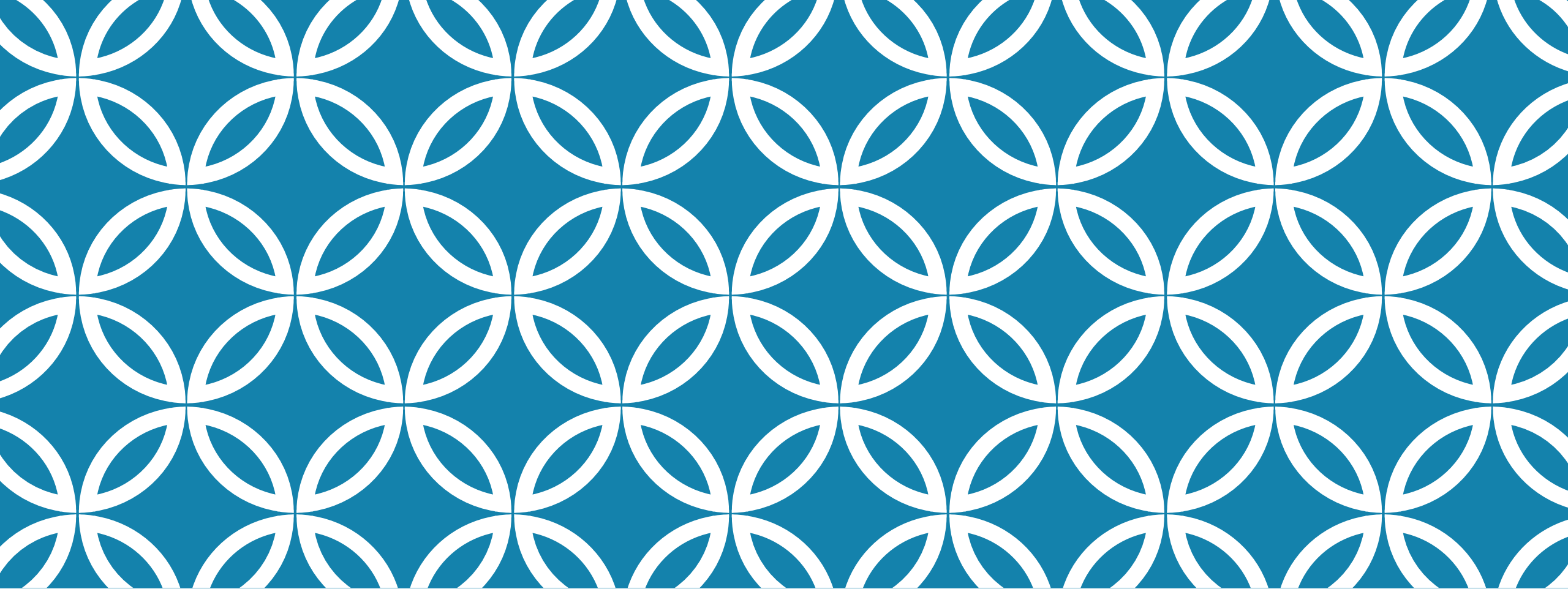




BRONCHIECTASIS

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ASST. PROF
DEPT. OF RESPIRATORY MED.

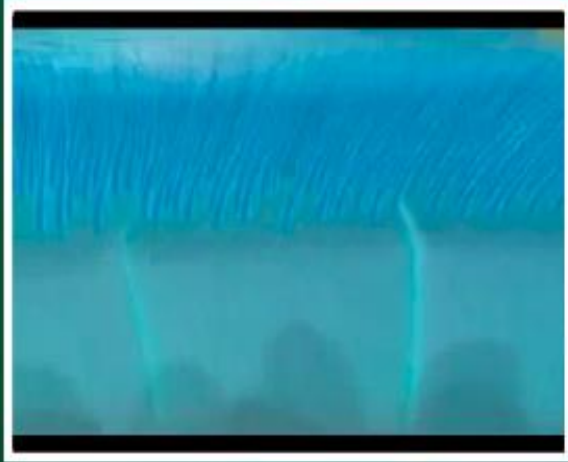
INTRODUCTION

- Abnormal irreversibly dilated and often thick-walled bronchi resulting from a variety of pathologic process that cause destruction of the bronchial wall and its surrounding supporting tissues
- Bronchiectasis represents the final common pathway of a number of infectious, genetic, autoimmune, developmental and allergic disorders and is highly heterogeneous in its aetiology, impact and prognosis.
- Bronchiectasis not due to cystic fibrosis (“non-CF bronchiectasis”, henceforth referred to simply as bronchiectasis) is characterised radiologically by permanent dilation of the bronchi, and clinically by a syndrome of cough, sputum production and recurrent respiratory infections



Airway Defense Mechanisms

Mucociliary clearance



Adaptive Immunity

- Immunoglobulins
- T and B lymphocytes

Innate immunity

Cellular components

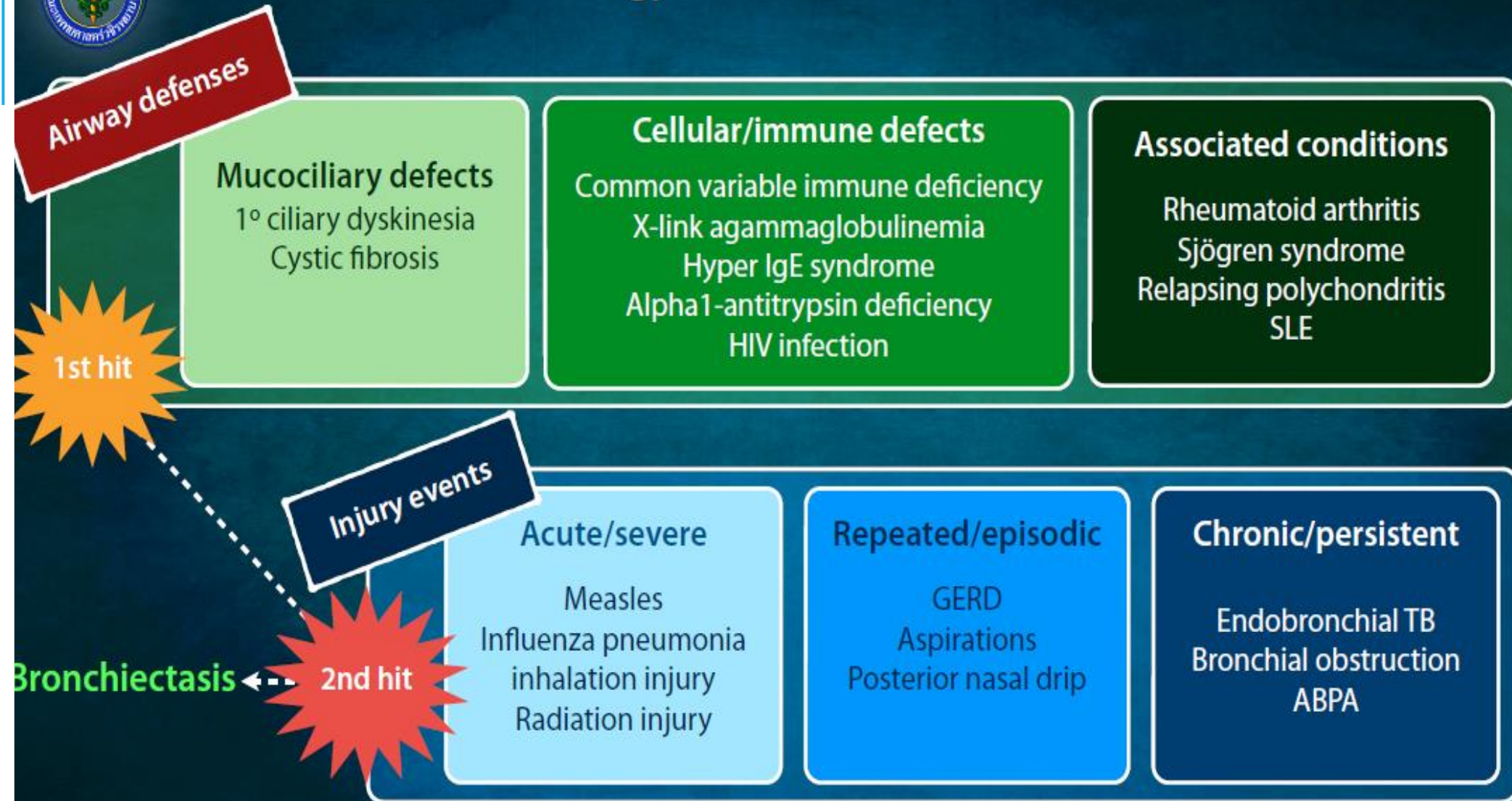
- Neutrophils
- Macrophages and dendritic cells
- NK cells

Protein components

- Toll-like receptors
- Antimicrobial proteins: Lysozymes, lactoferrins, peroxidase, defensin, cathelicidins
- Inflammatory cytokines: interferons, cytokines, chemokines, complements

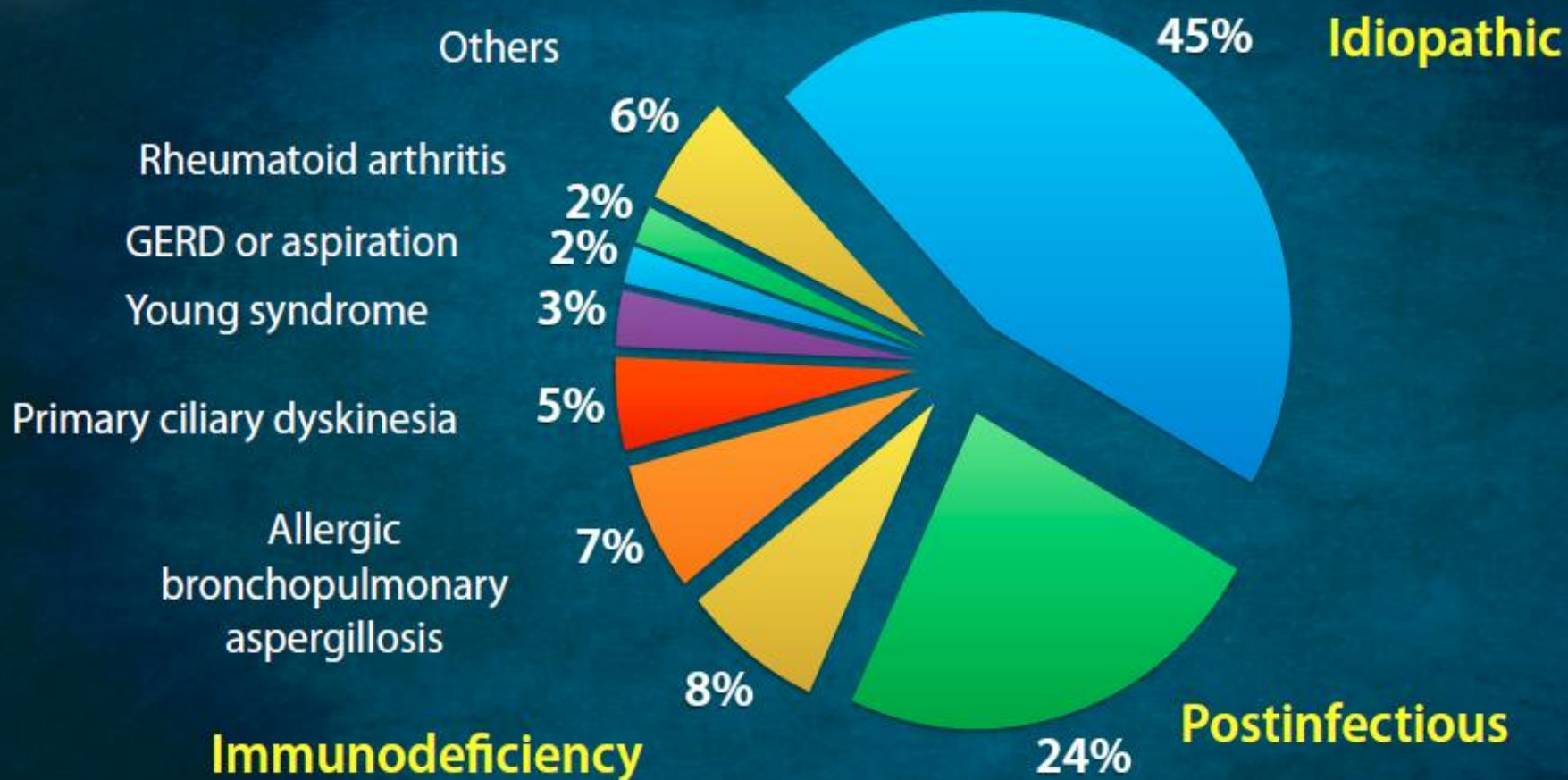


Etiology of Bronchiectasis





Reported Etiologies of Bronchiectasis



Quast T M, Self A R, Browning R F et al. *Dis Mon* 2008; 54: 527-539.

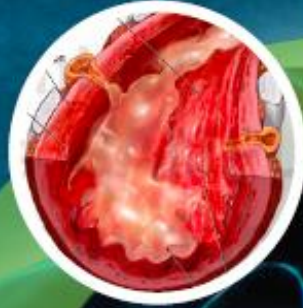
Pasteur M C, Helliwell S M, Hughton S J et al. *Am J Respir Crit Care Med* 2006; 100: 2183-2189.



Pathogenesis of Bronchiectasis: **The Vicious Cycle**

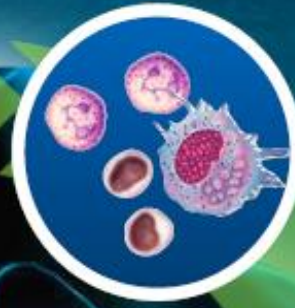
Infection

with acute inflammation
and recruitment of
inflammatory cells



Release

of inflammatory cytokines
peroxidases, proteinases
elastase, etc.



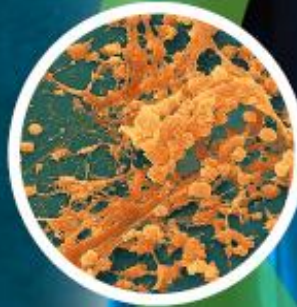
Destruction

of mucociliary and
cartilagenous supporting
structures



Colonization

and biofilm formation
intermittent dispersals



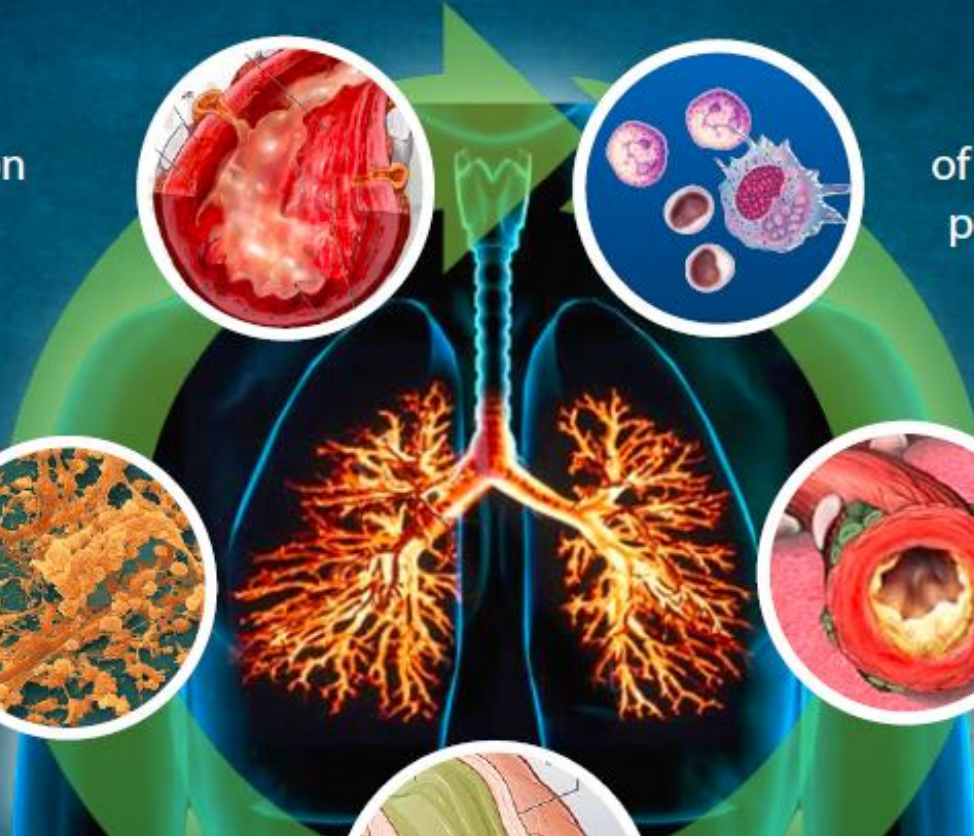
Impairment

mucociliary clearance
sputum retention



Loss

of ventilatory
function

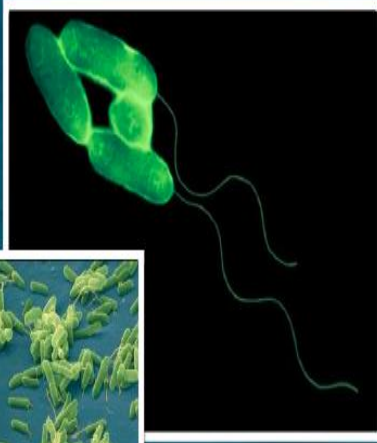




Pseudomonas aeruginosa in Bronchiectasis

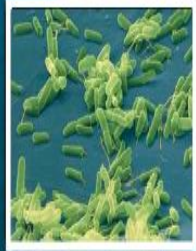
Lipopolysaccharide

- Systemic inflammation



Quorum sensing

- Production of lactone
- cell-cell signaling



Alginate

- Adherence to the epithelial cells

Pyocyanin

- Disruption of the epithelial cell wall
- Impairment of ciliary function

Flagellum

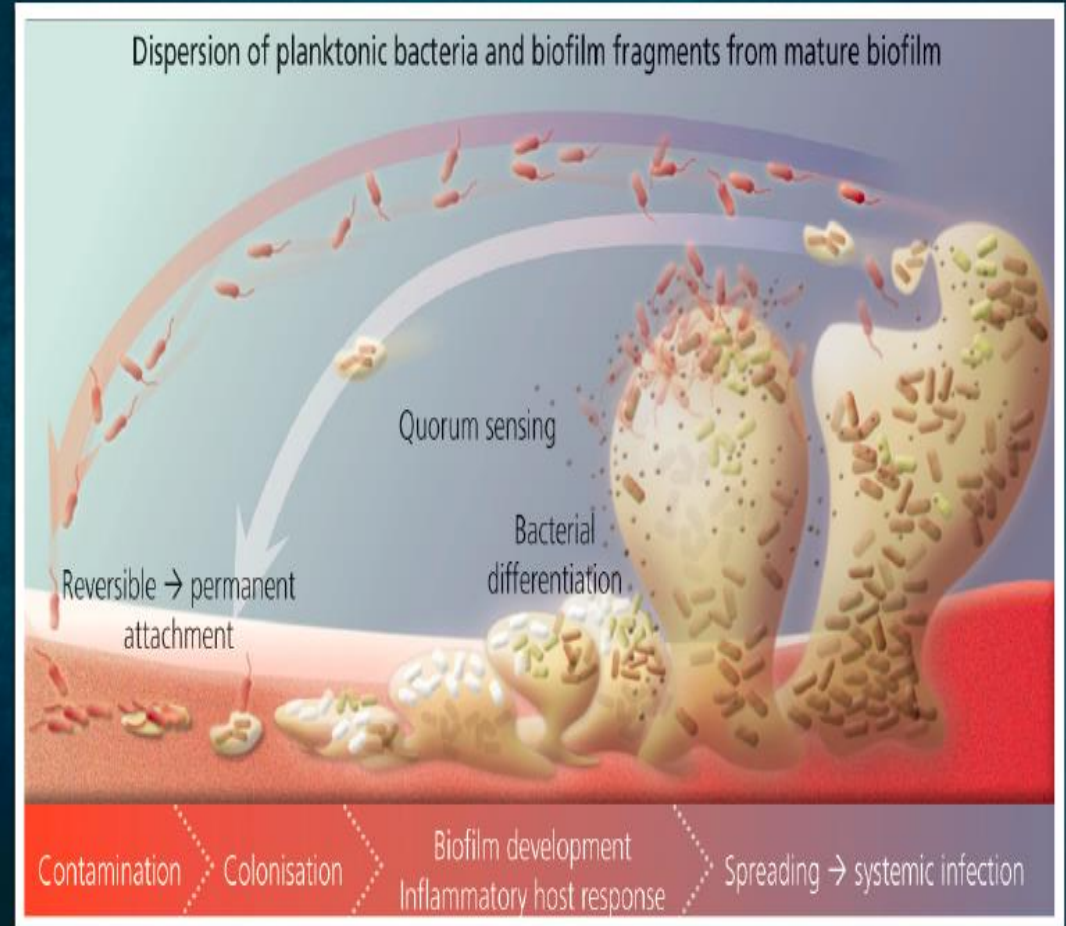
- Mobility
- Release of the proinflammatory chemokines on attachment

Pili

- Adherence to lipid membrane
- Release of toll-like receptors
- Recruitment of phagocytic cells

Barker A F, Moulton B C. *Clin Chest Med* 33 (2012) 211-217.

Role of Biofilms



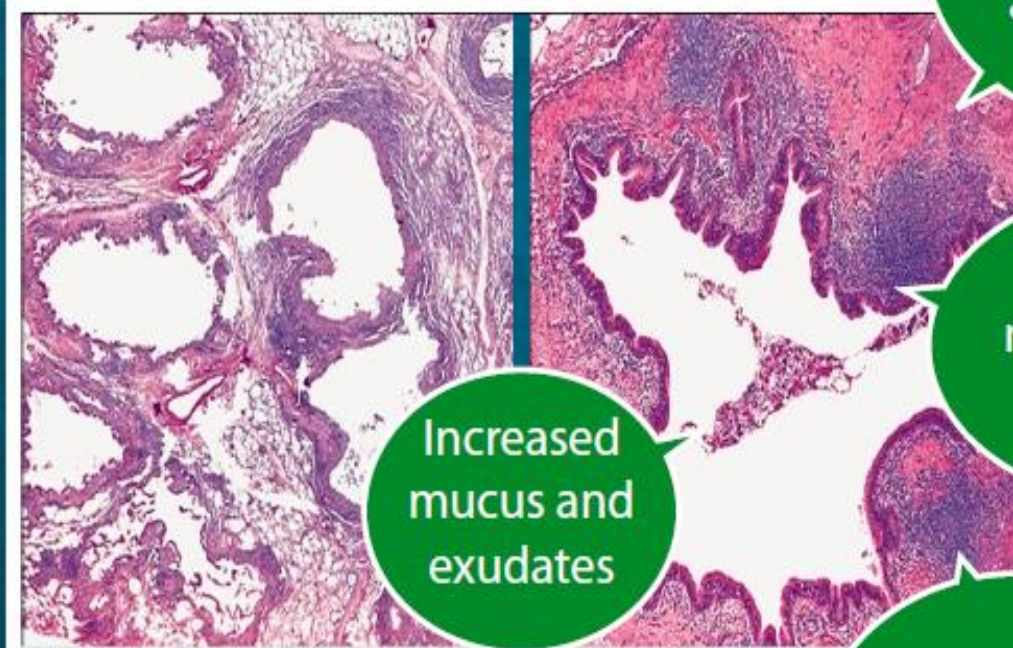
Adapted from Beckford-Ball J. <http://woundsinternational.wordpress.com>



Histologic Changes in Bronchiectasis



Normal bronchus



Increased
mucus and
exudates

Cartilage
destruction
and fibrosis

Mucosal and
mucous gland
hyperplasia

Inflammatory
cells
infiltration

Bronchiectasis



Diagnosis of Bronchiectasis: **General Consideration**

**Definitive diagnosis
Severity of impairment**

**Underlying or
associated condition(s)**

**Microbiology of
the bronchiectatic airway**



Clinical Manifestations of Bronchiectasis

Clinical Features of bronchiectasis

History

Chronic productive cough*
Sputum production*
Reported bouts of respiratory tract infection

Physical examination

Wheezing, rhonchi, crackles
Clubbing
Cyanosis

Clinical features of the associated/causative condition(s)

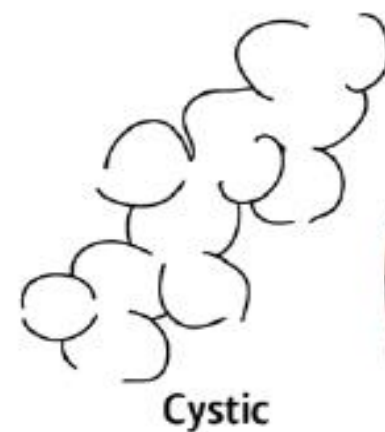
Bronchial obstruction
localized wheezing

ABPA
Prominent wheezing

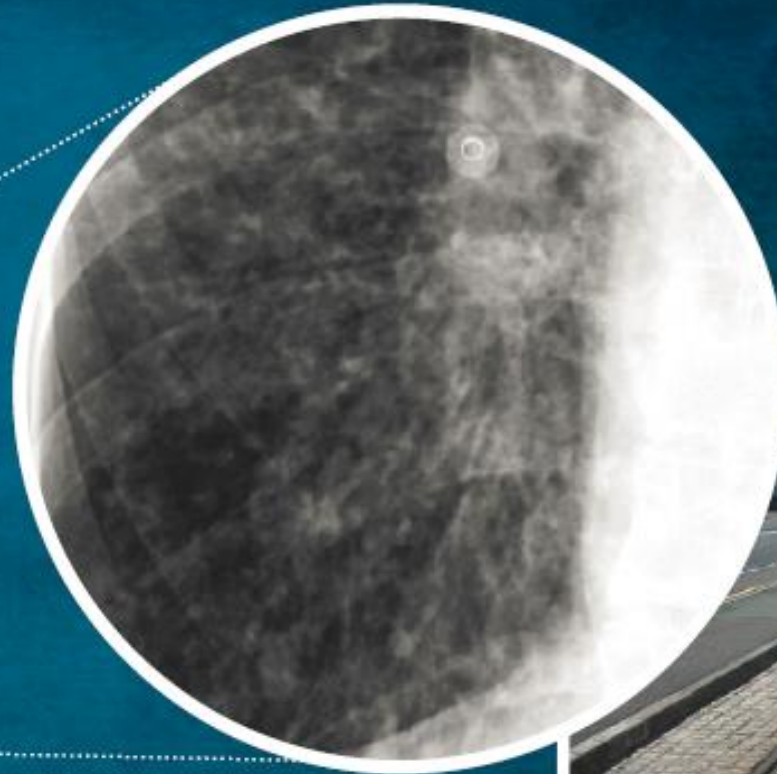
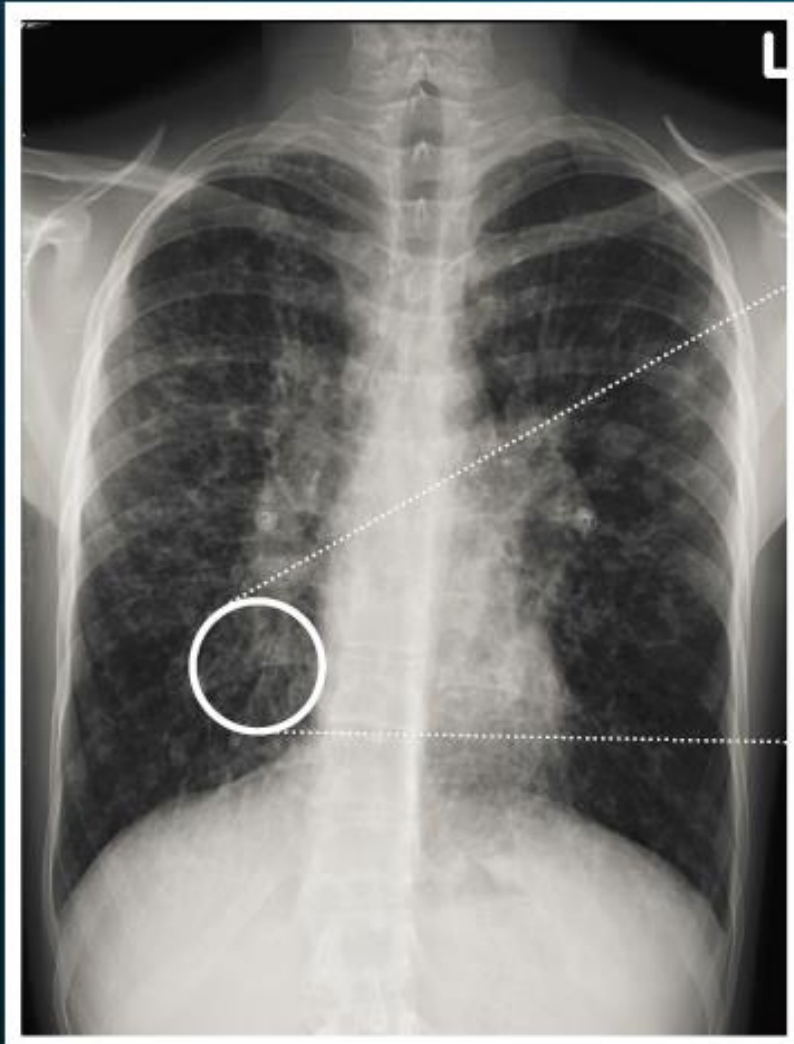
CTDs
Arthritis
Sicca syndrome

PCD, CF, Young Syndrome
Recurrent sinus disease
Infertility

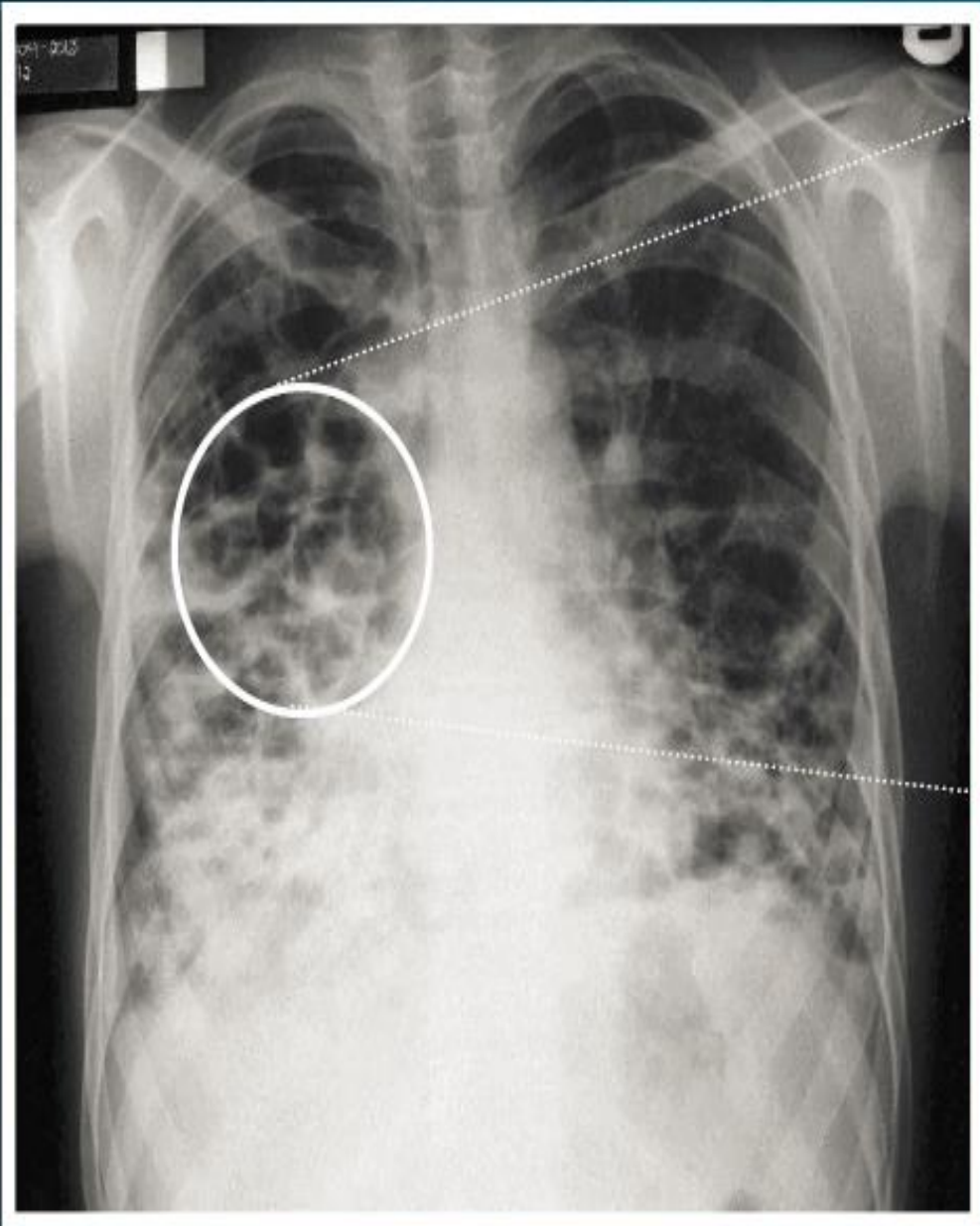
Pathological Classification of Bronchiectasis



RADIOLOGY

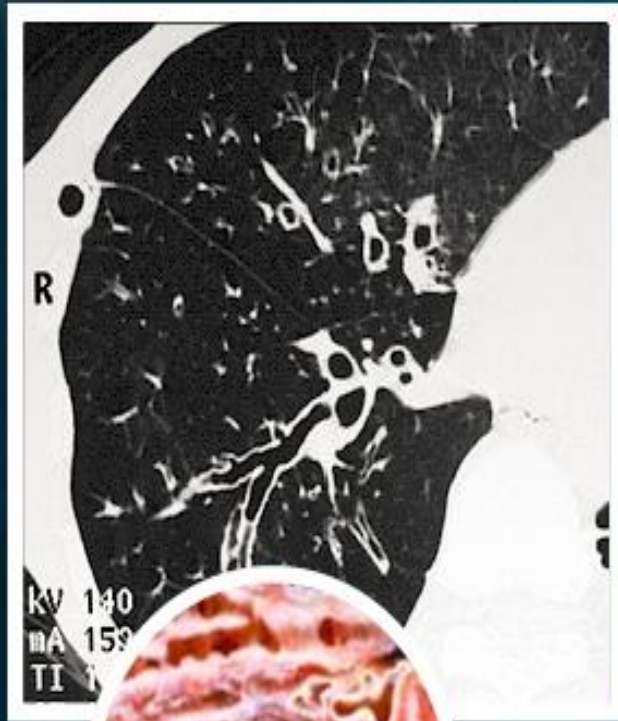


Bronchial wall thickening and widening
with parallel configuration
"Tram track" sign

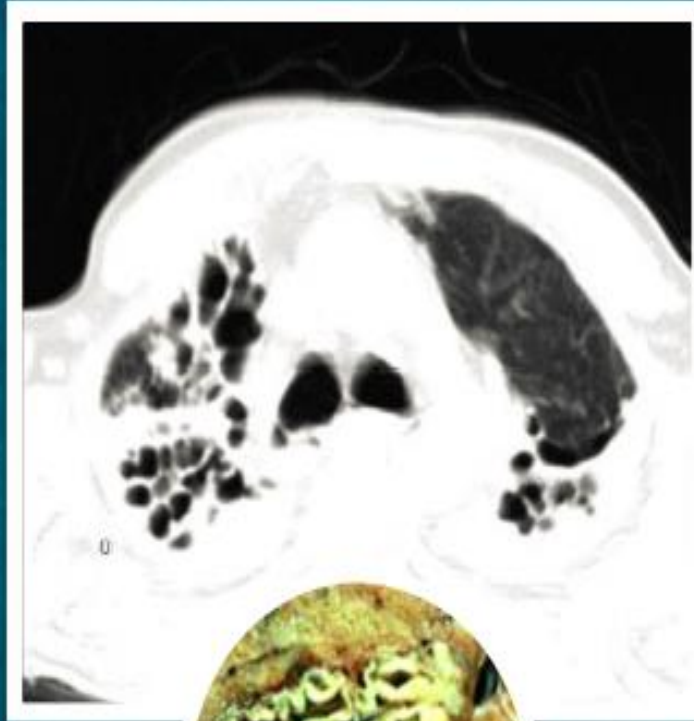


Conglomerating cysts of varying size
and wall thickness

"Honeycomb" sign



Cylindrical



Saccular/Varicoid



Cystic

PFT AND ABG



- Supportive evidence of airway disease (**Obstructive defect**)
- Severity assessment (**Severe impairment = poor prognosis**)
- Bronchodilator therapy (**Positive bronchodilator response**)
- Oxygen therapy (**Hypoxemia**)

ADDITIONAL TESTS

Test/Procedure	Suggestive clinical features	Etiology
Quantitative immunoglobulins (IgG, IgA, IgM)	Concomitant sinus disease, recurrent infection	Common variable immune deficiency
Aspergillous-specific IgG, IgE level, aspergillus skin testing	Asthma, central bronchiectasis, prominent mucus plugging	Allergic bronchopulmonary aspergillosis
IgE level	Eczema, staphylococcal infections, retained primary teeth	Hypergammaglobulinemia E (Job syndrome)
Alpha-1 antitrypsin level	Emphysema	Alpha-1 antitrypsin deficiency
Sweat chloride, nasal potential difference or CF mutation screen	Concomitant sinus disease, younger age, upper lobe disease	Cystic fibrosis
Bronchoscopy	Unilateral focal disease	Bronchial obstruction

Test/Procedure	Suggestive clinical features	Etiology
Bronchoscopy with mycobacterial cultures	"Tree-in-bud" on HRCT, nodules, cavity, scoliosis, pectus	Nontuberculous mycobacteria and tuberculosis
Ciliary biopsy, ciliary functional testing, nasal nitric oxide	Childhood onset, sinus or ear infections, situs inversus, infertility	Primary ciliary dyskinesia
Swallow evaluation of esophageal pH measurement	M avium disease	Gastroesophageal reflux disease or aspiration
IgG subclass levels, response to immunization, tests for qualitative immune defects	Childhood onset, recurrent infections, dysmorphic features	Congenital immunodeficiency
Serology for autoimmune disease	Arthritis, sicca syndrome	Rheumatoid arthritis, Sjögren syndrome
Serology for HIV infection	Opportunistic infections, recurrent infections	HIV disease

Mucociliary defects

Ciliary biopsy/function test
Sweat chloride
CF mutation screening

Cellular/immune defects

Quantitative immunoglobulins
IgG or IgE levels
AAT level
Serology for HIV

Associated conditions

Serology for CTDs:
ANA, Anti-Sm
Anti-Ro, Anti-La
etc.

Acute/severe

Measles
Influenza pneumonia
inhalation injury
Radiation injury

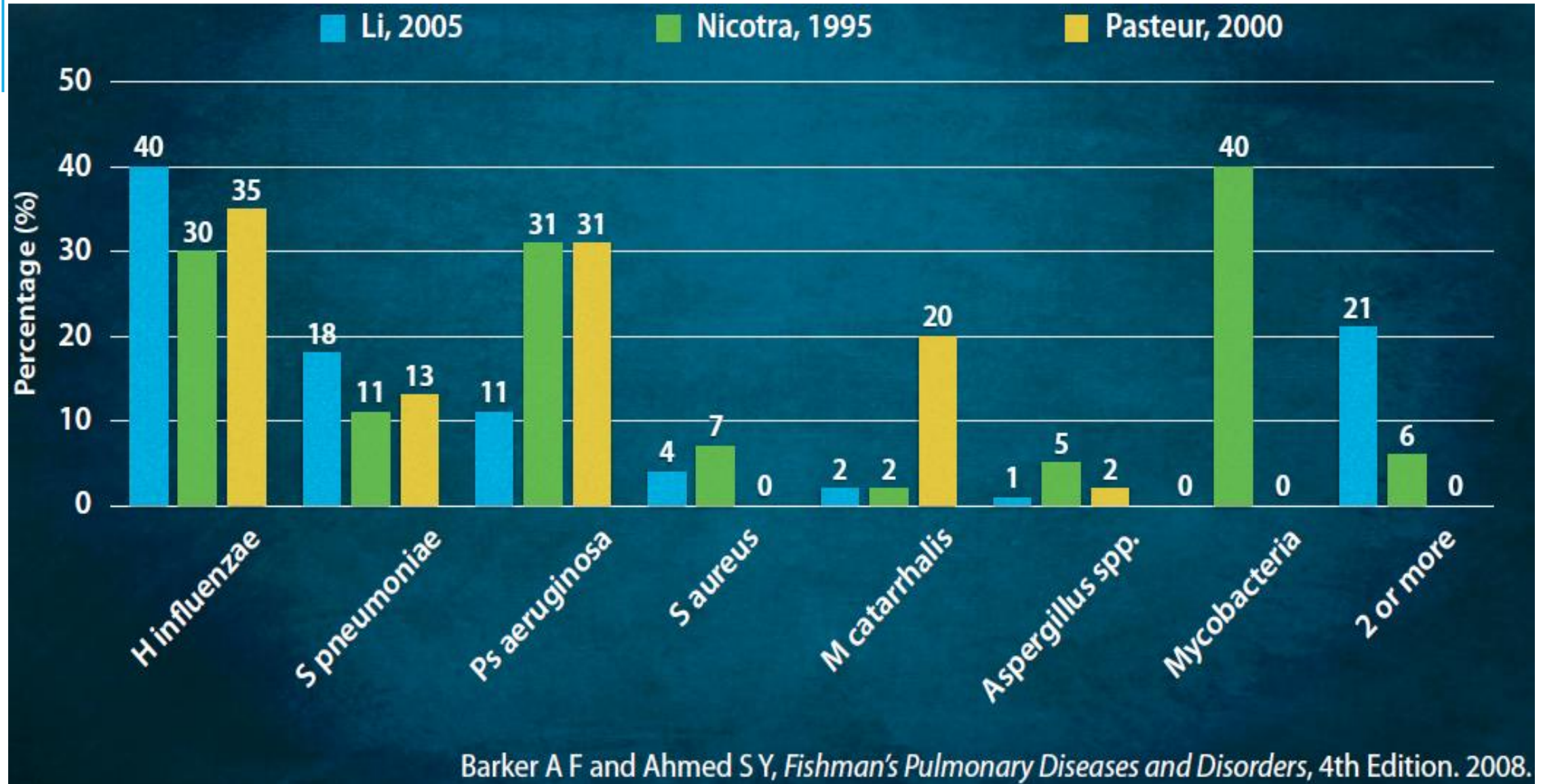
Repeated/episodic

Esophageal pH
Swallow evaluation

Chronic/persistent

Bronchoscopy
Aspergillus IgG/IgE
Aspergillus allergy test

MICROBIOLOGY



MANAGEMENT- COLE'S VICIOUS CYCLE HYPOTHESIS

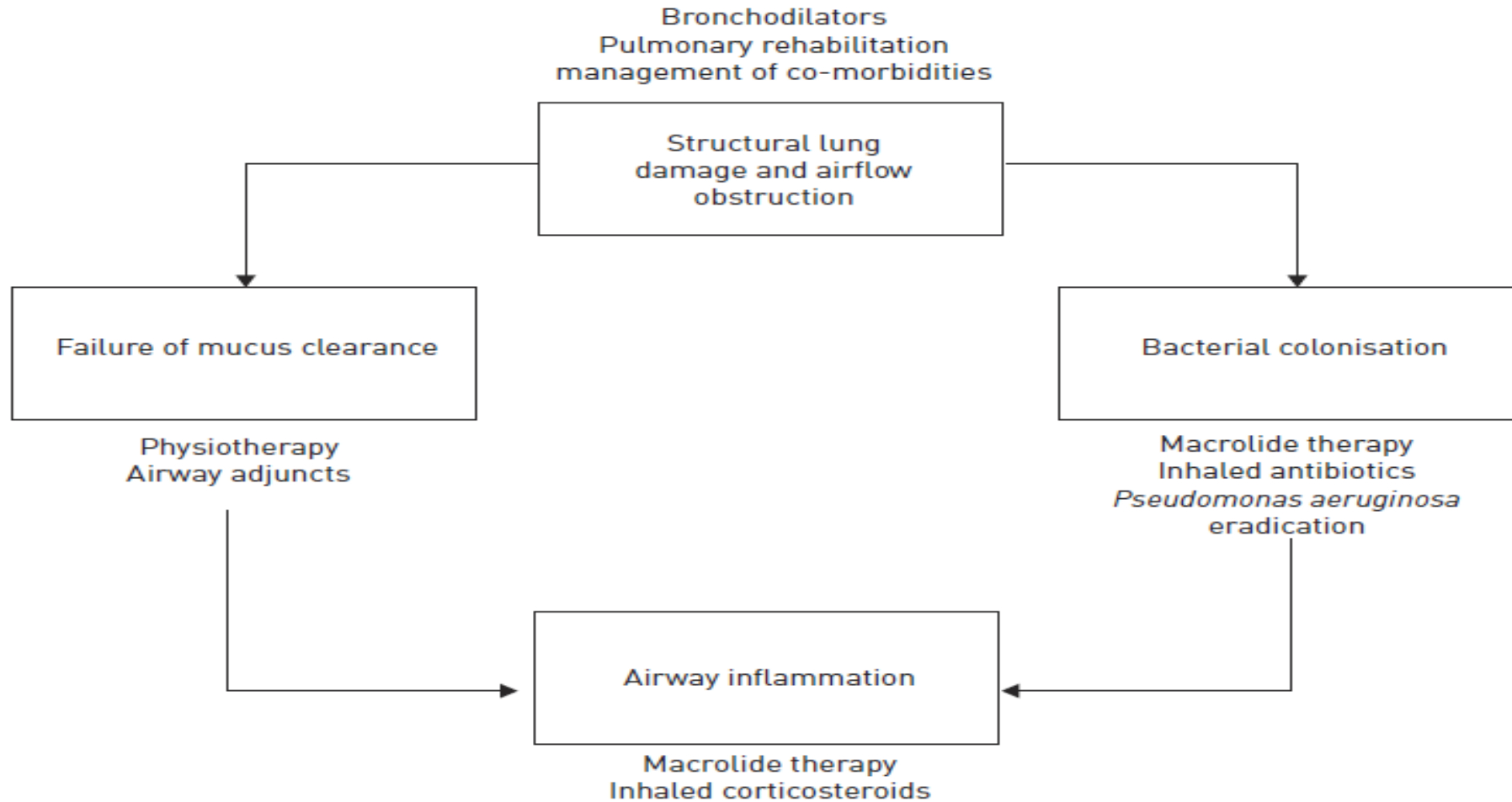


TABLE 3 The Bronchiectasis Severity Index

Domain	Points
Age years	
<50	0
50–69	2
70–79	4
≥80	6
Body mass index kg·m⁻²	
<18.5	2
≥18.5	0
FEV₁ % predicted	
>80	0
50–80	1
30–49	2
<30	3
Hospital admissions in the past 2 years	
Yes	5
No	0
Exacerbation frequency in the past 12 months	
0–2	0
≥3	2
MRC dyspnea score	
1–3	0
4	2
5	3
Bacterial colonisation	
<i>Pseudomonas aeruginosa</i>	3
Other PPMs	1
None	0
Radiological severity	
≥3 lobes involved or cystic bronchiectasis	1
<3 lobes involved	0

0–4 points: low risk of hospitalisation and mortality; 5–8 points: moderate risk of hospitalisation and mortality; ≥9 points: high risk of hospitalisation and mortality.

TREATMENT MODALITIES

- AIRWAY CLEARANCE
- PULMONARY REHABILITATION
- ANTI-MICROBIAL THERAPY
- INHALED CORTICOSTEROIDS AND BRONCHODILATORS
- INHALED ANTIBIOTICS
- LTOT
- SURGERY- LOBECTOMY, LUNG TRANSPLANTATION
- VACCINATION AGAINST PNEUMONOCOCCAL AND INFLUENZA
- SPUTUM SURVEILLANCE FOR NTM AND PSEUDOMONAS AERUGINOSA

How macrolides achieve their beneficial effects is unclear. Alongside their antimicrobial effects, macrolides have anti-inflammatory effects including inhibition of inflammatory cell migration, cytokine secretion and possible attenuation of the production of reactive oxygen species [63, 64] Other mechanisms that have been proposed to explain macrolide benefit include reduction of biofilms surrounding virulent Gram-negative organisms such as *P. aeruginosa* and promotion of gastric emptying that may reduce potential for acid reflux [65, 66].

Macrolides are therefore effective, but the key question is in which patients they should now be used. BTS guidelines recommend consideration of long-term oral antibiotics for patients with ≥ 3 exacerbations per year or those chronically colonised with *P. aeruginosa* [2]. These guidelines were written before the publication of the three recent trials and, given that the EMBRACE trial showed benefit in patients with one or more exacerbations per year, these recommendations may change. In clinical practice, macrolides are most frequently used in patients with three or more exacerbations per year, in patients with *P. aeruginosa* and also in patients with less frequent exacerbations who continue to have significant impairment of quality of life despite standard treatment. Further research needs to explore the best dosage and schedule for

TABLE 1 Summary of three double blind randomised controlled trials of macrolides in non-CF bronchiectasis

	EMBRACE: New Zealand		BLESS: Australia		BAT: Netherlands	
	Placebo	Azithromycin 500 mg three times per week	Placebo	Erythromycin 400 mg twice daily	Placebo	Azithromycin 250 mg once daily
Subjects n	70	71	58	59	40	43
Male %	29	32	43	36	30	42
Mean age years	59.0	60.9	63.5	61.1	64.6	59.9
Baseline data						
FEV1 % predicted at baseline	67.3	67.1	70.1	66.9	82.7	77.7
Exacerbation rate pre-trial	3.93 (mean)	3.34 (mean)	Not reported	Not reported	4.0 (median)	5.0 (median)
SGRQ	36.6	31.9	38.1	36.7	40.2	40.6
Outcomes						
Change in FEV1 with treatment	−0.04	0	−4.0	−1.6 [#]	−0.10	1.03 [#]
Change in SGRQ from baseline	−1.92	−5.17	−1.3	−3.9	−4.12	−12.18 [#]
Total exacerbations in 12 months during trial n	178	109	114	76	78	39
Mean exacerbation rate during trial (per patient)	2.54	1.54 [¶]	1.97	1.27 [#]	1.95	0.91 [¶]

SGRQ: St. George's Respiratory Questionnaire. [#]: p<0.05 compared with placebo. [¶]: p<0.001 compared with placebo group.



INHALED ANTIBIOTICS

TOBRAMYCIN

GENTAMICIN

COLISTIN

AZTREONAM

AMOXICILLIN

CIPROFLOXAN

LIPOSOMAL CIPROFLOXACIN

STEP WISE MANAGEMENT OF BRONCHIECTASIS

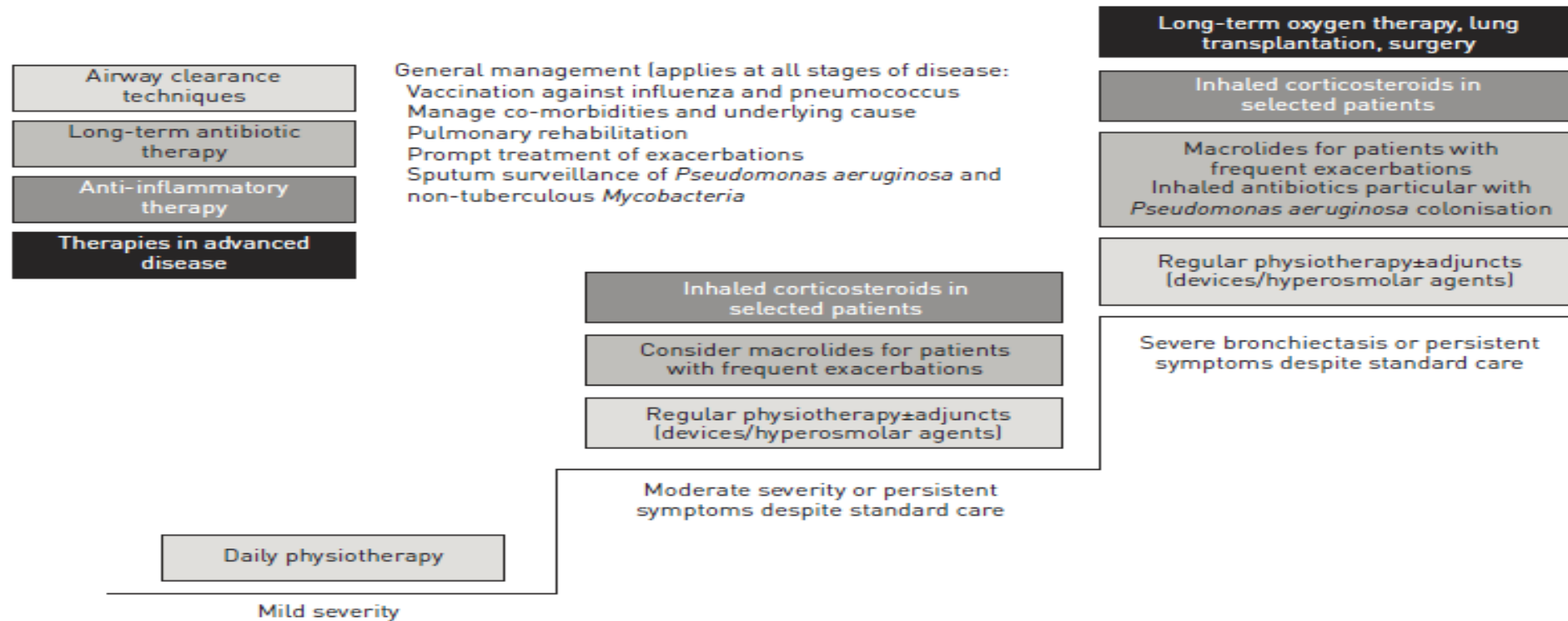


FIGURE 2 The stepwise management of non-CF bronchiectasis. Alternative oral antibiotics such as β -lactams or tetracyclines may be appropriate for patients intolerant or not suitable for macrolides.

NEWER THERAPIES

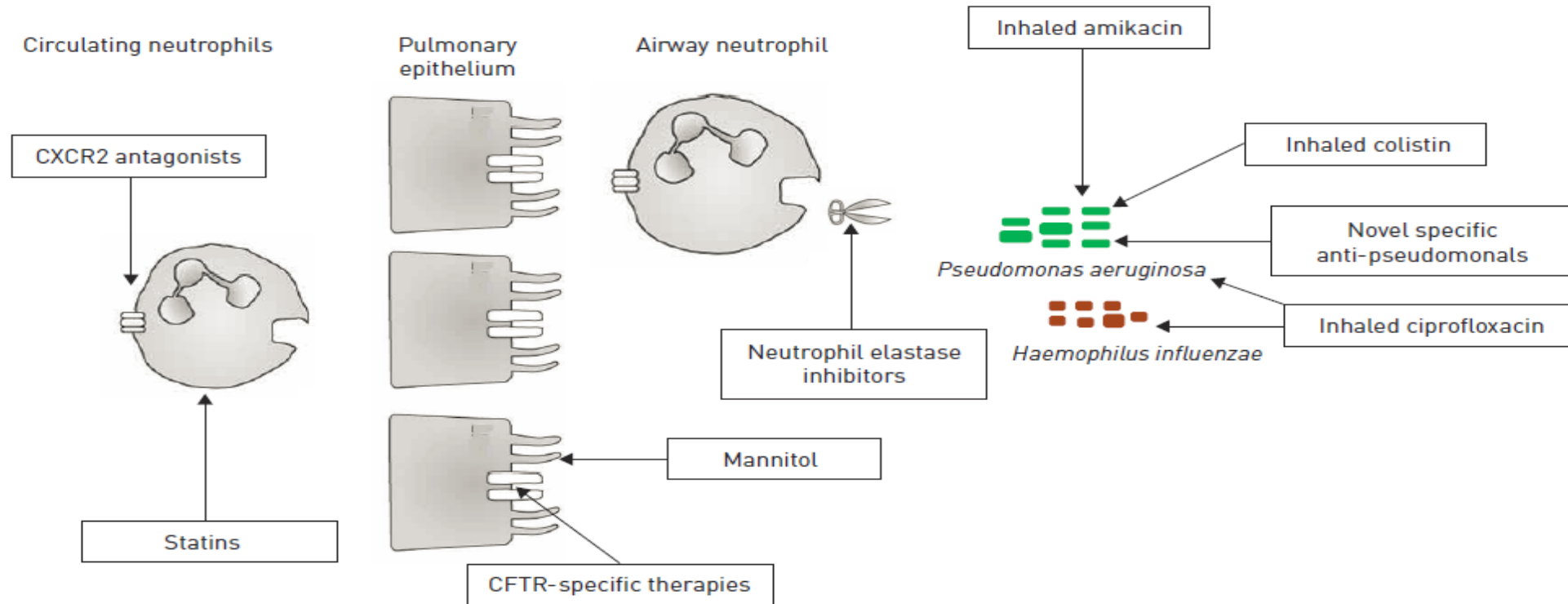


FIGURE 3 New therapies in development for bronchiectasis and their possible role. CFTR: cystic fibrosis transmembrane conductance regular.



THANK YOU!