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ERS International Congress 2022: highlights from the Respiratory Infections Assembly

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Shareable abstract (@ERSpublications)

This highlights article provides valuable insight into the latest scientific data and updates in clinical practice from Assembly 10 (Respiratory Infections) at #ERSCongress2022 <https://bit.ly/3iowTc8>

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Abstract

The European Respiratory Society International Congress took place both in person, in Barcelona, Spain, and online in 2022. The congress welcomed over 19 000 attendees on this hybrid platform, bringing together exciting updates in respiratory science and medicine from around the world. In this article, Early Career Members of the Respiratory Infections Assembly (Assembly 10) summarise a selection of sessions across a broad range of topics, including presentations on bronchiectasis, nontuberculous mycobacteria, tuberculosis, cystic fibrosis and coronavirus disease 2019.

Introduction

The annual European Respiratory Society (ERS) Congress is the largest scientific and medical conference for respiratory research, bringing together experts from across the world. The congress provides an excellent opportunity to hear about new and exciting developments in the field of respiratory medicine from a broad range of clinical and scientific topics. Assembly 10 is the Respiratory Infections Assembly, which covers all pulmonary and respiratory infection issues, with a strong focus on pneumonia, antibiotic resistance, bronchiectasis, tuberculosis, nontuberculous mycobacteria and adult cystic fibrosis. It can be challenging to keep up to date with the wide variety of sessions on offer at the ERS Congress, so in this article, Early Career Members share some of the highlights of sessions from Assembly 10.

Group 10.01: respiratory infections and bronchiectasis

Bronchiectasis: how recent advances in research can support personalised medicine in practice

This Hot Topics session on bronchiectasis consisted of a phenomenal line-up of speakers presenting the latest clinical, translational and technological innovations in bronchiectasis, outlining further areas for research.

Sanjay Chotirmall (Singapore, Singapore) presented an exciting overview of the latest methods and findings of the microbiome in the pathophysiology and clinical management of bronchiectasis, focusing on lessons learned. Data in bronchiectasis have shown that a reduction in microbiome diversity during exacerbations is associated with a higher exacerbation frequency and mortality, demonstrating that the



microbiome has prognostic implications for patients [1]. S. Chotirmall provided several enlightening examples of network analysis integration with visual demonstrations of the differences in functionality and cross-talk between microbial organisms interacting together at baseline, during and after exacerbation, and before and after treatment in bronchiectasis, suggesting that microbial “interactions” with other microbes, host and environment, may potentially be more important than microbial identity [2]. Understanding the microbiome may also help deepen our understanding of infection, antibiotic treatment and the development of antimicrobial resistance. It may also assist in unwrapping the pathophysiology of overlap diseases represented by different microbiota profiles [3]. The functional effects of the microbiome are hugely important in providing recognition of considering microbes and their associated networks to stratify patients in the era of precision medicine [4]. The gut–lung microbiome reveals interorgan relationships suggesting that a disrupted gut–lung microbiome may be associated with worse bronchiectasis disease [5]. Advances in the analysis of next-generation sequencing may be used to further complement and build upon our current understanding of the microbiology and microbiome in bronchiectasis, providing improved patient stratification with prognostic significance [6].

James Chalmers (Dundee, UK) followed with an elegant discussion on the inflammatory process in bronchiectasis and the shift in the goal of finding appropriate anti-inflammatory therapies to prevent disease progression. While highlighting significant breakthroughs that have transformed our understanding of bronchiectasis over the last 10 years, not least through EMBARC (the European Bronchiectasis Registry) and numerous epidemiological studies identifying predictors of poor outcomes, there are still deficits in our understanding of the pathophysiology and targeted treatment of bronchiectasis. Studies have demonstrated different inflammatory phenotypes in bronchiectasis, predominantly neutrophil and neutrophil extracellular trap phenotypes, supporting the concept of targeting neutrophilic inflammation with existing and novel therapies [7, 8]. The development of direct novel anti-inflammatory therapies, such as dipeptidyl peptidase-1 (DPP1) inhibition, are potential game-changers in the management of bronchiectasis. A landmark randomised controlled trial with 6 months of the DPP1 inhibitor brensocatic demonstrated a significantly prolonged time to first exacerbation at both 10- and 25-mg doses compared to placebo, and a dramatic reduction in inflammation across the board [9]. More recently, eosinophilic bronchiectasis has been described as a specific entity, affecting approximately 20% of bronchiectasis patients. After accounting for infection status, raised blood eosinophil counts were shown to be associated with shortened time to exacerbation [10]. Inflammation underlies much of the disease heterogeneity in bronchiectasis and precision medicine for inflammatory endotypes will be key for future management of the disease.

Harm Tiddens (Rotterdam, the Netherlands) discussed how technological innovation can support physicians making decisions in bronchiectasis. A systematic review of the diagnosis and quantification of bronchiectasis using computed tomography (CT) or magnetic resonance imaging in 2020 showed that the most often used criterion for bronchiectasis was an inner airway/artery ratio ≥ 1.0 (42%); however, no validation studies for this cut-off value were found. 42 different scoring methods were described to quantify bronchiectasis. Clearly, validated and age-specific cut-off values are needed to better diagnose and quantify bronchiectasis in future studies [11]. H. Tiddens has been at the forefront of technological innovations in bronchiectasis, showing that fully automatic methods of assessing airway/artery analysis and airway tapering may provide a roadmap for artificial intelligence in bronchiectasis, potentially replacing time-consuming manual annotations and visual scoring methods to quantify abnormal widening, thickening and tapering of airways in bronchiectasis [12, 13].

Finally, Stefano Aliberti (Milan, Italy) gave a clinical overview of what is needed to build a multidisciplinary team for the optimal management of bronchiectasis in any geographical location, highlighting the importance of multidisciplinary work to optimise patient outcomes. The session finished with a lively discussion among the audience and panel members summarising how we can apply this information in a clinical setting and what may optimise patient outcomes in the future.

Bronchiectasis

Micheál Mac Aogáin (Dublin, Ireland) opened the bronchiectasis session by highlighting the need to move beyond the traditional single pathogen-centric model towards a more holistic and integrated understanding of the complex interaction between microbial and host environment, to potentially further biomarker discovery and pave the way for more personalised therapy [14]. He showed the role of antimicrobial resistance, whereby airway resistance genes are associated with time to next exacerbation and decline in lung function. A clinical assessment of *Neisseria* species followed this; this a typical upper airway commensal was shown to weaken barrier integrity and promote inflammation in primary epithelial cells, possessing distinct transcriptomic and metabololipidomic signatures in the mouse lung [4]. Finally, he outlined how dysregulation of the bacteriome and mycobioime within the gut–lung axis resulted in a

“high-risk” patient group. This group was characterised by increased airway *Pseudomonas* accompanied by gastrointestinal *Bacteroides* and *Saccharomyces*, resulting in more severe clinical and radiological bronchiectasis, including increased exacerbations.

Nicole Lapinel (New Orleans, LA, USA) and Timothy Aksamit (Rochester, MN, USA) presented work from the US Bronchiectasis and NTM Research Registry to provide better insight into the diagnosis, pathophysiology aetiologies and management approaches of bronchiectasis. N. Lapinel highlighted that patients with increased frequency of exacerbations experience the most significant disease burden related to deterioration in lung function, reduced quality of life, increased medication use and morbidity. T. Aksamit complemented this work by showing how exacerbation frequency strongly predicts future exacerbations over 4 years. Robert Stockley (Birmingham, UK) presented a late-breaking abstract from the EARCO registry, reporting the presence of α_1 -antitrypsin deficiency mutation and its association with bronchiectasis, emphysema and lung function using high-resolution CT. Wojciech Dolliver (Boston, MA, USA) highlighted the use of the ROSE (radiology, obstruction, symptoms, exposure) criteria to stratify patients from the COPDGene cohort to show how the coexistence of COPD and bronchiectasis results in a worse prognosis, with a higher risk of future exacerbations and death than in those with COPD only, bronchiectasis only or neither condition.

Lidia Perea Soriano (Barcelona, Spain) showed patients with elevated interleukin-1 β had significantly reduced airway cilia beat angle and amplitude, associated with thicker, more purulent mucus and more severe disease. Amelia Shoemark (Dundee, UK) followed by highlighting the underdiagnosis of pathogenic or likely pathogenic variants in motile ciliopathy genes in patients with bronchiectasis. Jamie Cheong (London, UK) showed how digital tablet-based devices can be used to monitor the development of ototoxicity (hearing or balance problems due to a medicine) following treatment with intravenous aminoglycosides for chronic suppurative lung disease.

What's new in COVID?

This session aimed to describe the novel results in coronavirus disease 2019 (COVID-19) infection, starting with airway remodelling in the COVID-19 lung. Vincent Geudens (Leuven, Belgium) highlighted the need to characterise airway changes in COVID-19. He showed increased airway visibility in large and small airways with high heterogeneity, demonstrating that COVID-19 remodels the large and small airway structures, similar to idiopathic pulmonary fibrosis. Regarding airway microbiota, Sabine Stadler (Lausanne, Switzerland) presented novel profiles associated with total lung capacity (TLC) after severe COVID-19. A distinct oropharyngeal microbiota was found in patients with impaired TLC, diffusing capacity of the lungs for carbon monoxide and desaturation between 3 and 12 months after infection. Two speakers presented results from clinical trials. Adrian R. Martineau (London, UK) discussed a phase 3 randomised controlled trial (CORONAVIT) that found vitamin D had no effect on preventing COVID-19 or another acute respiratory infection. Andreas Tiezt (Basel, Switzerland) showed encouraging results from the EMPATHY phase 2 trial, which found faster clinical recovery with ensivibep, a designed ankyrin repeat protein [15], in patients with mild-to-moderate COVID-19.

Identifying patients at risk of deterioration is a key research priority in COVID-19. Ana Motos Galera (Barcelona, Spain) discussed results from the CIBERESUCICOVID study showing the effect of corticosteroid treatment on reducing 90-day and in-hospital mortality. Chloe Hughes (Dundee, UK) showed that changes in the peripheral blood transcriptome regarding neutrophil activity, coagulation and interferon signalling are related to an increased risk of major cardiac events after hospitalisation with COVID-19. Regarding novel risk factors, Elien De Waele (Sint-Niklaas, Belgium) talked about the impact of biological ageing in terms of telomere length on clinical severity in hospitalised patients. Luke Daines (Edinburgh, UK) discussed risk factors, including social deprivation, pre-existing depression and anxiety, and age <70 years, associated with persistent breathlessness after hospitalisation. Alexander Holm (Gothenburg, Sweden) showed early data suggesting the longstanding effects on the lipid composition of the pulmonary surfactant in COVID-19 patients treated in intensive care.

The session finished with a late-breaking abstract regarding the real-world effectiveness of sotrovimab for the early treatment of COVID-19, presented by Carolina Reyes (San Francisco, CA, USA). Sotrovimab was associated with reduced risk of 30-day all-cause hospitalisation and facility-reported mortality, and its clinical effectiveness persisted during the Delta and early Omicron waves.

Pneumonia

In this session, presenters discussed patient care, cell and molecular biology and epidemiology of pneumonia and COVID-19. Four speakers looked at associations between COVID-19 and pneumonia. Yan

Hui Giam (Dundee, UK) opened the session by discussing the role of AMP-activated protein kinase (AMPK) activity in COVID-19 and pneumonia. She showed associations between elevated resistin and disease severity but found that neither AMPK nor Nrf2 activity influenced pneumonia severity. Athanasios Konstantinidis (Ioannina, Greece) analysed the major differences between COVID-19 pneumonia and community-acquired pneumonia (CAP). COVID-19 pneumonia was complicated more frequently with longer hospital stay and need for mechanical ventilation and intensive care unit (ICU) admission, despite having less severe pneumonia presentation than patients with CAP. Kseniia Bielsludtseva (Dnipropetrovsk, Ukraine) discussed the role of plasminogen activator inhibitor (PAI)-1 in COVID-19 and bacterial pneumonia. PAI-1 was significantly increased in COVID-19, indicating disruption of the fibrinolysis system.

Updates on therapies and treatment tools were presented by five speakers. Chuan Yen Sun (Taipei, Taiwan) demonstrated that cefoperazone-sulbactam and piperacillin-tazobactam prolonged infusion had similar clinical efficacy and outcomes in treating pneumonia, taking into account the resolution of symptoms, clinical effectiveness and in-hospital mortality, and improvement of clinical, radiological and laboratory tests. Kasia Kiarostami (Barcelona, Spain) compared the efficacy of systemic treatment with telavancin or linezolid on the endotracheal tube (ETT)-biofilm methicillin-resistant *Staphylococcus aureus* (MRSA) load and thickness in a model of mechanically ventilated piglets with MRSA pneumonia reproducing ICU conditions, finding that telavancin had increased activity against ETT MRSA biofilm. Daniel Lozano-Rojas (Leicester, UK) discussed a new method of mechanically predicting pneumonia mortality level with the help of routinely collected data. This method avoids complex sampling frameworks, while complementing existing pneumonia guidelines. Taiki Furukawa (Nagoya, Japan) presented his work on an artificial intelligence algorithm for mortality and long-term hospitalisation prediction, using integrated electronic health records for hospitalised with pneumonia. Maria Hein Hegelund (Hillerød, Denmark) showed that undernourished patients admitted with CAP have an increased mortality risk at 30 days, highlighting the importance of in-hospital nutritional screening.

Finally, Luiz Alberto Ruiz Iturriaga (Barakaldo, Spain) showed that in hospitalised patients with pneumococcal pneumonia, severe lymphopenia was a strong predictor of severity and 30-day mortality, and urged early stratification of these patients. Shaun Thein (Birmingham, UK) presented work showing that neutrophils from patients with CAP are immature and have reduced migratory capabilities.

Respiratory infections: state of the art

This State of the Art session covered recent developments in pneumonia, understanding the lung microbiome, vaccination in chronic lung disease and tuberculosis.

Leopoldo Segal (New York, NY, USA) opened the session by discussing evidence that microbial functions contribute to host inflammatory damage and pathogen susceptibility. Specific airway microbiome composition, particularly enrichment of oral commensal taxa, has been associated with worse prognoses in both non-COVID-19 [16] and COVID-19 pneumonia [17]. L. Segal proposed that the microbiome may modulate immune responses to infection. Supporting this, he presented data showing that enrichment for oral commensal bacteria in the lungs of patients with tuberculosis and HIV was associated with impaired interferon responses [18, 19]. Relationships between the microbiome and host responses are complex, and the need for further research was highlighted.

On the topic of diagnostic advancements in tuberculosis, Daniela Maria Cirillo (Milan, Italy) described the negative impact of the COVID-19 pandemic, widening the gap between numbers of people diagnosed and those falling ill with tuberculosis, and a need for improved tests for disease diagnosis, treatment monitoring and outcome prediction. The positive predictive value of many predictive tools is currently deemed insufficient [20], but amongst the most promising is a three-gene assay utilising finger-prick blood sampling [21]. For monitoring active disease and treatment, in particular, in multidrug-resistant (MDR) tuberculosis, comprehensive, validated, time- and cost-effective susceptibility testing is needed utilising targets identified from whole-genome sequencing (WGS) studies [22, 23]; the World Health Organization is currently evaluating promising targeted sequencing approaches, releasing a public call for data.

Discussing vaccine utility, Tobias Welte (Hannover, Germany) explained that susceptibility to subsequent infections in chronic lung disease has begun to be understood; in asthma, for example, reduced interferon response to viral infection has been identified [24]. Critically, a major risk factor for future exacerbations is previous exacerbations [25], and bacterial and viral infections represent important targets for exacerbation prevention. Whilst vaccinations for pathogens including *Haemophilus influenzae* [26] and *Bordetella pertussis* [27] are available, both vaccination rates [28] and effectiveness require improvement [29].

Replicating SARS-CoV-2 vaccine development, research must be directed towards utilising new technology, rapid vaccine production and alternative delivery methods, as well as development of combination vaccines to improve compliance and reduce exacerbation rates.

Christoph Lange (Borstel, Germany) concluded the session by summarising new drugs and treatment regimens in tuberculosis. Recent investigation of drug regimens in children has allowed reduction in treatment duration from 6 to 4 months [30], and substitution of rifampicin with rifapentine and ethambutol with moxifloxacin also facilitated reduction in adult treatment duration [31]. Additionally, successful 6-month triple-drug therapy of bedaquiline, pretomanid and linezolid [32] has been evidenced for MDR tuberculosis treatment, and drug dosages have been further optimised to reduce associated severe adverse event occurrence [33]. Unfortunately, wide implementation of these regimens has been prevented by the unavailability of rifapentine [34] and pretomanid in many countries, lack of resistance testing for pretomanid and high cost [35]. However, many new medicines are under investigation, with 17 compounds currently in phase 1 and 2 trials, providing further hopes for successful treatment.

Fight to antimicrobial resistance: the role of new diagnostics (a European perspective from the Value-Dx consortium)

In this session, presenters discussed the appropriate use, development and major advances of diagnostic tools for respiratory infections from a clinical and epidemiological perspective.

Maurizio Sanguinetti (Rome, Italy) named antibiotic resistance as a global cause of mortality, and emphasised the importance of microbiological and serological testing in antibiotic use [36–38]. Rapid test usage, such as urine antigen testing and PCR, is considered promising in pathogen diagnostics in the future. Molecular detection tests are still considered the “gold standard” due to comprehensive application in both bacterial and viral lower respiratory tract infections [39–44]. Additionally, well-timed diagnostic methods can lead to appropriate de-escalation of antibiotic treatments [45]. Rapid multiplex tests should be used to improve antibiotic stewardship by prescribing appropriate antibiotics earlier and avoiding unnecessary therapy [46, 47].

Cristina Aymerich (Utrecht, the Netherlands) discussed the importance of monitoring the epidemiology of microbial aetiology in community-acquired acute respiratory tract infections. C. Aymerich highlighted that the increased detection of antimicrobial-resistant species is a serious challenge to medicine, requiring greater precautions around possible transmission, pathogenicity, high susceptibility of “naïve” population and absence of possible vaccination and treatment. The COVID-19 pandemic has led to a wider uptake of PCR testing for both respiratory viruses and other pathogens leading to increased detection of microbes in patients with respiratory infections [48]. However, C. Aymerich urged caution when diagnosing co-infections, where the risk of over-testing might impact antimicrobial stewardship.

Maarten Postma (Groningen, the Netherlands) discussed the use of large-scale point-of-care diagnostics in predicting antimicrobial resistance, finding it beneficial in around one fifth of cases. Despite the increased cost of testing in addition to the overall cost of consultations, M. Postma concluded that these diagnostics may be beneficial tools to reduce antimicrobial resistance.

Bojana Beovic (Ljubljana, Slovenia) encouraged the use of rapid microbiological diagnostics at the bedside to improve antibiotic use, highlighting the importance of antimicrobial stewardship and the potential to be cost effective.

Lungs on fire: respiratory infections?

Four real-life cases were presented to an expert panel for a lively discussion to reach a step-by-step approach, differential diagnoses and management plans.

Case 1 was submitted by M. Saad (Italy). A 60-year-old Brazilian female presented with difficult-to-treat asthma with recurrent admission and corticosteroid use. Investigations showed high eosinophil count (1350 cells per mm³) and IgE (763 UI·mL⁻¹), but a negative *Aspergillus* IgE/IgG, vasculitis screen and stool parasitic screen. CT showed bilateral pulmonary infiltrates and electromyography showed peripheral neuropathy. She was treated with mepoliumab (anti-IL-5) for antineutrophil cytoplasmic antibodies-negative eosinophilic granulomatosis with polyangiitis with a good initial response, but later deteriorated with an eosinophilia and new cerebral and pulmonary infiltrates. A gastroscopy performed for epigastric symptoms showed *Strongyloides* larvae, diagnosing *Strongyloides* hyperinfection syndrome, allowing for ivermectin treatment. The definition of eosinophilia with pulmonary symptoms was highlighted: blood eosinophilia (≥ 500 cells per mm³), pulmonary symptoms and radiographic evidence of pulmonary disease,

often with histopathological evidence of eosinophilia and/or increased eosinophils in bronchoalveolar fluid (>10%) [49]. Various causes, including infection, drugs and vasculitis, were discussed and the need to re-review patients with partial response to treatments was emphasised.

Case 2 was submitted by S. Yuvarajan (India). A 52-year-old female with breathlessness and haemoptysis post-COVID-19 was investigated with a bronchoscopy showing an endobronchial smooth globular mass and microscopy identifying hyphae, diagnosing pulmonary mucormycosis. This is an angioinvasive fungal infection common in immunosuppressed (including post-COVID-19) hosts. Symptoms include nasal discharge, nasal/ facial pain, visual loss and headaches. Fungal pneumonia is a rare cause of pulmonary artery pseudoaneurysms, which have a high risk of rupture leading to massive haemoptysis. Pulmonary mucormycosis is rare but increasing post-pandemic and a high index of suspicion is required for diagnosis.

Case 3 was submitted by D. Rodrigo (Sri Lanka). A 50-year-old male with a background of ulcerative colitis, immunosuppressed on infliximab presented with persistent fevers despite antibiotics and antituberculosis treatment. Extensively investigated with negative antinuclear antibody, rheumatoid factor and HIV, and no positive microbiology from various samples (bronchoalveolar lavage and lung biopsy). Key findings were a bicytopenia, hepatosplenomegaly on ultrasound and bone marrow aspiration showing haemophagocytosis, as well as a significantly elevated ferritin and serum triglyceride level, confirming the diagnosis of haemophagocytic lymphohistocytosis (HLH). HLH is a life-threatening immune syndrome caused by massive cytokine storm from highly stimulated but ineffective immune responses. Symptoms can mimic infections, hepatitis, encephalitis and fever of unknown origin but the use of biomarkers (ferritin, triglycerides and cytopenia) can aid diagnosis. Treatment is usually with a combination of etoposide and corticosteroids but the underlying driver of secondary HLH must be treated.

Case 4 was submitted by S. Wickramasinghe (Sri Lanka). A 65-year-old with persistent radiological changes and a right lower lobe cavitating lesion was diagnosed with pulmonary actinomycoses after an endobronchial ultrasound showing Gram-positive bacteria and confirmed actinomycosis. Actinomycosis is an uncommon infection, often presenting with cervicofacial symptoms, and only 15% accounting for pulmonary presentations. Risk factors include excess alcohol consumption and poor oral hygiene. Actinomycosis generally has a low mortality rate if recognised and treated with antibiotics.

Group 10.02: tuberculosis and nontuberculous mycobacterial disease *Advances in epidemiology, diagnosis and treatment of tuberculosis*

In this oral session, seven presenters gave 5-min presentations on their work on tuberculosis covering epidemiology, screening programmes, contact tracing and post-tuberculosis sequelae.

Hayoung Choi (Seoul, Republic of Korea) aimed to evaluate the risk of long-term mortality in 55 739 tuberculosis survivors in Korea when followed up for at least 1 year after study enrolment. The mortality risk in tuberculosis survivors was 1.62-fold higher than in age- and sex-matched controls, even after adjusting for potential confounders including sociodemographic characteristics and comorbidities. Male sex, heavy alcohol consumption, lowest income quintile and higher Charlson comorbidity index were associated with increased mortality [50].

Jinsoo Min (Seoul, Republic of Korea), in a prospective cohort study, evaluated tuberculosis culture conversion rates between drug-susceptible and isoniazid-monoresistant pulmonary tuberculosis (PTB). While 7% of drug-susceptible tuberculosis patients remained positive at 2 months, 17% of isoniazid-monoresistant patients remained culture positive at the end of 2 months, although this was not statistically significant. Patients with *katG* mutation had higher proportion of 2-month culture positivity, which was similar to isoniazid-monoresistant patients. J. Min concluded that prompt changes of treatment based on *katG* mutation detected by genotypic testing would be useful before identifying isoniazid resistance on phenotypic tests.

In a systematic review to determine the prevalence and pattern of radiological sequelae and abnormal spirometry in patients who had completed therapy for PTB, Ayush Goel (New Delhi, India) found that in 81 studies including >14 000 participants, 40–86% patients showed radiographic abnormality on chest radiography with prevalence of fibrosis and bronchiectasis being nearly 70% and 35–86% respectively on CT scan. More than 70% of the studies showed at least 40% of patients developing some abnormality on spirometry, of which the obstructive pattern was the most common finding. Louis Yeung (Sydney, Australia) also presented similar findings in an Australian cohort of treated PTB patients where significant prevalence of impaired lung function was found. Of concern, a high proportion of patients had airflow obstruction which would be consistent with COPD. The presence of airflow obstruction persisted beyond

12 months of completing PTB treatment. Both these studies highlighted the high burden of post-tubercular lung damage, emphasising the need to follow up this cohort post-treatment.

Conor Tweed (London, UK) analysed data collected in the REMoxTB trial to investigate symptom profile in follow-up for patients who had successfully completed standard tuberculosis therapy and whether these symptoms could predict treatment success at 18 months [51]. Symptoms were reported by 25% of the participants in the 12 months after treatment completion. Chest pain and weight loss (both 18%), cough (17.6%), fever (10.3%) and dyspnoea (7.7%) were the most common symptoms. This study concluded that clinical trial datasets do represent an opportunity to evaluate post-tuberculosis morbidity and should be considered when evaluating new tuberculosis regimens.

Darryl Braganza Menezes (Birmingham, UK) studied usage of WGS to investigate tuberculosis outbreaks in the UK, where they compared epidemiologically linked cases with subsequent WGS to determine subsequent sizes of outbreaks. 167 incidents were investigated with nine tuberculosis outbreaks events over 7 years and 35 active cases generated 2511 contacts from contact tracing investigations. They found that WGS cluster investigations demonstrated transmission links greater than those demonstrated by epidemiological investigations alone. Hence, the study concluded that social network analysis may represent a better model for contact tracing.

Dominik Zenner (London, UK) analysed key drivers behind differences in tuberculosis yield in four large migrant tuberculosis screening programmes (UK, the Netherlands, Sweden and Italy) to inform tuberculosis control planning. Significant associations between tuberculosis screening yield and increasing age, migrant typology, higher tuberculosis incidence in the country of origin, tuberculosis case contact, period of screening and additional programmatic effects were found.

Update on nontuberculous mycobacterial pulmonary diseases

In this mini-symposium, presenters discussed state-of-the-art updates in nontuberculous mycobacterial (NTM) disease, considering recent evidence and recently published guidance. Christoph Lange (Borstel, Germany) opened the symposium with the presentation of new 2022 management guideline recommendations for less-common NTM pulmonary diseases [52]. These guidelines give a clear, differentiated approach to management options and the strategy for selecting antibacterial therapy for different groups of patients and different NTM pathogens [53].

Claire Andrejak (Amiens, France) described the main pathological conditions and species of NTM that can lead to the development of NTM pulmonary disease [54, 55]. C. Andrejak highlighted the importance of screening for NTM in populations at risk to gain a timely diagnosis and identify an effective antimicrobial therapy regimen [55–59]. In addition to the above, the speaker drew attention to additional risk factors for the development of NTM pulmonary disease, which included impaired airway clearance in patients with anatomical deformation of the chest or in older women with a low body mass index [60, 61].

Jakko van Ingen (Nijmegen, the Netherlands) discussed common issues that arise when selecting the molecule and dosage of therapies for the treatment of NTM infection [53, 62, 63]. Despite the development and research of a large number of new molecules, the pharmacokinetics and pharmacodynamics of antibiotics and their effective concentrations in the blood serum of patients during the treatment of NTM pulmonary disease remain uncertain [64]. J. van Ingen highlighted the importance of using a personalised medicine approach in the future, which would be based on certain criteria of outcomes predictors and treatment effectiveness [65, 66].

Group 10.03: adult cystic fibrosis

Advances in cystic fibrosis research

Group 10.03 is a newly established group within Assembly 10, focussing on adult cystic fibrosis. In this session, presenters discussed new developments in cystic fibrosis, ranging from new therapies to the impact of air pollution on the airways. Using *Pseudomonas aeruginosa* cystic fibrosis clinical isolates, Agustina Llanos (Labège, France) showed that LasB elastase, a *P. aeruginosa* virulence factor, exhibits higher activity during the early stages of infection, compared to when chronic infection is established. A. Llanos suggested that a LasB anti-virulence drug would be most effective in people with cystic fibrosis who have early-stage *P. aeruginosa* infections.

Claire Kim (Boston, MA, USA) investigated the long-term safety of lumacaftor/ivacaftor (LUM/IVA) treatment in people with cystic fibrosis during the year 2020. Data from the US Cystic Fibrosis Foundation

and UK cystic fibrosis patient registries supported, despite study limitations, an overall favourable benefit-risk profile of LUM/IVA.

Carolin Steinack (Zurich, Switzerland) studied a cohort of adults with cystic fibrosis and at least one copy of the F508del *CFTR* mutation. Glucose metabolism was measured pre- and post-elexacaftor/tezacaftor/ivacaftor (ETI) treatment using the standardised oral glucose tolerance test. ETI treatment significantly improved glucose metabolism. Concurring with previous findings [67], significant changes were also observed in lung function, body mass index and sweat chloride.

Orla O'Carroll (Dublin, Ireland) explored the complex relationship between ETI and anxiety in people with cystic fibrosis. People with cystic fibrosis completed a seven-item generalised anxiety disorder questionnaire pre- and 1 month post-ETI treatment. Overall, a trend towards improving anxiety scores was observed with ETI treatment but anxiety worsened for a few. Mechanisms contributing to the relationship remain unclear.

Sphingolipids (bioactive structural components of cell membranes) appear dysregulated in people with cystic fibrosis. Through liquid chromatography mass spectrometry analysis of plasma from people with cystic fibrosis pre- and 1 month post-ETI treatment, Dirk Westhölter (Essen, Germany) found that ETI treatment alters plasma sphingolipid profiles towards a favourable outcome [68].

In cystic fibrosis, air pollution is associated with increased frequency of exacerbations and risk of initial acquisition of *P. aeruginosa* and *S. aureus*, and decreased lung function [69]. Using the *Scnn1b*-transgenic (Tg) mouse model that overexpresses the epithelial Na⁺ channel producing a cystic fibrosis-like phenotype, Marion Blayac (Créteil, France) simulated atmospheres representative of an urban city and a highly polluted megacity, taking into account seasonal variation to examine the effects of air pollution in cystic fibrosis. Summer-like and Beijing-like winter type atmospheres induced greater expression of pro-inflammatory cytokines in *Scnn1b*-Tg mice. The anti-inflammatory cytokine IL-10 measured following exposure only increased in wild type mice. M. Blayac suggested that air pollution could increase cystic fibrosis disease severity by worsening of existing lung phenotype.

Mucus has a yield stress that is significantly increased in cystic fibrosis [70]. James Shemilt (Manchester, UK) introduced a mathematical approach to modelling the mucus layer in a small airway, taking into account yield stress. The model showed that a sudden decrease in viscoelasticity of mucus (e.g. by applying a mucolytic) could trigger airway closure due to mucus plugging. J. Shemilt suggested that the application of this method to whole-lung modelling could be used to predict the effects of inhaled therapies in people with cystic fibrosis.

Conclusion

Assembly 10 encompasses a broad range of clinical and scientific topics in areas such as bronchiectasis, NTM, cystic fibrosis, COVID-19 and tuberculosis. Here, we have presented a selection of presentations from numerous high-quality respiratory infection sessions at the 2022 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.

Provenance: Commissioned article, peer reviewed.

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