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EDITORIAL

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World Bronchiectasis Day: It is time for global action to promote equity of care

"Our experience as a family over the years has been that there is just not enough information and understanding about paediatric bronchiectasis. It has been misunderstood and mistreated for far too long" Zena and Ed Powell.

On July 1, 2023, as we celebrate the second World Bronchiectasis Day, it is time to reflect upon the need to increase awareness of bronchiectasis and to promote global collaboration so as to reduce its high burden for patients, their families and the health system.[1]

The global incidence and prevalence of pediatric bronchiectasis unrelated to cystic fibrosis (CF) (henceforth referred to as bronchiectasis and the focus of our editorial) are increasing.[2] Once believed to be rare, the wide availability of chest computed tomography combined with increased recognition has led to the awareness that it is not an uncommon disorder. However, it remains a neglected chronic lung disease, especially in children and in resource-limited settings.[3] While often going unrecognized, the burden of bronchiectasis on children, families and the health system is large. One prospective cohort study described the substantial impact of bronchiectasis upon a child and adolescent's quality of life (QoL) where in any given month 30% attended healthcare, 50% received antibiotics, and 25% were absent from school or childcare.[4] In Australia in 2016, each pediatric bronchiectasis exacerbation requiring hospitalization cost the health system $22,407 United States dollars.[5] Yet, there is large inequity in the delivery of services for people with bronchiectasis within and between settings, even in resource-rich countries like Australia.[6]

Enabling optimal treatment requires diagnosis, which is dependent upon recognition and awareness of the disease. This requires education and implementation strategies that address primary care physicians, pediatricians, pulmonologists and parents about the significance of chronic wet cough and its treatment, the basic elements of pediatric bronchiectasis management.

Diagnosing pediatric bronchiectasis promptly is important for several reasons. The definition is based upon abnormally increased airway dilatation, and in children and adolescents, this is of critical importance as it may be reversible, at least in the early stages.[1] Making an early diagnosis is therefore a key objective in managing bronchiectasis in children and may also prevent the development of other complications.[7] Studies have shown most adults with bronchiectasis had symptoms (chronic wet cough) from childhood[8,9] and thus opportunities for an early diagnosis were missed. Importantly, these patients had more severe disease with poorer prognosis than those whose symptoms started during adulthood.[8] Arguably, adults with bronchiectasis who had symptoms as children could be considered a diagnostic and management failure. Second, early diagnosis with appropriate investigations can identify treatable underlying causes, for example, primary immunodeficiency[1] whereby targeted treatment will prevent further lung damage. Late diagnosis is also associated with prolonged periods of inappropriate treatment, often for "asthma," with the attendant fiscal costs and risk of side-effects. Lastly, early diagnosis with optimal management[7] will improve the patient's and their family's QoL, reduce on-going pulmonary damage and when pediatric bronchiectasis is reversible[1] it will be cost-saving by preventing future severe adult disease.

While the underlying mechanisms of bronchiectasis in children, adolescents, and adults with bronchiectasis share similarities, there are some important differences[1] in the clinical presentation, underlying causes, microbiology, treatment approaches and goals. Pediatric bronchiectasis is often caused by respiratory infections, such as complicated pneumonia, pertussis or protracted bacterial bronchitis or by genetic conditions, for example, CF, primary immune deficiency or primary ciliary dyskinesia, while that in adults is more commonly associated with underlying lung diseases and auto-immune disorders.[2] Thus, the diagnostic and treatment options may differ, especially age-dependent components, for example, lung function and airway clearance techniques. Also, children need supervision from their parents, and this may be another difficulty for both healthcare providers and families.

While the field of CF has made tremendous gains with disease-specific therapeutics, especially CF transmembrane conductance regulator modulators, other causes of bronchiectasis have been neglected, this despite the larger global burden of bronchiectasis unrelated to CF with poorer outcomes that are largely related to inequity of care.[6,10] Nevertheless, the experience of CF care have also taught us that attention to care through a multidisciplinary care approach (e.g., optimizing nutrition, appropriate antibiotic use, airway clearance, intensive treatment in specialized centers) is of outmost importance as the QoL and longevity of people with CF improved substantially (from <2-years to >40-years), even before introducing disease-modifying medications.[11]

In recognition of the above, the European Respiratory Society (ERS) funded a child bronchiectasis clinical research collaboration (CRC) in March 2021, called Child-BEAR-Net[12] (Children's Bronchiectasis Education, Advocacy and Research Network, <www.improveBE.org>). While Child-BEAR-Net's impact lags behind their well-established adult counterpart (EMBARC), its collaboration among 20 countries along with the European Lung Foundation (ELF), has started to make important strides. Members include representatives from Australia, Europe, Asia, Africa, and South

America, along with the ELF and a parent advisory group. With a focus on patient-centered needs, to date it has:

- Established an international collaboration of consumers, scientists, and clinicians with expertise in pediatric bronchiectasis;
- Developed an international consensus of quality standards for managing children and adolescents with bronchiectasis,[13] based upon the ERS clinical practice guideline for child and adolescent bronchiectasis[7];
- Derived a statement for defining respiratory exacerbations in children and adolescents with bronchiectasis for clinical trials[14];
- Consolidated a road map of priorities based upon the needs of patients/parents of children and adolescents with bronchiectasis[15];
- Launched an international pediatric bronchiectasis registry;
- Obtained international consensus on the clinical and research priorities[15];
- Developed a core-outcome-set for intervention studies (manuscript in review); and
- Contributed to resources for education and advocacy (see website).

At the forefront of the above are the voices of parents of children with bronchiectasis and adolescents/adults diagnosed with bronchiectasis in childhood. Without their voices and input (along with input from Jeanette Boyd from the ELF), all the above would have had far less impact. For example, in our international survey, the two highest clinical needs expressed by parents/patients were having an action management plan for exacerbations and access to physiotherapists, while the two highest health practitioners' research priorities related to eradication of airway pathogens and optimal airway clearance techniques.[15] We thank the many parents/patients and international community of health professionals who completed the surveys that informed four of the documents[13–15] above.

The current priorities and needs of parents/patients were also outlined on the road map of priorities based upon the needs of patients/parents of children and adolescents with bronchiectasis.[15] The document set out 10 research priorities. Among these are:

1. To improve phenotyping and personalized treatment. There is growing recognition of the heterogeneity of bronchiectasis, identifying disease subtypes could help tailor treatment to individual patients based upon their specific needs and disease characteristics.
2. There is a need for new therapies that can improve outcomes and QoL for children and adolescents with bronchiectasis.
3. Ongoing research should focus upon identifying risk factors for exacerbations and developing strategies to prevent and manage them.
4. The need for improved QoL, which so greatly affect children and adolescents with bronchiectasis and their families.

There is now hope that there will be more dedicated research on bronchiectasis, including interest from big pharma. This will help to achieve treatment goals of preserving lung function, optimizing lung growth, halting disease progression and even reversing mild bronchiectasis, while optimizing QoL, and preventing exacerbations and complications. As with other chronic airway diseases, adoption of "treatable traits" addressing pulmonary disease, the underlying etiology, comorbidities, and environmental and lifestyle factors at the individual patient level is likely to assist clinical management and improve patient outcomes.[16] This approach will be aided by studies identifying distinct phenotypes (classifying disease according to observable patient characteristics) and endotypes (classifying disease by their underlying pathobiological pathways), which will decrease the proportion of patients categorized as idiopathic bronchiectasis and promote patient-focused precision medicine. Finally, new dedicated or repurposed therapies of mucolytics, various modified inhaled antibiotics, and inhibitors of dipeptidyl peptidase 1 (DPP1), an enzyme that is critical to the activation of neutrophil enzymes have undergone or are undergoing clinical trials.

World Bronchiectasis Day is to raise awareness and it is also a day to recognize the strength and resilience of patients and families living with this condition. Ed recently shared his journey <https://europeanlung.org/en/people-and-partners/your-experiences/ed-powell-my-experience-of-bronchiectasis/> and Zena shared the efforts she went to at securing a diagnosis for Ed at the 2021 ERS conference <https://europeanlung.org/en/people-and-partners/your-experiences/zena-powell-parent-perspectives-and-input-into-the-ers-guidelines/>. Collectively, we as healthcare providers and researchers need to forge ahead along with patients to push systems to enable best-evidenced practice care, promote relevant high-quality research, and reduce the inequity in the provision of services to improve the lives of children and adolescents with bronchiectasis and their families. This is necessary to help families for generations to come to receive a prompt diagnosis and treatment. It is time for global action to promote equity of care for people with bronchiectasis.

"In our opinion the work we are involved with as part of the Child BEAR net team is positively impacting the diagnosis, treatment, management and future research of the condition. Helping families for generations to come to get timely diagnosis and treatment."

Figure. Picture of Ed and Zena Powell.

AUTHOR CONTRIBUTIONS

Oleksandr Mazulov - conceptualization (equal), writing original draft (equal), writing review and editing (equal), supervision (equal), Zena Powell and Ed Powell - conceptualization (equal), writing editing (equal), Andrew Bush - conceptualization (equal), writing original draft (equal), writing review and editing (equal), supervision (equal), Anne B Chang - conceptualization (equal), writing original draft (equal), writing review and editing (equal), supervision (equal), Ahmad Kantar - writing review and editing (equal), supervision (equal), Keith Grimwood - conceptualization (equal), writing original draft (equal), writing review and editing (equal), supervision (equal), Bulent Karadag - writing review and editing (supporting), other Child-BEAR-Net committee members - writing review and editing (supporting).

CONFLICTS OF INTEREST STATEMENT

Drs Alexopoulou, Bush, Constant, Douros, Fortescue, Griese, Hector, Karadag, Hill, Kantar, Mazulov Midulla, Moeller, Proesmans, Yerkovich, Zacharasiewicz have nothing to disclose. Ms Boyd, Powell and Wilson, and Mr Collaro also have nothing to disclose. Drs Chang and Grimwood report grants from the National Health and Medical Research Council, and the Medical Research Futures Fund, Australia, during the conduct of the study. Dr Chang is also an independent data management committee member for clinical trials of an unlicensed vaccine (GlaxoSmithKline), and monoclonal antibody (AstraZeneca); an advisory member of study design for an unlicensed product for chronic cough (Merck), and personal fees from being an author of two UpToDate chapters that are outside the submitted work. Dr Chalmers reports grants, and personal fees from AstraZeneca, grants, and personal fees from Boehringer Ingelheim, personal fees from Chiesi, grants and personal fees from GlaxoSmithKline, grants from Gilead Sciences, grants and personal fees from Insmed, personal fees from Novartis, and personal fees from Zambon that are outside the submitted work. Dr Grigg reports grants and personal fees from OM Pharma, personal fees from GlaxoSmithKline, personal fees from Novartis, personal fees from Omron, and personal fees from AstraZeneca that are outside the submitted work. Dr Zacharasiewicz reports personal fees for lectures from AstraZeneca, personal fees for lectures from Chiesi, and personal fees from Vertex Pharmaceuticals, personal fees from Novartis, and personal fees from Sanofi that are outside the submitted work.

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