South African Thoracic Society position statement on the management of non-cystic fibrosis bronchiectasis in adults: 2023

A Goolam Mahomed,[1] MB BCh, FCP (SA), FCCP; **S D Maasdorp,**[2] MB ChB, MMed (Int Med), FCP (SA), Cert Pulmonology (SA) Phys;
R Barnes,[3] BSc (Physio), MSc (Physio), PhD; **H van Aswegen,**[4] PhD; **A Lupton-Smith,**[5] BSc (Physio), PhD;
B Allwood,[6] MB BCh, FCP (SA,) Cert Pulmonology (SA) Phys, MPH, PhD;
G Calligaro,[7] BSc Hons, MB BCh, FCP (SA), MMed (Int Med), Cert Pulmonology (SA) Phys;
C Feldman,[8] MB BCh, DSc, PhD, D Med (honoris causa), FRCP, FCP (SA);
I S Kalla,[8] MB BCh, PhD, FCP (SA), FCCP, Cert Pulmonology (SA) Phys, Cert Critical Care (SA)

[1] *Louis Pasteur Private Hospital, Pretoria, South Africa*
[2] *Division of Pulmonology and Critical Care, Department of Internal Medicine, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa*
[3] *Department of Physiotherapy, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa*
[4] *Department of Physiotherapy, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*
[5] *Division of Physiotherapy, Department of Health and Rehabilitation Sciences, Stellenbosch University, Cape Town, South Africa*
[6] *Division of Pulmonology, Department of Internal Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*
[7] *Division of Pulmonology, Department of Internal Medicine, Faculty of Health Sciences, University of Cape Town, South Africa*
[8] *Department of Internal Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*

Corresponding author: *A Goolam Mahomed (akhtergm@telkomsa.net)*

Background. Bronchiectasis is a chronic lung disorder that affects the lives of many South Africans. Post-tuberculosis (TB) bronchiectasis is an important complication of previous pulmonary TB and a common cause of bronchiectasis in South Africa (SA). No previous statements on the management of bronchiectasis in SA have been published.
Objectives. To provide a position statement that will act as a template for the management of adult patients with bronchiectasis in SA.
Methods. The South African Thoracic Society appointed an editorial committee to compile a position statement on the management of adult non-cystic fibrosis (CF) bronchiectasis in SA.
Results. A position statement addressing the management of non-CF bronchiectasis in adults in SA was compiled. This position statement covers the epidemiology, aetiology, diagnosis, investigations and various aspects of management of adult patients with non-CF bronchiectasis in SA.
Conclusion. Bronchiectasis has largely been a neglected lung condition, but new research has improved the outlook for patients. Collaboration between interprofessional team members in patient management is important. In SA, more research into the epidemiology of bronchiectasis, especially post-TB bronchiectasis and HIV-associated bronchiectasis, is required.
Keywords. Bronchiectasis, non-cystic fibrosis, management.

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The South African Thoracic Society mandated a multidisciplinary team of healthcare providers to compile a position statement on the management of non-cystic fibrosis bronchiectasis in South Africa (SA). International guidelines on the management of bronchiectasis were reviewed and used as a basis from which the current position statement was compiled. This is the first position statement on the management of adult non-cystic fibrosis bronchiectasis in SA. A description of the epidemiology and aetiology of bronchiectasis is provided, as well as guidance on its diagnosis and management.
The position statement provides guidance on the management of bronchiectasis to healthcare providers, policymakers and regulatory authorities.

Bronchiectasis is a heterogeneous disease with multiple causes affecting the airways that results in irreversible dilatation of the bronchi, and is clinically characterised by a chronic cough, sputum production and frequent exacerbations.[1,2] Cole's 'vicious cycle hypothesis' (Fig. 1) of an inciting infection resulting in damage to the airways and impaired mucociliary clearance, leading to persistent airway inflammation, mucus accumulation, recurrent respiratory tract infection and further airway damage, is a well-recognised model for explaining the underlying pathogenesis of bronchiectasis.[3]

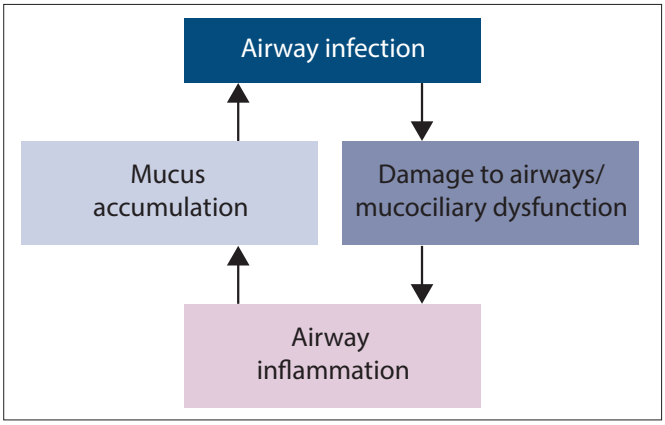

Fig. 1. Pathogenesis of bronchiectasis.

More recently, Flume *et al.*[4] described the complex pathogenesis of bronchiectasis as a 'vortex' whereby impaired airway mucociliary clearance and secretion accumulation impair normal host immunity, resulting in recurrent and/or persistent infection, which elicits a host inflammatory response that causes airway injury and remodelling, ultimately leading to bronchiectasis.

Bronchiectasis affects the lives of many South Africans, but it is a neglected condition, and very little local research is available for review. No previous statements on the management of bronchiectasis in South Africa (SA) have been published. Given that 2019 was the 200th anniversary of the first description of bronchiectasis by Laënnec in 1819, the Council of the South African Thoracic Society (SATS) resolved to develop a consensus statement on the management of adult non-cystic fibrosis (CF) bronchiectasis in SA to celebrate this occasion. An editorial committee under the leadership of Prof. Akhter Goolam Mahomed and Dr Shaun Maasdorp was appointed to perform this task.

Our objective was to provide a position statement that will act as a template for the management of adult patients with bronchiectasis in SA. The position statement is aimed at all healthcare practitioners including primary care practitioners (GPs), physician specialists, pulmonologists, nurses, physiotherapists, surgeons, pharmacists, and ancillary specialists such as microbiologists and radiologists. We hope that it will serve as a stimulus to conduct local research in the field of bronchiectasis, as we have many unanswered questions, and we would also like it to serve as a template for guidance to policymakers and regulatory authorities. A separate consensus document on the management of CF has been published by the South African Cystic Fibrosis Association.[5] The management of CF-associated bronchiectasis is discussed in detail in that document, and therefore will not be covered in the current document.

Members of the editorial committee comprised a balance of specialist representatives with an interest in bronchiectasis from the various academic sectors and private practice in SA. Each expert member of the editorial committee was tasked with writing a section of the document, with particular reference to the content and evidence grading of the latest version of the British Thoracic Society[6] and European Respiratory Society[7] guidelines on the management of bronchiectasis, as well as the SA consensus guideline on the management of CF.[5] The members communicated with each other via e-mail and telephonically. The final draft document was compiled by the editorial committee and circulated among SATS Council members for further comment. These comments were considered by the editorial committee, and the final draft was then completed after a final face-to-face meeting of the committee at the 2022 SATS Congress in Cape Town.

Recommendations

- In South Africa, the most common aetiology of bronchiectasis is post-infectious, with tuberculosis being the most important pathogen.
- A work-up for secondary causes of bronchiectasis should be performed in all patients diagnosed with diffuse bronchiectasis.
- The investigation of choice for the diagnosis of bronchiectasis should be a thin-slice computed tomography scan of the chest (if a chest radiograph is non-diagnostic).
- Sputum Gram stain and culture should be a routine procedure in all cases of bronchiectasis and should be done initially, during follow-up visits, and before initiation of antibiotics in cases with exacerbations. This allows for targeted therapeutic interventions.
- Airway clearance techniques remain the mainstay of therapy.
- Bronchiectasis can coexist with other respiratory and systemic illnesses. These need to be identified and treated independently.
- All patients should receive an annual influenza vaccination and the pneumococcal vaccination, and should be vaccinated against COVID-19. The dosing schedule should be determined by the most current guidelines published.

Position statement

1. Epidemiology

There is marked regional variation in the prevalence of bronchiectasis. In the USA, the prevalence of bronchiectasis was estimated to be 139 per 100 000 among adult patients.[8] Bronchiectasis becomes more common with increasing age. Among US Medicare patients aged ≥65 years, the estimated prevalence was 701 per 100 000.[9] Patients enrolled in the US Bronchiectasis Research Registry were mostly female (79%), and the mean age at diagnosis was 57 years.[10] A UK population-based cohort study found the prevalence of bronchiectasis to be 566 per 100 000 in women and 485 per 100 000 in men.[11] Bronchiectasis was similarly more common in women, and the median age at diagnosis was 61.8 years.[11] The age-adjusted mortality rate for women with bronchiectasis was 1 437.7 per 100 000, a rate that was 2.26 times higher than that of the general population.[11] Similarly, among men, the age-adjusted mortality for patients with bronchiectasis was 1 914.6 per 100 000, which was 2.14 times higher compared with the general population.[11] In Germany, the prevalence of bronchiectasis was 67 per 100 000, with a higher prevalence of 192 per 100 000 in patients aged >65 years.[12] Patients with bronchiectasis in India tend to be younger (median age 56 years) than European and US patients and are more likely to be male (56.9%).[13] The highest prevalence of bronchiectasis was reported from China, with 1.2% (1 200 per 100 000) of individuals aged >40 years being diagnosed with bronchiectasis.[14] However, bronchiectasis is by no means a condition that only affects older people.

Table 1. Conditions associated with bronchiectasis[3,18]

Post-infectious
Mycobacterial infection, especially tuberculosis
Viral infection, such as measles, whooping cough, COVID-19
Pneumonia
Mucociliary disorders
Cystic fibrosis
Primary ciliary dyskinesia
Secondary to bacterial infection
Obstruction
Foreign body, tumour, mycobacterial infection
Immune dysfunction
Primary: Hypogammaglobulinaemia, selective hyperglobulinaemia, neutrophil abnormalities
Secondary: HIV, chemotherapy, allergic bronchopulmonary aspergillosis, malnutrition, extremes of age
Rheumatic/inflammatory conditions
Rheumatoid arthritis, inflammatory bowel disease
Miscellaneous
Congenital tracheobronchomegaly, Marfan's syndrome, alpha-1-antiprotease deficiency syndrome, chronic obstructive pulmonary disease, asthma, aspiration

Both idiopathic and post-tuberculosis (TB) bronchiectasis are found in children and young adults.[15] Bronchiectasis is prevalent among patients with HIV.[16,17] Although population-based studies are lacking in Africa, it is highly likely that bronchiectasis is common and frequently under-diagnosed given the high burden of infectious pulmonary diseases, especially pulmonary TB and HIV, on this continent.

2. Aetiology

The list of conditions associated with bronchiectasis is extensive, as indicated in Table 1.[3,18] There is marked geographical variation in the aetiology of bronchiectasis.[15] In India, TB (35.5%) followed by other infections (22.4%) are the main causes of bronchiectasis.[13] These figures contrast strikingly with an Australian bronchiectasis cohort, where post-infective bronchiectasis (28.1%) was common, but post-TB bronchiectasis was only found in 1.8%.[19] In a European cohort, the most common causes of bronchiectasis included infections, connective tissue disease, immunodeficiency and asthma.[20] However, idiopathic bronchiectasis still made up 40% of the study population, and this is common to all registries, especially if an exhaustive evaluation is not performed.[20]

2.1 Post-TB bronchiectasis

It is interesting to appreciate that, for the first 150 of the 200 years since it was first described, bronchiectasis was strongly associated with TB, yet until recently most modern publications from low-TB settings fail to fully acknowledge TB as a major global cause of non-CF bronchiectasis. It has recently been estimated that 155 million TB survivors are currently alive,[21] with many of them having some form of residual impairment.[22] The proportion of non-CF cases attributable to TB naturally varies substantially according to the population background incidence of TB, for example being estimated at 12% in Taiwan[23] and 36% in the recent European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) study in India.[13] Viewed the other way, the finding of bronchiectasis after TB also appears to vary widely, ranging from 4 - 11% on chest radiographs to 35 - 86% on the more sensitive computed tomography (CT) scan imaging.[24] Recently, chest radiographic imaging in a prospective Malawian cohort found bronchiectasis in ≥1 lobe in 44.2% of adult patients after treatment completion.[25]

TB may result in damage to a number of different compartments of the lung, namely the parenchyma, large and small airways, vessels and pleura.[26] Post-TB bronchiectasis therefore forms one of a cluster of possible manifestations involved in the umbrella term 'post-TB lung disease' and may coexist with, among others, small-airways disease (or TB-associated obstructive lung disease) and lung fibrosis in any one individual patient.[26]

Post-TB bronchiectasis appears to have a male preponderance, probably reflecting the well- known male preponderance of TB,[13] affects the upper lobes more commonly than other causes of non-CF bronchiectasis, and is more likely to be unilateral.[23] However, the affinity for the middle and lower zones is often under-appreciated, being involved in ~60% of post-TB bronchiectasis cases.[13] Additionally, post-TB bronchiectasis appears to be more frequently associated with a 'frequent exacerbator' phenotype compared with other causes,[13] and although most commonly associated with airflow obstruction, is also more frequently associated with low forced vital capacity compared with other causes.[13]

Isolation of other organisms in post-TB bronchiectasis patients is not uncommon, but appears to vary substantially by geographical location, with common organisms including *Pseudomonas aeruginosa*, non-tuberculous mycobacteria (NTM), *Haemophilus influenzae* and *Klebsiella pneumoniae*.[13,23,27]

Interestingly, there is emerging evidence suggesting that the Bronchiectasis Severity Index (BSI) and FACED score (forced expiratory volume in 1 second (FEV_1), age, colonisation with *P. aeruginosa*, number of pulmonary lobes affected, and dyspnoea) are unable to adequately predict exacerbations and readmissions in post-TB bronchiectasis, but do demonstrate an association with mortality.[28]

3. Diagnosis

The main symptom of bronchiectasis in adults is a chronic cough productive of mucopurulent sputum,[18] although bronchiectasis can also occur in the absence of sputum production. Associated symptoms such as dyspnoea, weight loss, fatigue and haemoptysis may develop as the disease progresses.[18] Any history of persistent mucopurulent sputum production therefore raises the possibility of underlying bronchiectasis.[6] However, in patients who are not immunocompromised, reactivation adult TB occurs in the upper lobes, which in the upright position allows for spontaneous drainage of mucus. These patients therefore often do not present with a productive cough, and this has been referred to as 'dry bronchiectasis'. A comprehensive clinical history and meticulous clinical examination can reveal additional symptoms and signs associated with an underlying cause of bronchiectasis, for example a history of steatorrhoea with CF or the finding of situs inversus with Kartagener's syndrome.[29] The diagnosis of bronchiectasis can often be suspected on chest radiographic imaging, but thin-slice CT has superior sensitivity and specificity and is therefore the imaging modality of choice for confirmation of disease. Morphologically, bronchiectasis on CT images can have a cylindrical, varicose or cystic appearance.[29] Current

criteria for diagnosing bronchiectasis on CT imaging include:

- a broncho-arterial ratio (internal diameter of bronchus/outer diameter of accompanying pulmonary artery) >1 ('signet-ring sign')
- absence of normal airway tapering towards the lung periphery ('tram track' appearance)
- visible small bronchi within 1 cm from the costal visceral pleura or abutting mediastinal pleura
- thickened bronchial walls
- thick secretions in airways
- mosaic attenuation on expiratory CT views.[6,30,31]

The fixed cut-off value for the broncho-arterial ratio has recently been contested, because age- and disease-related changes in both the airway and vessel diameter can occur that may decrease the sensitivity and specificity of this measurement.[32] Magnetic resonance imaging of the chest, by which both structural and functional aspects of the lungs can be measured, is rapidly developing as an imaging modality for respiratory diseases and may play an important role in the future management of bronchiectasis.[32]

4. Management

The main principles of treating patients with bronchiectasis are to identify and treat the underlying cause, as well as optimally managing secretions (often mucopurulent), recurrent airway infections and persistent airway inflammation that can lead to worsening lung function over time (Fig. 2). Exacerbations of bronchiectasis contribute significantly to morbidity, mortality and healthcare costs and are therefore a major target for prevention, early recognition and expedited treatment. An exacerbation of bronchiectasis is defined as deterioration in ≥3 of the symptoms of coughing, sputum volume and/or consistency, sputum purulence, dyspnoea and/or exercise tolerance, fatigue and/or malaise, and haemoptysis over at least a 48-hour period, in addition to a clinician's decision that a change in treatment for bronchiectasis is required.[33] The frequent-exacerbator phenotype, defined as ≥3 exacerbations per year, carries the highest risk for recurrent exacerbations, reduced quality of life and increased mortality over a 5-year period.[34]

Fig. 2. Bronchiectasis management. (HRCT = high-resolution computed tomography; TB = tuberculosis; NTM = non-tuberculous mycobacteria; FACED = forced expiratory volume in 1 second, age, colonisation with Pseudomonas aeruginosa, numbers of pulmonary lobes affected and dyspnoea; BSI = Bronchiectasis Severity Index.)

4.1 Airway clearance

Airway clearance techniques (ACTs) are non-pharmacological interventions used to facilitate removal of retained secretions from the airways of patients with chronic respiratory diseases such as bronchiectasis.[35] Short-term goals for the management of patients living with bronchiectasis using ACTs include more effective removal of retained and infected secretions to relieve symptoms of

dyspnoea and to improve lung ventilation. Long-term goals for patient management using ACTs include minimising the risk of further airway damage, improving exercise capacity to optimise functional independence, reducing the number of disease exacerbations and hospitalisations per year, and improving disease-specific quality of life (QoL) and cough-related QoL.[6,7] ACTs consist of a variety of strategies used by physiotherapists in their management of patients living with bronchiectasis during the acute exacerbation stage and the chronic stage of their disease.[36] Physiotherapists are essential in assisting and training patients with regard to the most appropriate methods of airway clearance. CT imaging, if available, should be reviewed to complement physiotherapy patient management by identifying the affected lung segments.[6] The choice of ACT used depends on preference, the age and level of comprehension of each individual patient, and the presence or absence of contraindications to the use of each ACT.[36] The chosen ACT should form part of the patient's daily routine. The frequency and duration of airway clearance sessions should be tailored to the individual patient's requirements and may alter during periods of exacerbation.[6] Typically, treatment is performed twice a day, for a minimum of 10 minutes to a maximum of 30 minutes per session; however, during an exacerbation, treatment frequency and duration can be adapted as required depending on each individual patient's clinical presentation and needs.[6]

The ACTs perceived to be most effective during acute exacerbation and the stable stage of the disease include active cycle of breathing technique, directed huffing or forced expiratory technique, gravity-assisted body positioning (postural drainage), modified body positioning for postural drainage (no head-down tilt), oscillating positive expiratory pressure (PEP) devices, continuous PEP therapy (PEP mask), and exercise therapy.[16,34-36] Manual chest physiotherapy techniques such as percussion, shaking and vibration combined with gravity-assisted positioning or modified postural drainage may be used for patients who struggle to expectorate their secretions when using other ACTs.[6] A lesser-known but effective and inexpensive ACT is slow expiration with the glottis held open in a lateral decubitus position (ELTGOL – *l'Expiration Lente Totale Glotte Ouverte en decubitus Latéral*) and is worth considering in the management of these patients, in isolation or in combination with other ACTs.[37]

Muco-active therapy should be considered if ACTs are not effective and should be co-ordinated with ACTs to ensure that the overall effect is optimal.[38] The use of mucolytic therapy in patients with non-CF bronchiectasis has not been adequately studied. It is therefore frequently advised to use similar guidelines as for patients with CF, where isotonic saline or hypertonic saline nebulisation therapy is recommended as mucolytic agent. Hypertonic saline (7%) has an immediate effect, and ACTs should therefore be used during or directly after administration of this drug.[38] If hypertonic saline does not seem to enhance secretion clearance after 4 weeks of use, it should be stopped. Other mucolytic agents such as carbocysteine and erdosteine can be considered, although evidence regarding efficacy is limited.[38] Humidification with sterile water can also be considered.

In patients with features of reactive airway disease or asthma, or severe airflow obstruction (FEV_1 <1 L/min), consider pretreatment with bronchodilator therapy before administration of muco-active therapy and ACTs. Short-acting beta-2-agonists such as salbutamol via a metered dose inhaler or nebuliser device are recommended.

4.2 Pulmonary rehabilitation

Pulmonary rehabilitation is defined as 'a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors'.[39] Patients with bronchiectasis frequently present with reduced exercise capacity, muscle weakness and low levels of physical activity, all of which contribute to worsening dyspnoea.[40] Pulmonary rehabilitation should be offered to patients living with bronchiectasis who suffer from shortness of breath (Modified Medical Research Council Dyspnoea Scale ≥1) that limits their physical functioning and those with reduced exercise capacity.[6,40] Exercise consists of a variety of activities, such as aerobic (cardiovascular) training and resistance (strength) training. Exercise prescription should follow a comprehensive assessment,[40,41] be individually tailored, and follow the principles used for chronic obstructive pulmonary disease (COPD). Inspiratory muscle training should be considered in conjunction with exercise training to optimise training effects.[42] Education sessions, tailored to the needs of individuals living with bronchiectasis, form an essential part of pulmonary rehabilitation programmes.[6,7,38] The benefits of pulmonary rehabilitation include improvements in exercise capacity, cough symptoms and QoL, and in some cases reduced episodes of exacerbation.[43] These benefits are usually obtained within 6 - 8 weeks of attendance and maintained up to 6 months following completion of pulmonary rehabilitation.[7] Maintenance programmes should be considered for patients upon pulmonary rehabilitation programme completion. Patients who are scheduled for surgical intervention for their bronchiectasis should receive preoperative pulmonary rehabilitation to ensure that optimal physical conditioning is achieved prior to surgery.[6,7]

4.3 Health dialogue (education) and self-management

Education should be provided to each individual living with bronchiectasis, and the sessions should be tailored to the needs of such individuals. Dialogue sessions should include explaining the pathophysiology of the condition to the individual, identifying appropriate ACTs to use for secretion management, management strategies for dyspnoea during episodes of disease exacerbation, the importance of physical exercise and hydration, and relevant inhalation therapy.[6]

4.4 Exacerbations of bronchiectasis

Acute exacerbations of bronchiectasis are characterised by acute bacterial infection, although viral infection may precede and trigger this. An exacerbation of bronchiectasis is defined as a change in ≥3 of the following symptoms for >48 hours: cough, change in sputum volume and/or consistency, sputum purulence, haemoptysis, shortness of breath, and fatigue and/or malaise. Antibiotic therapy is the cornerstone of treatment and reduces sputum bacterial load as well as airway and systemic inflammation.[44] Therapy should be tailored to previous sputum bacteriology results (if known), a history of success or failure of prior regimens, and the presence of allergy to antibiotics. Sputum should be routinely obtained for Gram staining and culture prior to antibiotic administration. In addition

to excluding *Mycobacterium tuberculosis,* sputum should also be sent for NTM culture. Patients may have received multiple courses of antibiotics in the past, which increases the likelihood of resistant organisms. A chest radiograph may be obtained if pneumothorax or pneumonia is suspected.

Frequently isolated pathogens in bronchiectasis include *H. influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus* (methicillin sensitive and resistant), *P. aeruginosa* (especially mucoid types), and, less frequently, *Streptococcus pneumoniae*.[45,46] Afebrile and/or stable patients can usually be treated with an oral antibiotic, while intravenous treatment is reserved for patients with a clinical need for hospital admission, failure of oral therapy, or pathogens that are resistant to available oral agents. The choice of agent should be made according to whether the colonising organism is sensitive or resistant to a beta-lactam, and whether *P. aeruginosa* has been cultured. The respiratory fluoroquinolones (moxifloxacin, levofloxacin) are reasonable empirical and broad-spectrum options if the sputum bacteriology is unknown. In patients known to have *P. aeruginosa* airway infection and with no quinolone resistance, ciprofloxacin (500 - 750 mg twice a day) is recommended.

Use of a single nebulised antibiotic for an infective exacerbation is not recommended.

Clinical severity, treatment failure or confirmed resistance requires the administration of intravenous antibiotics. In patients with *P. aeruginosa* infection, the question of whether to use combination antibiotics is controversial, and has not been well studied; a meta-analysis of this practice in CF bronchiectasis was inconclusive.[47] A common practice is to start with a single agent (for example, an antipseudomonal beta-lactam cephalosporin or carbapenem) and to add an aminoglycoside if the patient is acutely ill and pseudomonal pneumonia seems possible. If methicillin-resistant *S. aureus* (MRSA) is isolated, the patient can be treated with oral linezolid, co-trimoxazole (if sensitive) or intravenous vancomycin.

The optimal duration of therapy is not well defined but is usually 10 - 14 days. There are no good-quality data comparing shorter v. longer regimens, and the recommendation of 14 days of antibiotics in other international guidelines is based on expert consensus only.[7]

The isolation of *P. aeruginosa* is an important prognostic and therapeutic consideration in patients with bronchiectasis, as it is associated with a decline in lung function and an increased frequency of exacerbations, hospital admissions and deaths.[48,49] Eradication of *P. aeruginosa* cultured for the first time is an attractive treatment target (Table 2); however, data on this therapy are limited, and studies are small. In one controlled trial, 35 patients with new *P. aeruginosa* were randomised to ceftazidime/tobramycin intravenously followed by three months of nebulised tobramycin 300 mg; 12 months later, 54% of the eradication group and 29% of the placebo group were free of *P. aeruginosa* in sputum.[50]

Table 2. *Pseudomonas aeruginosa* eradication

***P. aeruginosa* cultured**
Ciprofloxacin 500 - 750 mg twice a day × 14 days followed by inhaled colistin, gentamicin or tobramycin × 3 months
Intravenous antipseudomonal beta-lactam ± aminoglycoside × 14 days, followed by inhaled colistin, gentamicin or tobramycin × 3 months

4.5 Stable bronchiectasis

Daily oral non-macrolide antibiotic therapy (for example, amoxicillin 500 mg twice daily and doxycycline 100 mg twice daily) for bronchiectasis has not been well studied and is reserved for patients with ≥3 exacerbations per year who are not candidates for long-term macrolide administration and are not colonised with *P. aeruginosa*.[51] Patients with chronic airway infection with *P. aeruginosa* can try inhaled antibiotic therapy. This is an attractive strategy for chronic suppression, as there is negligible systemic absorption and the antibiotic reaches exponentially higher concentrations in the airways than if given intravenously. Inhaled antibiotic options for patients with chronic *P. aeruginosa* infection include gentamicin, tobramycin, amikacin and colistin. Inhaled antibiotics should be preceded by administration of short- or long-acting bronchodilator therapy followed by muco-active therapy and ACTs.[7] Intermittent intravenous antibiotics are not part of routine care outside of acute exacerbations, but may be given to patients with resistant organisms before thoracic or non-thoracic surgery to reduce bacterial burden and sputum production and optimise postoperative lung function.

4.6 Anti-inflammatory treatment

Patients with bronchiectasis who have recurrent exacerbations (≥3 per year) and are not colonised with *P. aeruginosa* should be offered long-term anti-inflammatory therapy with a macrolide.[7] However, prior to the introduction of macrolide therapy it is important to exclude the possibility that the cause of the bronchiectasis is NTM, as use of a single-agent macrolide may be associated with the development of drug-resistant NTM infection, especially *Mycobacterium avium-intracellulare*, the treatment of which is primarily macrolide based. In patients with chronic *P. aeruginosa*, macrolides can also be added if they continue to have exacerbations despite inhaled antipseudomonal antibiotic therapy. Macrolides are antibiotics with anti-inflammatory and immunomodulatory effects that have been proven to significantly reduce exacerbation frequency in patients with bronchiectasis. Their use was extrapolated from the CF literature, but several randomised controlled trials in patients with non-CF bronchiectasis have confirmed their benefit in terms of reducing exacerbation frequency.[51-53] Adverse effects of macrolide therapy include QT-interval prolongation, hearing loss and increased bacterial resistance (Table 3).[1] Inhaled corticosteroid therapy should not be routinely provided to patients with bronchiectasis, unless to treat a concomitant condition for which it is specifically indicated (e.g. asthma or COPD): a meta-analysis found insufficient evidence of benefit.[53] A trial of therapy is therefore advised only in adults with difficult-to-control symptoms or marked bronchial hyper-responsiveness.

4.7 Role of surgery

Since bronchiectasis is associated with a decline in lung function over time, a conservative approach to lung resection surgery is advised to preserve functional lung parenchyma as much as possible. In patients with localised bronchiectasis and recurrent infections, haemoptysis and/or mycetoma in the affected part of the lung, or localised infection with resistant organisms such as NTM or multidrug-resistant or extensively drug-resistant TB, lung resection surgery

can be considered.[54,55] Patients with diffuse bronchiectasis would probably not benefit from lung resection surgery, so medical therapy remains the mainstay of treatment. Bilateral lung transplantation is an option in selected patients with diffuse bronchiectasis, and referral to a specialised transplant centre should be considered.[56]

4.8 Causes of bronchiectasis with specific treatment

A rational approach to establishing an aetiological diagnosis is required. The justification for investigating a secondary aetiology is that in a few conditions, specific therapeutic interventions have potential benefits with minimal adverse effects. The conditions where interventions with a specific aetiology may have a significant impact on outcome include immunoglobulin deficiency syndromes, allergic bronchopulmonary aspergillosis (ABPA) and NTM infections. The recommended therapy for these conditions includes intravenous or subcutaneous immunoglobulins for patients with defective antibody production, oral corticosteroids with antifungal agents for ABPA, and specific antimicrobial agents if the diagnosis of NTM has been confirmed microbiologically. The approach as described in the British Thoracic Society guideline for the management of bronchiectasis[6] is endorsed by the SATS. In general, patients with diffuse bronchiectasis would require exclusion of conditions associated with a generalised impairment of airway mucosa function such as CF or primary ciliary dyskinesia, or a generalised immune dysfunction disorder such as immunoglobulin deficiency or HIV. A comprehensive clinical history and examination should guide the clinician in the extent of the diagnostic work-up. Routine investigations would usually include a full blood count, urea, creatinine and electrolyte profile, liver function tests and glucose determination. Assessment for underlying common immune dysfunction disorders includes HIV testing, IgG, IgM and IgA evaluation, as well as IgG subclasses and pneumococcal antibody testing. Sweat chloride or conductivity testing (see the SA consensus guideline on the management of CF[5]) should be included in the diagnostic work-up of patients with diffuse bronchiectasis or sinobronchitis. In patients with features of asthma, screening for ABPA should be performed by means of total IgE, *Aspergillus*-specific IgE or *Aspergillus* precipitants. Sputum cultures, including mycobacterial cultures, are required in all patients with bronchiectasis. Often an underlying cause cannot be identified, and referral to an immunologist may be required.

4.9 Immunisations

It is advisable that all patients with underlying chronic respiratory conditions receive vaccinations. All adults should be offered annual influenza vaccination with the trivalent/quadrivalent inactivated influenza vaccine.[57,58] Patients with bronchiectasis who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown should receive a pneumococcal conjugate vaccine (PCV13) followed by a dose of pneumococcal polysaccharide vaccine (PPSV23).[59,60] The efficacy of pneumococcal vaccination may be reduced in patients with immunoglobulin deficiency syndromes. Antibody titres to pneumococcal antigens may be required to confirm an adequate immune response. An inadequate antibody response would necessitate repeat pneumococcal vaccination. Guidance on the timing intervals and dosing schedule are published in the SA pneumonia guideline.[57]

Patients with bronchiectasis should also receive the COVID-19 vaccine. Data on the efficacy of all COVID-19 vaccines in this population group, especially patients with combined variable immunodeficiency syndrome (CVID), are limited. The only data available for a similar population group are from patients on immunosuppressive therapy for solid-organ transplants. In this cohort of patients, the vaccine is recommended even with the probability of reduced humoral efficacy, as these patients have preserved cell-mediated immunity. Patients with CVID should be immunised with two doses of COVID-19 vaccine.[61,62] Literature to support an additional COVID-19 vaccine dose to CVID patients is limited. However, data extrapolated from solid-organ transplantation recipients undergoing immunosuppressive treatment suggest that there is merit in receiving booster doses 9 months after receiving the last dose to counteract waning immunity.[61,62]

5. Prognosis

Age-adjusted mortality rates in patients with bronchiectasis were double that of the general population in a UK population-based cohort study.[11] Factors associated with a worse prognosis include older age and comorbidities, lower FEV_1, lower body mass index, recurrent exacerbations, *P. aeruginosa* colonisation, a greater extent of disease and worsening dyspnoea.[63,64] Several scoring systems, such as the BSI,[63] accessible by means of an online calculator (http://www.bronchiectasisseverity.com/15-2/), the Bronchiectasis Aetiology

Table 3. Differences between inhaled and oral macrolide antibiotics

Inhaled antibiotics	Macrolide antibiotics
Advantages	Advantages
High concentrations delivered to airways	Easy to use, low treatment burden and relatively cheap
Lower rate of resistance	Reduce exacerbations
Lower collateral damage	Anti-inflammatory effects
Low systemic absorption	
Disadvantages	Disadvantages
Concern over tolerance with nebulised formulation	Gastrointestinal and other side-effects
Deposition erratic	Antibiotic resistance
Time consuming	Non-tuberculous mycobacteria colonisation must be excluded
Rotating regimens	Cardiovascular events/drug interactions (Q-Tc prolongation)
Limited data in patients without Pseudomonas aeruginosa	Long-term efficacy and tolerance

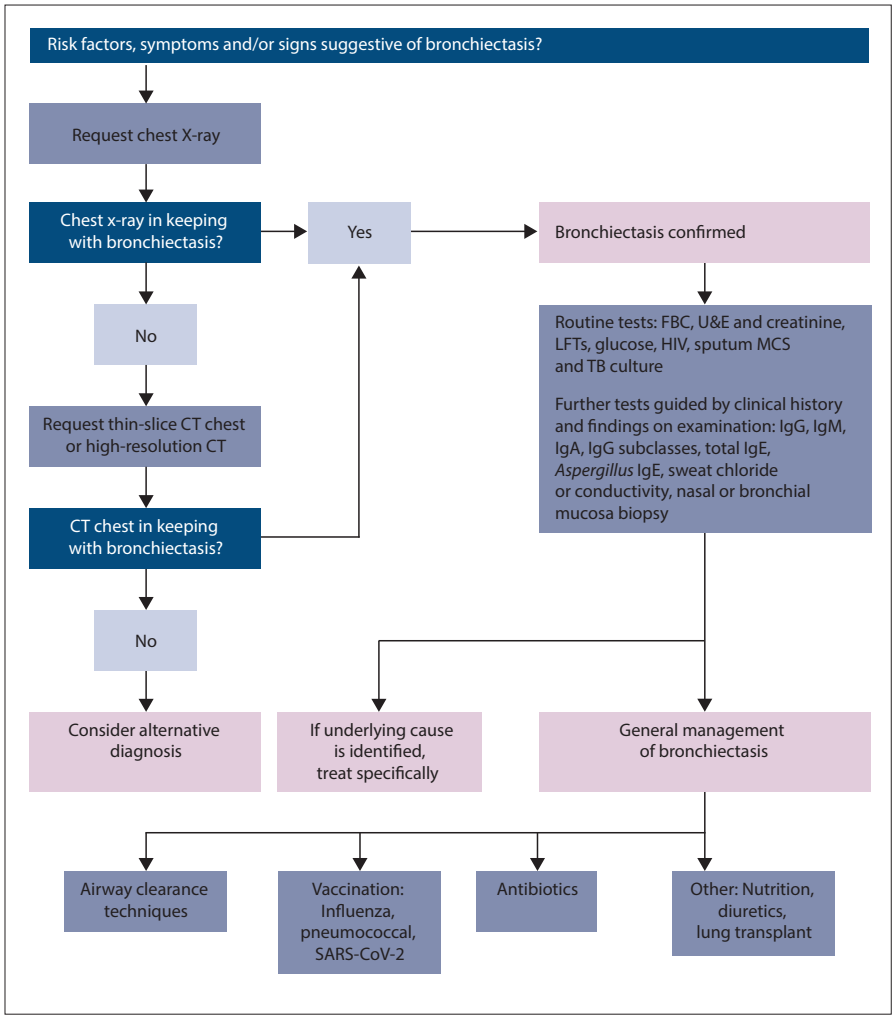

Fig. 3. Algorithmic approach to bronchiectasis. (CT = computed tomography; FBC = full blood count; U&E = urea and electrolytes; LFTs = liver function tests; MCS = microscopy, culture and sensitivity; TB = tuberculosis; IgG = immunoglobulin G; IgM = immunoglobulin M; IgA = immunoglobulin A; IgE = immunoglobulin E.)

Comorbidity Index (BACI),[65] FACED[64] and E-FACED (incorporating exacerbations),[66] have been developed for predicting severity and prognosis in patients with non-CF bronchiectasis.

6. Follow-up

Bronchiectasis is a chronic condition with variable rates of lung function decline, dependent on colonisation with pathogenic bacteria, especially *Pseudomonas* and *S. aureus*, exacerbation frequency, and adherence to airway clearance therapy. Patients should therefore be followed up frequently, at least 3 - 6-monthly, for clinical review. Apart from the general history and physical examination, adherence to ACT schedules, as well as spirometry, should form part of routine assessment at each visit. Sputum for microscopy, culture and sensitivity should be assessed 3-monthly (if possible), and this should include culture for TB to exclude infection with NTM. For patients on long-term treatment with macrolides, hearing should be assessed annually, and macrolides should be discontinued if any deterioration in hearing is found, while also referring the patient appropriately for audiology assessment.

7. Conclusion

An algorithmic approach to bronchiectasis is provided in Fig. 3. Bronchiectasis has largely been a neglected lung condition, but the establishment of the EMBARC database and recent new research into the condition have improved the outlook for patients. We have made progress in research into ACTs and some progress in the use of appropriate antibiotics for this condition. The importance of collaboration among interprofessional team members in patient management, with clear communication regarding management goals, collective planning for hospital discharge and follow-up in the community to ensure optimal clinical outcomes, cannot be over-emphasised. However, several questions remain unanswered. In SA we have the opportunity to conduct research into the epidemiology of bronchiectasis, post-TB bronchiectasis, which seems to be a distinct entity, and HIV-associated bronchiectasis.

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Disclaimer. This position statement is only intended for guidance on general management of patients. Each patient must be individually managed. The final responsibility for management of any patient rests on the managing physician and healthcare provider.

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