EMBARCing on a new era for bronchiectasis: a review series for the Seventh World Bronchiectasis Conference

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It is our pleasure to introduce a review series in the *European Respiratory Review* for the World Bronchiectasis Conference 2024, covering key clinical topics and perspectives for future research in this exciting field. This is a time of great progress and change in the field of bronchiectasis. The past 10 years have seen an acceleration of clinical research with major advances in our understanding of the epidemiology, pathophysiology and heterogeneity of the disease [1]. Most original articles or reviews on the topic of bronchiectasis published in the past 10–15 years will refer to the fact that bronchiectasis has been a neglected or "orphan" condition. Bronchiectasis has historically been a poor relation to the closely related airway diseases such as cystic fibrosis, asthma and even COPD, where greater therapeutic progress and research investment has been made.

This is now changing, as bronchiectasis emerges from the shadows as an area of exciting research advancement. A new generation of anti-inflammatory therapies such as dipeptidyl peptidase-1/cathepsin C inhibitors are in advanced clinical development [2], based on a shift in understanding of bronchiectasis from a problem of impaired mucociliary clearance leading to bacterial infection, towards conceptualising the disease as an inflammatory airway condition. There has been a rapid expansion in the number of clinical trials being performed across the spectrum of anti-infectives, anti-inflammatories/immunomodulators and mucoactive treatments [3]. This has been driven by a global advocacy effort that has raised the profile of the disease, and deepened our understanding of the patient population and disease pathophysiology. As a result, bronchiectasis is entering a new era where it can no longer be described as neglected.

This review series aims to highlight this great progress and identify areas of future research focus. The series has been developed by the European Multicentre Audit and Research Collaboration (EMBARC), a European Respiratory Society clinical research collaboration [1]. Active since 2012 and representing a network of bronchiectasis clinicians and researchers which involves colleagues in more than 32 countries, EMBARC has made an important contribution to the progress we are now seeing in the field of bronchiectasis. The bronchiectasis community is uniquely collaborative and unified and it is this "team bronchiectasis" approach which has led to the development of global registries that have enrolled more than 20 000 patients [4–8], have facilitated translational research through global biobanks and collaboration with basic scientists, and which is now helping to deliver international clinical trials. EMBARC is proud to have developed this series with each review combining emerging and talented investigators with established experts.

The topics covered in this series include some of the areas of greatest progress and also identify some of the most unmet needs. The epidemiology of bronchiectasis is reviewed by Mattia Nigro and co-workers,

who explore the increasing prevalence of the disease, as well as our deeper understanding of patient characteristics and variation across regions which have been revealed by large scale registries.

Bronchiectasis research, and the development of new treatments, have been greatly limited by a lack of understanding of the pathophysiology. The lack of *in vivo* and *in vitro* models to study the disease means that most of the data we need to understand the disease must come from humans. This is now happening as detailed studies using modern multi-omics technologies are unveiling new pathways, endotypes and treatable traits [9]. Perea *et al.* [10] expertly review the pathophysiology.

Infection is a key component of the pathophysiology and such a crucial treatable trait that it is deserving of its own review. This is particularly the case as advances in sequencing technology transform our understanding of traditional microbiology towards a molecular age in which we understand infections in terms of disruption of the normal lung microbiota. Mac Aogáin *et al.* [11], review our understanding of infection, from conventional culture to next generation sequencing.

Non-tuberculous mycobacterial (NTM) pulmonary disease presents unique clinical challenges due to the difficulties in recognition and diagnosis, limited understanding of the prognosis or when to treat, and complex treatment regimens which are often poorly tolerated and not always effective [12]. A neglected disease within a neglected disease, NTM pulmonary disease remains an area with limited clinical trial evidence. Van Braeckel *et al.* [13], introduce the clinical challenges of managing NTM infections.

Exacerbations are key events in the natural history of bronchiectasis as they place the patient at risk of more exacerbations, whilst deceasing quality of life, driving lung function decline and being associated with increased mortality [14]. Understanding, preventing and treating exacerbations are reviewed by De Angelis *et al.* [15].

Personalised medicine in key to the management of a heterogeneous disease. Personalised or precision medicine depends on the identification of subgroups of patients defined by specific biology (known as endotypes) and treatable traits. To do this, biomarkers which can be applied in clinical practice are needed. Great advances have been made in defining subgroups of patients with bronchiectasis and Johnson *et al.* [16] review the underexplored area of bronchiectasis biomarkers.

The next article in the series reviews bronchiectasis in Asia. We felt that bronchiectasis has made enormous progress in recent years, but progress has not been equitable and uniform. Most studies into epidemiology and pathophysiology of bronchiectasis arise from the global north and particularly Western Europe and the USA, while the burden of bronchiectasis in regions with a high prevalence of tuberculosis is believed to be very large [17]. Registries in India and Korea have revealed markedly different patient characteristics and treatment patterns compared with Europe and the USA [5, 8]. It is therefore essential to understand more about the unique characteristics and healthcare challenges of bronchiectasis in Asian countries.

Finally, treatment of bronchiectasis is receiving more and more attention with an increasing number of trials of therapies including antibiotics and anti-inflammatory drugs, but the central pillar of bronchiectasis management remains airway clearance and exercise [18]. To emphasise this our key commissioned review on management focuses on non-pharmacological management and particularly airway clearance [19, 20].

Taken together, these reviews represent a comprehensive and in-depth exploration of key issues in the field from internationally recognised experts actively researching these areas.

The seventh World Bronchiectasis Conference will take place in Dundee, Scotland from the 4–6 July 2024, a few days after we celebrate the third World Bronchiectasis Day on 1 July 2024. The first World Bronchiectasis Conference was held in Hannover in Germany in 2016, hosted by Professor Tobias Welte. Tobias sadly passed away too soon on the 10 March 2024 and we take this opportunity to recognise the lasting legacy of Tobias in pulmonary medicine, including the field of bronchiectasis. Since its inception, the World Bronchiectasis Conference has been a key opportunity for clinicians and scientists working in this field to come together and share the latest research, discuss clinical problems, and to advocate for this field. The World Bronchiectasis Conference 2024 will be a celebration of progress and a recommitment to do more to advance the field for the benefit of our patients. We hope you enjoy and learn from this series of papers celebrating the World Bronchiectasis Conference 2024.

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