Reclaiming the name 'bronchiectasis'

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> The beginning of wisdom is to call things by their proper name
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> — Confucius, *The Analects of Confucius*

Diseases should be defined by what they are, not by what they are not. The way we classify and name things has a significant impact on our behaviour and on our perception of their importance.[1] Here we argue that clinicians and researchers should stop using the term 'non-cystic fibrosis' bronchiectasis to describe this common and disabling disease.

Diseases are classified by putting patients into groups based on similarities so that we can better understand natural history, epidemiology and treatment. The International Classification of Diseases (ICD) provides a common language for reporting and monitoring diseases. This allows clinicians and researchers to compare and share data in a consistent and standard way—between hospitals, regions and countries and over periods of time. It facilitates the collection and storage of data for analysis and evidence-based decision-making.[2] Bronchiectasis is a recognised code in ICD-10, J47.

Bronchiectasis is a pathological description of abnormal, usually permanent dilation of the bronchi which may be a feature of a wide range of clinical disorders. These include severe infections (including bacteria, viral and fungal diseases), immune deficiencies, autoimmune disorders, channelopathies, ciliary disorders and hypersensitivity reactions. Despite the heterogeneity in aetiology, 50%–70% of adults are typically classified as idiopathic and postinfective.[2 3]

Data on the epidemiology of bronchiectasis show a progressive increase in reported morbidity. Hospitalisations are increasing in the USA at a rate of 2%–3% per year, and in Europe, data show an average increase in age-adjusted incidence of 2.9% per year in Germany, and there has been an increase of 3% per annum in bronchiectasis-related deaths from the UK.[4–6] This is a disease that is increasingly being diagnosed and is placing a significant burden on healthcare resources.

Defining bronchiectasis by what it is not implies that it is somehow less common or less important than cystic fibrosis (CF). It is certainly not less common, as estimates of prevalence from the USA Medicare system suggest a prevalence of 52/100 000.[5] These figures are a substantial underestimate and the true figure may be double this. Age-standardised hospital admission rates are 2–6 per 100 000 population in Europe.[6] It is not less important. People who suffer from the disease have significant morbidity and get no benefit or reassurance from knowing that CF has a worse prognosis.[7] This is not to understate the importance of CF but simply to emphasise that bronchiectasis is a very important group of disease entities in their own right.

Bronchiectasis has historically been a neglected condition and has received little interest from academic funding bodies, medical charities or the pharmaceutical industry, who do not view bronchiectasis as a priority area for investment.[2] The link with CF has had a major impact on research and drug development. The majority of therapies to reach late-phase clinical trials in bronchiectasis have involved the repurposing of therapies previously developed for CF.[8–11] The results have been a number of negative clinical trials, as some therapies developed for CF either fail to work entirely,[8 9] perhaps because of differences in pathophysiology and drug tolerability between bronchiectasis and CF, or have had some positive results but failed to meet their primary end-points.[10 11] Bronchiectasis requires research into the specific pathophysiology, development of specific drug therapies, and to achieve this it needs a clear identity.

This identity is crucial because bronchiectasis itself needs to be better understood and better defined. CF is a genetic disorder defined by the presence of recognised genotypes and dysfunction of the CF transmembrane conductance regulator (CFTR). By definition, it is a permanent and progressive disorder. The diagnosis of bronchiectasis, by contrast, requires the demonstration of permanent abnormal dilatation of bronchi and a compatible clinical history. The former is typically based on a single 'snap-shot' high-resolution CT scan performed at diagnosis. Data suggest that, particularly in children but also in adults, bronchiectatic dilatation leading to a diagnosis of 'non-CF' bronchiectasis can resolve, either spontaneously or as a result of treatment.[12 13] Additionally, some patients present the clinical syndrome of bronchiectasis without visible bronchial dilatation on CT. How do we define a condition without a consistent objective gold standard? We need to understand whether the clinical syndrome of bronchiectasis is truly an anatomical disorder or whether bronchial dilatation is simply a manifestation of a poorly characterised small airways inflammatory disorder.

In adults, 10%–20% of patients with COPD may have bronchiectasis by radiographic criteria on CT scan, but as highlighted in a recent editorial, it is unclear to what extent bronchiectasis is a primary disorder, a complication of COPD or an overlap syndrome.[14] In difficult asthma, airway wall thickening and bronchial dilatation is also seen.[15] Whether such changes are permanent is unclear, while clinicians and guideline writers remain uncertain as to whether to call this an aetiology of bronchiectasis.[16]

We need to work towards a better understanding of the pathophysiology of bronchiectasis in order to define the disease by more than a radiographic appearance and the absence of CF.

The term non-CF bronchiectasis may also be misleading as it is often applied to populations of patients who have never been tested for CF. British Thoracic Society guidelines recommend testing for CF, by sweat test and/or CFTR genotyping, in patients younger than 40 years of age or those with features typical of CF such as upper lobe disease or recurrent isolation of *Pseudomonas aeruginosa* and *Staphylococcus aureus*.[16] The average age of patients with bronchiectasis in the UK is between 60 and 70 years, and only between 10% and 20% are colonised with these pathogens.[17] It makes no logical sense to define these patients' condition as the absence of a disease for which the majority of patients have not even been tested.

The use of the term non-cystic fibrosis is a relatively recent phenomenon—starting from its first pathological description by Laennec in 1819, the disease was known simply as bronchiectasis. The first use of the term 'non-cystic fibrosis bronchiectasis' identifiable on PUBMED was in 1992, with this term perhaps developing as an unhelpful by-product of the

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surge in research into CF that followed the discovery of the CF gene in 1989.[18] We hope there will be a similar surge in interest, investment and therapeutic advance in bronchiectasis—what Hurst recently referred to as the 'age of bronchiectasis'. Progress should start with defining what the disease is rather than what it is not.[19]

Patients do not recognise the term non-CF bronchiectasis, and the vast majority of patient information uses the much simpler and better recognised term of bronchiectasis.

The heterogeneity of bronchiectasis is sometimes cited as a reason for not considering it a 'real' disease entity. This is unhelpful and in our opinion, bronchiectasis is no more heterogeneous than many other common respiratory disorders. In CF, there is now disease subtyping with the classifications of CFTR-related disease and CFTR-related metabolic syndrome indicating the challenges of even precisely defining an autosomal recessive single gene disorder.[20] Bronchiectasis is the final common pathway and diagnostic label for a wide range of disease processes, but the same is clearly true of COPD and asthma. COPD is not 'non-asthmatic airflow obstruction' and bronchiectasis is not 'non-cystic fibrosis'.

The editors of *Thorax* recognise the importance of names on public perceptions having famously championed the renaming of exacerbations as 'lung attacks' in the hope of attracting greater interest in their prevention and treatment.[1] Bronchiectasis deserves to reclaim the name it held for over 150 years. We challenge researchers and authors to call this disease by its ICD classification and the editors of *Thorax* to request revision of any manuscript submitted to *Thorax* to remove the term 'non-cystic fibrosis' in reference to bronchiectasis.

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REFERENCES

1 Fitzgerald JM. Targeting lung attacks. *Thorax* 2011;66:365–6.
2 Kelly MG, Murphy S, Elborn JS. Bronchiectasis in secondary care: a comprehensive profile of a neglected disease. *Eur J Intern Med* 2003;14:488–92.
3 Chalmers JD, McHugh BJ, Doherty CJ, *et al*. Vitamin-D deficiency is associated with chronic bacterial colonisation and disease severity in non-CF bronchiectasis. *Thorax* 2012;68:39–47.
4 Ringshausen FC, de Roux A, Pletz MW, *et al*. Bronchiectasis-associated hospitalizations in Germany, 2005–2011: a population-based study of disease burden and trends. *Plos ONE* 2013;8:e71109.
5 Seitz AE, Olivier KN, Adjemian J, *et al*. Trends in bronchiectasis among medicare beneficiaries in the United States, 2000 to 2007. *Chest* 2012;142:432–9.
6 Bronchiectasis. *The European Lung White Book* 2014;15:176–83.
7 Lavery K, O'Neill B, Elborn JS, *et al*. Self-management in bronchiectasis: the patients' perspective. *Eur Respir J* 2007;29:541–7.
8 O'Donnell AE, Barker AF, Ilowite JS, *et al*. Treatment of idiopathic bronchiectasis with aerosolized recombinant human DNase I. rhDNase Study Group. *Chest* 1998;113:1329–34.
9 Barker AF, O'Donnell AE, Flume P, *et al*. Aztreonam for inhalation solution in patients with non-cystic fibrosis bronchiectasis (AIR-BX1 and AIR-BX2): two randomised double-blind, placebo-controlled phase 3 trials. *Lancet Respir Med* 2014;2:738–49.
10 Bilton D, Tino G, Barker AF, *et al*. Inhaled mannitol for non-cystic fibrosis bronchiectasis: a randomised, controlled trial. *Thorax* 2014;69:1073–9.
11 Haworth CS, Foweraker JE, Wilkinson P, *et al*. Inhaled colistin in patients with bronchiectasis and chronic pseudomonas aeruginosa infection. *Am J Respir Crit Care Med* 2014;189:975–82.
12 Gaillard EA, Carty H, Heaf D, *et al*. Reversible bronchial dilatation in children: comparison of serial high-resolution computer tomography scans of the lungs. *J Radiol* 2003;47:215–20.
13 Yap VL, Metersky ML. Reversible bronchiectasis in an adult: a case report. *J Bronchology Interv Pulmonol* 2012;19:336–7.
14 Hurst JR, Elborn JS, Soyza AD. COPD-Bronchiectasis overlap syndrome. *Eur Respir J* 2015;45:310–3.
15 Gupta S, Siddiqui S, Haldar P, *et al*. Qualitative analysis of high-resolution CT scans in severe asthma. *Chest* 2009;136:1521–8.
16 Pasteur MC, Bilton D, Hill AT. British Thoracic Society guideline for non-CF bronchiectasis. *Thorax* 2010;65(Suppl 1):i1–58.
17 Chalmers JD, Goeminne P, Aliberti S, *et al*. Derivation and validation of the bronchiectasis severity index: an international multicentre observational study. *Am J Respir Crit Care Med* 2014;189:576–85.
18 Taylor RF, Hodson ME, Pitt TL. Auxotrophy of Pseudomonas aeruginosa in cystic fibrosis. *FEMS Microbiol Lett* 1992;71:243–6.
19 Hurst JR. Microbial dysbiosis in bronchiectasis. *Lancet Respir Med* 2014;2:945–7.
20 Bombieri C, Claustres M, De Boeck K, *et al*. Recommendations for the classification of diseases as CFTR-related disorders. *J Cyst Fibros* 2011;10(Suppl 2):S86–102.