Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

A large meta-analysis of 147 252 children in 31 birth cohort studies examined the relation between asthma and wheeze occurrence with preterm birth.[6] An association between school-age asthma and preterm birth (odds ratio 1·40, 95% CI 1·18–1·67), independent of birth weight, was reported. Others have obtained similar results for an association between preterm birth and wheezing.[7] Another meta-analysis[8] suggests that caesarean section, a procedure often done for women with pre-eclampsia, is also associated with a 20% increased risk of asthma.

Finally, asthma in early life might be linked to the subsequent development of COPD. Most patients with COPD also have features of asthma, and differentiation between the two disorders is often difficult. This issue has been highlighted in many reports in the past 2 years and has been comprehensively reviewed by Postma and Rabe.[9] Patients with asthma–COPD overlap syndrome (ACOS) are usually excluded from clinical trials and, depending on their clinical features, might be misdiagnosed and given incorrect treatment. The Dutch hypothesis, originally suggested by Orie,[10] stated that differentiation of asthma from COPD in adults depends on clinical expression as modified by age, sex, and the environment (eg, infection and smoking). Postma and colleagues[11] have updated this hypothesis in modern terms. Full clinical phenotyping, as suggested by Orie, is still extremely valuable. Rather than simply labelling patients as having asthma, COPD, or ACOS, they should be fully characterised with genomics and systems biology approaches. Ultimately, such approaches will be necessary to clearly distinguish between these two disorders, fully understand their unique aspects and their overlap, and define new treatments.[12]

Dietary modifiers of fetal development hold the key to prevention of asthma and other complex diseases, and the application of systems biology approaches to multi-omic data will also be needed to fully understand the biochemistry of disease development.

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Bronchiectasis: working together for better evidence

There remains limited evidence to guide the treatment of patients with bronchiectasis. 2014 was characterised by great optimism, followed by disappointment as large randomised clinical trials—such as those for inhaled aztreonam, mannitol, and colistin—failed to reach their primary endpoints. As a result, we remain without a licensed therapy for this disabling disease.[1] No such large phase 3 studies have been reported in 2015, and we await results of major trials of inhaled antibiotics, which are due to be reported in 2016. Nevertheless, 2015 could mark the beginning of a revolution in our understanding of bronchiectasis; a series of high-quality studies and international programmes have started to unravel the complex pathophysiology of the disease and to lay the foundation for clinical breakthroughs.

Identification of the underlying cause of bronchiectasis is crucial for ongoing management. A cohort study of 1258 patients from six European

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countries reported that the frequency of idiopathic disease was 18–58%, while that of disease with a post-infective cause ranged from 5% to 43%.[2] 164 (13%) patients had an underlying cause that required a specific treatment. Clear geographical variations in disease cause were noted, but there was no association between underlying cause and severity, suggesting that all patients with bronchiectasis need to undergo protocolised testing for cause of disease.[2]

Geographical variation in the cause of bronchiectasis is even more marked outside Europe, with up to 60% of patients in the USA having disease caused by non-tuberculous mycobacteria (NTM), which is less common in Europe (2–9% of patients in some reports).[2] In 2015, several small translational studies have added to our understanding of disease mechanisms. One of these is Szymanski and colleagues' whole-exome sequencing study[3] of 69 patients with pulmonary NTM infection and bronchiectasis, and 18 of their unaffected family members. The investigators reported a high frequency of mitral valve prolapse, pectus excavatum, and joint hypermobility in these patients, and that these features were associated with several immune genes (eg, *STAT1*, *IRF8*, *CARD9*, *CLEC4D*, and *MPEG1*) and cilia genes, and with the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. This finding suggests that NTM-associated bronchiectasis might have a characteristic morphology and genetic susceptibility, but large studies in diverse populations are needed.[3]

Frequent and severe exacerbations of bronchiectasis are both independently associated with mortality.[4] Gao and colleagues[5] identified respiratory viruses in a large proportion of exacerbations. Viruses—most frequently coronaviruses, rhinovirus, and influenza A/B viruses—were identified in 49 of 100 exacerbations (in 58 patients). Although many bronchiectasis exacerbations might have a viral cause, viruses were detected in 11 (19%) patients when they were clinically stable, suggesting that viral carriage or delayed viral clearance could be a factor leading to exacerbations.[5]

Bronchiectasis is characterised by airway neutrophilia, a form of inflammation that is relatively resistant to existing therapies like inhaled corticosteroids.[6] The chemokine receptor CXCR2 is expressed on neutrophils, and antagonism of CXCR2 can reduce neutrophil recruitment to the lung. A phase 2A proof-of-concept study of AZD5069, a CXCR2 antagonist, has been performed in 52 patients with bronchiectasis.[6] Sputum neutrophil count was decreased by 38% in the active treatment group compared with placebo. Surprisingly, this decrease was associated with an increase in the concentrations of some sputum and serum cytokines, and did not result in a reduction in exacerbations.[6] Larger studies are needed, since this trial was not powered to detect clinical benefits.

Early-phase studies need sensitive and responsive clinical trial endpoints. Unfortunately, unlike cystic fibrosis, for which forced expiratory volume in 1 s (FEV1) is an accepted trial endpoint, FEV1 is poorly responsive to treatment in bronchiectasis. Lung clearance index (LCI), a measure of ventilation inhomogeneity in the peripheral airways, is potentially a more sensitive and responsive measure than FEV1, but further assessment is needed. In Grillo and colleagues' study[7] of 32 stable and 32 exacerbating patients with bronchiectasis, LCI was reproducible across visits but did not change significantly with exacerbation or short-term treatments.

Although these studies improve our understanding of bronchiectasis and can inform future work, a reminder of how far we need to go in clinical medicine was provided by Welsh and colleagues' overview of Cochrane systematic reviews.[8] Summarising 21 systematic reviews, the authors identified poor

evidence for most therapies in clinical use, including inhaled corticosteroids, hypertonic saline, and long-term antibiotics. They called for a coordinated effort to stimulate further research and highlight the need for better clinical trial endpoints.[8]

A major step towards achieving this goal was taken in 2015 with the launch of a €50 million programme of work across Europe. Led by Stuart Elborn from Queen's University Belfast, UK, this EU-funded programme represents the largest investment in bronchiectasis research worldwide, and it aims to develop two new inhaled antibiotics for bronchiectasis.[9] The programme will also address challenges in drug development through validation of new clinical trial endpoints, including LCI, sputum biomarkers, and microbiome characterisation.[9] Moreover, the programme will provide long-term support for the European Bronchiectasis Registry (EMBARC), which began recruitment in February, 2015, and aims to gather data from up to 10 000 patients across Europe while building a sustainable framework for future multicentre clinical trials.

These developments give us great optimism for the coming years in bronchiectasis research. However, 2015 was also notable for the sad loss of a friend and colleague, David Serisier.[10] A member of the international advisory board of *The Lancet Respiratory Medicine* and a passionate and exceptionally talented researcher, Serisier made many important contributions to bronchiectasis, the most notable of which was the landmark Bronchiectasis and Low-dose Erythromycin Study (BLESS) study.[11] His passion and energy inspired everyone in the field, and he is greatly missed.

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The complex challenge of chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) continues to be a leading cause of morbidity and mortality in developed countries. As a heterogeneous disease with few disease-altering therapies it presents a complex challenge. Several studies published in 2015 have substantially contributed to our understanding of the disease process and its treatment modalities.

COPD has long been thought to be caused by a rapid decline in forced expiratory volume in 1 s (FEV_1) as a result of lung damage. Although cigarette smoking is the predominant and most common cause of disease development, environmental pollution, ageing, recurrent respiratory illnesses and infections, and genetic factors have all been reported as important contributors. Using three independent cohorts (the Framingham Offspring Cohort, the Copenhagen City Heart Study, and the Lovelace Smokers Cohort), Lange and colleagues[1] showed that decreased baseline airflow in young adulthood (age <40 years), along with normal rates of decline in FEV_1 (<40 mL per year), can result in development of grade 2 COPD or higher, as defined by the Global Initiative for