Post-TB Bronchiectasis: Is Effective Medical Management Possible?

Vincent M. Balanag Jr., MD, FPCCP
“It should be remembered that bronchiectasis in association with inactive tuberculosis is a benign disease.”

“However, if symptoms are severe (especially hemoptysis) resection is the only cure.”

“Thoracoplasty or other collapse measures may be palliative value in controlling hemorrhage in cases where resection is contraindicated.”
“If there are symptoms, considerable relief may be obtained by the temporary use of penicillin or aureomycin.”

“Some patients who have abundant cough and sputum may obtain considerable relief by moving to a warm, dry climate.”
“If there are symptoms, considerable relief may be obtained by the temporary use of penicillin or aureomycin.”

“Some patients who have abundant cough and sputum may obtain considerable relief by moving to a warm, dry climate.”

David Salkin, California Medicine 1950
Keys to Effective Medical Management

1. Good understanding of the etiology and pathogenesis of the disease
2. Clear and generally-accepted diagnostic criteria
3. Management principles aimed at clinically relevant outcomes
4. Treatment options that are efficacious & effective
5. Systematic approach to treatment
Bronchiectasis

- Persistent or progressive condition characterized by dilated, thick-walled bronchi. ¹

1. *BTS Bronchiectasis Guideline, 2010*
Bronchiectasis

- Due to destruction of the elastic and muscular components of bronchial wall, usually due to acute or chronic infection.\(^2\)

2. *ACCP Evidence-based Clinical Practice Guidelines, 2006*
Detection of bronchiectasis

Focal bronchiectasis
- Congenital bronchial atresia
- Extrinsic compression
- Endobronchial malignancy
- Foreign body
- Broncholithiasis
- Airway stenosis

Diffuse bronchiectasis
- Peripheral predominance
- Central predominance

Peripheral predominance
- Upper lung predominance
- Lower lung predominance
  - Idiopathic
  - Postinfectious
  - Repeated aspiration
  - Fibrotic lung disease
  - Posttransplant rejection
  - Hypogammaglobulinemia

Central predominance
- Right middle lobe and lingula predominance
- Allergic bronchopulmonary aspergillosis
- Mounter-Kuhn's syndrome
- Williams-Campbell syndrome

Atypical mycobacterial infection (MAI)
- Immotile cilia syndrome
Bronchiectasis in TB

- Co-existence of bronchiectasis and TB was first noted by Laennec in 1819.

- Granger in 1878 first stressed that:
  - Bronchiectasis may appear in the course of active tuberculosis, or
  - Develop as a sequela of inactive tuberculosis, or
  - TB itself may engraft on already developed bronchiectasis
Bronchiectasis in TB

• Bronchiectasis has been accepted as a universal sequela of tuberculosis

• Earlier studies, many dating from pre-chemotherapy era, show presence of bronchiectasis in 68% to 100% of TB cases
Post-TB Bronchiectasis: prevalence

• 100 patients who completed 9 months of supervised TB treatment,
• All with residual lung lesions (fibrosis, fibro-cystic areas, cavity) by x-ray:
• Pre-treatment extent of lesions
  ➢ 37 moderately-advanced TB
  ➢ 63 far-advanced TB
• All subjected to bronchography

Bronchographic sequelae vs. pre-treatment extent of lesions

<table>
<thead>
<tr>
<th></th>
<th>Moderately-advanced</th>
<th>Far-advanced</th>
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<tbody>
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<td>Normal</td>
<td>10 (27.0)</td>
<td>4 (16.4)</td>
<td>14 (14.0)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>17 (46.0)</td>
<td>45 (71.4)</td>
<td>62 (62.0)</td>
</tr>
<tr>
<td>Others</td>
<td>10 (27.0)</td>
<td>14 (22.2)</td>
<td>24 (24.0)</td>
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<tr>
<td>Total</td>
<td>37 (100)</td>
<td>63 (100)</td>
<td>100 (100)</td>
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### Bronchographic sequelae vs. pre-treatment smear status

<table>
<thead>
<tr>
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<th>Smear-positive</th>
<th>Smear-negative</th>
<th>Total</th>
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<td>Normal</td>
<td>12 (15.4)</td>
<td>2 (9.1)</td>
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<tr>
<td>Bronchiectasis</td>
<td>46 (59.0)</td>
<td>16 (72.7)</td>
<td>62 (62.0)</td>
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<tr>
<td>Others</td>
<td>20 (25.6)</td>
<td>4 (18.2)</td>
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<tr>
<td>Total</td>
<td>78 (100)</td>
<td>22 (100)</td>
<td>100 (100)</td>
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*Sahoo, et al. Ind J Tub (1988)*
Post-TB Bronchiectasis: definition

• Bronchiectasis in the presence of inactive TB (Salkin, 1960).

• Cylindrical or saccular dilatation of the bronchial tree occurring in an area of previous tuberculosis (Hamel, 1962).
Post-TB Bronchiectasis: pathogenesis

- Tuberculous bronchitis - spillage of tuberculous exudate from parenchymal focus or ruptured lymph nodes into the bronchial tree
- Bronchial obstruction due to hilar TB adenopathy, with secondary infection
- Traction from contracting scar tissue in neighboring lung parenchyma (traction bronchiectasis).
Tuberculous Bronchitis

NORMAL

INFLAMMATORY IRREGULARITY
STENOSIS AND OBLITERATION OF BRONCHIAL LUMEN

EARLY BRONCHIAL DILATATION

LATE BRONCHIAL DILATATION
TB Hilar Lymphadenitis
Traction Bronchiectasis
Bronchiectasis: Pathology

- Bronchial dilatation is associated with **destructive** and **inflammatory** changes in the walls of **medium-sized airways**, often at the level of segmental or subsegmental bronchi.

- Airway inflammation is **primarily mediated by neutrophils** and results in up-regulation of enzymes such as elastase and matrix metalloproteinases.

- The normal structural components of the wall, including cartilage, muscle, and elastic tissue, are **destroyed and may be replaced by fibrous tissue**.

- The dilated airways frequently contain pools of **thick, purulent material**, while more peripheral airways are often occluded by secretions or obliterated and replaced by fibrous tissue.
Bronchiectasis: Pathology

• Additional microscopic features include bronchial and peribronchial inflammation and fibrosis, ulceration of the bronchial wall, squamous metaplasia, and mucous gland hyperplasia.

• The parenchyma normally supplied by the affected airways is abnormal, containing varying combinations of fibrosis, emphysema, bronchopneumonia, and atelectasis.

• As a result of inflammation, vascularity of the bronchial wall increases, with associated enlargement of the bronchial arteries and anastomoses between bronchial & pulmonary arterial circulations.
Bronchiectasis: Pathology

- Normal Bronchus
  - Wall
  - Mucous gland
  - Cilia
  - Air passageway
  - Mucus

- Bronchiectasis
  - Loss of cilia
  - Increased mucus
  - Destruction of wall
Bronchiectasis

Clinical Course
• Chronic sputum production
• Recurrent respiratory infections/pneumonia
• Airflow obstruction
• Respiratory failure

Cardinal Symptoms
• Cough
• Sputum production
• Dyspnea
• Hemoptysis
Post-TB Bronchiectasis: Diagnosis

• Bronchiectasis
  – history of chronic sputum production, recurrent lower respiratory infections or hemoptysis
  – HRCT findings consistent with bronchiectasis:
    • *Bronchial dilatation*
      – Signet ring sign” interdiameter of bronchus greater than its adjacent pulmonary artery (1.5x or more)
      – Tramlines - non-tapering or flaring of bronchi towards the periphery
    • *Presence of bronchi in the outer lung fields (within 1-2 cm of pleura)*
Post-TB Bronchiectasis: Diagnosis

• **Tuberculous etiology**
  – previous clinical, radiographic or bacteriologic diagnosis of TB
  – Upper lobe or right middle lobe location of bronchiectasis

• **Inactive TB disease**
  – “healed” or “stable” lesions
  – absence of cavitation
  – sputum negative for TB bacilli
# CT Findings in Post-TB Bronchiectasis

Cartier et al, AJR 1999.

<table>
<thead>
<tr>
<th>CT Findings</th>
<th>Previous Tuberculosis</th>
<th>Childhood Infection</th>
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<tr>
<td>Zonal Predominance</td>
<td>%</td>
<td>%</td>
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<td>Upper</td>
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<td>Middle</td>
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<td>None</td>
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<td>0</td>
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<td>Cross-sectional Distribution</td>
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<tr>
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<tr>
<td>Central</td>
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<td>7</td>
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<tr>
<td>Mixed</td>
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## CT Findings in Post-TB Bronchiectasis

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<th>CT Findings</th>
<th>Previous Tuberculosis</th>
<th>Childhood Infection</th>
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<tr>
<td>Laterality</td>
<td>%</td>
<td>%</td>
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<tr>
<td>Unilateral</td>
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<td>Bilateral</td>
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<tr>
<td>Asymmetric</td>
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<td>89</td>
</tr>
</tbody>
</table>

Cartier et al, AJR 1999.
Assessing Severity of Bronchiectasis

- Radiographic extent (HRCT)
- Sputum characteristics: volume, color
- Frequency of acute exacerbations
- Dyspnea rating (MRC, Borg scale, BDI)
- Exercise capacity (6-MWT)
- Health-related QOL (SGRQ)
- PFT/Spirometry (FEV1, RV, RV/TLC)
- Arterial blood gases (PO2, PCO2)
Radiographic Extent

• Scoring system proposed by Bhalla et al, (Radiology 1991).
  – Each lobe (considering lingula and middle lobe as independent) is scored as:
    ➢ 0 = no bronchiectasis
    ➢ 1 = cylindrical bronchiectasis in a single segment
    ➢ 2 = cylindrical bronchiectasis in more than 1 segment
    ➢ 3 = cystic bronchiectasis
  – Maximum score: 18 points:
    • Mild : 1-5 points
    • Moderate: 6-9 points
    • Severe: >9 points
Sputum volume

- Bronchiectatic lesions in the upper lobes → the amount of expectoration is slight in relation to the ectasia;

- Abundant cough and sputum are indicative of bronchiectasis in the dependent portions of the lung; or of superimposed infection

Salkin, 1950
Sputum volume

• Sputum volume is associated with extent of bronchiectasis and presence of small-airway abnormalities (Ooi et al, Radiology, 2002)

• Sputum volume is correlated with extent of CT lesions (Ramos et al, LCP 2008)
Sputum color

• Sputum color predicted bacterial colonization in non-CF bronchiectasis:
  - mucoid: 5%
  - mucopurulent: 43.5%
  - purulent: 86.4%

• Other independent factors associated with purulent sputum
  - varicose or cystic bronchiectasis
  - FEV1 < 80% predicted

Murray et al. ERJ (2009)
Airflow obstruction in TB


• In 100 pts fully treated with tuberculosis in a tertiary teaching hospital in India, prevalence= 46%
  – Mild (FEV1 > 60%) = 75%
  – Moderate (FEV1 40-59%) = 10%
  – Severe (FEV1 <40%) = 15%
• Prospective study of 40 pts with clinically-stable, CT-diagnosed bronchiectasis, 80% related to PTB
• HRCT Scores (extent of bronchiectasis)
  – Mild (1-5): 14 (35%)
  – Moderate: 15 (37.5%)
  – Severe: 11 (27.5%)
• Pulmonary function
  – Normal: 2 (5%)
  – Obstructive alone: 6 (15%)
  – Restrictive alone: 14 (35%)
  – Obstructive and restrictive: 18 (45%)

Ramos et al, LCP 2004
Airflow Obstruction in TB

- Previous TB is an independent risk factor for obstructive lung disease, even if the lesion is minimal (OR=2.56, 95% CI 1.84-3.56) (Lee et al, J Korean Med Sci 2011)
- Prior TB is independently associated with an increased risk of airflow obstruction (OR=1.37, 95% CI 1.13-1.67) (Lam et al, Chest 2010)
- History of TB is associated with presence airflow obstruction (OR=6.31, 95% CI 2.67-15.0) (Idolor et al, 2010)
Cause of airflow obstruction?

• Bronchospasm affecting larger airways and retained secretions are contributors to airway obstruction; no significant correlation between extent of bronchiectasis and pulmonary resistance (Pande, et al. Thorax 1971).

• Airflow obstruction in bronchiectasis is linked to evidence of intrinsic disease of the small and medium airways (bronchial wall thickness) and not to bronchiectatic abnormalities, emphysema or retained endobronchial secretions (Roberts et al. Thorax, 2000).
Principles and General Approach to Management

• ACCP evidence-based CPG (2006):
  – The goals of treatment generally are:
    • To improve symptoms of cough, sputum production and dyspnea
    • To prevent progression of airway damage
  – Goals of pharmacotherapy:
    • enhance bronchodilation and enhance mucociliary clearance
    • prevent and treat recurrent infection
    • mobilize secretions
Principles and General Approach to Management

• BTS Bronchiectasis Guidelines (2010):
  – Identify and treat underlying cause to prevent disease progression [D]
  – Maintain or improve pulmonary function [D]
  – Improve quality of life by reducing daily symptoms and exacerbations [D]
  – In children, achieve normal growth and development [D]
Treatment Options

• Antibiotics
• Mucolytics
• Bronchodilators
• Corticosteroids
• Chest physiotherapy
• Pulmonary rehabilitation/exercise
• Vaccination
Antibiotics

• Indicated for the treatment of exacerbations and chronic active disease

  – Before starting antibiotics, a sputum sample should be sent off for culture [BTS,D]

  – Empirical antibiotics should be started while waiting sputum microbiology [BTS,D]
Antibiotics

• Previous sputum bacteriology results can be useful in deciding which antibiotic to use.

• Antibiotics can be modified subsequently once the pathogen is isolated only there is no clinical improvement and treatment should be guided by antibiotic sensitivity results.

• Failure to respond to an antibiotic course should prompt a repeat sputum culture.

BTS Bronchiectasis Guidelines, 2010
Antibiotics

• If there are no previous bacteriology, first-line treatment is amoxicillin 500 mg TID clarithromycin 500 mg BID for 14 days [B].

• High dose oral regimens (e.g., amoxicillin 1 gm TID or 3 gm BID) may be needed in patients with severe bronchiectasis chronically colonized with Hemophilus influenzae [B]

• Ciprofloxacin should be used in patients colonised with Pseudomonas aeruginosa with cautious use in the elderly [B]

BTS Bronchiectasis Guidelines, 2010
IV Antibiotics

• Intravenous antibiotics should be considered when patients are:
  – Particularly unwell
  – Have resistant organisms
  – Have failed to respond to oral antibiotics

• Likely apply to patients with Pseudomonas aeruginosa

BTS Bronchiectasis Guidelines, 2010
Combination Antibiotics

• Not required in patients colonized with:
  – H. influenzae, Moraxella catarrhalis, Strep pneumo or methicillin-sensitive Staph aureus

• Should be used:
  – for infections due to strains of Pseudomonas aeruginosa that are resistant to more than one antipseudomonal antibiotics including ciprofloxacin. or
  
  – if the clinician suspects the patient will require many subsequent antibiotic courses to reduce the development of drug resistance

BTS Bronchiectasis Guidelines, 2010
Long-term antibiotics

• Should be considered in:
  – patients having ≥3 exacerbations per year requiring antibiotic therapy
  – patients with fewer exacerbations that are causing significant morbidity

• Long-term nebulized antibiotics should be considered in patients chronically colonized with P. aeruginosa.

BTS Bronchiectasis Guidelines, 2010
Prolonged-use Antibiotics

• Prolonged use antibiotics improve clinical response, and may improve quality of life and reduce time to first exacerbation,
  – nebulized gentamicin

• They may not reduce exacerbation rates or improve lung function

Clinical Evidence, 2011
Macrolides

Systematic Review and Meta-Analysis (Gao, et al. PLOS ONE March 2014)

• Population: clinically-stable non-CF bronchiectasis defined by HRCT

• Intervention: Long-term macrolide treatment (≥ 2 months): Roxithromycin, erythromycin & azithromycin, 8-52 wks.

• Comparison: placebo or usual care
Macrolides

• Significantly decreased the number of patients with exacerbations and the frequency of exacerbations, but not admissions for infective exacerbations, in adults and children

• Led to statistically significant improvement in QoL but not 6MWT, in adults

• Resulted in significantly larger increases in FEV1 and FVC from baseline, in adults but not in children

• Might increase the risk of diarrhea and abdominal discomfort, but not overall adverse events

Gao et al. PLOS One 2014
Mucolytics

BTS Bronchiectasis Guideline, 2010

• “Recombinant human DNase should not be used in adults with bronchiectasis.” [A]

• “Recombinant human DNase should not be used in children with bronchiectasis.” [D]
Mucolytics

• Recombinant **DNAse should be avoided** in non-CF bronchiectasis, except in the context of a clinical trial.

• High doses of **bromhexine with antibiotics may help** with sputum production and clearance, but long-term data and robust clinical outcomes are lacking.

• **Erdosteine may be a useful adjunct** to physiotherapy in stable patients, but robust long-term trials are required.

• Evidence is insufficient to permit evaluation of the routine use of other mucolytics.

Cochrane Review (2014)
Bromhexine

- Bronchiectasis by bronchography/CT, in clinical exacerbation (cough, >20 ml sputum)
- RCT, double-blind
- Bromhexine 30mg TID plus ceftazidime 1 gm od vs. placebo plus ceftazidime

- Reduced sputum volume at about 2 wks
- Improved symptom scores (difficulty of expectoration, cough and quality of sputum) at about 2 weeks

Erdosteine

• Elderly patients with bronchiectasis and mucus hypersecretion
• Open-label, parallel trial
• Erdosteine plus chest physiotherapy vs. chest physiotherapy alone

- Erdosteine had significant improvement in FEV1, FVC
- Erdosteine shows significant improvement in mucus volume production

Erdosteine

• Office of Orphan Products Development (OOPD) of the Food and Drug Administration (FDA) has granted orphan drug designation for its drug candidate, Erdosteine®, for the treatment of bronchiectasis. Erdosteine is a mucolytic with antibacterial, anti-inflammatory, and antioxidant properties.
Bronchodilators

ACCP Evidence-based CPG, 2006:

• “In patients with bronchiectasis with airflow obstruction and/or bronchial hyperreactivity, therapy with bronchodilators may be of benefit.”
  – Level of evidence, expert opinion;
  – Benefit, small;
  – Grade of recommendation, E/C.
Bronchodilators

BTS Bronchiectasis Guideline, 2010

• “It seems appropriate to assess patients with airflow obstruction for reversibility to $B_2$-agonist and anticholinergic bronchodilators and to institute therapy where lung function or symptoms improve with therapy.” [D]

• “Methyxanthines have no routine role in bronchiectasis.” [D]
Bronchodilators

• **B2-agonists**
  – Frequently prescribed in bronchiectasis
  – Theoretically may be beneficial; increase ciliary beat frequency in vitro
  – No data to support its efficacy

• **Oral methyloxanthines** *(Clin Evid, 2011)*
  – Often used in bronchiectasis
  – No good-quality trials
  – “may use on empirical or trial basis”
Inhaled CS

• BTS Bronchiectasis Guideline, 2010

  – Inhaled steroids should not be used routinely in children with bronchiectasis (outside of use for those patients with additional asthma). [D]

  – In adults, current evidence does not support routine use of inhaled steroids in bronchiectasis (outside of use for those patients with additional asthma). [D].
Inhaled CS

• Cochrane Review (2009)
  – There is insufficient data to recommend the routine use of inhaled steroids in stable state bronchiectasis;
  – Therapeutic trial might be justified in patients with difficult to control symptoms.
Oral CS

• Cochrane Review (2011)
  – There are no randomized trials upon which to base recommendations about the use of oral corticosteroids in acute or stable bronchiectasis.
Physiotherapy

• Patients should be made aware of airway clearance techniques:
  – active cycle breathing techniques [A]
  – oscillating positive expiratory devices [A]
  – forced expiration technique [A]

• Inclusion of postural drainage should be considered [B]

BTS Bronchiectasis Guidelines. 2010
Physiotherapy

• Adjuncts to airway clearance techniques:
  – Sterile water inhalation to facilitate clearance [B]
  – Nebulized normal saline to increase sputum yield, reduce sputum viscosity and improve ease of expectoration [B]
  – Nebulized hypertonic saline, pretreated with a bronchodilator in those with BHR [D]
  – Nebulized B2 agonist to enhance clearance [B]
  – NIV/IPPB to augment TV and reduce work of breathing [D]

BTS Bronchiectasis Guidelines. 2010
Exercise

• BTS Bronchiectasis Guidelines, 2010
  – Pulmonary rehabilitation should be offered to individuals who have breathlessness affecting ADL [B]
  – Inspiratory muscle training can be used in conjunction with conventional pulmonary rehabilitation to enhance the maintenance of training effects [B]

• Clinical Evidence, 2011
  – Inspiratory muscle training may improve quality of life and exercise endurance
Vaccination

• **Cochrane Database Syst Rev, 2007**
  – 23-valent pneumococcal vaccine:
    • The study found a significant reduction in acute infective respiratory exacerbations in the PV group compared to the control group, OR=0.48 (95%CI 0.26, 0.88); number needed to treat to benefit = 6 (95%CI 4, 32) over 2-years.

  • Current but limited evidence support the use of 23-valent pneumococcal vaccine as routine management in adults with bronchiectasis. Circumstantial evidence also support the use of routine 23-valent pneumococcal vaccination in children with bronchiectasis.
Vaccination

• **Cochrane Database Syst Rev, 2007**
  
  – Influenza vaccine:
    
    • No eligible trials were identified and thus no data were available for analysis.
    
    • There is neither evidence for, nor against, routine annual influenza vaccination for children and adults with bronchiectasis.
Treatment approach to Bronchiectasis

- Bronchiectasis
  - Localized
    - Treatment of underlying disease (if possible)
    - Surgery
      - For example, substitution for immunoglobulin deficiency
  - Generalized
    - Physiotherapy, breathing therapy
    - Exacerbation?
      - Oral/IV antibiotic therapy for 7–10 days
    - Obstruction?
      - Betasypathomimetics, Anticholinergics
    - Frequent exacerbations, colonization with *Pseudomonas*, severe symptoms
      - Inhaled antibiotic treatment
      - If required inhaled corticosteroids
      - If required macrolide antibiotics
      - Consider transplantation

Jessica Rademacher, and Tobias Welte, 2011
**Persistent Asthma: Daily Medication**

Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.

**Step 1**
**Preferred:** Low-dose ICS
**Alternative:** Cromolyn, LTRA, Nedocromil, or Theophylline

**Step 2**
**Preferred:** Low-dose ICS + LABA
**Alternative:** Medium-dose ICS

**Step 3**
**Preferred:** High-dose ICS + LABA
**Alternative:** Medium-dose ICS + either LTRA, Theophylline, or Zileuton

**Step 4**
**Preferred:** High-dose ICS + LABA
**Alternative:** Consider Omalizumab for patients who have allergies

**Step 5**
**Preferred:** High-dose ICS + LABA + oral corticosteroid
**Alternative:** Consider Omalizumab for patients who have allergies

**Step 6**
Step up if needed
(first, check adherence, environmental control, and comorbid conditions)

Assess control

Step down if possible
(and asthma is well controlled at least 3 months)

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**Quick-Relief Medication for All Patients**
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

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**Key:** Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. EIB, exercise-induced bronchospasm; ICS, inhaled corticosteroid; LABA, long-acting inhaled beta₂-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta₂-agonist
### Stepwise Management of Stable COPD

<table>
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<th>Stage 0</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4</th>
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<tr>
<td><strong>At Risk</strong></td>
<td><strong>Mild</strong></td>
<td><strong>Moderate</strong></td>
<td><strong>Severe</strong></td>
<td><strong>Very Severe</strong></td>
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<tr>
<td>Chronic Symptoms (Cough and Sputum Production)</td>
<td>FEV₁ ≥ 80% Predicted</td>
<td>FEV₁ 50% to 79% Predicted</td>
<td>FEV₁ 30% to 49% Predicted</td>
<td>FEV₁ &lt;30% Predicted or Chronic Respiratory Failure or Right-Sided Heart Failure</td>
</tr>
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</table>

- **Stage 0**
  - FEV₁ Normal
  - Chronic Symptoms (Cough and Sputum Production)
- **Stage 1**
  - Mild
  - FEV₁ ≥ 80% Predicted
- **Stage 2**
  - Moderate
  - FEV₁ 50% to 79% Predicted
- **Stage 3**
  - Severe
  - FEV₁ 30% to 49% Predicted
- **Stage 4**
  - Very Severe
  - FEV₁ <30% Predicted or Chronic Respiratory Failure or Right-Sided Heart Failure

**Stage 1 Treatment**
- Add long-acting bronchodilator(s) for relief of persistent dyspnea
- Add inhaled corticosteroids for persistent dyspnea on bronchodilator(s) or repeated exacerbations

**Stage 2 Treatment**
- Add pulmonary rehabilitation
- Add long-term oxygen to correct arterial hypoxemia

**Stage 3 Treatment**
- Consider pulmonary rehabilitation for patients who are persistently dyspneic despite therapy with long-acting bronchodilators and inhaled corticosteroids
- Add short-acting bronchodilator for relief of intermittent dyspnea

**Stage 4 Treatment**
- Consider transplantation or other surgical treatment

**General Management**
- Smoking cessation for all smokers
- Vaccinations against influenza and pneumococcal infection for those older than 65 years
# Grading of Clinical Severity of Bronchiectasis

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<th>Parameter</th>
<th>MILD</th>
<th>MODERATE</th>
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<td>Sputum volume</td>
<td>0-50 ml/day</td>
<td>50-150 ml/day</td>
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<tr>
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<td>mucopurulent</td>
<td>purulent</td>
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<td>AE per year</td>
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<td>&gt;6</td>
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<tr>
<td>Dyspnea grade</td>
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<td>Grade 1-2</td>
<td>Grade 3-4</td>
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<tr>
<td>Limitation of activities</td>
<td>None</td>
<td>Mild to moderate</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>Spirometry</td>
<td>Normal</td>
<td>Mild defects</td>
<td>Moderate to severe defects</td>
</tr>
<tr>
<td>Resting ABG</td>
<td>Normal</td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>
Stepwise approach to Bronchiectasis

**Mild**
- Adequate hydration
- Vaccination
- Antibiotic therapy for acute exacerbations
- Specific treatment, if available

**Moderate**
- Prolonged or cyclic antibiotics
- Mucolytics
- Bronchodilators
- Chest Physiotherapy
- Pulmonary Rehabilitation
- Surgical resection, if focal

**Severe**
- Long-term oxygen therapy
- Inhaled/oral corticosteroids
- Lung Transplantation
Common isolates: out-patients

• 45 patients with symptomatic bronchiectasis seen at the OPD (2014)

• Common pathogens:
  – Moraxella catarrhalis: 15 (67%)
  – Streptococcus pneumoniae: 5 (11%)
  – Coagulase-neg staph aureus: 4 (9%)
  – Acinetobacter spp: 6 (13%)
  – Pseudomonas aeruginosa: 4 (9%)

Yu & Raymond, LCP 2014
Common isolates: admitted pts.

- 84 patients admitted with acute exacerbations of post-TB bronchiectasis (2008-2010):

- Common pathogenic organisms:
  - Moraxella: 19 (24%)
  - Pseudomonas: 15 (19%)
  - Acinetobacter: 9 (11%)

Carabbacan & Jocson, LCP 2011)
## Sensitivity Pattern

<table>
<thead>
<tr>
<th></th>
<th>MORAXELLA</th>
<th>PSEUDOMONAS</th>
<th>ACINETOBACTER</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO-AMOXYCLAV</td>
<td>13/13 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEFTRIAXONE</td>
<td>16/16 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COTRIMOXAZOLE</td>
<td>3/15 (20%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ERYTHROMYCIN</td>
<td>3/12 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIPROFLOXACIN</td>
<td>8/12 (75%)</td>
<td>11/14 (79%)</td>
<td>6/6 (100%)</td>
</tr>
<tr>
<td>LEVOFLOXACIN</td>
<td>7/9 (78%)</td>
<td>3/3 (100%)</td>
<td></td>
</tr>
<tr>
<td>CEFTAZIDIME</td>
<td>10/12 (83%)</td>
<td>4/5 (80%)</td>
<td></td>
</tr>
<tr>
<td>GENTAMYCIN</td>
<td>9/12 (75%)</td>
<td>6/7 (86%)</td>
<td></td>
</tr>
<tr>
<td>AMIKACIN</td>
<td>12/13 (92%)</td>
<td>6/8 (75%)</td>
<td></td>
</tr>
<tr>
<td>PIPER-TAZOBACTAM</td>
<td>10/13 (77%)</td>
<td>8/8 (100%)</td>
<td></td>
</tr>
<tr>
<td>IMIPENEN</td>
<td>7/9 (78%)</td>
<td>7/7 (100%)</td>
<td></td>
</tr>
<tr>
<td>AZTREONAM</td>
<td>8/11 (73%)</td>
<td>3/5 (60%)</td>
<td></td>
</tr>
</tbody>
</table>

Carabbacan & Jocson, LCP 2011)
Keys to Effective Medical Management: Post-TB Bronchiectasis

- Good understanding of the etiology and pathogenesis of the disease
- Clear and generally-accepted diagnostic criteria
- Management principles aimed at clinically relevant outcomes
- Treatment options that are efficacious & effective
- Systematic approach to treatment
Thank You.
Bronchiectasis

• Persistent or progressive condition characterized by dilated, thick-walled bronchi. ¹

• Due to destruction of the elastic and muscular components of bronchial wall, usually due to acute or chronic infection.²

• Increased bronchial artery proliferation and arteriovenous malformations.²

1. BTS Bronchiectasis Guideline, 2010
2. ACCP Evidence-based Clinical Practice Guidelines, 2006
• Relationship of extent of bronchiectasis on CT and clinical parameters of disease:
  – sputum volume, character and duration
  – dyspnea grade, limitation of activity and number of exacerbations
• Patients with stable bronchiectasis confirmed by HRCT (n=40); 80% with prior TB
• HRCT score: Mild (1-5 segments)=35%; Moderate (6-9 segments)=37%; Severe (>9 segments)=28%
Correlation between CT extent and clinical parameters (Ramos et al. LCP 2004)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Spearman’s Rank Correlation Coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum years</td>
<td>0.1994</td>
<td>0.2173</td>
</tr>
<tr>
<td>Sputum volume</td>
<td>0.3192</td>
<td>0.0447</td>
</tr>
<tr>
<td>Sputum color</td>
<td>0.2053</td>
<td>0.2038</td>
</tr>
<tr>
<td>Dyspnea grade</td>
<td>0.1449</td>
<td>0.3725</td>
</tr>
<tr>
<td>Limitation in activity</td>
<td>0.0555</td>
<td>0.7339</td>
</tr>
<tr>
<td>No. of exacerbations</td>
<td>0.0788</td>
<td>0.6289</td>
</tr>
<tr>
<td>PFT</td>
<td>0.3259</td>
<td>0.0402</td>
</tr>
<tr>
<td>ABG</td>
<td>-0.0440</td>
<td>0.7876</td>
</tr>
</tbody>
</table>
# Bronchiectasis Severity Index

<table>
<thead>
<tr>
<th>Severity Criteria</th>
<th>Levels</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt; 50</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>50-69</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>70-79</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>80+</td>
<td>8</td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>≥ 18.5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&lt; 18.5</td>
<td>2</td>
</tr>
<tr>
<td>Predicted FEV1</td>
<td>&gt;80%</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>50-80%</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>30-49%</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&lt;30%</td>
<td>3</td>
</tr>
<tr>
<td>Hospital admissions in the past 2 years</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>5</td>
</tr>
</tbody>
</table>
## Bronchiectasis Severity Index

<table>
<thead>
<tr>
<th>Severity Criteria</th>
<th>Levels</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacerbation frequency in the last 12 months</td>
<td>0-2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3 or more</td>
<td>2</td>
</tr>
<tr>
<td>MRC dyspnea score</td>
<td>1-3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Colonisation status</td>
<td>Not colonised</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Chronic colonisation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>P. Aeruginosa colonisation</td>
<td>3</td>
</tr>
<tr>
<td>Radiological severity</td>
<td>&lt; 3 lobes</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3 or more lobes or cystic changes</td>
<td>1</td>
</tr>
</tbody>
</table>
# Bronchiectasis Severity Index

<table>
<thead>
<tr>
<th>Points</th>
<th>1 year outcome</th>
<th>4 year outcome</th>
<th>1 year outcome</th>
<th>4 year outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 points</td>
<td>0-2.8%</td>
<td>0-5.3%</td>
<td>0-3.4%</td>
<td>0-9.2%</td>
</tr>
<tr>
<td>5-8 points</td>
<td>0.9-4.8%</td>
<td>4-11.3%</td>
<td>1-7.2%</td>
<td>9.9-19.4%</td>
</tr>
<tr>
<td>9+ points</td>
<td>7.6-10.5%</td>
<td>9.9-29.2%</td>
<td>16.7-52-6%</td>
<td>41.2-80.4%</td>
</tr>
</tbody>
</table>

**MORTALITY**

**HOSPITALISATION RATE**
“There is no cure or effective treatment for bronchiectasis.”

“There are no publication guidelines on the management of bronchiectasis in contrast to the phlethora of those in asthma, COPD, lung cancer and pneumonia.”

Tsang & GL Tipper, IJTLDD 2004
“General consideration such as adoption of good nutrition, quitting smoking and exposure to fresh air should be recommended.”

“There is no evidence that the benefits of pulmonary rehabilitation for COPD can be extrapolated to bronchiectasis patients.”

Tsang & GL Tipper, IJTLD 2004
Clinical Parameters

• Independent variables in assessing severity and response to treatment in bronchiectasis:

1. Lung extent of bronchiectasis (HRCT)
2. Airflow obstruction (FEV1, FEV1/FVC, PEF)
3. Lung hyperinflation (RV, RV/TLC)
4. Dyspnea (MRC, Borg scale, BDI)

Quality-of-Life

• Patients who are microbiologically cured of TB have substantially lower health quality compared to both those with similar pulmonary risk actors and to healthy populations)

• Average SGRQ scores:
  – vs. persons with similar risk factors: up to 62% lower
  – vs. healthy subjects of same age/PFT: lower

Pasipanodya 2007; Jones 2003; Domingo-Salvany 2002
Delphi study on NCFB

- 10 experts on non-cystic fibrosis bronchiectasis:
- Areas of consensus (≥70% agreement):
  1) 10 to 14 days duration of antibiotics for exacerbations of NCFB
  2) Combination antibiotics should not be given for acute exacerbations of NCFB regardless of history of Pseudomonas colonization,
  3) Some type of airway clearance technique should be used for stable NCFB
  4) Recommended treatment end points for NCFB include sputum volume, sputum color and exacerbation frequency and
  5) Recombinant DNAase and inhaled corticosteroids should not be routinely used for NCFB.