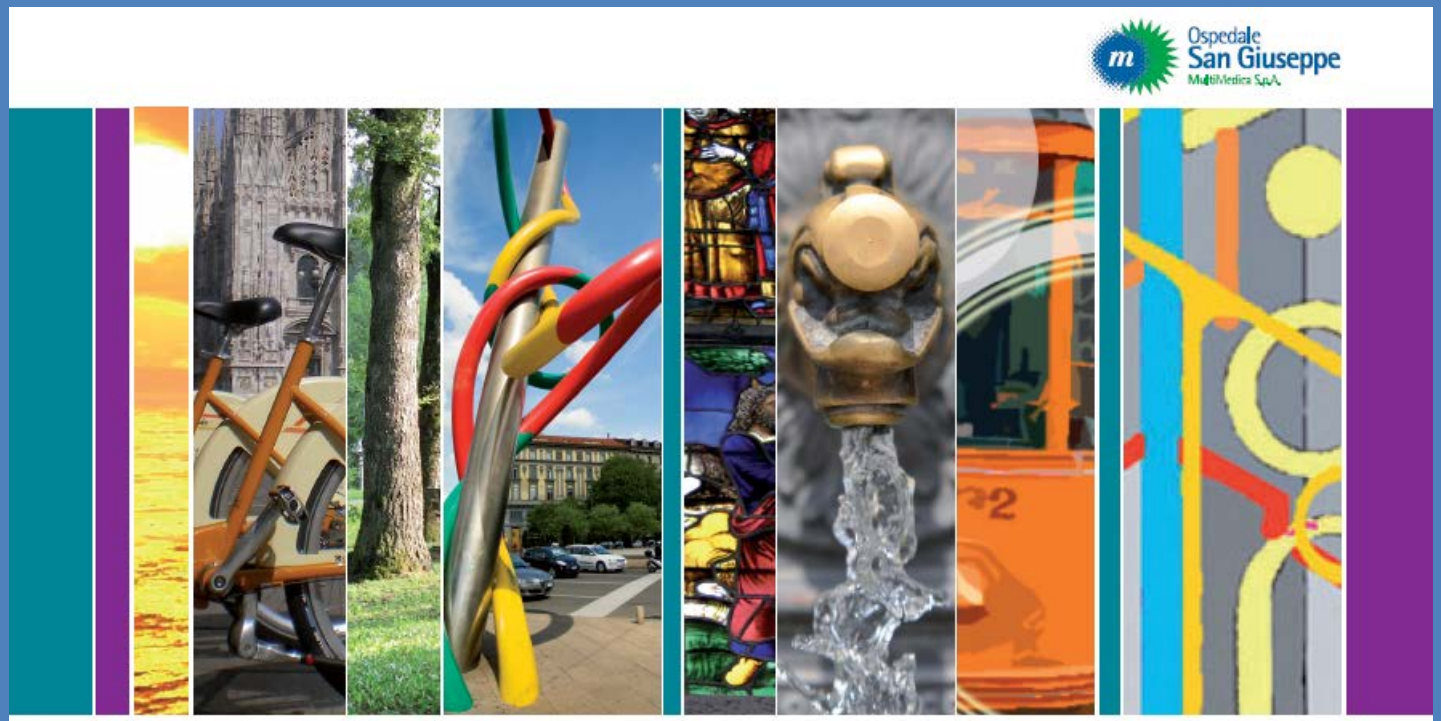


UPDATE SULLE BRONCHIECTASIE

Bruno del Prato
Napoli

ORIGINAL RESEARCH

A Novel Microbiota Stratification System Predicts Future Exacerbations in Bronchiectasis

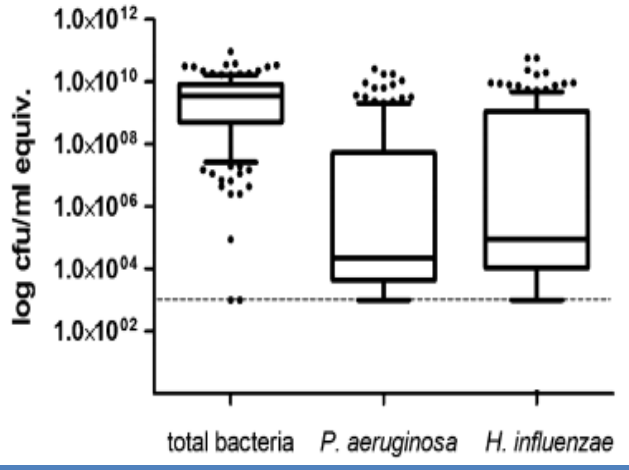
2015

Geraint B. Rogers[1], Nur Masirah M. Zain[2], Kenneth D. Bruce[2*], Lucy D. Burr[1], Alice C. Chen[1], Damian W. Rivett[3], Michael A. McGuckin[1], and David J. Serisier[1,4*]

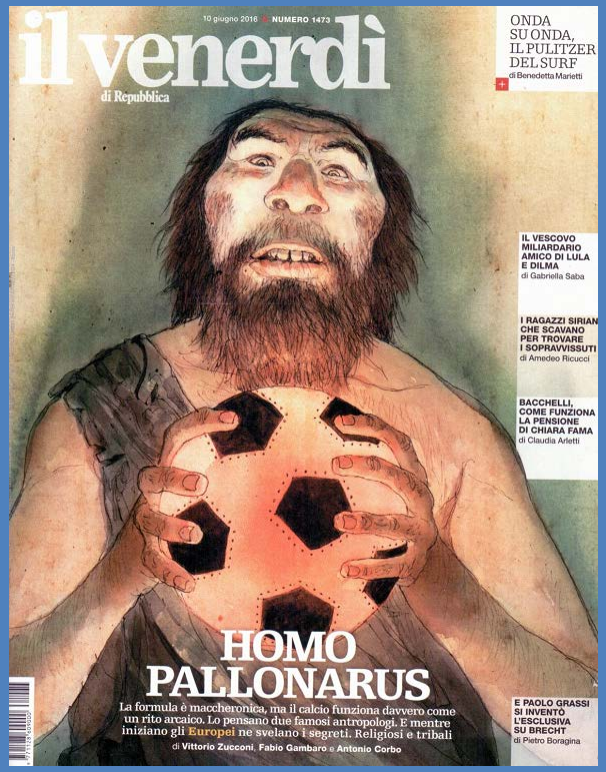
[1]Immunity, Infection, and Inflammation Program, Mater Research Institute, University of Queensland, and Translational Research Institute, Woolloongabba, Queensland, Australia; [2]Institute of Pharmaceutical Science, King's College London, and [3]Division of Ecology and Evolution, Department of Life Sciences, Imperial College London, London, United Kingdom; and [4]Department of Respiratory Medicine, Mater Adult Hospital, South Brisbane, Australia

In conclusion, this stratification system provides highly clinically relevant output from complex bacterial community data that surpasses culture-based techniques. In subjects with non-CF bronchiectasis this system enabled future exacerbation risk to be predicted, including in the substantial subset of subjects with dominant bacterial taxa that are not ordinarily identified by culture and have not previously been considered to be pathogenic.

…quale è il reale impatto di "taxa" batterici dominanti spesso non identificati con normali culture …….
Sono patogeni ? Quale è il loro effetto patogenetico ?



A BOLOGNA UN TEAM DI SCIENZIATI HA ESAMINATO **IL MICROBIOMA** INTESTINALE DI DECINE DI PERSONE : NEI CENTENARI HA CARATTERISTICHE UN PO' PARTICOLARI…



E SE L'ELISIR DI LUNGA VITA SI TROVASSE NELLA PANCIA?

di Alex Saragosa

A Bologna, un team di scienziati ha esaminato il **microbioma** intestinale di decine di persone: nei centenari ha caratteristiche un po' particolari

Da tempo la scienza cerca di svelare i meccanismi della longevità, tentando di capire quanto per essa contino Dna, dieta, abitudini di vita e semplice fortuna. Un gruppo di ricercatori dell'Istituto di Tecnologie biomediche del Cnr e dell'Università di Bologna ha ora indagato su un altro versante: il ruolo che può esercitare sulla durata della vita il microbioma batterico che ci portiamo nella pancia.

«Il microbioma intestinale svolge compiti essenziali per la salute» dice Marco Severgnini, ingegnere biomedico dell'Itb-Cnr. «In particolare, ci aiuta a digerire bene gli alimenti, per esempio producendo acidi grassi a catena corta facilmente assimilabili, ma anche tenendo alla larga i batteri patogeni e producendo vitamine e sostanze antinfiammatorie. Oggi sappiamo che avere un microbioma sbilanciato può portare a disturbi, come l'obesità o l'eccessiva permeabilità intestinale, che consente a tossine e microrganismi di entrare nel sangue, con danni alla salute». Essere accompagnati lungo la vita dai «batteri giusti» potrebbe quindi essere il viatico indispensabile per superare i cento anni.

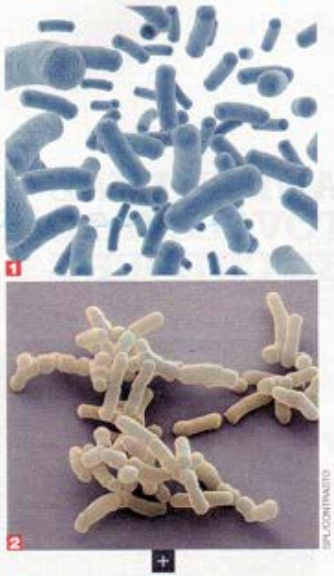
Per capire se lo sia davvero Severgnini e colleghi hanno esaminato il microbioma di decine di persone dai 20 anni in su, fra le quali 24 di oltre 105 anni di età, tutte provenienti dall'area bolognese, per avere un campione il più omogeneo possibile per quanto riguarda dieta e ambiente.

I risultati mostrano che anche il microbioma invecchia insieme a chi se lo porta dentro: mentre i giovani hanno nel loro intestino soprattutto batteri «buoni», come Ruminococcaceae e Lachnospiraceae, più si invecchia e più compaiono nuove specie, fra cui alcune che sarebbe meglio tenere alla larga, come gli Enterobatteri. «Questo è probabilmente dovuto al fatto che se si vive a lungo i batteri da cui siamo circondati riescono a poco a poco a farsi strada nel nostro organismo. Per esempio abbiamo trovato nel microbioma di anziani i batteri che normalmente si trovano sulle gengive».

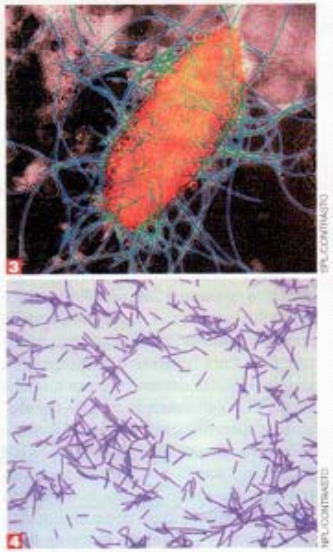
Diventano ultracentenari quelli che evitano questo declino? «Non esattamente, anche il loro microbioma appare invecchiato. Ma in loro si riscontra anche una parallela proliferazione di specie che svolgono attività antinfiammatoria e protettiva del rivestimento intestinale, come il Bifidobacterium e l'Akkermansia, che probabilmente contrastano l'azione negativa di altri batteri. Inoltre negli ultracentenari abbiamo scoperto la presenza di Christensenellaceae, batteri che sembrano ridurre il rischio di obesità. Da studi su gemelli si sa che questi batteri si trovano soprattutto in persone dotate di certe varianti genetiche. Potrebbe essere quindi che i geni dei centenari, oltre a preservarne direttamente la salute, "attirino" i batteri giusti».

Ma allora si potrebbe imitare il «microbioma di Matusalemme», per esempio assumendo bevande che contengano i microrganismi giusti? «Non ci conterei molto» dice Severgnini. «Si sa che il microbioma è molto difficile da cambiare: persino dopo una cura di antibiotici che lo alteri completamente, tende a ritornare come era prima».

Lo conferma una recente ricerca compiuta dal microbiologo Oluf Pedersen, dell'Università di Copenaghen, che ha riesaminato i sette migliori studi fatti finora sull'efficacia delle bevande probiotiche, quelle con i «batteri buoni», concludendo che mentre sembrano essere utili per chi ha certi disturbi intestinali, non c'è la prova che cambino il microbioma di persone sane. Per diventare centenari, quindi, meglio insistere su dieta sana e attività fisica sperando poi di aver ereditato i geni (e i batteri) giusti. ◻



BATTERI «BUONI» E «CATTIVI» CHE SI TROVANO NEL MICROBIOMA INTESTINALE: [1] AKKERMANSIA, [2] BIFIDOBACTERIUM, [3] ENTEROBACTER, [4] LACHNOSPIRACEAE CLOSTRIDIUM



TASK FORCE REPORT
Eur Respir J 2016; In press ;CTED PROOF

Research priorities in bronchiectasis: a consensus statement from the EMBARC Clinical Research Collaboration

Stefano Aliberti[1], Sarah Masefield[2], Eva Polverino[3], Anthony De Soyza[4,5], Michael R. Loebinger[6], Rosario Menendez[7], Felix C. Ringshausen[8], Montserrat Vendrell[9], Pippa Powell[2] and James D. Chalmers[10] on behalf of the EMBARC Study Group[11]

What are the prevalence and characteristics of microbiological colonisation in patients with bronchiectasis across Europe (including bacteria, viruses, fungi, nontuberculous mycobacteria and resistant microorganisms)?

Consensus statements

1) We suggest studies of the microbiome (incorporating bacteria and potentially fungi) in bronchiectasis linked to detailed clinical phenotyping data.

2) A longitudinal study of the bacteriology of bronchiectasis incorporating data on antibiotic resistance is needed.

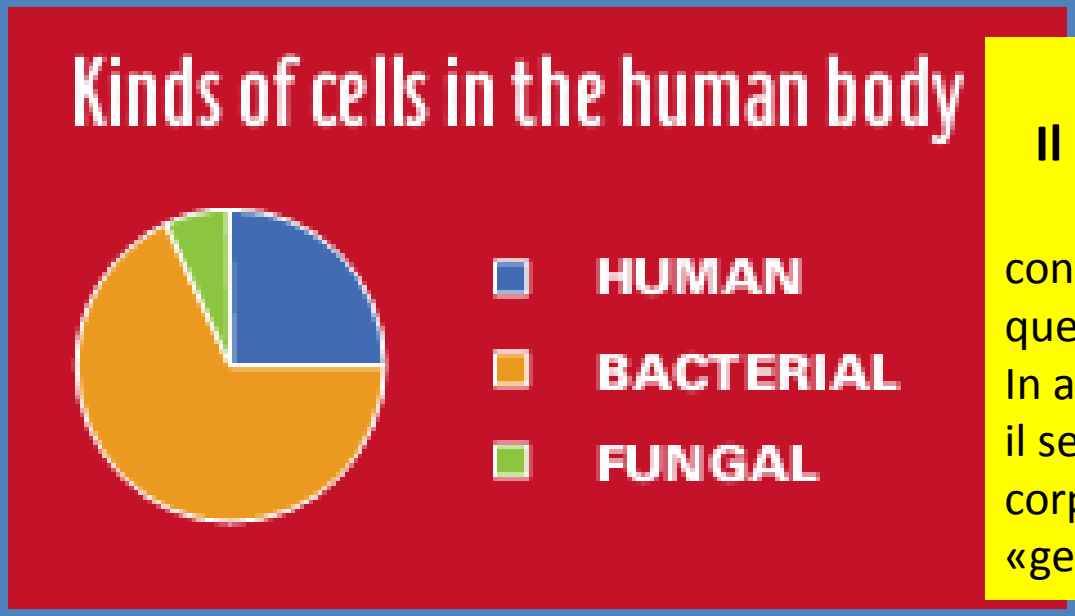
55 key research priorities

Il microbioma è definito come la collezione completa dei microbi (batteri, funghi, virus ecc) che coesistono naturalmente nel corpo umano.

Lo studio del microbioma umano può condurre a nuovi concetti e linee guida di valore nel campo della nutrizione umana, nella scoperta di nuovi farmaci e nella medicina preventiva. Tali studi possono accrescere enormemente la nostra comprensione di malattie complesse quali l'obesità, il cancro e le malattie immunitarie come ad esempio l'asma

BIODIVERSITÀ NEL MICROBIOMA UMANO: IMPLICAZIONI SUI PROCESSI COGNITIVI E COEVOLUTIVI

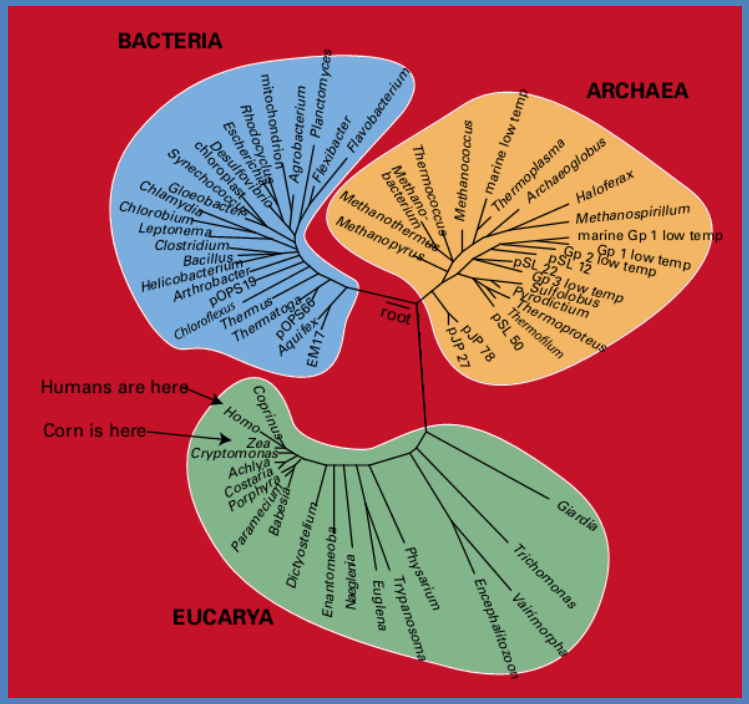
Massimo Pregnolato
Dipartimento di Chimica Farmaceutica
QuantumBiolab
Università degli Studi di Pavia
Viale Taramelli 12



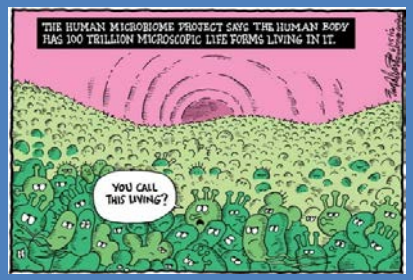
MICROBIOMA
Il genoma delle comunità microbiche che vivono nel corpo umano
contiene circa 100 volte più geni rispetto al quelli del genoma umano.
In altre parole il «metagenoma umano» cioè il set di tutti i genomi contenuti nel nostro corpo è circa 100 volte più esteso del «genoma umano» finora considerato !

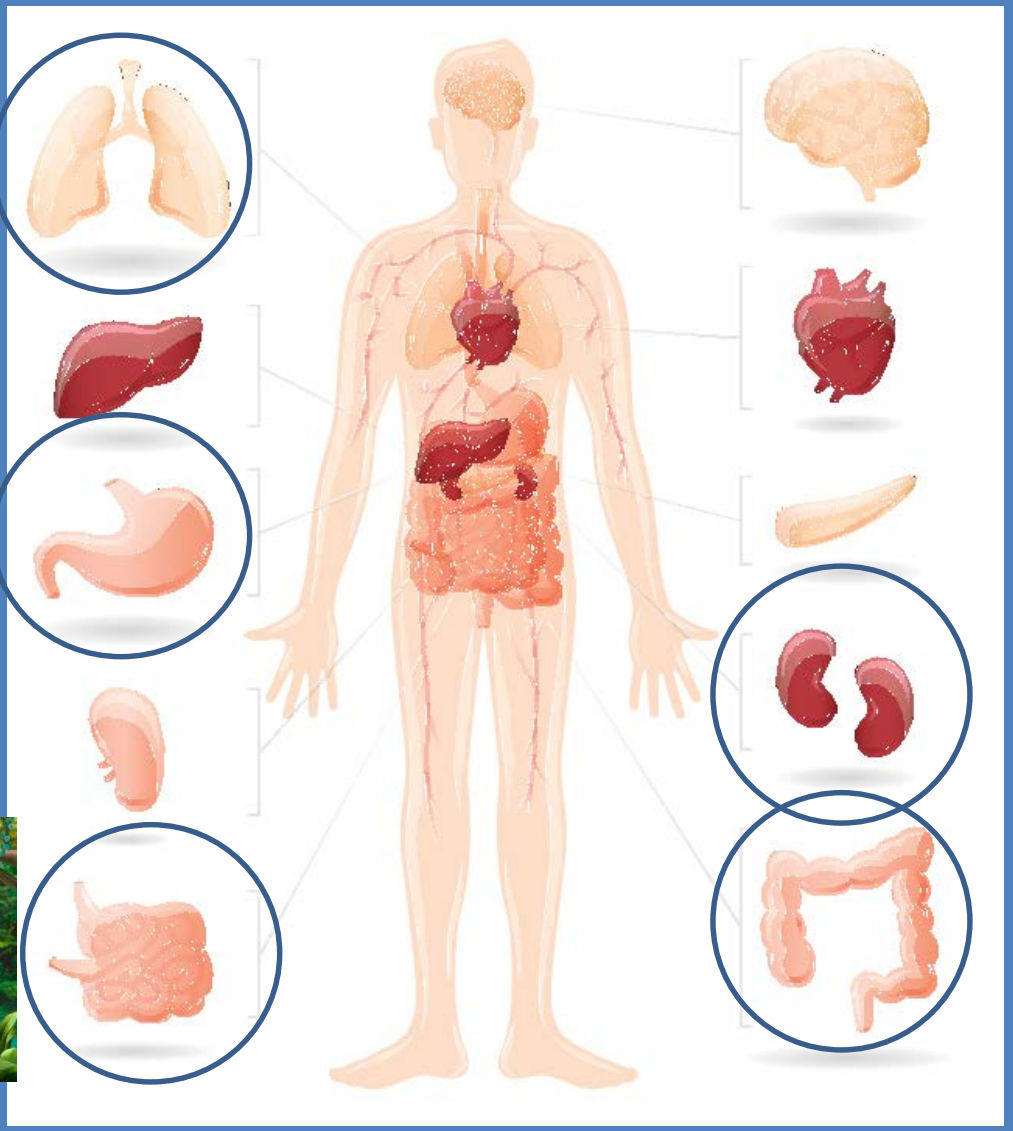
Abstract: Un corpo fisico umano medio è costituito da circa 1013 (10,000,000,000,000 o circa dieci trilioni) di cellule. I microorganismi che risiedono nel corpo umano adulto sono stimati intorno a 1014 cellule, il che equivale a dire che il 90% del nostro corpo non è umano.

Ovviamente le cellule umane continuano a contribuire per la maggior parte del nostro peso corporeo in quanto essendo i batteri residenti costituiti da cellule molto più piccole di quelle umane il loro peso collettivo è solo di circa 900 grammi.



Concetto di biodiversità





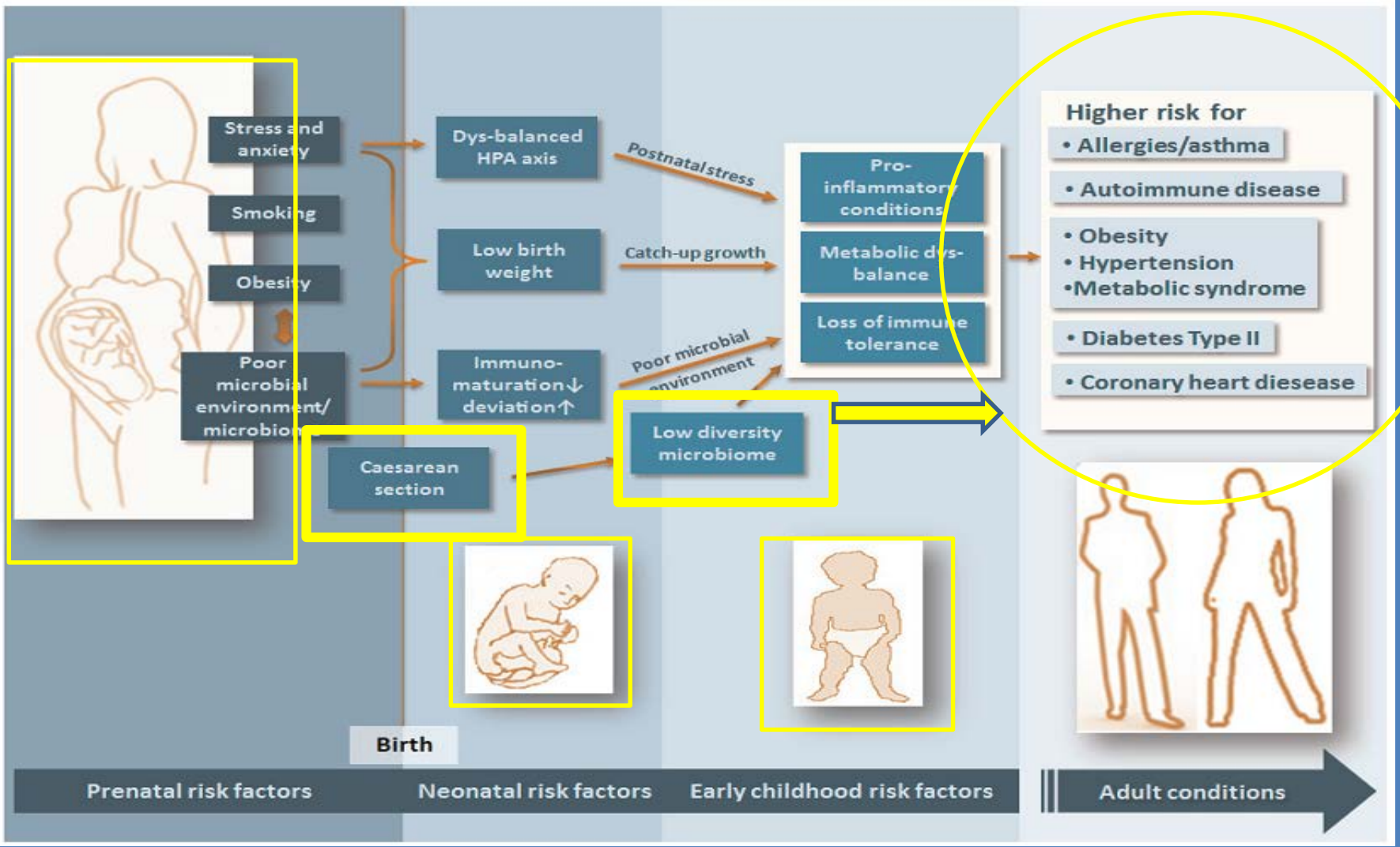
La biodiversità del microbioma umano è presente in tutti i nostri organi ed apparati

The mucosal microbiome in shaping health and disease

Petra Ina Pfefferle[1,2] and Harald Renz[2,3]*

Evoluzione della DIVERSITA' del microbioma dalla vita fetale alla età adulta

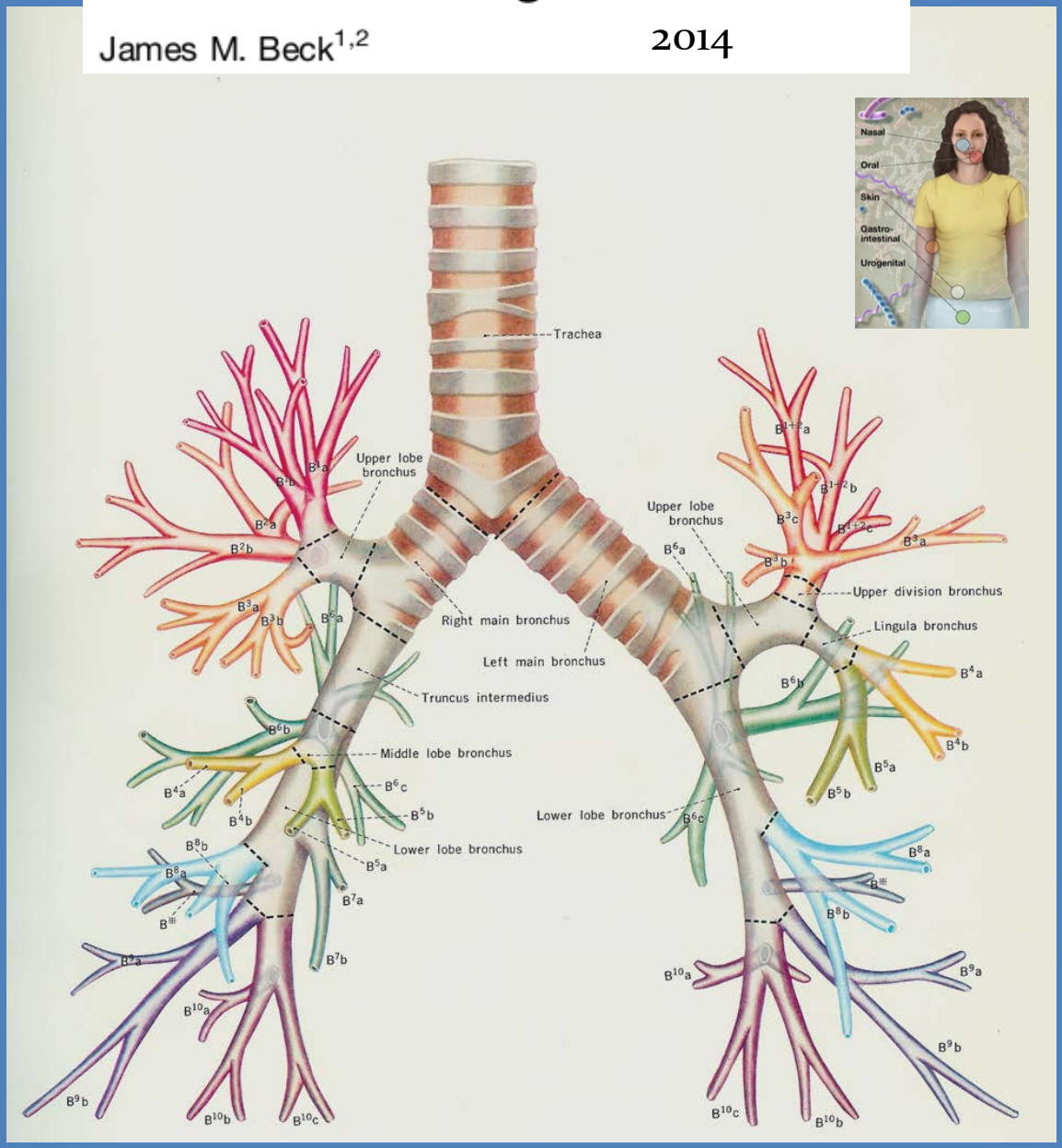
Figure I. Pre- and postnatal environmental factors pave the way for later chronic inflammatory disease through the microbiome

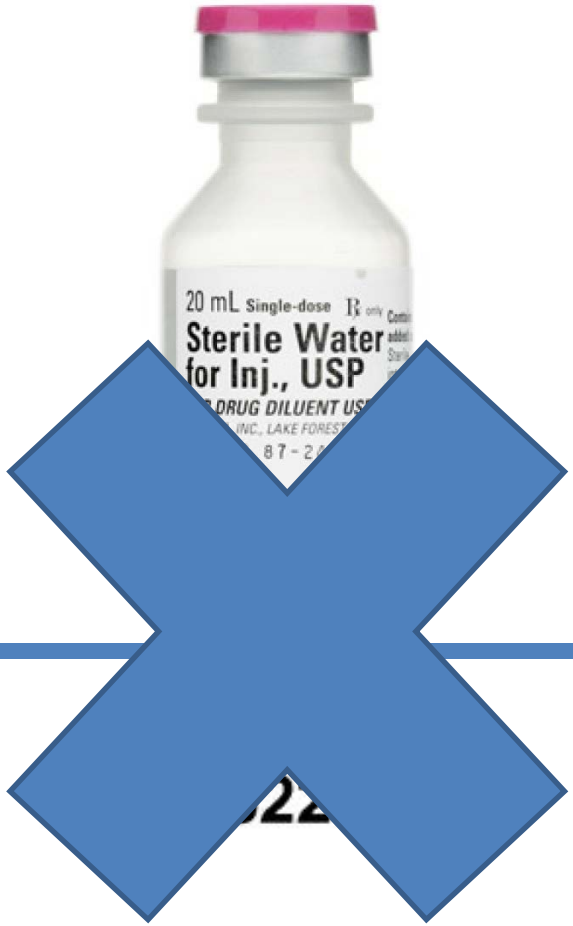


ABCs of the Lung Microbiome

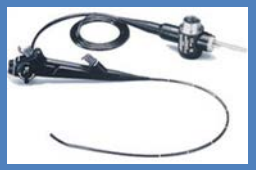
James M. Beck[1,2]

2014



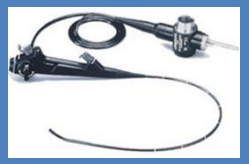


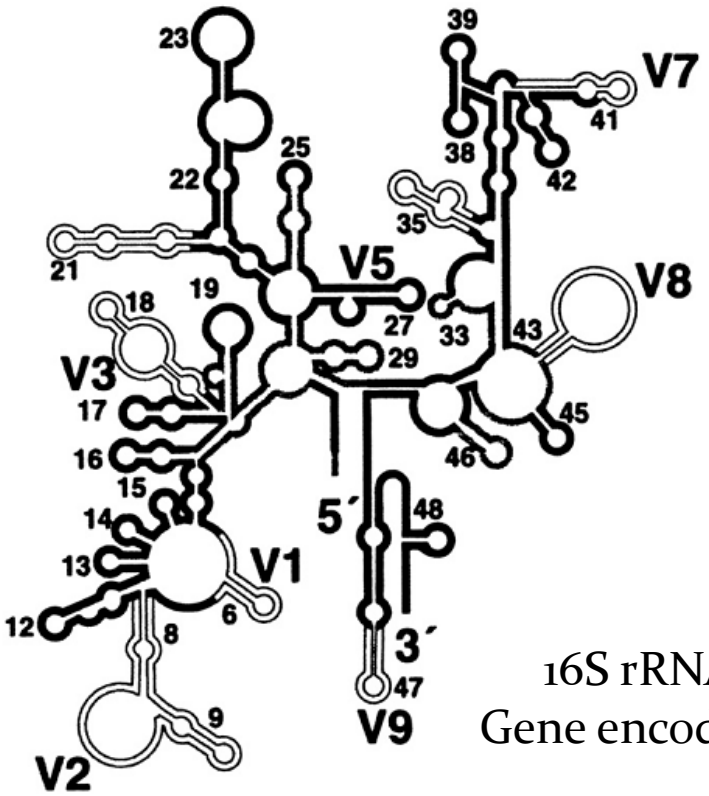
STERILE | R



ABCs of the Lung Microbiome

James M. Beck[1,2]





16S rRNA
Gene encoding

Figure 1. Secondary structure model of the 16S rDNA. V1 through V9 indicate major hypervariable regions, which are sequenced to identify organizational taxonomic units; V4 and V6 are unlabeled. Reprinted by permission from Reference 4.

The microbiome is a population of microbes assembled at a particular time and in a particular location.

Le principali ricerche sul microbioma polmonare si basano sulla sequenziazione identificazione su BAL di una regione variabile di un gene <16S ribosomal RNA gene> NON PRESENTE NEI MAMMIFERI

ribosomal RNA

Fortunately, 16S rRNA is not present in mammals, and with proper controls the confounding effects of host DNA can be minimized

Ann Am Thorac Soc Vol 11, Supplement 1, pp S3–S6, Jan 2014

ORIGINAL RESEARCH

A Novel Microbiota Stratification System Predicts Future Exacerbations in Bronchiectasis

Geraint B. Rogers[1], Nur Masirah M. Zain[2], Kenneth D. Bruce[2*], Lucy D. Burr[1], Alice C. Chen[1], Damian W. Rivett[3], Michael A. McGuckin[1], and David J. Serisier[1,4*]

[1]Immunity, Infection, and Inflammation Program, Mater Research Institute, University of Queensland, and Translational Research Institute, Woolloongabba, Queensland, Australia; [2]Institute of Pharmaceutical Science, King's College London, and [3]Division of Ecology and Evolution, Department of Life Sciences, Imperial College London, London, United Kingdom; and [4]Department of Respiratory Medicine, Mater Adult Hospital, South Brisbane, Australia

I risultati di questo studio suggeriscono una diversa associazione clinica e prognostica collegata alla TAXA BATTERICA

- ***Correlazione certa tra bassa diversità ed espressione di malattia + severa***
- **La predominanza di Pseudomonas è associato con markers di malattia + severa,ridotta funzione polmonare ,frequenti riacutizzazioni e maggior uso di antibiotici……..**
- **La predominanza di Haemophilus è associato con riacutizzazioni polmonari meno frequenti ma maggiore risposta/attivazione infiammatoria locale e sistemica forse ad azione protettiva !**
- In pratica l 'aumento della risposta infiammatoria causato da Haemophilus LIMITA e previene la riacutizzazione in contrasto con l'infezione da Pseudomonas
- **Dubbi rimangono sul ruolo (in alcuni pazienti CULTURA NEGATIVI) di alcuni batteri non identificabili ordinariamente come i generi Veillonella e Prevotella e fino ad ora considerati NON patogeni**

Research Article

Neutrophilic Bronchial Inflammation Correlates with Clinical and Functional Findings in Patients with Noncystic Fibrosis Bronchiectasis

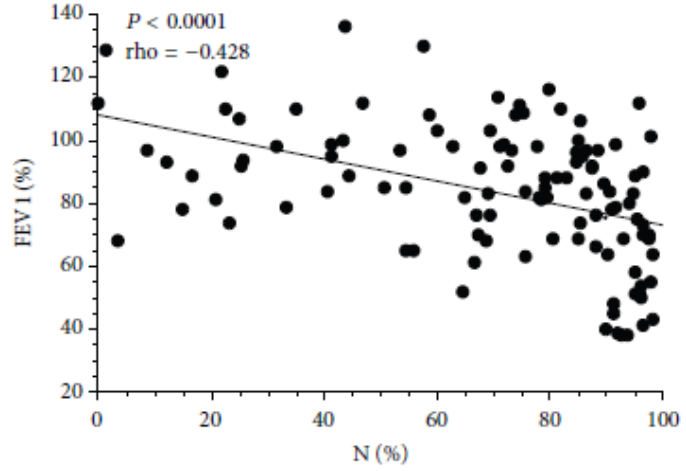
Hindawi Publishing Corporation
Mediators of Inflammation
Volume 2015, Article ID 642503, 6 pages
http://dx.doi.org/10.1155/2015/642503

Federico L. Dente, Marta Bilotta, Maria Laura Bartoli, Elena Bacci, Silvana Cianchetti, Manuela Latorre, Laura Malagrinò, Dario Nieri, Maria Adelaide Roggi, Barbara Vagaggini, and Pierluigi Paggiaro

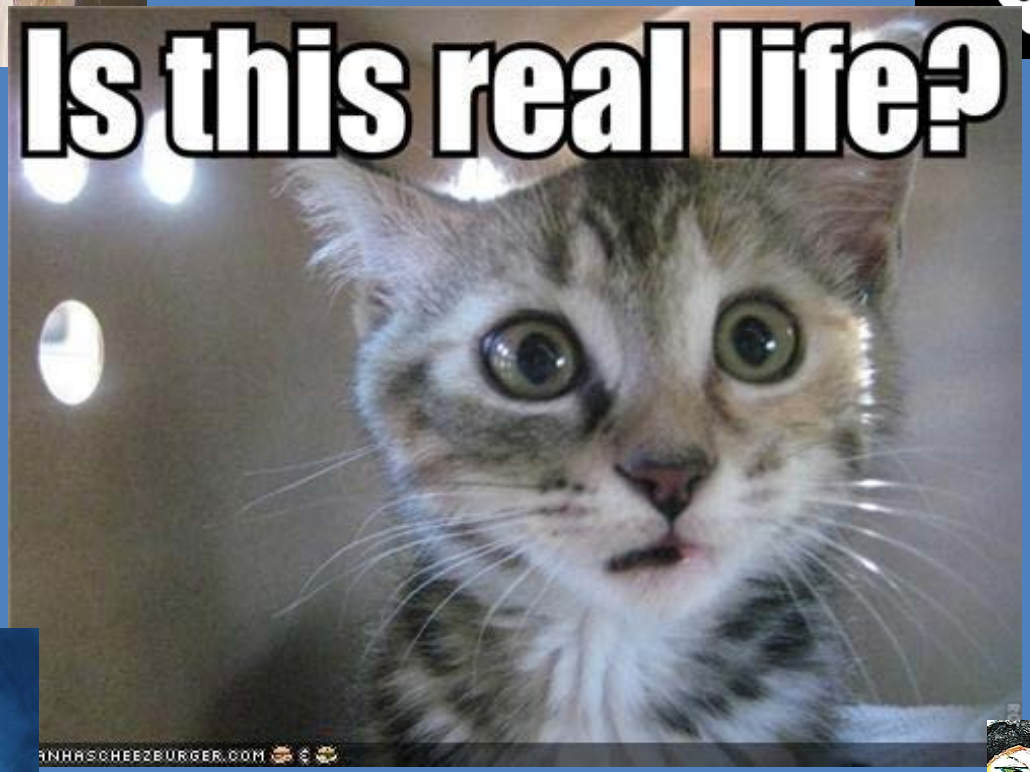
In conclusion, sputum neutrophilic inflammation in NCFB patients can be considered a good biomarker of disease severity, as confirmed by pulmonary function, disease duration, bacterial colonization, and BSI score.

Table 2: Biomarkers measured in the sputum, EBC, and exhaled air in the examined patients with NCFB.

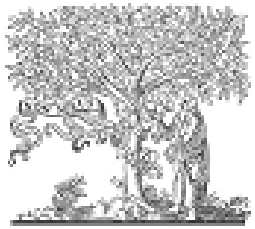
Sputum inflammatory cells	
Neutrophils, median (range), %	79.3 (1.5–98.1)
Eosinophils, median (range), %	0.8 (0–70.2)
Exhaled NO, ppb	22.5 (2–168)
MDA (EBC), nM	30.4 (6–116)



THE REAL WORLD



Journal of Infection (2015) 71, 28–36



ELSEVIER

BIAM British Infection Association

www.elsevierhealth.com/journals/jinf

Microbiology and outcomes of community acquired pneumonia in non cystic-fibrosis bronchiectasis patients

Eva Polverino [a], Catia Cilloniz [a], Rosario Menendez [b], Albert Gabarrus [a], Edmundo Rosales-Mayor [a], Victoria Alcaraz [a], Silvia Terraneo [c], Jordi Puig de la Bella Casa [d], Josep Mensa [e], Miquel Ferrer [a], Antoni Torres [a,*]

This is the first study in the literature analyzing a large CAP series to investigate demographics, clinical characteristics and microbial etiology of pneumonia in NCFBE patients.

[d] Department of Microbiology, Hospital Clinic of Barcelona, Spain
[e] Department of Infectious Disease, Hospital Clinic of Barcelona, Spain

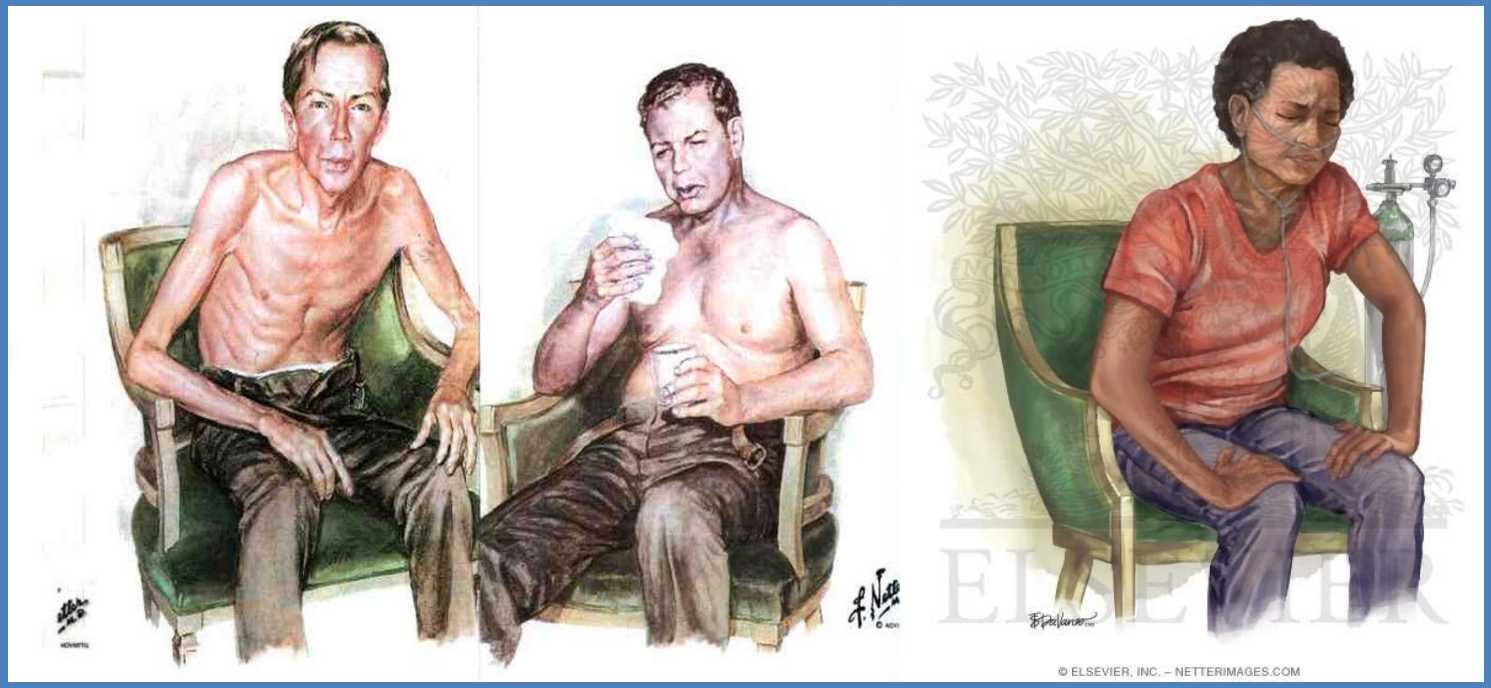
This is the first study in the literature analyzing a large CAP series to investigate demographics, clinical characteristics and microbial etiology of pneumonia in NCFBE patients.

Pazienti con CAP e Bronchiectasie (CAPBCTpz) *versus* Pazienti con CAP

RISULTATI :

- **Pazienti (CAPBCTpz) in genere più anziani e con maggiori comorbilità (molti con BPCO)**
- **uguale presentazione clinica , score di severità ed outcome (mortalità)**
- **uguale percentuale di isolamento microbico di S.pneumoniae**
- **CAPBCTpaz : maggiore presenza di P.aeruginosa ed Enterobacteriaceae**
- **CAPBCTpaz : Sottoposti a trattamento antibiotico empirico meno adeguato rispetto al gruppo CAP senza bronchiectasie !**

- The NCFBE-CAP group showed a lower rate of adequate empiric antibiotic therapy according to guidelines[18] in comparison with CAP.



Bronchiectasie nella BPCO
Bronchiectasie e BPCO

Recommendations for aetiological diagnosis of bronchiectasis

Rev Port Pneumol. 2016;

revista portuguesa de PNEUMOLOGIA portuguese journal of pulmonology

On behalf of the Pulmonology Portuguese Society Bronchiectasis Study Group, A. Amorim[a,*], F. Gamboa[b], M. Sucena[c], K. Cunha[d], M. Anciães[e], S. Lopes[f], S. Pereira[f], R.D. Ferreira[f], P. Azevedo[g], J. Costeira[h], R. Monteiro[i], J.C. da Costa[i], S. Pires[j], C. Nunes[k]

Prevalence of BE in obstructive airway diseases

Prevalence of BE in patients with COPD is highly variable (2–74%),[91,92] probably in relation with the criteria used to define BE. Several studies have confirmed a prevalence of approximately 50% in patients with moderate-severe COPD.[91,93,94]

The prevalence of BE in asthma is described between 17.5 and 28%.[18]

Bronchiectasis in Patients With COPD : A Distinct COPD Phenotype?

Anne E. O'Donnell

Chest 2011;140;1107-1108
DOI 10.1378/chest.11-1484

2015 NEW !!!

COPD–bronchiectasis overlap syndrome

John R. Hurst[1], J. Stuart Elborn[2] and Anthony De Soyza[3,4] on behalf of the BRONCH-UK Consortium[5]

Affiliations: [1]UCL Respiratory, University College London, London, UK. [2]Centre for Infection and Immunity, Queen's University, Belfast, UK. [3]Respiratory Medicine, Institute of Cellular Medicine, Newcastle University, Newcastle, UK. [4]Adult Bronchiectasis Service, Freeman Hospital, Newcastle upon Tyne Teaching Hospitals, Newcastle, UK. [5]For a list of the BRONCH-UK Consortium members see the Acknowledgements section.

Correspondence: John R. Hurst, UCL Respiratory, Royal Free Campus, University College London, London NW3 2PF, UK. E-mail: j.hurst@ucl.ac.uk

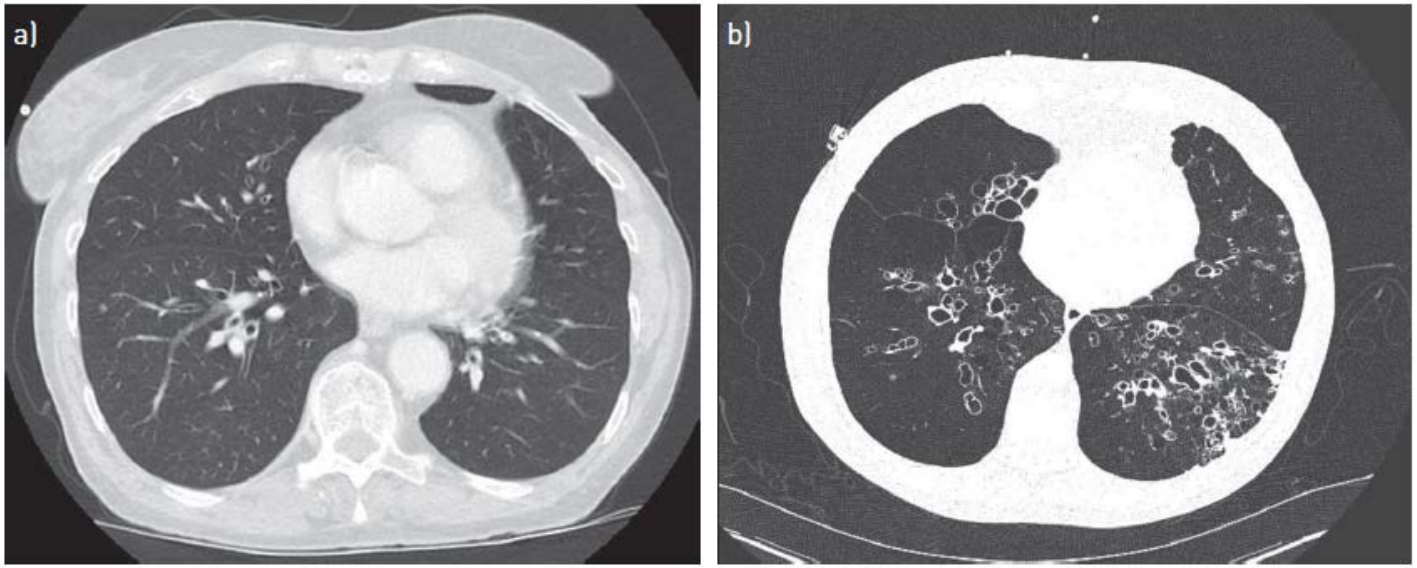


FIGURE 1 a) Typical airway wall changes in chronic obstructive pulmonary diagnosis are diffuse, and may be associated with co-existent emphysema on computed tomography. b) Airway wall changes in primary bronchiectasis may be localised or diffuse, and may be more severe resulting in cystic and/or varicose appearances.

Clinical phenotypes in adult patients with bronchiectasis

Eur Respir J 2016; 47:

Stefano Aliberti[1], Sara Lonni[1], Simone Dore[2], Melissa J. McDonnell[3], Pieter C. Goeminne[4,5], Katerina Dimakou[6], Thomas C. Fardon[7], Robert Rutherford[3], Alberto Pesci[1], Marcos I. Restrepo[8], Giovanni Sotgiu[2] and James D. Chalmers[7]

Centre
Dundee, UK
Leuven, Belgium
Monza, Italy
Galway, Ireland
Athens, Greece

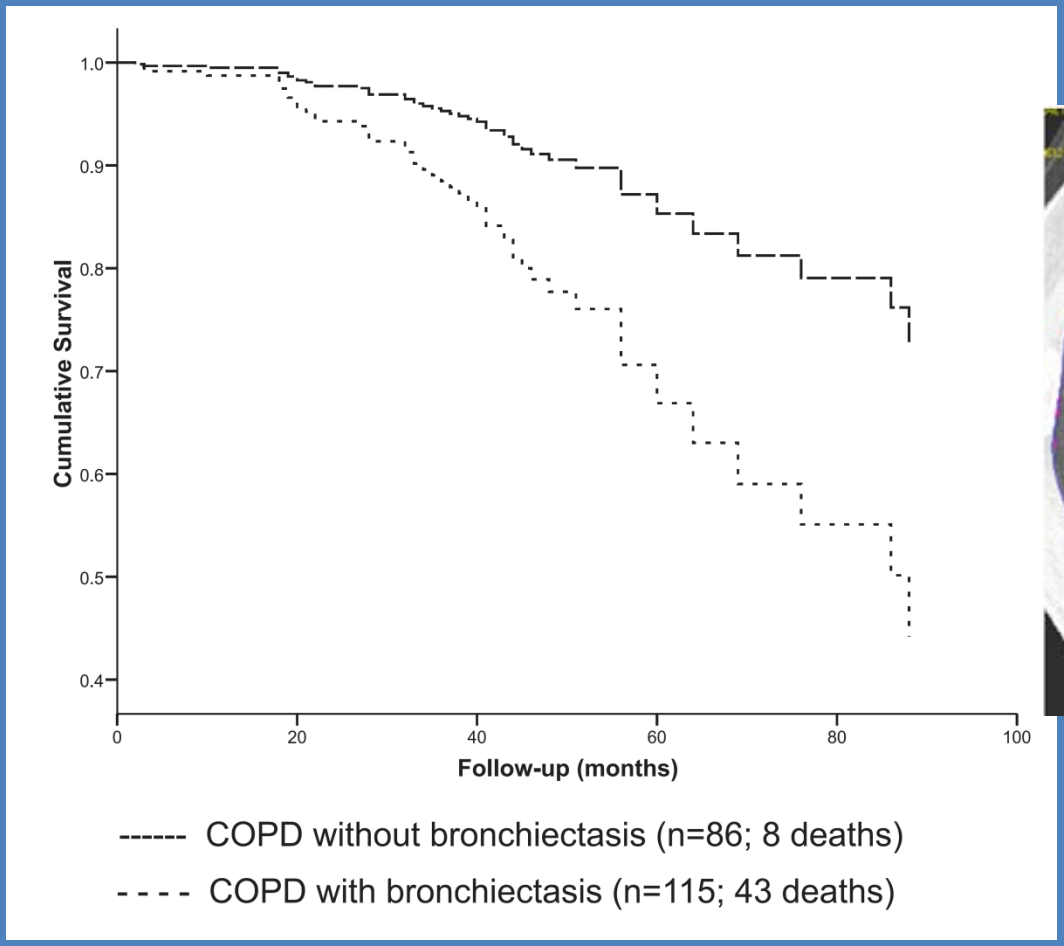
1145 patients

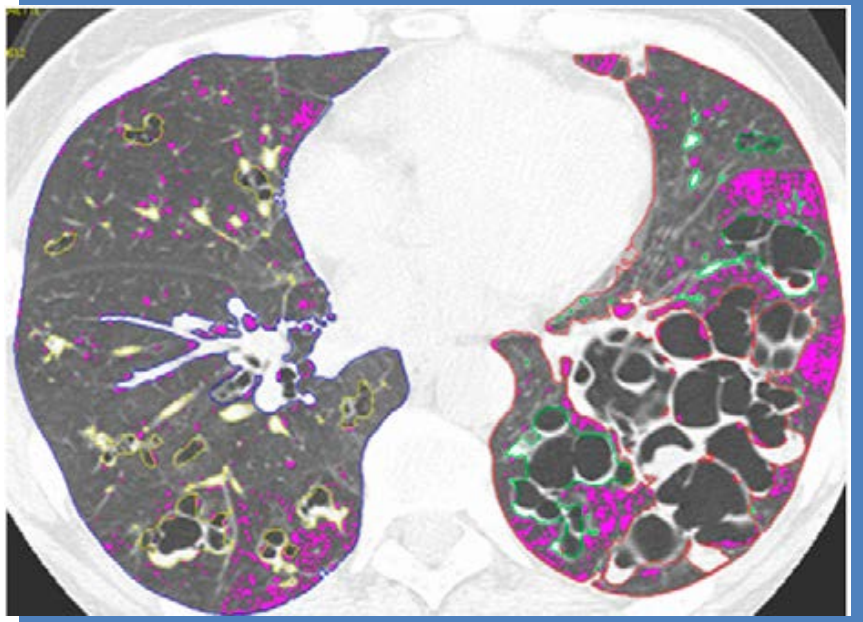
TABLE 3 Aetiology of bronchiectasis in the four clusters

	Cluster 1: "*Pseudomonas*"	Cluster 2: "Other chronic infection"	Cluster 3: "Daily sputum"	Cluster 4: "Dry bronchiectasis"	Overall p-value
Patients	179 (100)	273 (100)	373 (100)	307 (100)	
Idiopathic	46 (26)	86 (33)	131 (36)	110 (36)	0.09
Post-infective	63 (36)	54 (21)	96 (26)	77 (25)	0.004
COPD	21 (12)	29 (11)	50 (14)	20 (6.6)	0.03
Connective tissue disease	10 (5.6)	26 (9.8)	26 (7.1)	27 (8.9)	0.377
Immunodeficiency	11 (6.2)	17 (6.4)	14 (3.8)	14 (4.6)	0.436
ABPA	10 (5.6)	20 (7.6)	12 (3.3)	12 (3.9)	0.083
Asthma	2 (1.1)	10 (3.8)	8 (2.2)	15 (4.9)	0.071
Inflammatory bowel disease	3 (1.7)	6 (2.3)	12 (3.3)	3 (1)	0.233
Ciliary dysfunction	7 (4)	6 (2.3)	5 (1.4)	2 (0.7)	0.055
Aspiration	2 (1.1)	6 (1.9)	3 (0.8)	3 (1)	0.419
α_1-antitrypsin deficiency	0 (0)	1 (0.4)	3 (0.8)	6 (2)	0.091
Congenital	0 (0)	2 (0.8)	3 (0.8)	0 (0)	0.284
Other	2 (1.1)	1 (0.4)	2 (0.5)	15 (4.9)	<0.001

Data are presented as n (%), unless otherwise stated. COPD: chronic obstructive pulmonary disease; ABPA; allergic bronchopulmonary aspergillosis.

Mortalità





COPD with bronchiectasis : mortalità !!

EDITORIAL
ASTHMA AND BRONCHIECTASIS

Bronchiectasthma and asthmectasis!

Joan B. Soriano[1] and José Serrano[2]

Eur Respir J 2016; 47

Affiliations: [1]Instituto de Investigación Hospital Universitario de la Princesa (IISP), Universidad Autónoma de Madrid, Madrid, Spain. [2]Pneumology Dept, Hospital Comarcal de Inca, Inca, Spain.

Correspondence: Joan B. Soriano, Instituto de Investigación Hospital Universitario de la Princesa (IISP), Universidad Autónoma de Madrid, Diego de León 62, 28030 Madrid, Spain.
E-mail: jbsoriano2@gmail.com

Reconstruction of the first ever identification of bronchiectasis (plus asthma?). *Laennec*

- neutrophilic asthma
- A1-antitrypsin deficency
- respiratory tract Infections in childhood
- immunodeficiencies
- Allergic bronchopulmonary aspergillosis

…..a philosophical approach to this problem could be that individuals suffering with asthma and bronchiectasis should comprise a different population and present a new syndrome worth studying and naming……

Asthma and bronchiectasis exacerbation

Bei Mao[1,2,3], Jia-Wei Yang[1,2,3], Hai-Wen Lu[1] and Jin-Fu Xu[1,2]

Eur Respir J 2016; 47: 1597–1600. April 13 2016

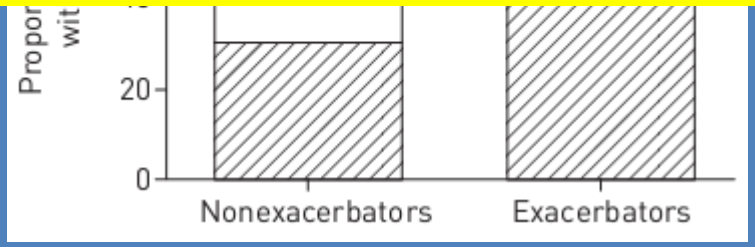
Affiliations:
[1]Dept of Respiratory and Critical Care Medicine, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China.

The existence of asthma was associated with an independent increase in risk of bronchiectasis exacerbation.

DIAGNOSTIC DIFFICULTIES IN CLINICAL PRACTICE

First question : bronchial hyperresponsiveness (BHR) very common among patients with only bronchiectasis …indistinguishable from patients with bct and asthma

Second question : complexity of deciding whether an episode of clinical and functional Impairment in a patient with asthma and bct corresponds to an asthma attack , to an exacerbaction of bct to both conditions simultaneously…..



Asthma	2.60 (1.15–5.88)	0.021
FEV_1 <50%	4.03 (1.75–9.26)	0.001
Extent >2 lobes	2.73 (1.16–6.45)	0.022
P. aeruginosa isolation	2.41 (1.00–5.79)	0.05

Factors associated with bronchiectasis exacerbation in all subjects according to the logistic regression analysis.

Galmiche JP, Zerbib F, Des Varannes B. Review article: respiratory manifestations of gastro-oesophageal reflux disease. Aliment Pharmacol Ther. 2008;27(6):449–64.
Lee AL, Button BM, Denehy L, Wilson JW. Gastro-oesophageal reflux in noncystic fibrosis bronchiectasis. Pulm Med. 2011;2011:395020.

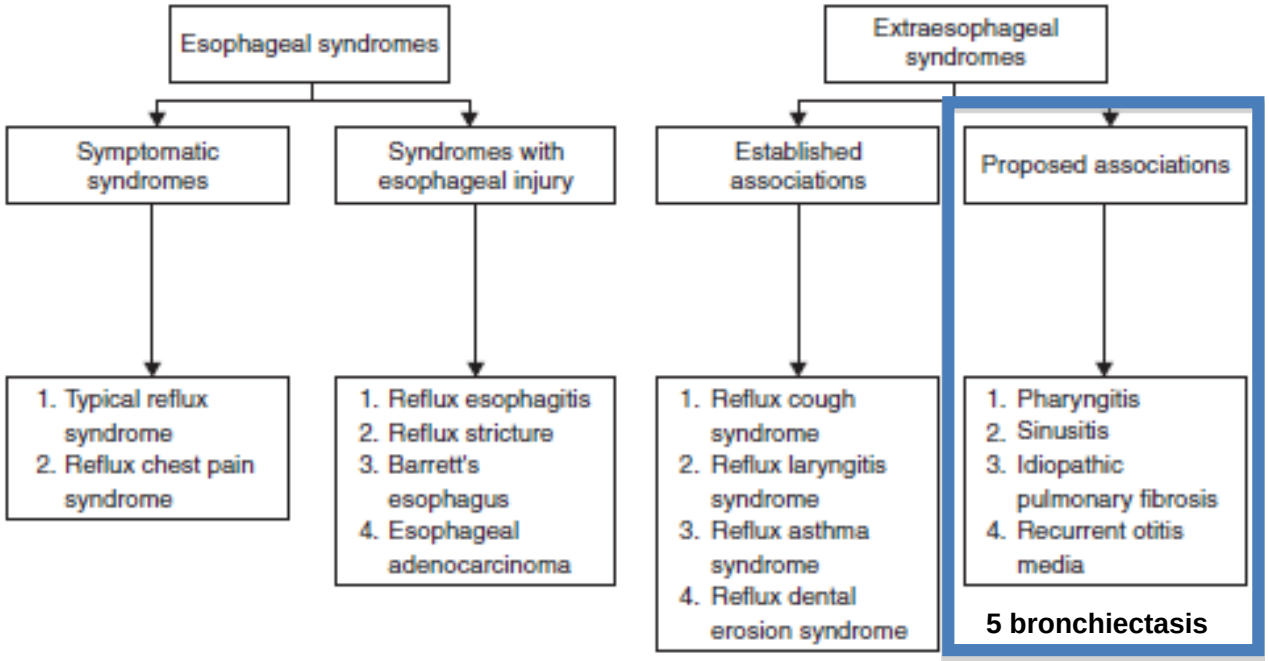


Figure 2 GERD manifestations.

Adapted from Montreal Consensus.

BRONCHIECTASIS **and** Gastro-oesophageal reflux disease

Bronchiectasie
Malattia Complessa
Indispensabile per una corretta Terapia :
Approccio multidisciplinare

THE REAL WORLD

On behalf of the British Thoracic Society Bronchiectasis (non-CF) Guideline Group: a sub-group of the British Thoracic Society Standards of Care Committee

What is the role of HRCT?

- HRCT is the radiological [illegible] ice to establish the diagnosis of bronchiectasis. **[D]**

DIAGNOSI !

What is an optimum HRCT protocol for defining bronchiectasis?

- Standard HRCT protocol, single detector CT scanner. **[D]**
  - patient position: supine, breath holding at full inspiration; optional ECG gating 120–140 kV; 100–180 mAs (dependent on patient habitus); acquisition time <1 s;
  - [illegible]
  - [illegible]
- Vo[illegible]D]
  - [illegible]ration
  - [illegible], pitch 0.9;
  - reconstruction with 'very or ultra sharp' kernel.

INDISPENSABILE :
USO DI TECNICHE/PROTOCOLLI
DI ESECUZIONE ESPERTI

What are the HRCT features of bronchiectasis?

- Bronchial wall dilation (internal lumen diameter greater than accompanying [illegible]ering) is the characteristic f[illegible]
- Bronchial wall thickening is often also present though harder to define. **[D]**

CARATTERISTICHE !

Can HRCT identify features of specific causes?

- HRCT f[illegible]rlying condition[illegible]ratory assessments. **[D]**
- HRCT images should be examined for features suggesting ABPA, cystic fibrosis, immotile cilia, opportunist mycobacteria and tracheobronchomegaly. **[D]**

SOSPETTO DIAGNOSTICO !

How are HRCT changes related to lung function?

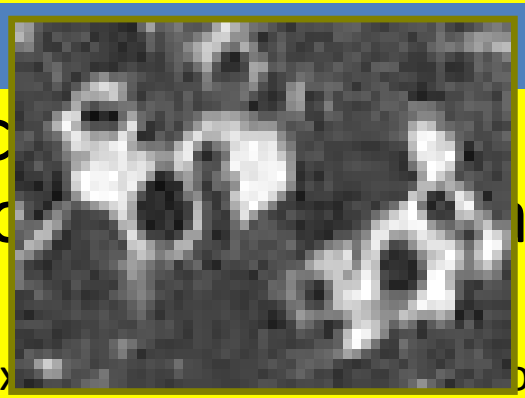
- The severity of bro[illegible]T correlates with measures of airflow [illegible]. **[D]**

SEVERITA' !

How often should radiological investigations be repeated?

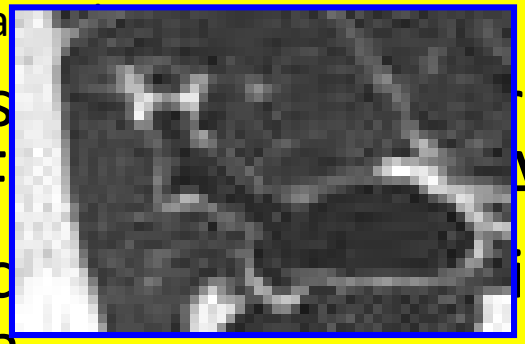
- Routine repeat chest x-ray or HRCT is not necessary; repeat imaging should be considered when there is clinical need. **[D]**

HRCT Diagnostic Criteria



- Diametro Bronc BD) più grande rispetto a quell diacente (SIGNET RING SIGN)
  - Scores 1 – mild - : IBD not ex of adjacent vessel
  - Scores 2- moderate- : IBD from two or three times
  - Scores 3 : - severe- : IBD exc

- Spessore della Par oè ispessimento peribronchiale : Pe keness (PbT)
  - Scores 1- mild- : PbT was e nt vessel
  - Scores 2 –moderate- : PbT t
  - Scores 3 – severe- :PbT grea

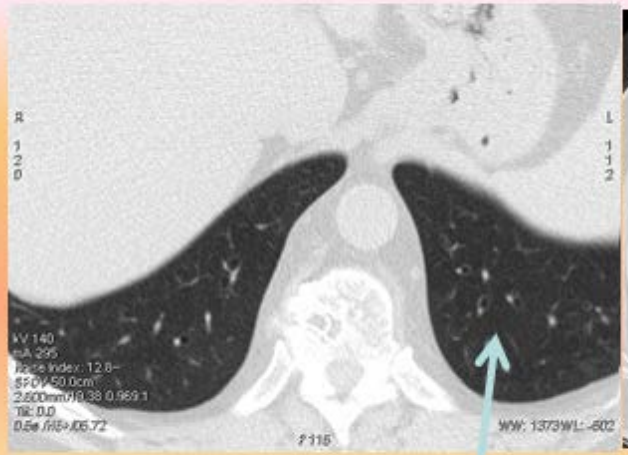


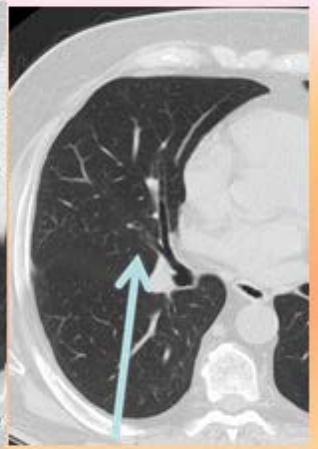
- Non riduzione/ass rogressivo e distale dei bronchi(LACK OF APERING)
- Riscontro di bronc) fin quasi alla superficie pleurica

M.Bhalla Radiology 1991 mod.

Segni HRCT-MDCT diretti

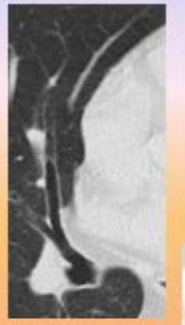
courtesy by M.Scuderi

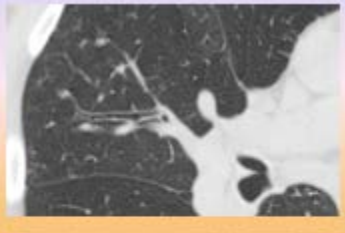


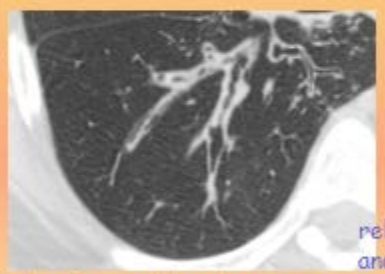


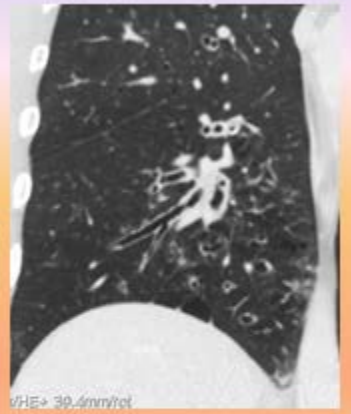
➢BRONCHOARTERIAL RATIO
➢SIGNET RING SIGN

LACK OF BRONCHIAL TAPERING







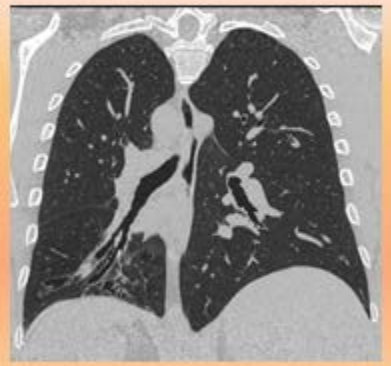


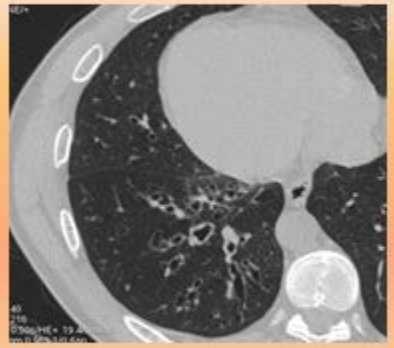
related to air flow limitation and severity of bronchiectasis

Bronchial wall thickening is a usual but inconstant feature of bronchiectasis. ...Minor to mild degrees of bronchial wall thickening are seen in normal subjects, those with asthma, individuals with lower respiratory tract viral infections and asymptomatic smokers.

courtesy by M.Scuderi

Segni HRCT-MDCT diretti

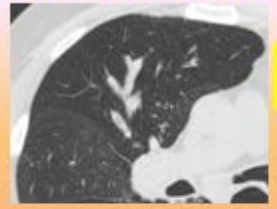




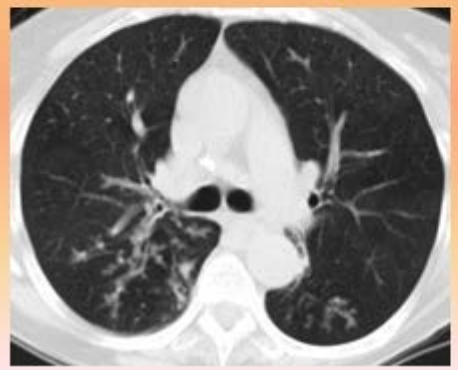
CROWDING

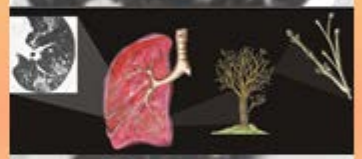
courtesy by M.Scuderi

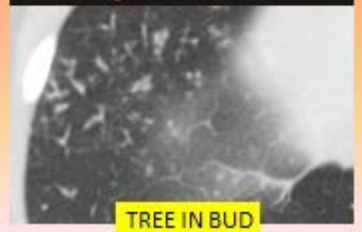
MUCOID IMPACTION



courtesy by M.Scuderi







TREE IN BUD

Recommendations for aetiological diagnosis of bronchiectasis

Rev Port Pneumol. 2016;

revista portuguesa de PNEUMOLOGIA portuguese journal of pulmonology

On behalf of the Pulmonology Portuguese Society Bronchiectasis Study Group, A. Amorim[a,*], F. Gamboa[b], M. Sucena[c], K. Cunha[d], M. Anciães[e], S. Lopes[f], S. Pereira[f], R.D. Ferreira[f], P. Azevedo[g], J. Costeira[h], R. Monteiro[i], J.C. da Costa[i], S. Pires[j], C. Nunes[k]

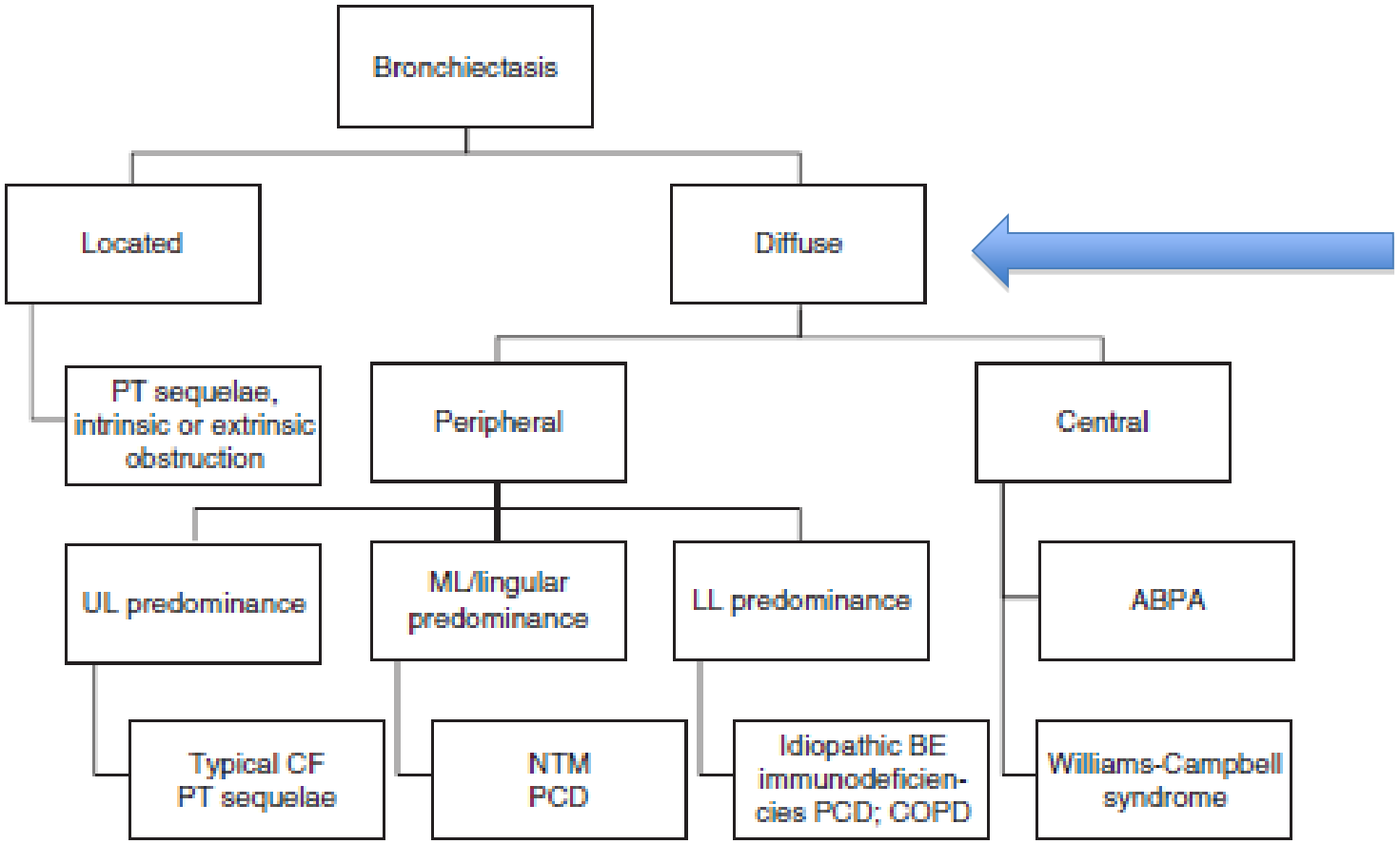
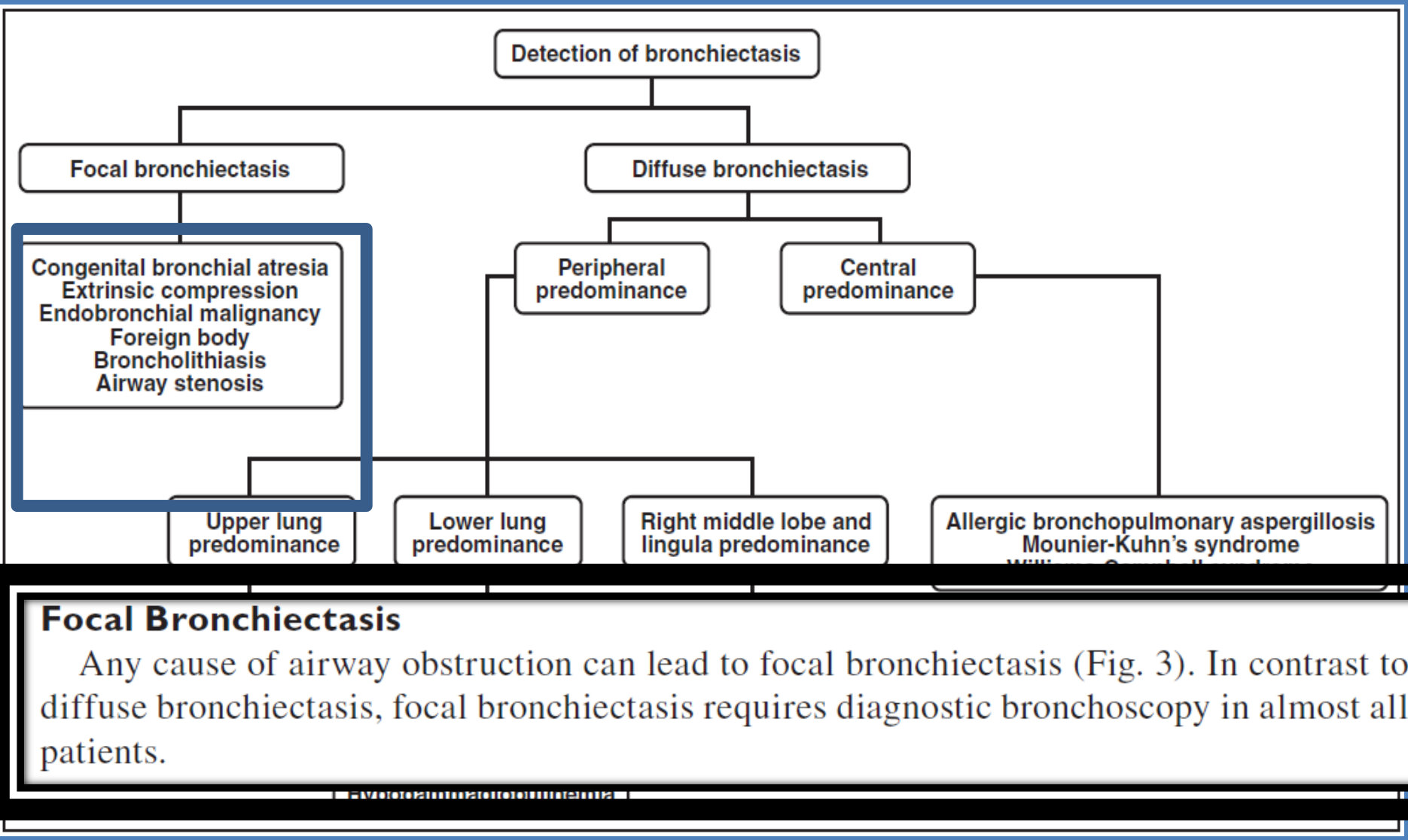


Figure 1 Radiological characteristics and aetiology. UL, upper lobe; ML, middle lobe; LL, lower lobe.

DISTRIBUTION FOCAL !



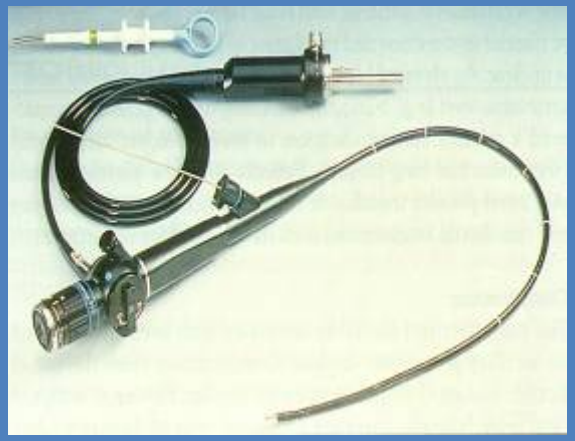
Focal Bronchiectasis

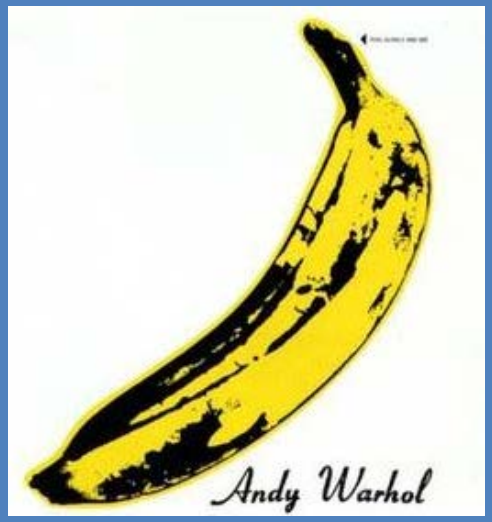
Any cause of airway obstruction can lead to focal bronchiectasis (Fig. 3). In contrast to diffuse bronchiectasis, focal bronchiectasis requires diagnostic bronchoscopy in almost all patients.

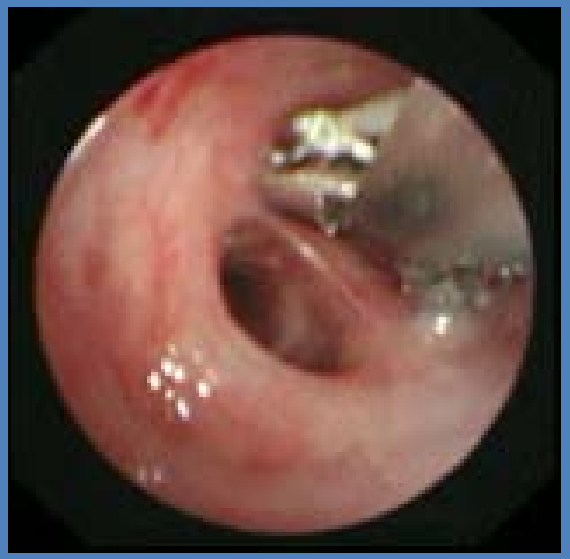
Luce Cantin[1]
Alexander A. Bankier
Ronald L. Eisenberg

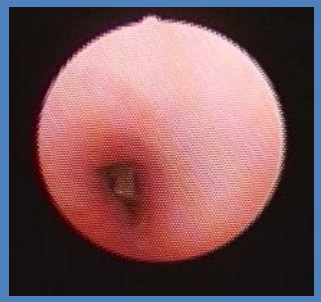
AJR:193, September 2009

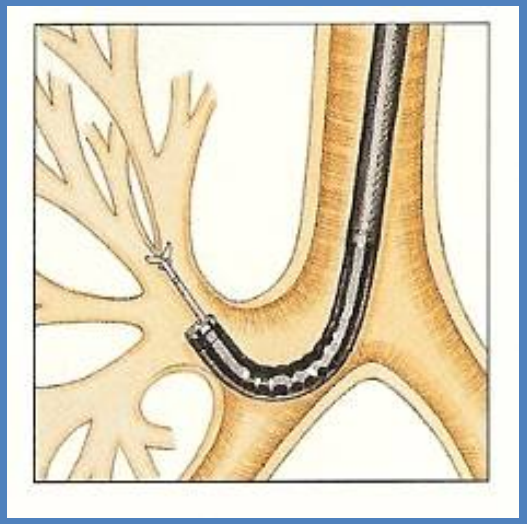
Fbs nelle bct localizzate

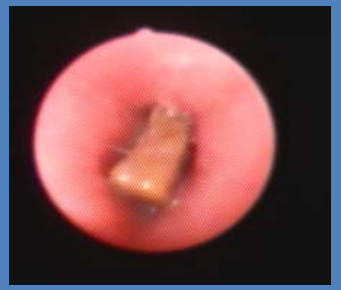






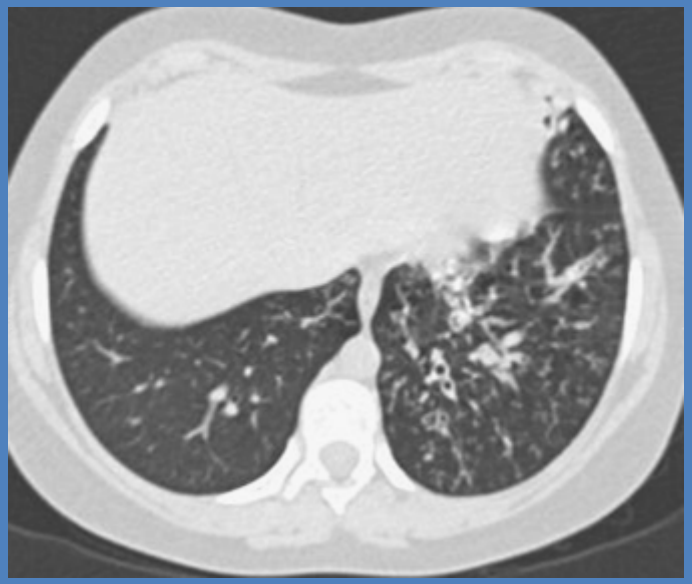




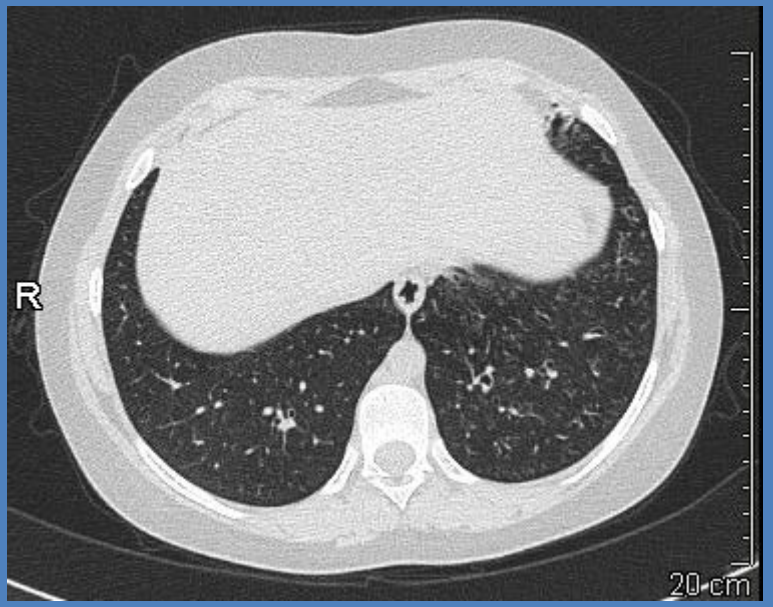


INDICAZIONE ALLA BRONCOSCOPIA (FBS) IN PAZIENTO CON BRONCHIECTASIE NON FC

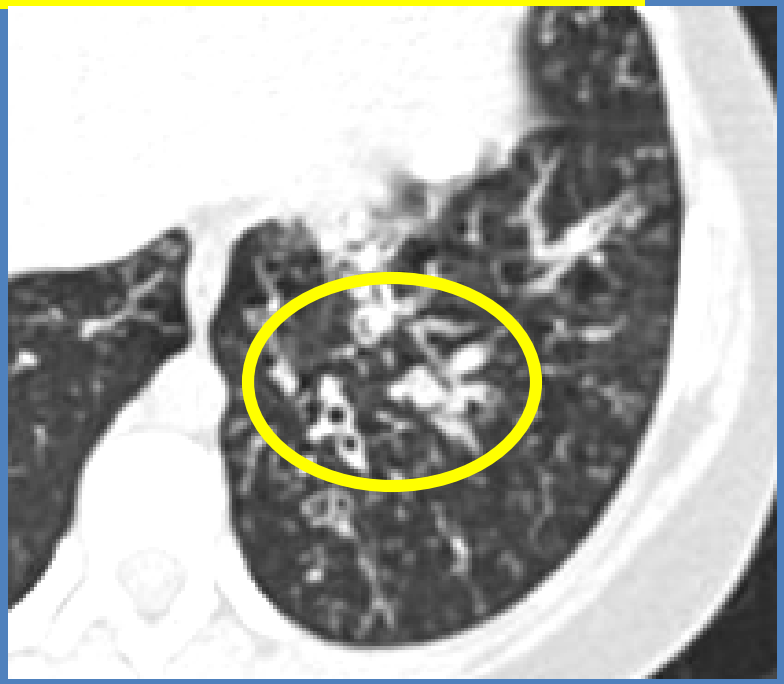
- può identificare e permettere la rimozione di un corpo estraneo nell'albero tracheobronchiale
- Può identificare alterazioni anatomiche e/o ostruzioni bronchiali misconosciute
- Può essere usato per identificare con certezze eventuali patogeni nelle basse vie respiratorie usando metodologie validate per il prelievo batteriologico come il BAL ed il brushing protetto soprattutto in pazienti con apparente malattia stabile
- Permette l' identificazione di "sindrome da aspirazione gastrica " in caso di riscontro di macrofagi con inclusioni lipidiche su BAL



Reversible bronchiectasis (pseudobronchiectasie)



BAL: *Haemophilus influenzae*



dopo 9 mesi

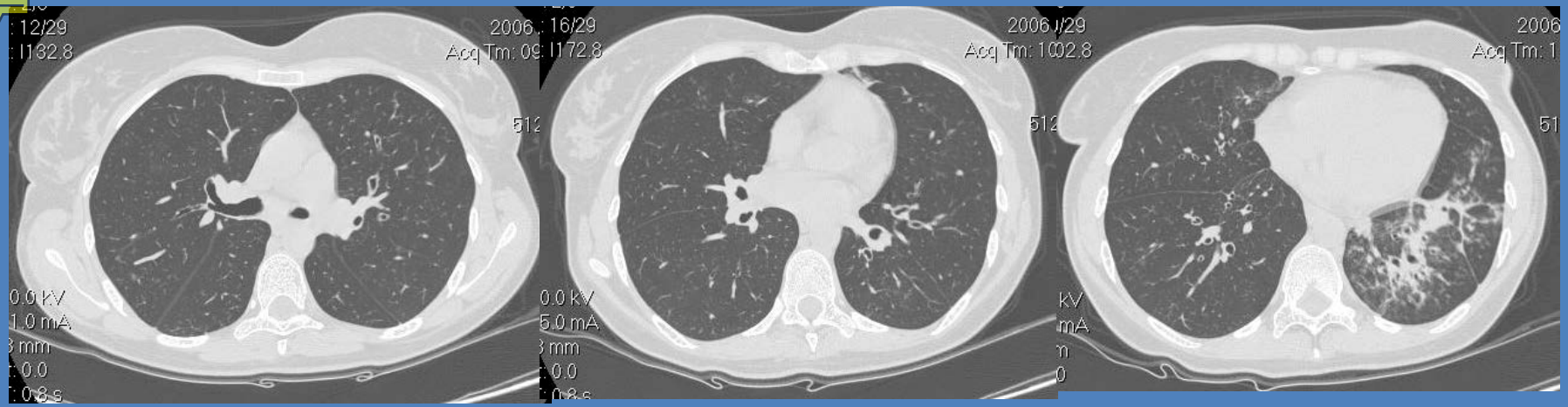
European Journal of RADIOLOGY

2002

- **Reversible bronchial dilatation in children: comparison of serial high-resolution computer tomography scans of the lungs**

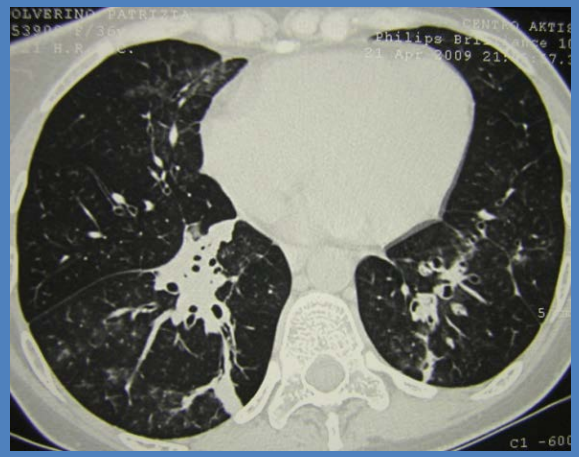
La diagnosi di BRONCHIECTASIE NEL BAMBINO deve essere fatta SOLO in presenza di segni clinici PERSISTENTI nel tempo associati ad un riscontro di BRONCHIECTASIE su una TAC del torace praticata dopo un ragionevole intervallo di tempo (almeno 2 anni secondo l'autore....)
....nel bambino si dovrebbero usare metodiche (multidetector four channel CT) che minimizzino il tempo e la dose di esposizione anche per ridurre la necessità di una sedazione.....

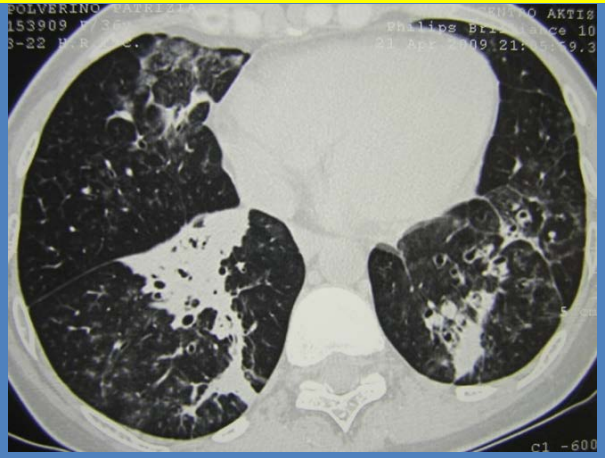
LA DIAGNOSI DI BRONCHIECTASIE NEI BAMBINI DEVE ESSERE FATTA CON " MOLTA CAUTELA"

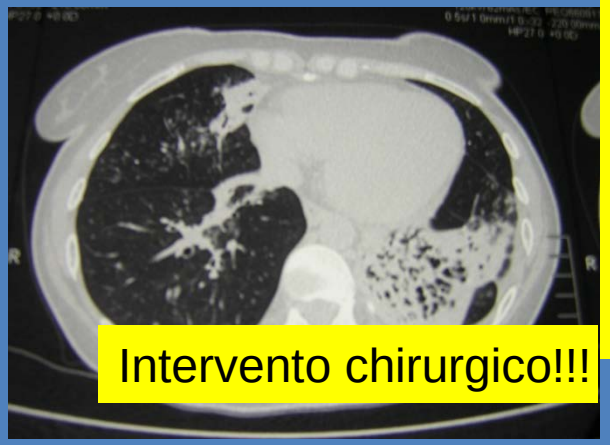


NELL'ADULTO

- **NON REVERSIBILITA' DELLE LESIONI**
- **LA MALATTIA SPESSO PROGREDISCE ANCHE SE VIENE PRATICATA UNA TERAPIA ADEGUATA !**







Intervento chirurgico!!!

2006 2008 2011

Bronchiectasie: Scoring system in CF

RADIOLOGICAL SCORING SYSTEM in CYSTIC FIBROSIS

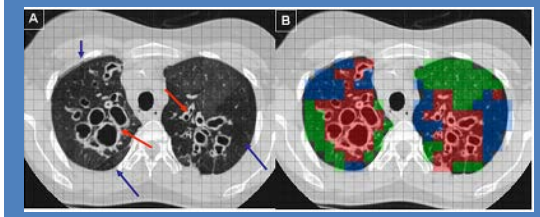
Bhalla CT score (bronchiectasis in cystic fibrosis)

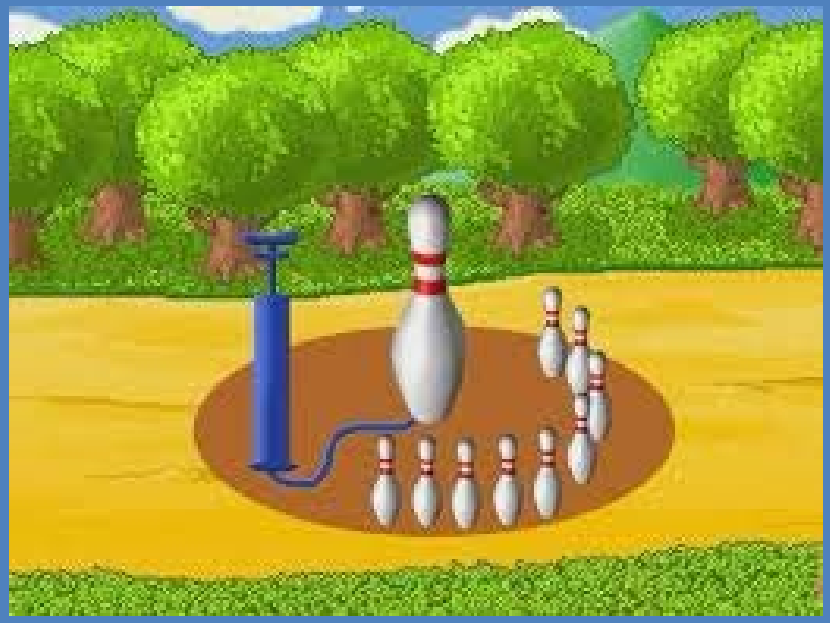
Category	Score			
	0	1	2	3
Severity of bronchiectasis	Absent	Mild (luminal diameter slightly greater than diameter of adjacent blood vessel)	Moderate (lumen 2–3 times the diameter of the vessel)	Severe (lumen > 3 times diameter of vessel)
Peribronchial thickening	Absent	Mild (wall thickness equal to diameter of adjacent vessel)	Moderate (wall thickness greater than and up to twice the diameter of adjacent vessel)	Severe (wall thickness > 2 times the diameter of adjacent vessel)
Extent of bronchiectasis (no. of BP segments)	Absent	1–5	6–9	> 9
Extent of mucus plugging (no. of BP segments)	Absent	1–5	6–9	> 9
Sacculations or abscesses (no. of BP segments)	Absent	1–5	6–9	> 9
Generations of bronchial divisions involved (bronchiectasis or plugging)	Absent	Up to 4th generation	Up to 5th generation	Up to the 6th generation and distal
No. of bullae	Absent	Unilateral (not > 4)	Bilateral (not > 4)	> 4
Emphysema (no. of BP segments)	Absent	1–5	> 5	
Collapse or consolidation	Absent	Subsegmental	Segmental or lobar	

Severe Advance Lung Disease (SALD) Scoring System

Chest Computed Tomography Scores Are Predictive of Survival in Patients with Cystic Fibrosis Awaiting Lung Transplantation

Martine Loeve[1,2], Wim C. J. Hop[3], Marleen de Bruijne[2,4,5], Peter T. W. van Hal[6], Phil Robinson[7], Moira L. Aitken[8], Jonathan D. Dodd[9], and Harm A. W. M. Tiddens[1,2]; on behalf of the Computed Tomography Cystic Fibrosis Survival Study Group*



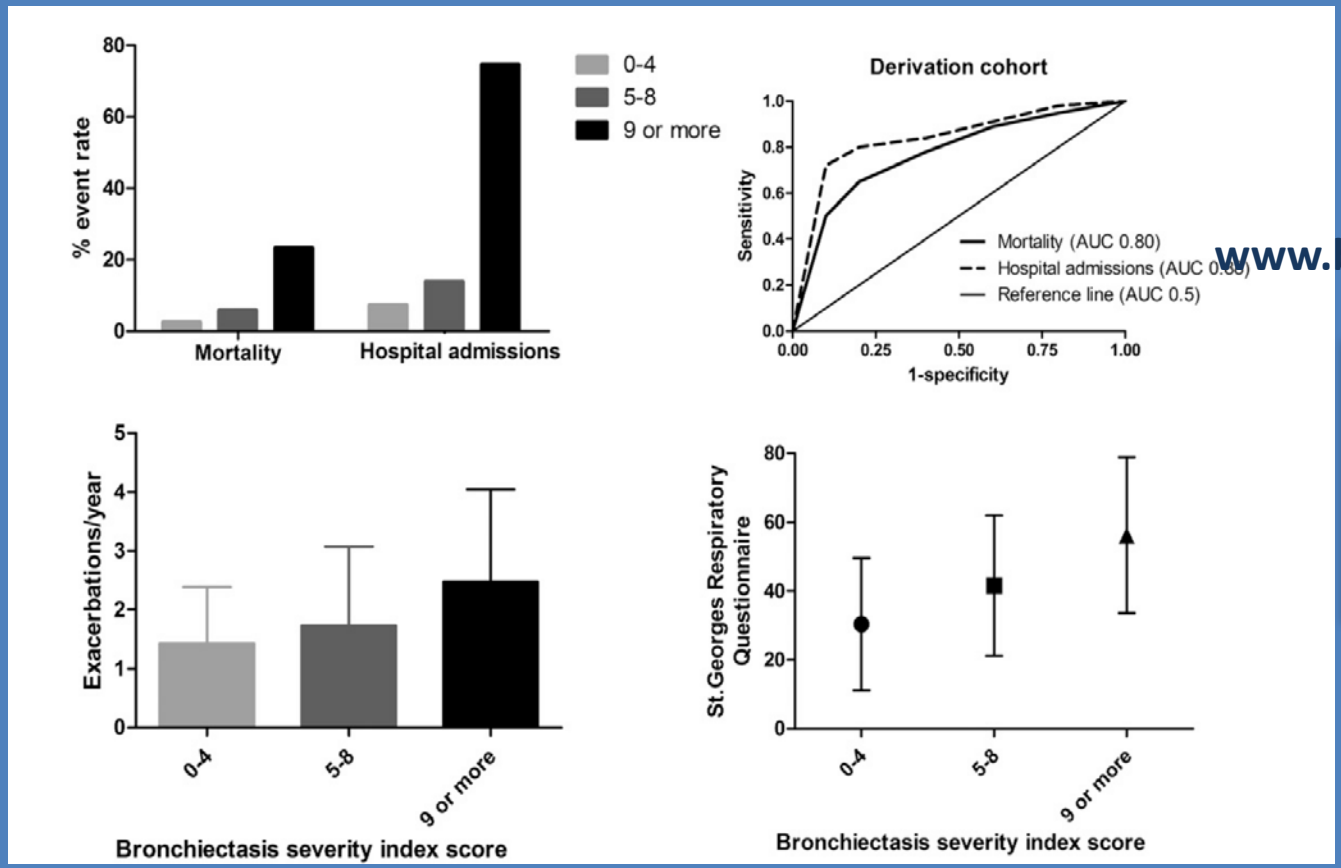


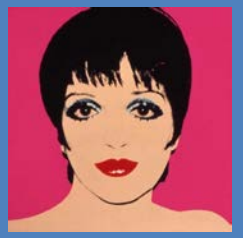
Bronchiectasie:
Scoring system in Non CF

The Bronchiectasis Severity Index

An International Derivation and Validation Study

James D. Chalmers[1], Pieter Goeminne[2], Stefano Aliberti[3], Melissa J. McDonnell[4,5], Sara Lonni[3], John Davidson[4], Lucy Poppelwell[1], Waleed Salih[1], Alberto Pesci[3], Lieven J. Dupont[2], Thomas C. Fardon[1], Anthony De Soyza[4,5], and Adam T. Hill[6]





www.bronchiectasisseverity.com

0-4 punti: Lieve
5-8 punti: Moderata
>9 punti : Grave

P, Aliberti S AJRCCM 201

ORIGINAL ARTICLE
BRONCHIECTASIS

Eur Respir J 2014; 43: 1357–1367

Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score

Miguel Á. Martínez-García[1,2], Javier de Gracia[2,3,4], Monserrat Vendrell Relat[2,5], Rosa-Maria Girón[6], Luis Máiz Carro[7], David de la Rosa Carrillo[8] and Casilda Olveira[9]

The outcome was 5-year all-cause mortality after radiological diagnosis "An easy-to-use multidimensional grading system accurately classifies bronchiectasis severity according to prognosis"

TABLE 6 Final score, cut-off points of the dichotomised variables and scoring of each variable

	Points
Chronic colonisation by *Pseudomonas aeruginosa*	
No	0
Yes	1
Dyspnoea mMRC score	
0–II	0
III–IV	1
FEV1 % predicted	
⩾50%	0
<50%	2
Age	
<70 years	0
⩾70 years	2
Number of lobes	
1–2	0
>2	1

Maximum score 7 points. mMRC: modified Medical Research Council; FEV1: forced expiratory volume in 1 s.

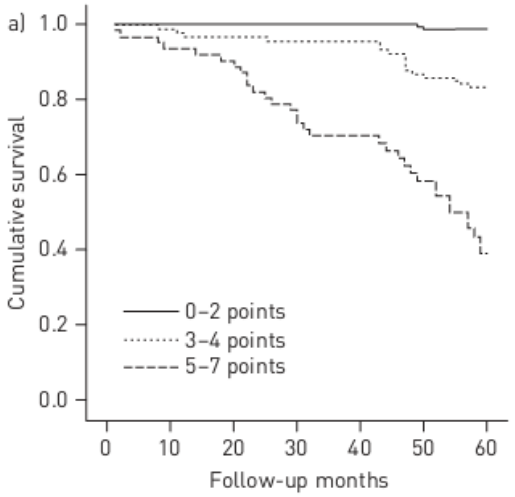


FIGURE 4 Kaplan–Meier curves for respiratory mortality

We conclude that this easy-to-use multidimensional grading system proved capable of accurately classifying the severity of bronchiectasis according to its prognosis.

The Bronchiectasis Severity Index
An International Derivation and Validation Study

James D. Chalmers[1], Pieter Goeminne[2], Stefano Aliberti[3], Melissa J. McDonnell[4,5], Sara Lonni[3], John Davidson[4], Lucy Poppelwell[1], Waleed Salih[1], Alberto Pesci[3], Lieven J. Dupont[2], Thomas C. Fardon[1], Anthony De Soyza[4,5], and Adam T. Hill[6]

ORIGINAL ARTICLE
BRONCHIECTASIS

Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score

Miguel Á. Martínez-García[1,2], Javier de Gracia[2,3,4], Monserrat Vendrell Relat[2,5], Rosa-Maria Girón[6], Luis Máiz Carro[7], David de la Rosa Carrillo[8] and Casilda Olveira[9]

Valutazione
Prognosi
In rapporto
alla severità

Identifica
Le Forme gravi

Stretto follow up

Impegno di risorse:
- Facilità di accesso del paziente al centro in caso di riacutizzazione.

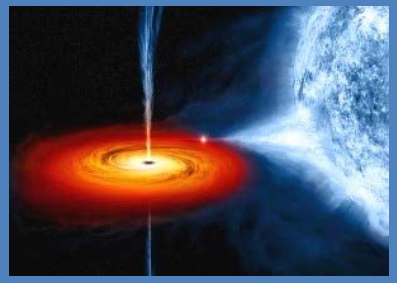
Prescrizione di device per FKT fuori dalle indicazioni convenzionali
- PEP mask
- CPAP
- BiLevel

Utilizzo di farmaci con modalità off label o attraverso protocolli di ricerca
- Antibiotico terapia a Lungo termine
- Antibiotici inalatori

Chalmers JD, Goeminne P, Aliberti S AJRCCM 2014

Bronchiectasie :TERAPIA

Approccio terapeutico integrato



A. Utilizzo di terapia antibiotiche inalatorie a lungo termine.

B. Utilizzo dei Macrolidi.

C. Riabilitazione e fisioterapia

Nessuna raccomandazione specifica nelle
linea guida, non farmaci con indicazione specifica oltre a quelle
comuni per tutti i pazienti con BPCO

Approccio terapeutico integrato

A. Utilizzo di terapia antibiotiche inalatorie a lungo termine.

B. Utilizzo dei Macrolidi.

C. Riabilitazione e fisioterapia

Management of bronchiectasis in adults

James D. Chalmers[1], Stefano Aliberti[2] and Francesco Blasi[3]

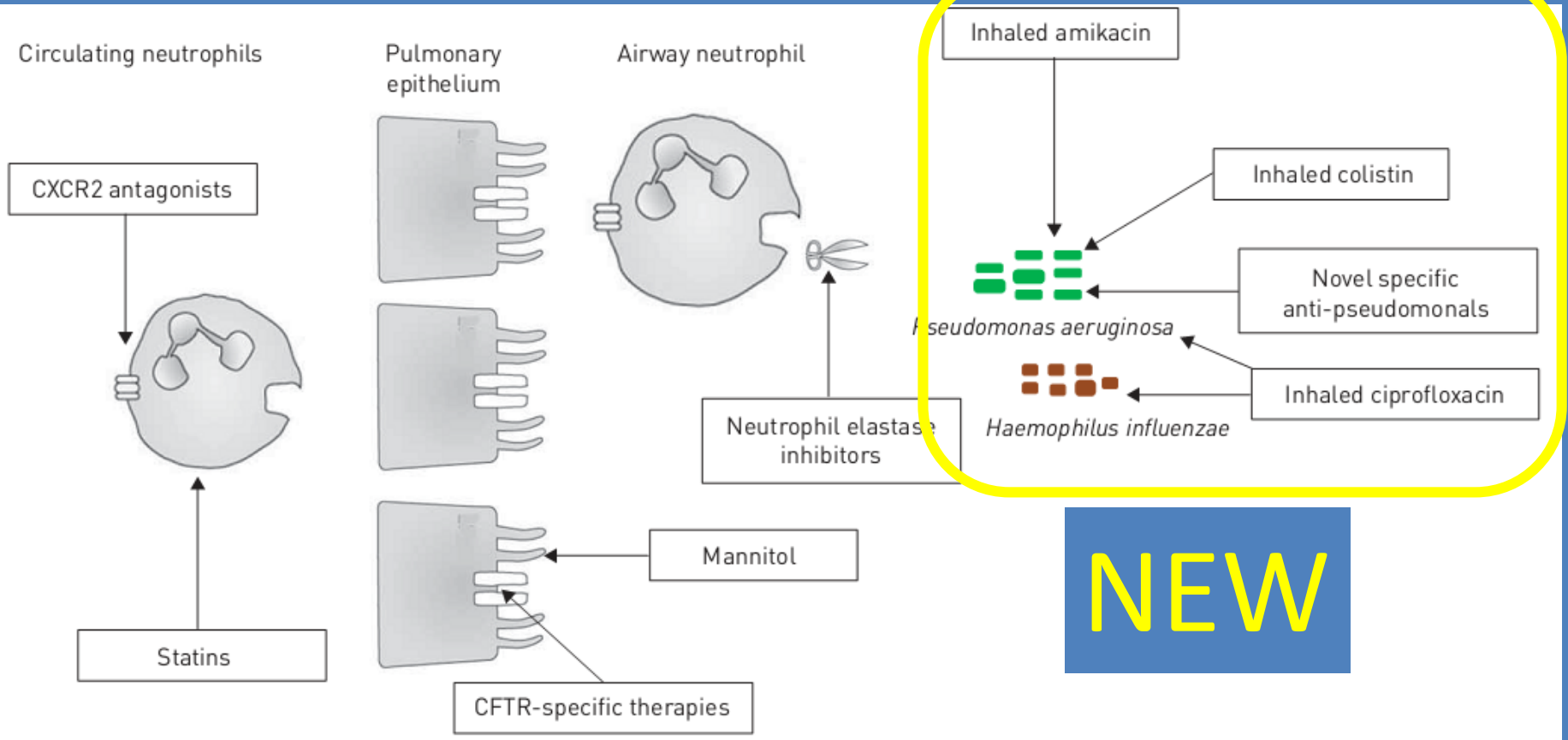


FIGURE 3 New therapies in development for bronchiectasis and their possible role. CFTR: cystic fibrosis transmembrane conductance regular.

Rationale for inhaled antibiotics

To reduce systemic side effects

(Tendinitis

To increase local concentration

ase)

The good example of CF:

the positive benefit (lung function, exacerbation, HRQoL)

Positive risk balance (safety/tolerability, resistance)

To reduce the risk of antibiotic resistance

Month on - month off

OBIETTIVO : Eradicazione di *P aeruginosa* in bronchiectasie non FC.

TABLE 2 Current state of development of inhaled antibiotic agents for non-cystic fibrosis bronchiectasis

Agent [ref.]	n	Current phase of development	Primary outcome	Duration	Patient population	Main results	Safety
Amoxicillin [78–80]	6 [78]; 3 [79]; 5 [80]	Three open label studies following failure of oral antibiotics	Sputum purulence	Continuous; 4 months/ 16 weeks	Bronchiectasis patients with purulent sputum that failed to clear following oral amoxicillin	Reduced sputum purulence; reduced neutrophil elastase activity ; reduced sputum volume; improved PEFR.	No issues identified.
Tobramycin [81]	A: 37; P: 37	Phase II study	*P. aeruginosa* bacterial load	28 days treatment (total duration 8 weeks)	*P. aeruginosa*-colonised patients; mean age 66 *versus* 63 years; FEV_1 mean 56 *versus* 53%	Significant reduction in *P. aeruginosa* load (mean difference 4.56 $\log_{10}$ cfu·mL^{-1}, p<0.01); 13/37 cleared *P. aeruginosa* from sputum; no significant change in FEV_1, p=0.41.	Increased dyspnoea, chest pain and wheezing; new resistance to tobramycin in 4/36.
Gentamicin [82]	A: 27; P: 30	Single-blind randomised controlled trial	Bacterial load	12 months	Patients colonised with any pathogens in at least three sputum samples in the preceding 12 months; two exacerbations in the previous year; able to tolerate test dose of gentamicin; FEV_1 >30% predicted; exsmokers of >1 year; not on long-term	Significant difference in bacterial load at 12 months (2.96 $\log_{10}$ cfu·mL^{-1} *versus* 7.67 $\log_{10}$ cfu·mL^{-1}, p<0.0001); reduction in exacerbations (median 0 in the gentamicin group, 1.5 in the saline group, p<0.0001); improved SGRQ and LCQ scores; reduced airway	Bronchospasm in 21.9%, two withdrawals; elevated serum gentamicin levels required dose reduction in one patient; no resistant isolates detected.
Colistin [83]	A: 73; P: 71	Phase III double-blind randomised controlled trial	Time to first exacerbation	6 months (patients withdrawn following exacerbation)			
Aztreonam [84]	AIR-BX1: A: 134; P: 132. AIR-BX2: A: 136; P: 138	2× phase III double-blind randomised controlled trial	QOL-B questionnaire score at week 4	Two 28 day treatment courses with alternating 28 day off treatment	Positive sputum for *P. aeruginosa* or other Gram-negative organisms (excluding *H.influenzae*) FEV_1 >20% predicted; chronic sputum production.	No difference in QOL-B at week 4 (mean difference 0.8 (95% CI −3.1–4.7, p=0.7) in AIR-BX1 and 4.6 (1.1–8.2, p=0.011) in AIR-BX2); no difference in QOL-B in both studies at week 12 (p=0.56 in both studies); no difference in time to first exacerbation.	AIR-BX1 adverse events leading to discontinuation: 22 *versus* 6%; AIR-BX2- adverse events leading to discontinuation: 10 *versus* 5%.
Ciprofloxacin DPI [86]	A: 60; P: 64	Phase II double blind randomised controlled trial	Bacterial load	28 days treatment with follow-up to 84 days	Idopathic or post-infective bronchiectasis; two or more exacerbations in the previous 12 months (one hospitalisation); able to produce sputum; culture positive for target microorganisms.	Mean difference in bacterial load −3.62 $\log_{10}$ cfu·mL^{-1} *versus* −0.27 $\log_{10}$ cfu·mL^{-1}, p<0.001; no significant differences in proportion of patients with exacerbations (36.7 *versus* 39.1%, p=0.6); no significant difference in SGRQ (mean difference −3.56, p=0.059).	10% of patients developed resistance (MIC >4 mg·L^{-1}) in the ciprofloxacin group; no difference in adverse events between groups.
Liposomal ciprofloxacin [87]	A: 20; P: 22	Phase II study double blind randomised controlled trial	Bacterial load after first 28-day treatment cycle with intervening 28-day off periods)	24 weeks (three 28 day treatment cycles)	*P. aeruginosa*-colonised patients; ≥2 exacerbations in previous 12 months.	Reduction in *P. aeruginosa* bacterial load −4.2 *versus* −0.08 $\log_{10}$ cfu·mL^{-1}, p=0.002; reduced number of exacerbations in the active treatment group (OR 0.2 95% CI 0.04–0.89, p=0.027); median time to pulmonary exacerbations reduced in the per protocol population (p=0.046).	No significant difference in minimal inhibitory concentrations to ciprofloxacin at day 28; no increase in adverse events.

PEFR: peak expiratory low rate; A: active; P: placebo; *P. aeruginosa*: *Pseudomonas aeruginosa*; FEV_1: forced expiratory volume in 1 s; cfu: colony forming units; SGRQ: St. Georges Respiratory Questionnaire; LCQ: Leicester Cough Questionnaire; QOL-B: quality of life bronchiectasis questionnaire; DPI: dry powder for inhalation; MIC: minimum inhibitory concentration.

STATE OF THE ART
MANAGEMENT OF BRONCHIECTASIS IN ADULTS

Management of bronchiectasis in adults

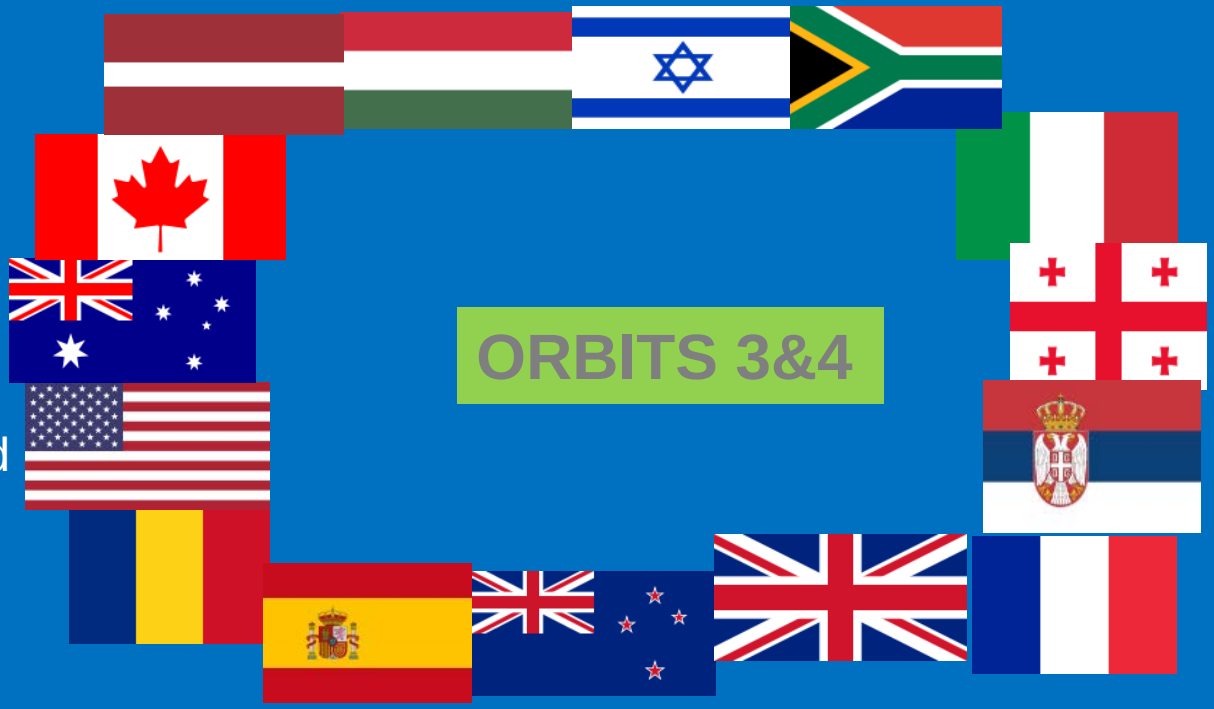
James D. Chalmers[1], Stefano Aliberti[2] and Francesco Blasi[3]

2015

ORBIT-3&4 Phase 3 Status January 2015

- 15 countries with 157 active sites

- Australia
- Canada
- France
- Georgia
- Hungary
- Israel
- Italy
- Latvia
- New Zealand
- Romania
- Serbia
- South Africa
- Spain
- United Kingdom
- USA



ORBIT 4

Studio multicentrico, randomizzato, in doppio cieco, controllato con placebo per valutare la sicurezza e l'efficacia di Pulmaquin® nella gestione delle infezioni polmonari croniche in presenza di *Pseudomonas aeruginosa* nei soggetti con bronchiectasia non da fibrosi cistica, con un'estensione in aperto di 28 giorni (ORBIT-4)

Ciprofloxacina per inalazione (Ciprofloxacin for Inhalation, CFI, 50 mg/ml), 150 mg in 3 ml

Ciprofloxacina libera per inalazione (Free Ciprofloxacin for Inhalation, FCI, 20 mg/ml), 60 mg in 3 ml

Obiettivo primario

L'obiettivo primario di questo studio è di valutare l'efficacia di Pulmaquin rispetto al placebo nella gestione delle infezioni polmonari croniche in presenza di *P. aeruginosa* nei soggetti con bronchiectasia non da Fibrosi Cistica (non FC) valutando il momento della prima esacerbazione polmonare nella Fase in doppio cieco.

Obiettivi secondari

Gli obiettivi secondari del presente studio sono di valutare quanto segue:

- Efficacia di Pulmaquin rispetto al placebo valutata dagli esiti clinici (comprese le esacerbazioni polmonari), dalla funzionalità polmonare, dagli esiti riferiti dal paziente e dal test di esercizio fisico nella Fase in doppio cieco.
- Risposta microbiologica nella Fase in doppio cieco e nell'Estensione in aperto.
- Sicurezza e tollerabilità di Pulmaquin rispetto al placebo nella Fase in doppio cieco.
- Sicurezza e tollerabilità di Pulmaquin nell'Estensione in aperto.

Antibiotici inalatori

Pro

- Eradicazione di Pa (solo??)
- Riduzione riacutizzazioni
- Riduzione dei ricoveri
- Lieve riduzione del declino del FEV1
- Lieve e non significativo miglioramento della QL

Contro

- Tosse
- Broncospasmo
- Emottisi

Brodt AM 2013

Approccio terapeutico integrato

Effetti avversi in bronchiectasie non FC.

Adverse events	Events/patients		Trials n	Risk ratio (95% CI)	p-value	I^2 %
	Antibiotic group	Control group				
Death	7/304 (2.3)	4/286 (1.4)	8	1.28 (0.44–3.71)	0.65	0
Withdrawal due to adverse events	37/304 (12.2)	35/286 (12.2)	8	1.00 (0.67–1.50)	0.99	0
Bronchospasm	26/260 (10.0)	6/266 (2.3)	7	2.96 (1.30–6.73)	0.01	0
Cough	15/97 (15.5)	14/101 (13.9)	2	0.54 (0.03–0.52)	0.69	76.3
Haemoptysis	6/97 (6.2)	5/101 (4.9)	2	1.26 (0.39–4.01)	0.70	0

Data are presented as n/N (%), unless otherwise stated.

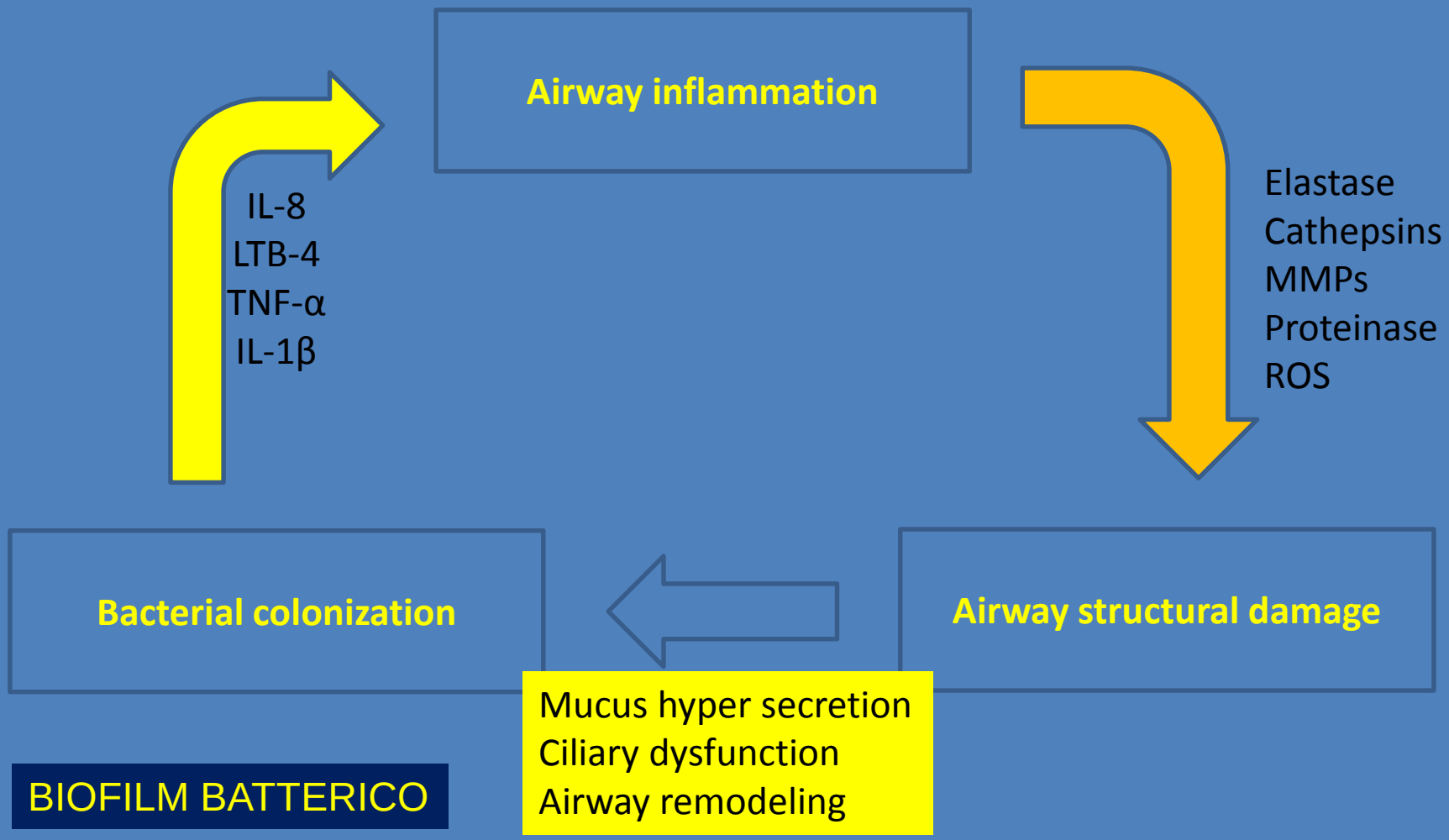
Approccio terapeutico integrato

A. Utilizzo di terapia antibiotiche inalatori a lungo termine.

B. Utilizzo dei Macrolidi.

C. Riabilitazione e fisioterapia

The vicious circle



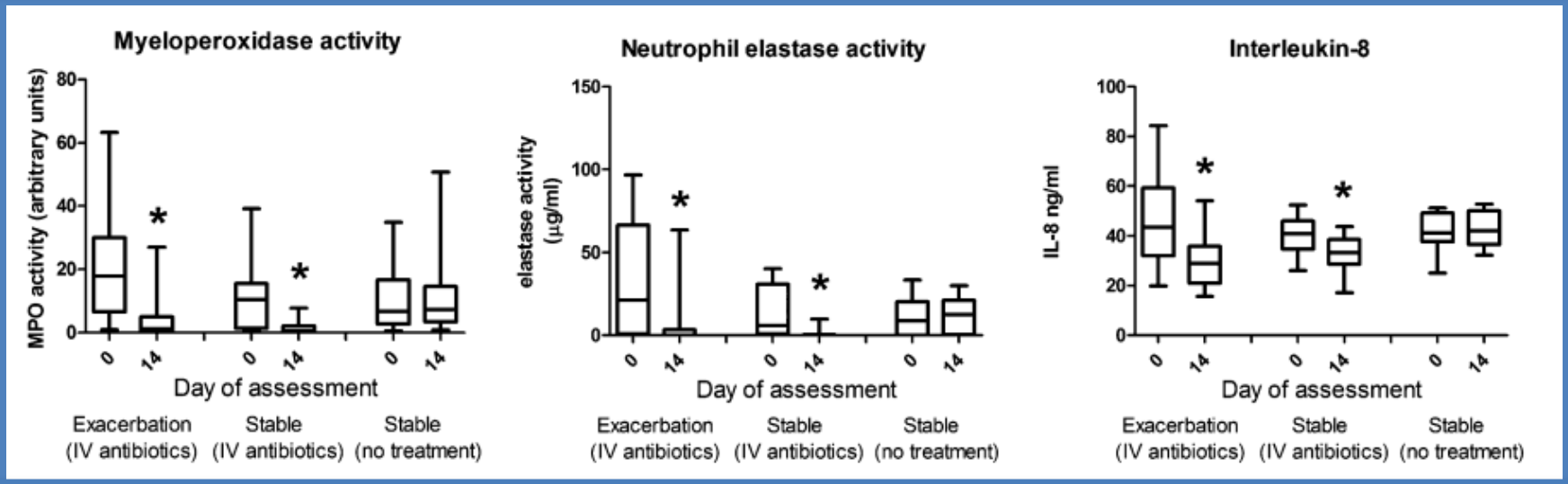
Short- and Long-Term Antibiotic Treatment Reduces Airway and Systemic Inflammation in Non–Cystic Fibrosis Bronchiectasis

James D. Chalmers[1], Maeve P. Smith[2], Brian J. McHugh[1], Cathy Doherty[3], John R. Govan[3], and Adam T. Hill[1,2]

[1]The University of Edinburgh/Medical Research Council Centre for Inflammation Research, The Queen's Medical Research Institute, Edinburgh, United Kingdom; [2]Department of Respiratory Medicine, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; and [3]School of Medicine and Veterinary Medicine, Cystic Fibrosis Group, Centre for Infectious Diseases, University of Edinburgh, Edinburgh, United Kingdom

Conclusions

Chronic colonization with high bacterial loads in non-CF bronchiectasis is associated with airway and systemic inflammation, a greater risk of exacerbations, and worse health-related quality of life. Short- and long-term antibiotic therapy reduces markers of airway and systemic inflammation. This study highlights the importance of monitoring sputum bacteriology when clinically stable and provides the evidence base for future intervention studies to reduce the bacterial burden in the airways.



Riduzione/rimodulazione dei mediatori di infiammazione sistemica

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						
FEV_1 % 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 FEV_1 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¶

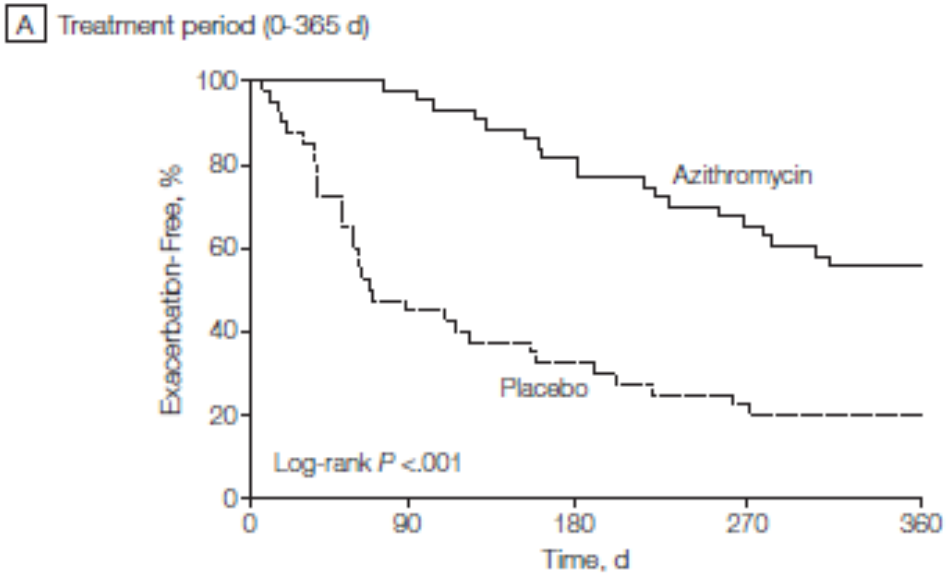
SGRQ: St. George's Respiratory Questionnaire. #: $p<0.05$ compared with placebo. ¶: $p<0.001$ compared with placebo group.

Effect of Azithromycin Maintenance Treatment on Infectious Exacerbations Among Patients With Non–Cystic Fibrosis Bronchiectasis

The BAT Randomized Controlled Trial

JAMA. 2013;309(12):1251-1259

Figure 2. Proportion of Patients Remaining Exacerbation Free



43 pts (52%) on AZI(250 mg daily) for 12 months

40 (48%) on placebo for 12 months

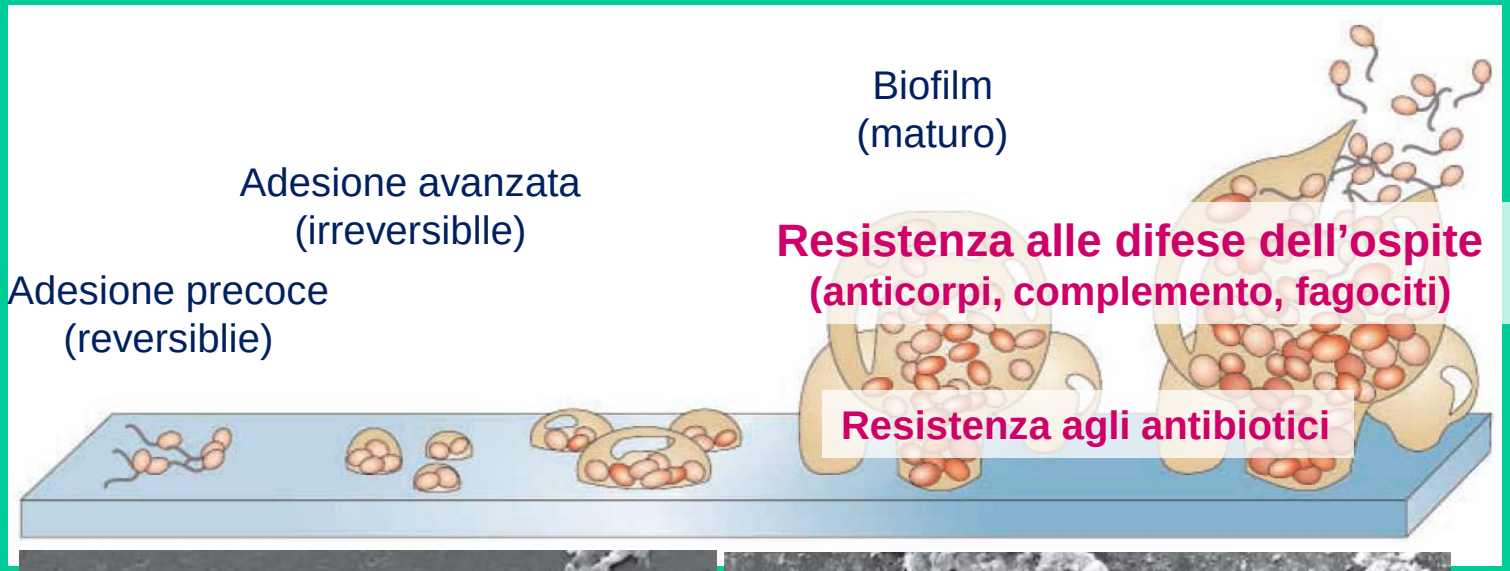
ITT analysis

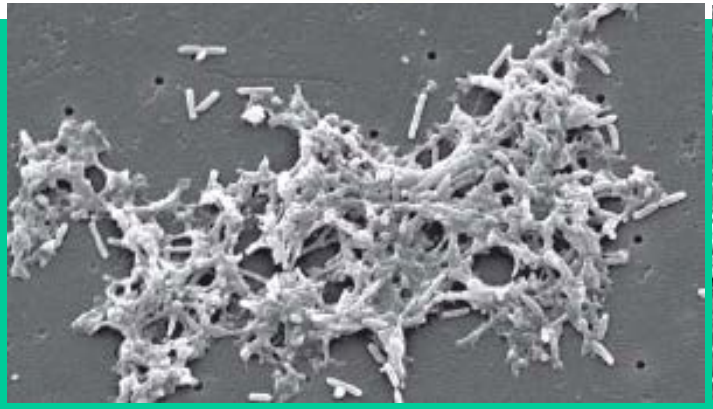
Median n of exacerbations:
- AZI group= 0 (IQR,0-1),
- Placebo= 2 (IQR, 1-3) (*P*.001).

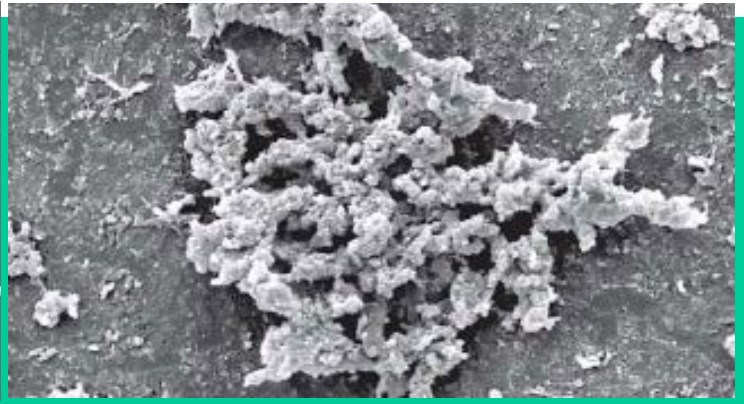
END POINT : EXACERBATION FREE

Macrolidi e biofilm batterici

Dispersione delle cellule
(emboli settici)







Quali antibiotici funzionano nel biofilm?

Beta-lattamici:

–bassa attività battericida

–migliore nei confronti di biofilm giovani

–***Macrolidi***

– ***inibizione del biofilm maturo in associazione con la tobramicina (claritromicina)***

–***Blocco/riduzione della comunicazione tra batteri (quorum sensing) nei biofilm da pseudomonas aeruginosa (azitromicina)***

–**Fluorochinoloni:**

–Elevata attività battericida

–Migliore attività sui biofilm maturi

Sanderson et al. Laryngoscope 2006; 116:1121–1126 modificato

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2010, p. 4409–4415 Vol. 54, No. 10
0066-4804/10/$12.00 doi:10.1128/AAC.00372-10

Efficacy of the Combination of Tobramycin and a Macrolide in an *In Vitro Pseudomonas aeruginosa* Mature Biofilm Model[▽]

Marie Tré-Hardy,[1]* Carole Nagant,[1] Naïma El Manssouri,[1] Francis Vanderbist,[2] Hamidou Traore,[2] Mario Vaneechoutte,[3] and Jean-Paul Dehaye[1]

Laboratoire de Chimie biologique et médicale et de Microbiologie pharmaceutique, Institut de Pharmacie, Université Libre de Bruxelles, CP 205/02, Bd. du Triomphe, 1050 Brussels, Belgium[1]; Laboratoires SMB, 26-28 rue de la Pastorale, 1080 Brussels, Belgium[2]; and Laboratory of Bacteriology Research, University of Ghent, Ghent, Belgium[3]

Received 18 March 2010/Returned for modification 26 June 2010/Accepted 31 July 2010

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2008, p. 3648–3663 Vol. 52, No. 10
0066-4804/08/$08.00+0 doi:10.1128/AAC.01230-07

Effects of Antibiotics on Quorum Sensing in *Pseudomonas aeruginosa*[▽]

Mette E. Skindersoe,[1]† Morten Alhede,[1] Richard Phipps,[1] Liang Yang,[1] Peter O. Jensen,[3] Thomas B. Rasmussen,[2] Thomas Bjarnsholt,[1] Tim Tolker-Nielsen,[1] Niels Høiby,[3] and Michael Givskov[1]*

Biomedical Microbiology, BioSys, Bldg. 227, Technical University of Denmark, Kgs. Lyngby DK-2800,[1] Physiology, Cultures & Enzymes Division, Chr-Hansen A/S, Bøge Allé 10-12, Hørsholm DK-2970,[2] and Department of Clinical Microbiology, Rigshospitalet, University of Copenhagen, Copenhagen DK-2100,[3] Denmark

Received 19 September 2007/Returned for modification 23 October 2007/Accepted 11 June 2008

During infection, *Pseudomonas aeruginosa* employs bacterial communication (quorum sensing [QS]) to coordinate the expression of tissue-damaging factors. QS-controlled gene expression plays a pivotal role in the virulence of *P. aeruginosa*, and QS-deficient mutants cause less severe infections in animal infection models. Treatment of cystic fibrosis (CF) patients chronically infected with *P. aeruginosa* with the macrolide antibiotic azithromycin (AZM) has been demonstrated to improve the clinical outcome. Several studies indicate that AZM may accomplish its beneficial action in CF patients by impeding QS, thereby reducing the pathogenicity of *P. aeruginosa*. This led us to investigate whether QS inhibition is a common feature of antibiotics. We present the results of a screening of 12 antibiotics for their QS-inhibitory activities using a previously described QS inhibitor selector 1 strain. Three of the antibiotics tested, AZM, ceftazidime (CFT), and ciprofloxacin (CPR), were very active in the assay and were further examined for their effects on QS-regulated virulence factor production in *P. aeruginosa*. The effects of the three antibiotics administered at subinhibitory concentrations were investigated by use of DNA microarrays. Consistent results from the virulence factor assays, reverse transcription-PCR, and the DNA microarrays support the finding that AZM, CFT, and CPR decrease the expression of a range of QS-regulated virulence factors. The data suggest that the underlying mechanism may be mediated by changes in membrane permeability, thereby influencing the flux of *N*-3-oxo-dodecanoyl-L-homoserine lactone.

Eur Respir J 2016; In press

TASK FORCE REPORT
IN PRESS | CORRECTED PROOF

Research priorities in bronchiectasis: a consensus statement from the EMBARC Clinical Research Collaboration

Stefano Aliberti[1], Sarah Masefield[2], Eva Polverino[3], Anthony De Soyza[4,5], Michael R. Loebinger[6], Rosario Menendez[7], Felix C. Ringshausen[8], Montserrat Vendrell[9], Pippa Powell[2] and James D. Chalmers[10] on behalf of the EMBARC Study Group[11]

What are the best molecule, dose, regimen and duration for long-term oral antibiotic therapy in patients with bronchiectasis (according to the presence or absence of P. aeruginosa *or other pathogens)?*

Three major studies recently demonstrated the efficacy of long-term macrolides in bronchiectasis in double-blind randomised trials [46–48]. Key questions remain regarding oral antibiotic therapy including: do macrolides have to be continued lifelong or can they be withdrawn (*e.g.* after 12 months)? The most appropriate dose and macrolide agent to minimise side-effects and development of antimicrobial resistance has not been determined. It is not known if alternative oral antibiotic agents such as tetracyclines or β-lactams are equally effective when given long term. As the maximum duration of macrolide treatment was 12 months, it is not known if the effectiveness of macrolides wanes over time, as antibiotic resistance develops or if effectiveness is sustained.

46 Wong C, Jayaram L, Karalus N, *et al.* Azithromycin for prevention of exacerbations in non-cystic fibrosis bronchiectasis (EMBRACE): a randomised, double-blind, placebo-controlled trial. *Lancet* 2012; 380: 660–667.

47 Altenburg J, de Graaff CS, Stienstra Y, *et al.* Effect of azithromycin maintenance treatment on infectious exacerbations among patients with non-cystic fibrosis bronchiectasis: the BAT randomized controlled trial. *JAMA* 2013; 309: 1251–1259.

48 Serisier DJ, Martin ML, McGuckin MA, *et al.* Effect of long-term, low-dose erythromycin on pulmonary exacerbations among patients with non-cystic fibrosis bronchiectasis: the BLESS randomized controlled trial. *JAMA* 2013; 309: 1260–1267.

Macrolidi

Pro

- Riduzione del numero di riacutizzazioni
- Miglioramento del SGRQ e lieve miglioramento del FEV1 (non significativo)
- Ridotta colonizzazione da Pseudomonas A.

Contro

- Epatotossicità
- Effetti gastrointestinali
- Alterazioni cardiovascolari
- Rischio di indurre resistenza in caso di infezione da NTM

IN QUALI PAZIENTI USARE I MACROLIDI ? > Frequenti riacutizzatori ? Riduzione della colonizzazione ? Riduzione della flogosi bronchiale ?

CHEST Original Research
BRONCHIECTASIS

Clinical Efficacy and Safety of Budesonide-Formoterol in Non-Cystic Fibrosis Bronchiectasis

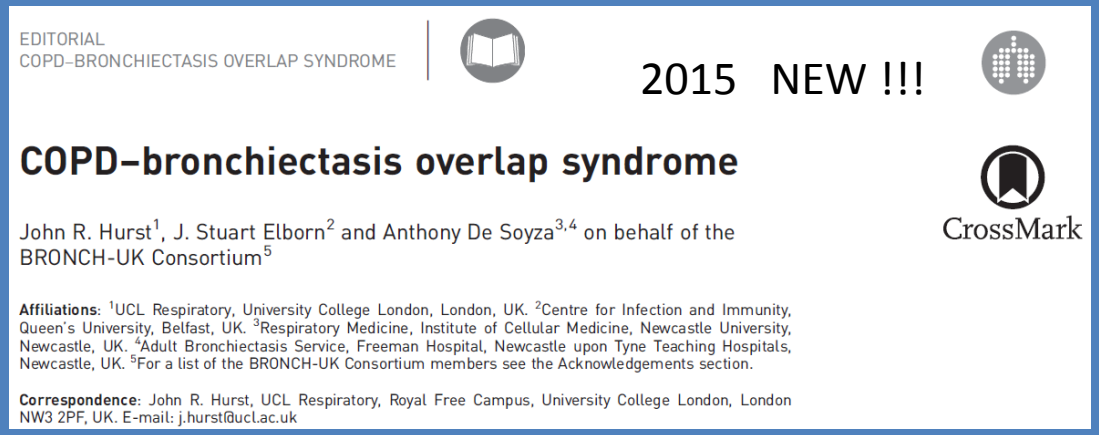
CHEST 2012; 141(2):461–468

Miguel Ángel Martínez-García, MD; Juan J. Soler-Cataluña, MD; Pablo Catalán-Serra, MD; Pilar Román-Sánchez, MD; and Miguel Perpiñá Tordera, MD

Conclusions: **Inhaled medium-dose formoterol-budesonide combined treatment in a single inhaler is more effective and safe compared with high-dose budesonide treatment in patients with non-CF bronchiectasis.**

- **Combined treatment >>>>>>**
- Reduction of dyspnea
- Decrease in cough days
- Decrease wheezing perceived
- Reduction in dose of rescue B2 agonist needed
- Improvement of HRQL

- **LABA and ICS are synergistic in :**
- reduction of mononuclear inflammation
- reduction of neutrophilic inflammation
- Reduction of airflow chronic bronchial obstruction and bronchial hyperresponsiveness



EDITORIAL
COPD–BRONCHIECTASIS OVERLAP SYNDROME

2015 NEW !!!

COPD–bronchiectasis overlap syndrome

John R. Hurst[1], J. Stuart Elborn[2] and Anthony De Soyza[3,4] on behalf of the BRONCH-UK Consortium[5]

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Treatments useful in COPD may not be widely effective in bronchiectasis and viceversa

•**Inhaled corticosteroids** provide perhaps the best example of this: they are widely used in COPD but not recommended for most patients with bronchiectasis.The reasons for this are unclear but reflect, in part, the diverse aetiology underlying bronchiectasis.

•**Inhaled antibiotics**, antipseudomonal agents in appropriate patients , are of benefit and appear in current bronchiectasis guidelines , but are not used routinely in stable COPD. Bronchiectasis guidelines suggest 14 days of antibiotics for treating bronchiectasis exacerbations but courses in COPD should be considerably shorter.Extrapolating this to COPD-associated bronchiectasis could greatly increase the use of antibiotics at a time when antimicrobial resistance is a major concern.

Approccio terapeutico integrato

A. Utilizzo di terapia antibiotiche inalatori a lungo termine.

B. Utilizzo dei Macrolidi.

C. Riabilitazione e fisioterapia

Approccio terapeutico integrato

Non Cystic Fibrosis Bronchiectasis

- Airway Clearance Techniques
- Postural drainage
- Non invasive ventilation
- Pelvic floor muscle training

Chronic Obstructive Pulmonary Disease

- Walking aids
- Breathing techniques
- Managing anxiety and panic
- Muscle Rehab.
- Respiratory muscle rehab.
- Oxigen therapy
- Airway clearance techinque
- Non invasive ventilation (Acute)
- Pelvic floor muscle training

Bott J et al. Guidelines for the physiotherapy management of the adult, medical, spontaneously breathing patient Thorax 2009

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Physiotherapy. 2015 Dec 1.

Short-term effects of three slow expiratory airway clearance techniques in patients with bronchiectasis: a randomised crossover trial.

Herrero-Cortina B[1], Vilaró J[2], Martí D[3], Torres A[4], San Miguel-Pagola M[5], Alcaraz V[3], Polverino E[3]

OBJECTIVE:

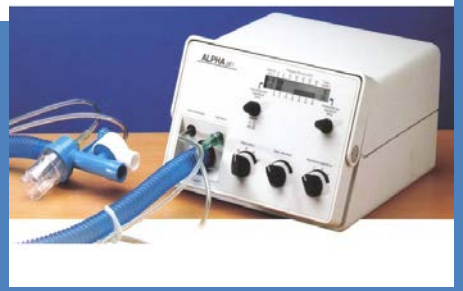
To compare the efficacy of three slow expiratory airway clearance techniques (ACTs).

INTERVENTIONS:

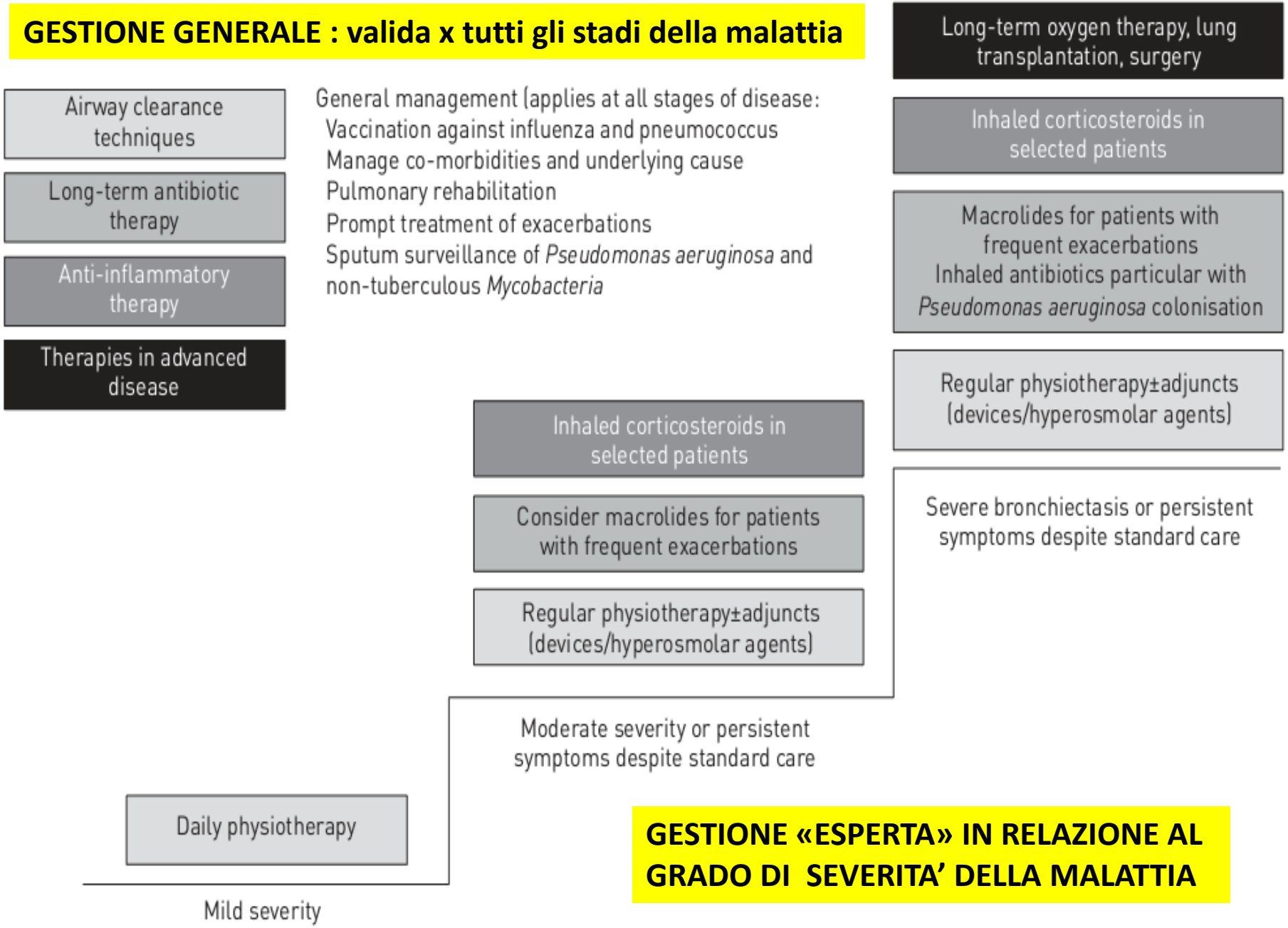
Autogenic drainage (AD), slow expiration with glottis opened in lateral posture (ELTGOL), and temporary positive expiratory pressure (TPEP).

CONCLUSIONS:

Slow expiratory ACTs enhance mucus clearance during treatment sessions, and reduce expectoration for the rest of the day in patients with bronchiectasis.



GESTIONE GENERALE : valida x tutti gli stadi della malattia



GESTIONE «ESPERTA» IN RELAZIONE AL GRADO DI SEVERITA' DELLA MALATTIA

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.

ambulatorio del paziente bronchiectasico ?

TASK FORCE REPORT
Eur Respir J 2016; In press CTED PROOF

Research priorities in bronchiectasis: a consensus statement from the EMBARC Clinical Research Collaboration

Stefano Aliberti[1], Sarah Masefield[2], Eva Polverino[3], Anthony De Soyza[4,5], Michael R. Loebinger[6], Rosario Menendez[7], Felix C. Ringshausen[8], Montserrat Vendrell[9], Pippa Powell[2] and James D. Chalmers[10] on behalf of the EMBARC Study Group[11]

55 key research priorities

Although historically considered a neglected disease, bronchiectasis has become a disease of renewed interest over the past decades in light of an increase in prevalence and an increasing burden on healthcare systems

There are no licensed therapies, and large gaps in knowledge in terms of epidemiology, pathophysiology and therapy…….

To date, treatment of bronchiectasis is mainly extrapolated from cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD), or based on expert opinions as high-quality evidence is still missing

This consensus statement identifies the key research priorities as determined by physicians caring for bronchiectasis patients, by the patients themselves, and by the friends and family helping care for them. This

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