug research for TB and possibilities to shorten treatment regimens to tackle issues including non-compliance and emergence of drug resistant mycobacteria (10). Magis-Escurra highlighted the results of a phase-3 clinical trial using a rifapentine-based regimen containing moxifloxacin, which demonstrated an effective reduction in treatment time to 4 months (11). Together with the establishment of the Unite4TB consortium,

there is a worldwide drive to accelerate drug development to obtain shorter, safe and effective treatments.

Finally, with the development of new guidelines for severe pneumonia currently in progress, Michael S. Niederman (New York, USA) initially emphasised current recommendations including combined beta-lactam and macrolides, rather than quinolones, as the back-bone of treatment for all(12). Consideration of individual pathogen and resistance, which may be targeted by novel antimicrobial agents, as well as inflammation in these patients is important(13). Of further consideration, patients with documented viral infection may still require antibiotic treatment, including in severe COVID-19, where biomarkers have a key role in clinical decision-making.

Precision Medicine for Airway Infections

James D. Chalmers (Dundee, UK), having been awarded the Cournand Lecture Award, presented an exciting overview of the inflammatory process in bronchiectasis and the shift in therapy goals. Despite progress over the last 10 years, there remain obstacles to overcome in furthering our understanding of the pathophysiology and targeted treatment of bronchiectasis. Translational studies and meta-analyses on prophylactic inhaled and oral macrolide antibiotics show that antibiotics can reverse the inflammatory process in bronchiectasis (14, 15). Yet, many patients worldwide are still not being offered proactive preventative care, which is integral to limiting disease progression. Recent studies have demonstrated different inflammatory phenotypes in bronchiectasis with studies in neutrophil elastase showing marked associations with exacerbations, lung function decline and *Pseudomonas* status in bronchiectasis (16, 17). Two-thirds of bronchiectasis patients have raised neutrophil elastase levels at baseline, hence the development of direct novel anti-inflammatory inhibitors such as DPP-1 are potential game-changers in the management of bronchiectasis (3). A landmark randomised controlled trial of Dipeptidyl Peptidase 1 (DPP1)-inhibition demonstrated a significantly prolonged time to first exacerbation and a reduction in inflammation compared to placebo (3). Drawing parallels with asthma, Chalmers highlighted how guidelines have evolved from focusing on bronchodilators that treat symptoms only to targeting the underlying pathophysiology to suppress inflammation and reduce exacerbations (18). A similar approach is needed in bronchiectasis, as large-scale genetic studies could potentially change the treatment landscape. Although we are steadily bridging the gap and moving towards precision medicine, work remains to transform the management of bronchiectasis.

Sanjay Chotirmall (Singapore, Singapore) followed with a discussion on the latest methods and findings of the bacteriome, mycobiome and virome across the spectrum of chronic lung disease, focusing on treatable and targetable traits. Data in bronchiectasis has shown that a loss of microbiome diversity during exacerbations is associated with a higher exacerbation frequency and higher mortality risk demonstrating that the microbiome has prognostic implications for patients (19, 20). A similar high-risk mycobiome signature and its prognostic role has been demonstrated in COPD.(21) Chotirmall discussed network analysis integration, functionality differences and cross-talk between microbial organisms interacting together in bronchiectasis (2). The microbiome's functional effects are important in recognising the need to consider microbes and their associated networks to stratify patients.

Holly R. Keir (Dundee, UK) presented a talk on the role of endotyping to profile the clinical heterogeneity, define mechanisms and identify clinically relevant biomarkers in bronchiectasis and COPD. In bronchiectasis, neutrophil extracellular traps (NETs) have been identified as a key marker of disease severity and treatment response(22). NETs were associated with worse quality of life,

future risk of hospital admission, and higher mortality. Short-term intravenous antibiotic treatment successfully reduced sputum NETs in bronchiectasis. 12-month prophylactic azithromycin was associated with a significant reduction in NETs in both bronchiectasis and asthma(23). Previous studies of neutrophil antagonists have shown conflicting results due to reduced neutrophil recruitment to the lung resulting in an increase in exacerbations (24-27). However, new therapies such as DPP-1inhibition may reduce neutrophil inflammation without dampening vital neutrophil functions such as recruitment and killing (3). It is hoped that endotyping may identify patients most likely to benefit from different types of therapies.

Nicolas Roche (Paris, France) presented the novel ERS living guidelines on the management of hospitalised patients with COVID-19. Given the critical situation worldwide in the midst of a pandemic, the ERS produced consensus-based guidance followed by evidence-based clinical practice guidelines. These were developed following a fast-track process in a six-month timeframe, despite the constant flow of new evidence. The Task Force conducted a systematic literature review of the latest available data to develop the guidelines, which offer a review of the most notable potential therapies for treating COVID-19 and recommendations on their effectiveness and suitability (28).

The session finished with an overview of patient perspectives from Marta Almagro (Barcelona, Spain) from the bronchiectasis patient advisory group from the European Lung Foundation (ELF) and EMBARC patient registry, highlighting the importance of patient involvement in research, clinical guidelines and educational activities. Patients and carers are the key stakeholders in every aspect of medical care, yet direct involvement of patients in clinical guidelines, clinical research studies or research consortia is relatively uncommon. Genuine patient engagement in the design, conduct, implementation and dissemination of clinical research and clinical guidelines can greatly enhance the quality and impact of such projects.

Respiratory infection and bronchiectasis outcomes

This session highlighted the challenges of long-term clinical outcomes in bronchiectasis, respiratory infection, and multiplex polymerase chain reaction (PCR) in clinical decision-making. Andrei Darie (Basel, Switzerland) opened the session by outlining the suitability of multiplex PCR from bronchoalveolar lavage combined with an antibiotic stewardship program to decrease the duration of inappropriate antibiotic therapy in hospitalised patients with severe pneumonia (29). In an outpatient setting, Benjamin Seeliger (Hannover, Germany) applied multiplex-PCR to reduce the time to tailored antibiotic therapy in lower respiratory tract infections of lung transplant recipients. These speakers highlighted rapid and sensitive molecular testing to improve clinical decision-making in both critical care and outpatient settings.

Three speakers used the EMBARC registry; Stefano Aliberti (Milan, Italy) identified potentially preventable or treatable risk factors in bronchiectasis deterioration, including exacerbation frequency, co-morbidities, lung function impairment, and *Pseudomonas aeruginosa* infection (30). Pieter Goeminne (Bornem, Belgium) expanded this perspective by using the EMBARC registry across 32 counties to identify changes in the quality of care following the 2017 ERS guidelines (31). Overall, there was an improvement in adherence to recommendations, with significant variation in the standard of care between counties. Following the introduction, the most significant improvement in adherence concerned the frequency of aetiological testing, sputum culture while stable for *P. aeruginosa*-focused eradication and antibiotic use in patients with frequent exacerbations. Raja Dhar (Kolkata, India) compared the EMBARC and Indian bronchiectasis registries to identify that bronchiectasis patients in India were generally younger, more likely to be male, and had greater

disease severity (32). He reported a higher mortality rate in India than Europe after adjusting for confounders, with the highest rate of exacerbations observed in patients with COPD, tuberculosis, and post-infection bronchiectasis.

Adrian Ceccato (Barcelona, Spain) transitioned the session towards respiratory infection, showing a reduction in mortality from corticosteroid treatment was limited to severely ill patients with community-acquired pneumonia (CAP) and high inflammatory response (33). Eleni Papakonstantinou (Basel, Switzerland) showed how serum heparan sulphate levels were significantly higher in moderate and severe acute exacerbations of COPD (AECOPD) than in stable conditions. The probability of infections at AECOPD is associated with the aetiology of infection, highlighting the opportunity to predict the development of AECOPD (34). Julie Worrell (Glasgow, UK) reported long-term transcriptional changes of immune-related genes in lung epithelial and stromal cells from acute influenza A viral infection. An immune cell-derived molecule, SpiB, was involved in upregulated antigen presentation of inflammatory chemokines and cytokines in lung epithelial cells adjacent to areas of inflammation following viral infection. Eihab Bedawi (Oxford, UK) assessed the performance of the RAPID score, a model for predicting mortality in patients with pleural infection, to predict outcomes in patients treated with intrapleural enzyme therapy. The RAPID score was highly predictive of mortality and length of hospital stay, highlighting the suitability of future avenues to assess targeted treatment.

ALERT: Bronchiectasis and COVID

The ALERT sessions showcased recent clinical trials in the treatment of bronchiectasis and COVID-19. Currently, there are no approved inhaled treatments available for patients with bronchiectasis (35). Charles Haworth (Cambridge, UK) opened the session with results from the phase-3 PROMIS-I study that examined the effect of colistimethate sodium (CMS) powder delivered twice-daily through the I-neb® AAD system on the frequency of pulmonary exacerbations in patients with bronchiectasis chronically infected with *P. aeruginosa*. The CMS I-neb system allowed delivery of a precise and reproducible dose to provide a significant increase in time-to-first exacerbation, 39% reduction in exacerbation, and 59% reduction in severe exacerbations over the 12-month study.

The phase-2 WILLOW study involved administering brensocatib, an oral DPP-1-inhibitor responsible for activating neutrophil serine proteases (3). Carlos Fernandez (Bridgewater, USA) reported that treatment with 10 to 25-mg brensocatib over 24-weeks showed a 40% decrease in exacerbation risk and 50% decrease in severe exacerbations in patients with bronchiectasis and a history of frequent exacerbations compared to placebo. The decreased exacerbation frequency provided new evidence for neutrophil serine proteases in the pathophysiology of bronchiectasis. While reduced neutrophil recruitment previously showed an increased risk of infection (36, 37), this trial also showed clinical benefit without compromising antibacterial defence. However, being a short-term trial, these findings should not be clinically directive.

The phase-2 STOIC trial, presented by Sanjay Ramakrishnan (Oxford, UK), described an open-label trial of budesonide, an inhaled glucocorticoid, as a treatment in adults within seven days of the onset of COVID-19 compared to usual care (38). Multiple early reports suggested that patients with chronic respiratory disease were under-represented in hospital admissions with COVID-19 (39, 40). It was hypothesised that this underrepresentation might be due to the widespread use of inhaled glucocorticoids, indicated by their use in chronic asthma and COPD to reduce exacerbations, which were often associated with viral infection. When administered to patients with early COVID-19 (not to be confused with mild COVID-19), the use of inhaled budesonide reduced the likelihood of

requiring urgent care, emergency department consultation, or hospitalisation with a quicker resolution of fever in patients (determined using either questionnaire or self-reporting).

The Recovery-Respiratory Support trial evaluated the effectiveness and safety of non-invasive respiratory strategies, such as continuous positive airway pressure (CPAP) and high-flow nasal oxygenation (HFNO), as an alternative to conventional oxygen therapy in hospitalised patients with confirmed or suspected COVID-19 acute respiratory failure(41). Bronwen Connolly (London, UK) outlined how these alternative strategies provide a potential strategy for avoiding invasive mechanical ventilation, especially if hospital intensive care units become overwhelmed. They showed that CPAP effectively reduced transition to tracheal intubation or mortality within 30-days, while HFNO provided no benefit.

How science conquered COVID-19: from big platform trials to patients

This session aimed to describe key studies into COVID-19 infection, including patient phenotyping, risk stratification and results of the international RECOVERY and REMAP-CAP trials.

Charlotte Summers (Cambridge, UK) opened the session by describing COVID-19 phenotypes from multicentre studies, including the ISARIC study (42). This study identified clusters of COVID-19 patients in the acute phase of the disease presenting with distinct gastrointestinal, blood disorders, pain-related symptoms, and typical symptoms (fever and cough). These highlighted distinct presentations of COVID-19, with clear multi-organ involvement. Patients were stratified into three main groups in the post-acute phase of the disease: resolution, long COVID or persistent critical illness (43). Identification and management strategies for each phenotype need to be considered to help treat these patients.

Results of the NIHR funded RECOVERY-RS trial were presented by Gavin D. Perkins (Birmingham, UK), who highlighted the need for international consensus on the use of non-invasive oxygen therapy in COVID-19 (44, 45). The RECOVERY-RS trial showed that while HFNO did not perform better than conventional oxygen therapy, CPAP decreased the need for mechanical ventilation at 30 days, and reduced intensive care admission compared to conventional oxygen therapy (41).

Utilising both expert and patient opinions to develop research prioritisation strategies for long COVID research was discussed next by Luke Daines. Patient priorities for new research into COVID-19 included reducing the burden of long COVID and finding new treatments. Using this novel research prioritization method, expert ideas can be tailored to provide answers to questions that matter most to patients (46).

Finally, the advantages of performing platform trials during a pandemic were highlighted by Lennie Derde (Utrecht, Netherlands). Platform trials utilise a shared control group and allow treatments to be dropped when proved inferior while the remaining trial continues (47). In COVID-19, RECOVERY-RS and REMAP-CAP utilised this method to show that corticosteroids and IL-6 receptor antagonists tocilizumab and sarilumab show clinical benefit in COVID-19 (48, 49), while other drugs including hydroxychloroquine, remdesivir and lopinavir were not beneficial (50). Platform trials are flexible and embed clinical practice and research together – which is of great value when rapid results are needed, such as in COVID-19.

Vaccination and infections

The exacerbation of chronic respiratory pathology has been complicated by the coronavirus pandemic process and due to poor vaccination levels worldwide. Even modern vaccination guidelines cannot be implemented properly to reduce the increasing incidence and mortality levels. This ERS/Industry joint session was devoted to discussing problematic questions and exploring new approaches for improving disease outcomes through immunization.

Leif E. Sander (Berlin, Germany) gave an overview of available vaccines against COVID-19, their mechanisms of immune stimulation and key effects. mRNA vaccines had shown higher efficacy levels (51) by significantly reducing hospitalisation in fully-vaccinated individuals (52). Higher coronavirus incidence among individuals after Vaxzevria usage comparatively to other vaccines was confirmed in all age groups in Germany. There was no difference between vaccines according to local reaction induction, however ChAdOx1-nCoV19 was associated with a significantly higher risk of systemic reactions (53). Studies indicated that the Delta-strain of the virus led to reduced immunity in elderly patients 6 month after vaccination (54) and was accompanied by low vaccine effectiveness (increased incidence, hospitalization and mortality rates) (55). As a conclusion Sander highlighted the importance of the third booster dosage for such risk groups with an aim to reduce breakthrough infection (56).

Tobias Welte (Hannover, Germany) focused on influenza emergency due to the high risk of hospital, post-hospital mortality (57) and cardiovascular complications (58). Welte discussed improvements in vaccination against influenza, including high dosage vaccine, new adjuvants and intradermal applications.

Jamie Correira de Sousa (Porto, Portugal) provided views on vaccination of adults against whooping cough. He named lack of booster vaccination, diagnostic difficulties, and poor immune response in adults as the main factors of severe chronic lung pathology in at-risk groups. Despite differences in views on pertussis vaccination in guidelines worldwide, Tdap is recommended for adult vaccination but it still meets barriers that prevent reaching a high vaccine uptake (59). Although there are a number of obstacles that currently limit an extensive roll-out of pertussis vaccination, there are a number of factors which may improve pertussis vaccination rates including harmonization of recommendations for adult vaccination schedules, identification of at-risk groups who can benefit more from a booster vaccine, educational interventions and new vaccine development.

Respiratory medicine meets other disciplines: emerging data of respiratory tract infections

A joint ERS/ESCMID session “Results from the current European Clinical Research Initiative on Antimicrobial resistance and emerging Infectious Diseases (ECRAID)” was devoted to discussing new diagnostic approaches to managing respiratory infections at a glance, including antibiotic usage optimization.

Maurizio Sanguinetti (Rome, Italy) observed the potential impact and relevance of diagnostics in managing respiratory tract infections from COVID-19 to hospital-acquired pneumonia. He announced a significant role of lower tract respiratory infections (LRI) in world mortality, especially due to *Streptococcus pneumonia*, *Staphylococcus aureus*, *P. aeruginosa*, which have become more

crucial during the coronavirus pandemic (60-62). The effective targeting and confirmation of CAP can be performed by well-prepared sputum samples cultures, RT-PCR and detection of viral etiology by rapid tests, which may also reduce overuse of antibiotics (63-65).

Maarten Postma (Groningen, Netherlands) and Evelina Taconelli (Verona, Italy) drew the audiences' attention to Value-Dx, a newly approved network tool for building an evidence-based algorithm in CAP management. Both speakers showed C-reactive protein as a rapid biomarker to guide antibiotic prescribing decision (66). Systematic reviews and meta-analyses showed that combination with laboratory, imagining and microbiological POCT could improve the accuracy of diagnosis and reduce inappropriate antibiotic prescriptions. Modelling forecasts for economic analyses of LRI identified demographical and geographical signs which could influence clinical and laboratory relative risks during overwhelming antibiotic treatment (67), increase the costs for general practitioners' service and increased adverse events due to AMR. However, the clinical network algorithm needs prospective validation to prove its effectiveness in clinical practice.

AMR was widely discussed in the presentation "Are antimicrobials still the future of respiratory infection therapy?" given by Stefano Aliberti (Milan, Italy). Several studies emphasized host-directed therapy, targeting host immune and inflammatory pathways to enhance immune response that could improve treatment outcomes in patients with infectious diseases. This has been confirmed by research on corticosteroids usage in COVID-19 pneumonia (48), macrolides in bronchiectasis (68), monoclonal antibody-based therapies (69-71). Recombinant human plasma has also shown promise in improving survival and attenuating lung injury (72, 73) with low propensity for resistance (74).

Adult Cystic Fibrosis

Covering topics from bench to bedside, this session focussed on the modulation, inflammation, microbiome and scoring systems for transplantation in adult cystic fibrosis patients.

Respiratory *P. aeruginosa* infections affect the majority of adult cystic fibrosis patients(75). Respiratory viral infections are associated with cystic fibrosis pulmonary exacerbations(76, 77), with human rhinovirus being the most frequently isolated respiratory virus from cystic fibrosis airways(76, 78). Adrian Endres (Frankfurt, Germany) applied a quantitative proteomics approach assessing the host-pathogen proteomes in an *in-vitro* model of *P. aeruginosa*-human rhinovirus co-infection in cystic fibrosis bronchial epithelial cells. Bacterial-viral co-infections induced host proteomic signatures distinct from single infections with either pathogen alone. Endres demonstrated that *P. aeruginosa* can modulate the inflammatory response to rhinovirus infection through proteolytic degradation of IL-6.

The three main families of unconventional T Cells; MAIT, *i*NKT and γδT have been poorly studied in the context of cystic fibrosis. Pauline Tossan (Tours, France) reported prospective data on circulating unconventional T cells from 62 patients from the Cystic Fibrosis Centre of Tours, France and 49 healthy donors. Detected by flow cytometry, there was an increased level of γδT cells in the blood of cystic fibrosis patients, whereas the levels were decreased for *i*NKT and MAIT cells. The expression of PD-1 and CD-69 was generally higher on unconventional T cell surfaces in cystic fibrosis patients, indicating that these sub-types displayed a highly activated phenotype and played a role in regulating the inflammatory response during cystic fibrosis.

Silvia Bresci (Florence, Italy) presented data from a multi-centre, prospective observational study determining the clinical impact of *Aspergillus* spp infection in 164 cystic fibrosis patients across 3 Italian centres. The project highlighted problems with classifying patients with *Aspergillus* infection and a need for further studies to evaluate the usefulness of *Aspergillus* galactomannan detection in sputum.

Dirk Westhölter (Essen, Germany) outlined immunophenotyping data revealing that circulating regulatory T cells are impaired in patients with cystic fibrosis and chronic *P. aeruginosa* infection(79). Patients with non-cystic fibrosis bronchiectasis showed higher levels of systemic of CD39 regulatory T cells (stable under inflammatory conditions) compared to cystic fibrosis. Higher lymphocyte populations were not altered by CFTR modulators indicating the need to re-evaluate the emergence of highly effective CFTR modulators anti-inflammatory therapies.

The current gold standard for lung transplantation referral can miss patients with atypical disease progression while simultaneously suggesting referral of patients with very stable lung disease(80, 81). In a single UK centre, Kavita Dave (Milton, Keynes, UK) showed that a 2-year mortality prediction model developed by Stanojevic *et al*.,(82) appropriately identified many patients for lung transplantation but could not identify 58% of those who had died. Better prediction models are needed given the variable course of disease progression.

Advances in treatment and management of tuberculosis and non-tuberculosis mycobacterium disease

In this oral session, 10 presenters gave 5-minute presentations on their work in TB and nontuberculous mycobacterial disease (NTM).

Kerri Viney (Geneva, Switzerland), from the World Health Organisation's (WHO) Global TB Programme, gave an update on definitions of drug resistance in TB (83). In June 2020, the WHO released updated guidelines on the treatment of extensively multi-drug resistant (XDR)-TB, encompassing three effective all-oral treatment regimens which are suitable for all patients with XDR-TB. These guidelines were updated in 2021 to reflect changes in the definition of pre-XDR and XDR TB. Olivia Conroy (London, UK) presented the results of a systematic review on implementing TB control strategies in Europe (84, 85) to highlight the need for clarity and acceptance of TB guidelines among healthcare workers while ensuring services are appropriately equipped.

Natalia Yatskevich (Minsk, Belarus) discussed the impact of WHO guidelines on treatment regimes in Belarus in a prospective study of a shorter standardized regimen in 222 patients. A modified shorter all-oral rifampicin-resistant (RR-TB) regime improved patient outcomes compared to those with extensive disease burden who had lower chances of eradication. In a study comparing the pharmacokinetics of a 'child-friendly' fixed-dose combination of rifampin and isoniazid and separate tables in 22 children with pulmonary tuberculosis, Aziza Pakhlavonoav (Moscow, Russia) concluded that there was no statistically significant difference in pharmacokinetic parameters between the treatments. Sudarsan Pothal (Puri, India) presented the results of a randomized control trial of metformin and anti-TB drug (ATD) versus ATD alone in 150 non-diabetic TB patients. The addition of metformin to the standard regimen showed increased sputum conversion and decreased prevalence of rifampicin resistance.

Three speakers discussed the impacts of TB in relation to various populations. Elena G Llorente (Barakaldo, Spain) presented the evolution and impact of tuberculosis treatment of elderly patients

as part of a multi-centre observational study conducted in Spain. Elderly patients were more likely to have extra-pulmonary and disseminated presentations, higher mortality and more hospital admissions. Previous studies have identified TB has a risk factor for COPD, in addition to being a differential diagnosis (86). Nuno Faria (Porto, Portugal) evaluated the impact of TB history on mortality and severe exacerbation outcomes in a retrospective study of 322 patients with COPD. A previous diagnosis of TB was significantly more likely to occur in GOLD Group C or D patients. There was a non-significant increase in severe exacerbations and mortality in COPD patients with a history of TB. Jee Whang Kim (Leicester, UK) discussed the impact of COVID-19 on TB infection rates during the COVID-19 pandemic in Leicester, UK. There was a marked reduction in active TB cases, especially during lockdown periods. Patients diagnosed during lockdown were significantly younger and smear-positive, suggesting under-detection of older and smear-negative cases. Kim advised that easing lockdown restrictions are likely to result in a resurgence of TB cases. With changes in healthcare, increased vigilance is needed to sustain effective TB control, including ensuring appropriate diagnosis in older people and smear negative cases.

Two presenters discussed treatment options in patients with NTM infection. Rachel Thomson (Brisbane, Australia) presented the results of OPTIMA, an open-label pilot trial of inhaled GM-CSF in antibiotic-resistant NTM infections with 21.8% of patients treated with at least 24-weeks of inhaled GM-CSF achieved sputum conversion, however this was not considered clinically significant. There was no improvement in clinical endpoints with a small reduction in bacterial load observed. Noeul Kang (Seoul, Republic of Korea) discussed clinical differences and risk factors associated with treatment failure following adjunctive surgical resection in patients with NTM. Post-operative complications can range from 20-30% after surgical resection in NTM disease (87-89). In this study, it was recommended that patients with NTM disease who achieve culture conversation more than 6 months after treatment initiation are closely monitored for recurrence and that patients with *Mycobacterium abscessus* infection had higher recurrence rates than patients with *Mycobacterium avium* infection.

New insights into nontuberculous mycobacteria disease: from diagnosis to treatment

Nontuberculous mycobacteria (NTM) can produce pulmonary and extrapulmonary disease in patients with and without prior comorbidities. This session aimed to improve awareness and knowledge of current epidemiology, diagnosis, and treatment options.

Marc Lipman (London, UK) gave an overview of changing NTM epidemiology. The global picture of NTM disease is that it is increasing over time, particularly in older populations(90, 91). Potential explanations for this increase are multifactorial, including modifications in the pathogen, the host, the environment and society(92). The future of NTM is likely to be more complex, there is an urgent need for applying robust national and international surveys to improve the identification of modifiable host and environmental risk factors(93).

Emmanuelle Cambau (Paris, France) reviewed the most important challenges of diagnosing NTM. To solve the diagnostic dilemma with pulmonary TB, NTM diagnosis needs both clinical expertise on NTM infection and lab expertise in NTM clinical microbiology(94). Furthermore, knowledge of the preferred microbiological tools for NTM identification, such as molecular identification and mass spectrometry MALDI-ToF, is required. Finally, antimicrobial susceptibility testing is mandatory in *M. abscessus*, relapses or recurrences, and other NTM with an unknown wild-type pattern (95). Cambu highlighted the new subcommittee in EUCAST (European Committee on antimicrobial susceptibility testing) focused on developing breakpoints and methods for antimycobacterial susceptibility testing.

Jakko van Ingen (Nijmegen, Netherlands) and Michael Loebinger (London, UK) discussed two case reviews showing the benefit and the limitations of the guideline-based therapies for NTM(95, 96). J. van Ingen presented a *M. kansasii* infection case successfully treated following the current recommendations. However, Loebinger presented a complicated *M. avium* complex infection case to expose the significant unmet needs, such as refractory disease, drug intolerance, relapse/reinfection, fungal co-infection, and mortality, that a significant number of patients still have despite following the guidelines. The talk concluded by emphasising the relevance of the guidelines and the importance of their limitations.

Claire Andrejak (Amiens, France) summarised the novel NTM treatments and approaches to solve the drug toxicity issue(97). Although there are promising *in-vitro* and *ex-vivo* data for the use of Clofazimine(98-100), Tedizolid(101, 102), Rifabutin(103), Beta-lactams(104), Bedaquilin and Delamanide(105, 106), and inhaled antibiotics(107-110), there is currently little evidence in multi-centre and randomized studies. Andrejak also reviewed the unresolved questions for the novel approach of bacteriophage-based therapy. In the era of antibiotic resistance, there is a need to improve the phage therapy outcome based on limiting the development of phage-resistant bacteria and combining phages with antibiotics to enhance their permeability.

Conclusion

The ERS Respiratory Infections Assembly encompasses a broad range of clinical and scientific topics in areas such as bronchiectasis, NTM, cystic fibrosis, COVID-19 and TB. The authors present a selection of presentations from numerous high-quality respiratory infection sessions at the 2021 ERS Congress. We hope this offers the reader the chance to be informed of some of the latest developments from Assembly 10 and encourage future participation in the ERS Congress.

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