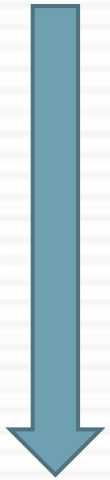
ASTHME ET DDB

Ali Ben Kheder - Fatma Tritar

Journées Francophones d'Allergologie - Nouméa - 9 Oct 2018

Asthme et DDB

Pauvreté de la littérature sur ce sujet !



2 pathologies portant sur les bronches

Publications DDB adultes (2000-2015)

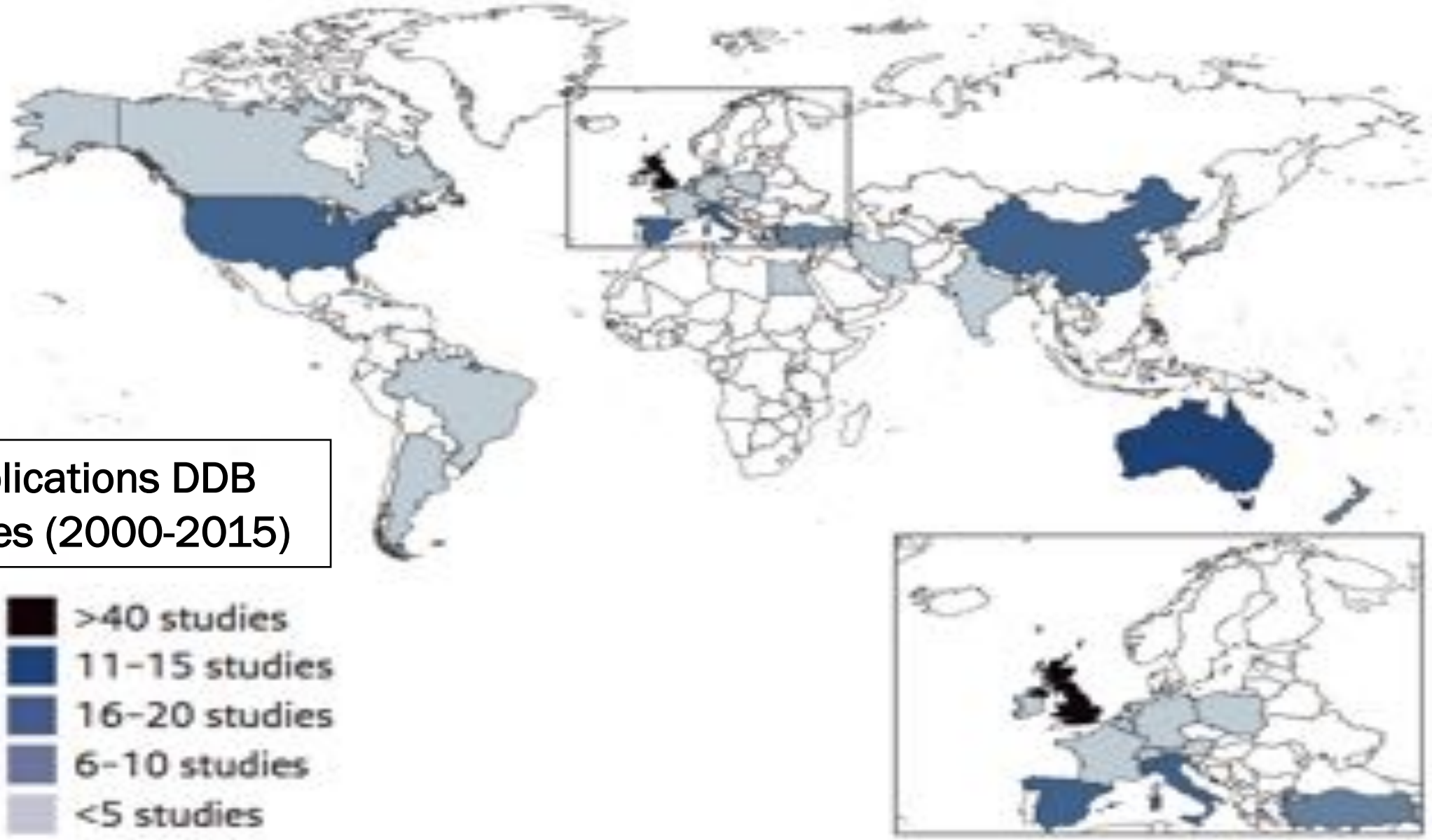
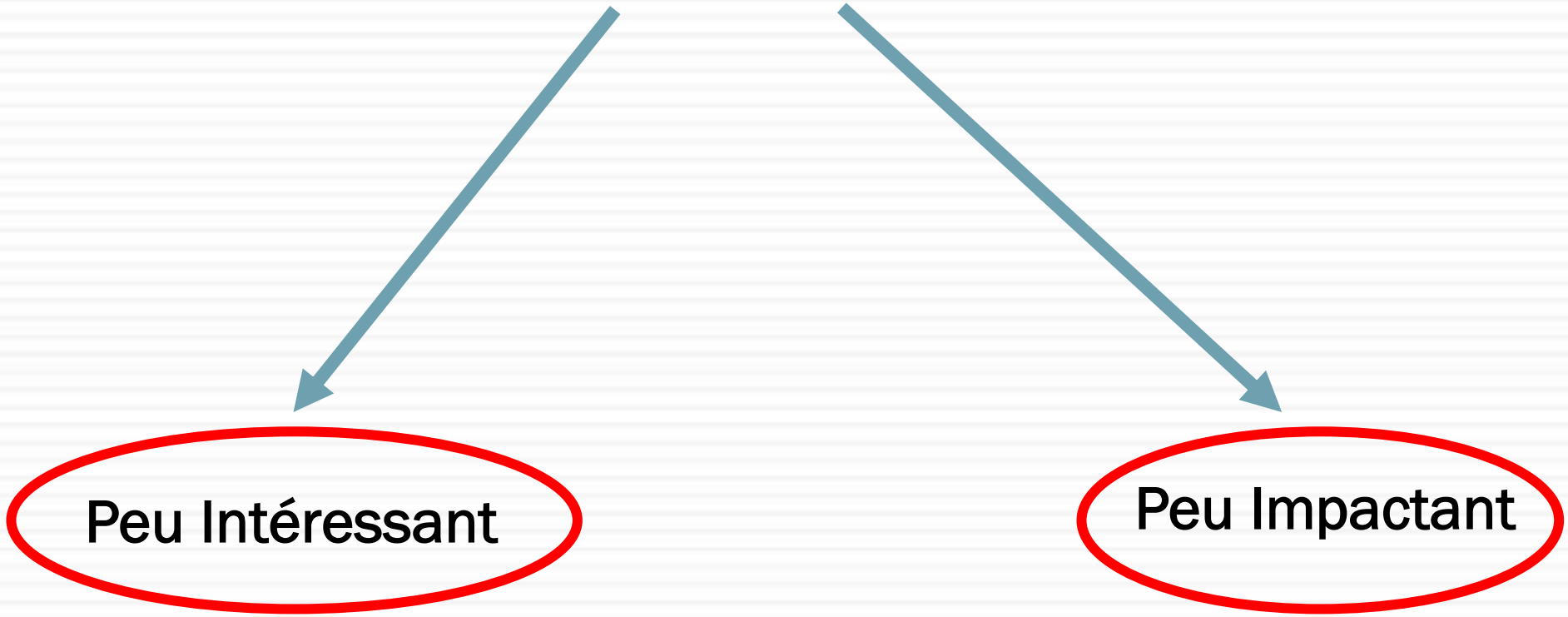


Figure 1 *Published original research studies in 2000–2015 on adult bronchiectasis worldwide (excluding cystic fibrosis).*

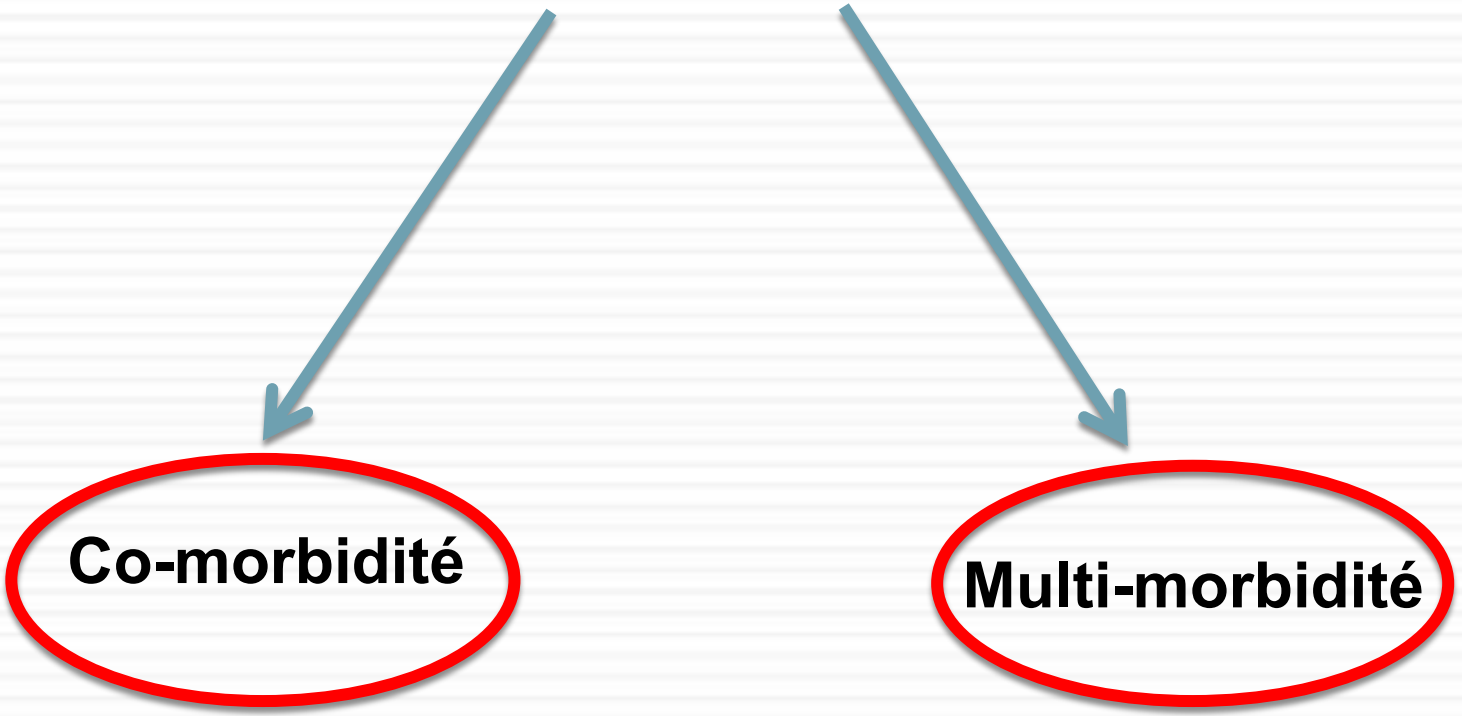
Asthme et DDB

Pauvreté de la littérature sur ce sujet !



Asthme et DDB

Entre Asthme et DDB : Existe-t-il un lien ?



Asthme et DDB

Les deux pathologies ont- elles une similitude clinique ?

Asthme et DDB

DDB sont-elles une évolution inéluctable de l'Asthme ?

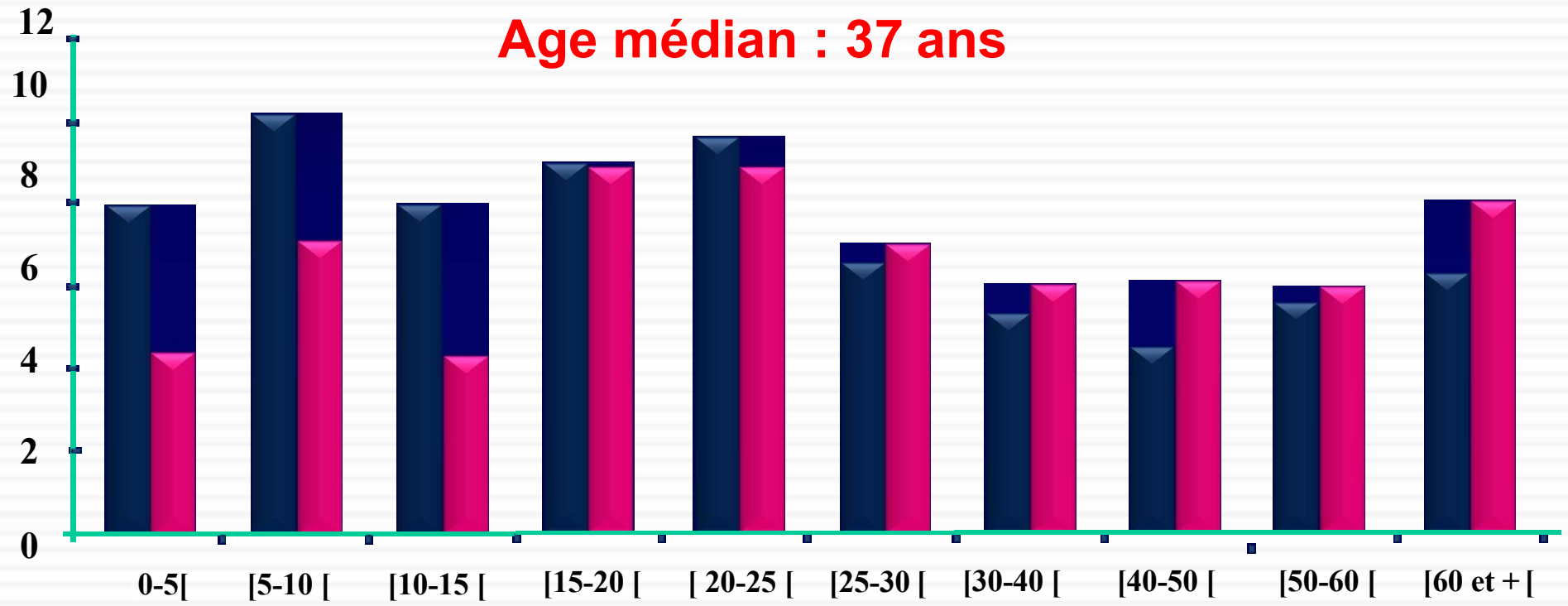
Asthme et DDB

Cette association comporte -t-elle un facteur de risque aggravant l'une ou l'autre pathologie ?

Asthme et DDB

Ces 2 affections ont-elles une évolution chronologique parallèle ?

Prévalence de l'asthme (33 million de personnes dans le monde)

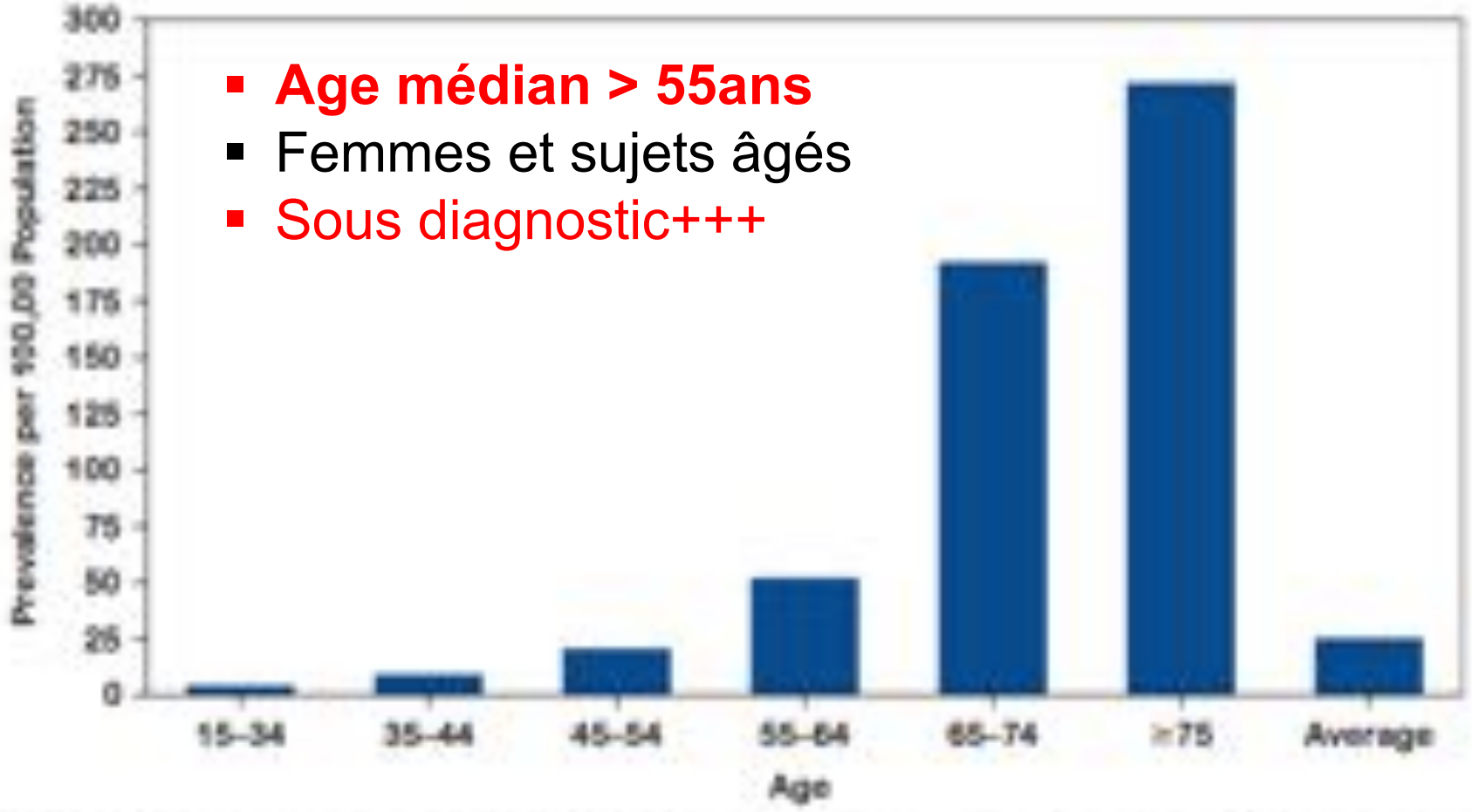


Jeunes : plus de garçons

Adultes : plus de femmes

IRDES Enquête Santé Protection Sociale 2006

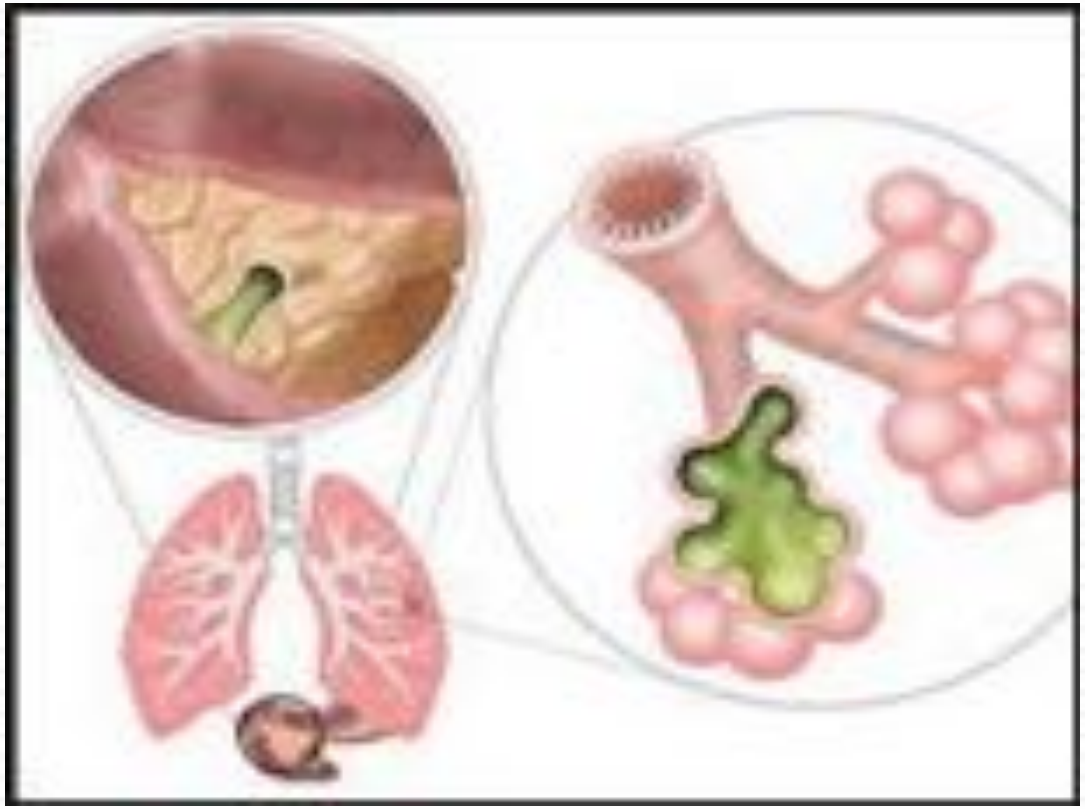
Prévalence des DDB inconnue (42 et 566 cas/100 0000 habitants)



- **Age médian > 55ans**
- Femmes et sujets âgés
- Sous diagnostic+++

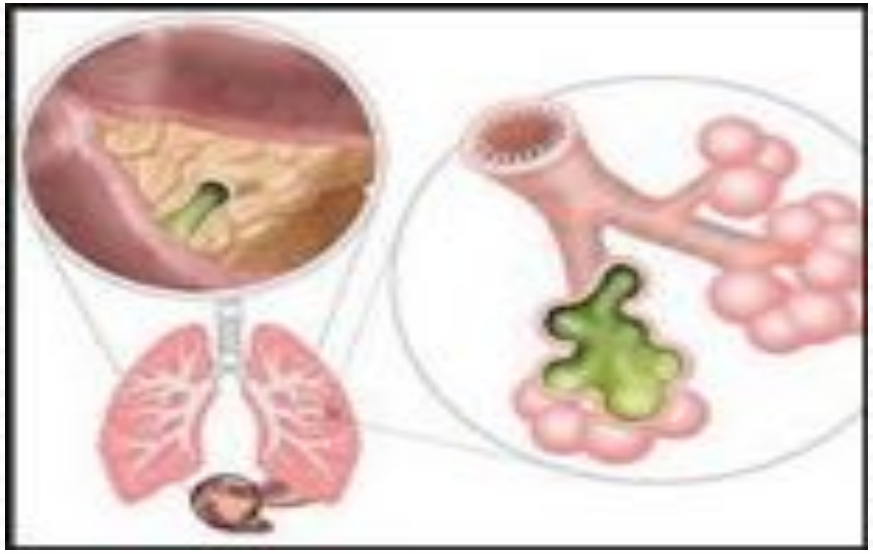
Bronchiectasis increases with age. It is likely to be much more common than reported here because it is not usually detected, reported, or treated (2).

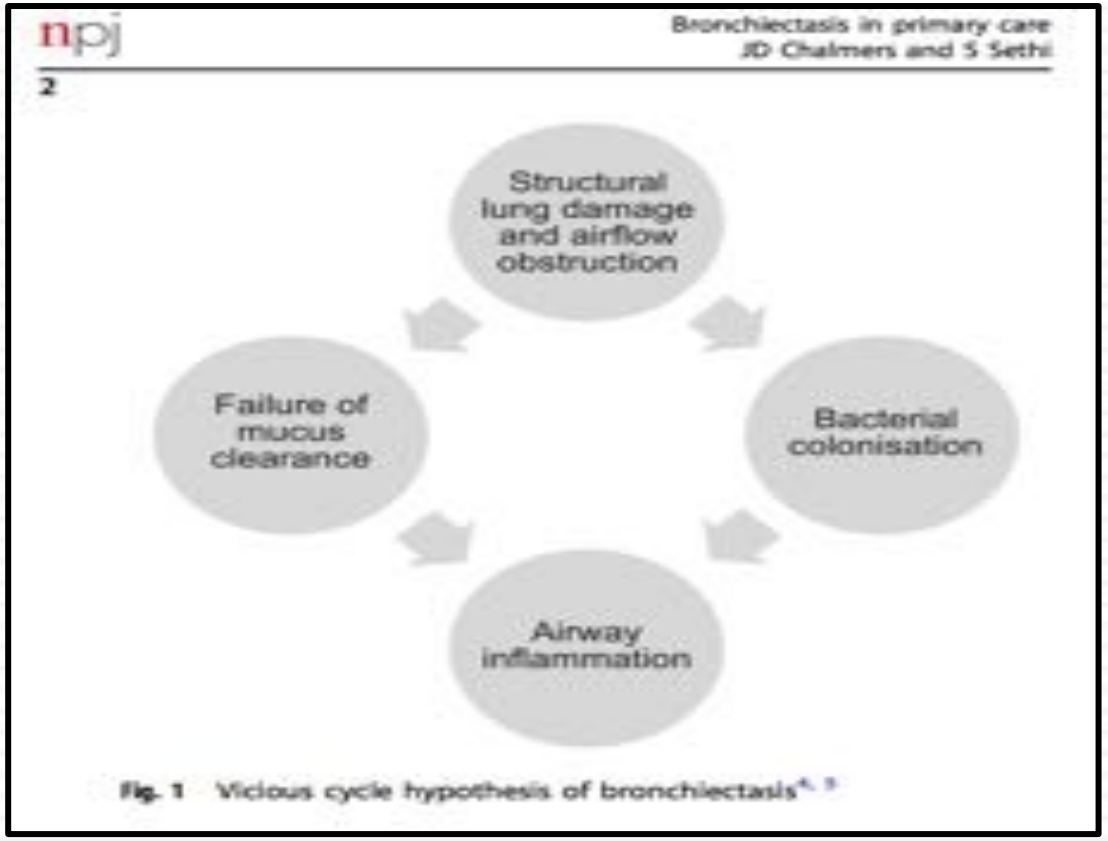
Bronchectasies (DDB)



Définition des bronchectasies (DDB)

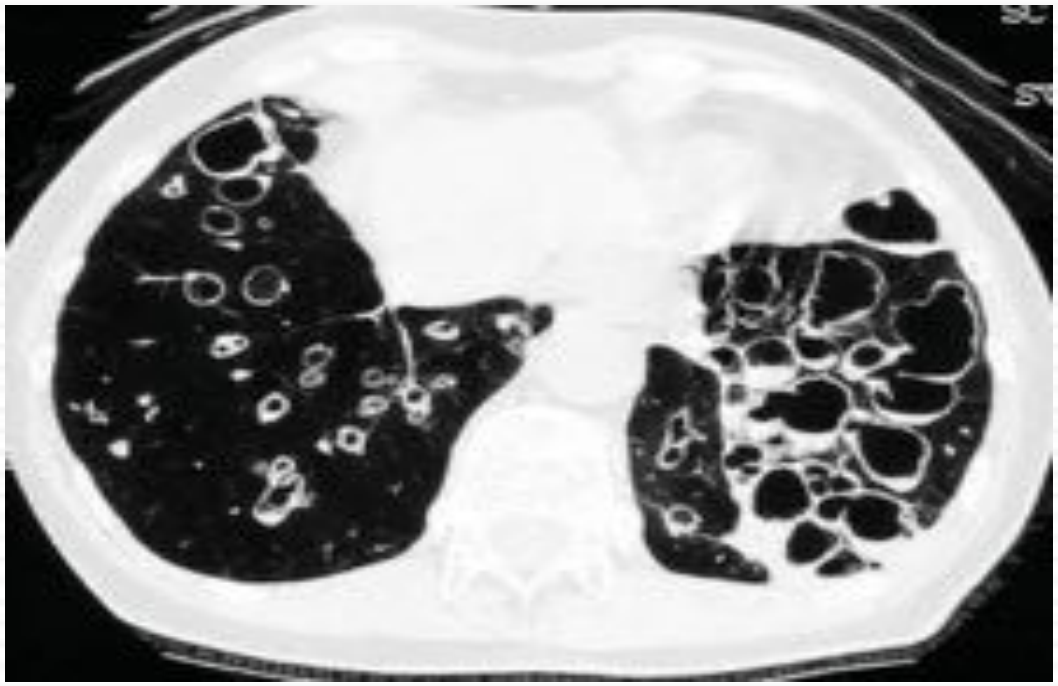
- Augmentation permanente et irréversible du calibre de plusieurs bronches dans
- un contexte de cercle vicieux fait d'infection, d'inflammation, de dommage tissulaire et d'altération de la clairance muco-ciliaire.

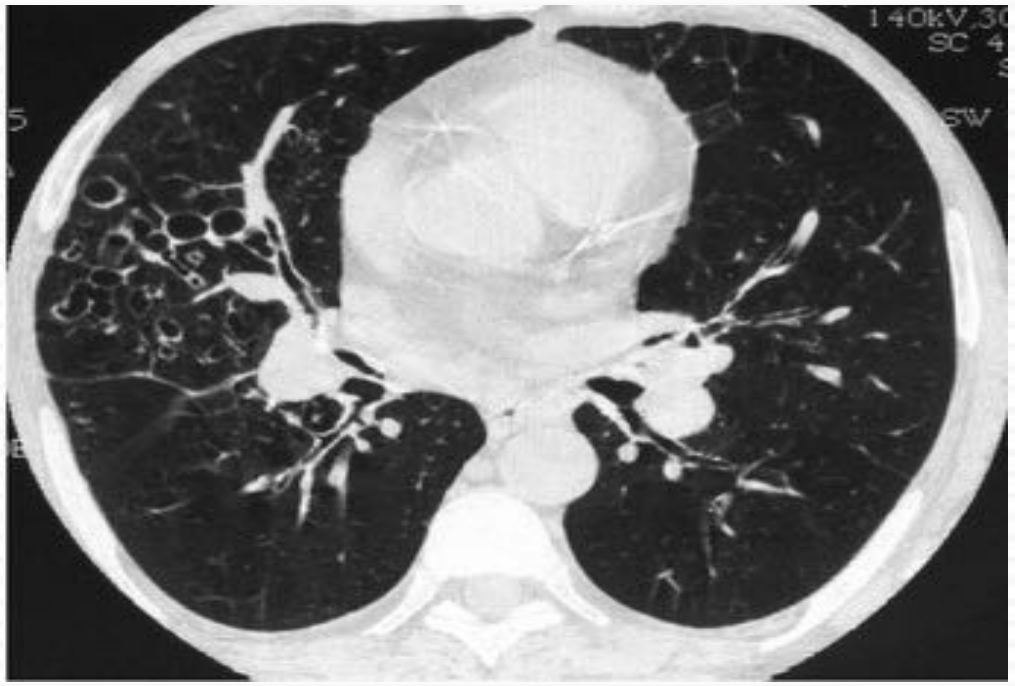




Bronchectasies (DDB) : diagnostic

- TDM-HR : gold standard ++
  - Dilatation de bronches : même calibre
  - Impactions mucoïdes





BRONCHECTASIE : ÉTIOLOGIES

Maladie inflammatoire RCH, Crohn, PR, Sjogren.... **Facteurs extrinsèques** Corps étranger Inhalation RGO Malformation postRx….	**Déficits immunitaires** humoral cellulaire **Maladies génétiques** Mucoviscidose DCP AAT	**Autres** ABPA Mycob non tuberculeuse Asthme….	**Post infectieuse** BK Rougeole, Coqueluche…. **Idiopathique**

BRONCHECTASIE : ÉTIOLOGIES

GUIDELINES FOR THE MANAGEMENT OF BRONCHIECTASIS IN PRIMARY AND SECONDARY CARE 2016

When to suspect the diagnosis

In Children:

- Chronic productive cough
- Asthma that is refractory to treatment
- A positive sputum culture for *S. aureus*, *H. influenzae* or *P. aeruginosa* in the setting of chronic respiratory symptoms
- Unexplained haemoptysis
- Persistent and unexplained physical signs or chest radiographic appearance

In Adults:

- Persistent productive cough - copious daily production of purulent sputum
- Frequent exacerbations
- Haemoptysis
- Persistent lung crackles on auscultation
- Finger clubbing
- Frequent bacterial colonisation of sputum (particularly *P. aeruginosa*)

EMBARC
The European Bronchiectasis Registry

ERS EUROPEAN RESPIRATORY SOCIETY

« European Multicentre Bronchiectasis Audit and Research Collaboration »

The management of bronchiectasis in Europe

Data from the European Bronchiectasis Registry (ERS)

James Chalmers University of Dundee, UK

ERJ Open Research 2016 2: 00081-2015; **DOI:** 10.1183/23120541.00081-2015

Recommandations basées sur la « vraie vie » sur la prise en charge des dilatations des bronches (DDB) de l'adulte

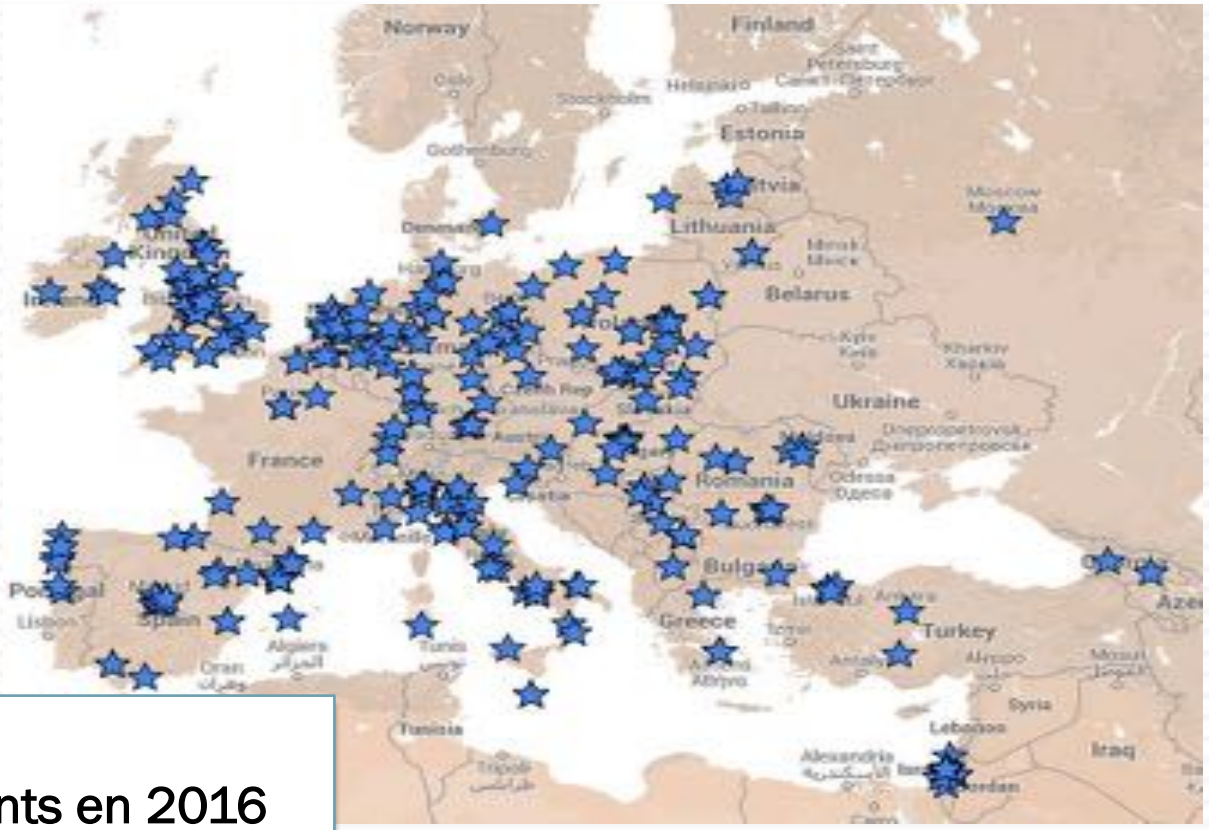
EMBARC

The European Bronchiectasis Registry

ERS EUROPEAN RESPIRATORY SOCIETY

Participation de 40 pays

232 Centres



Objectif

- 1000 patients en 2016
- 10000 patients en 2020

Key translational research questions

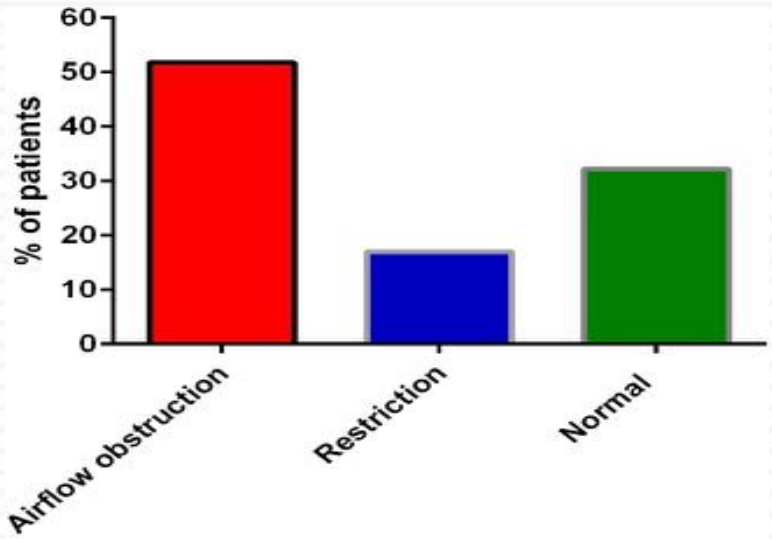
- What causes bronchiectasis?
- What causes bronchiectasis exacerbations?
- Development of new therapies and biomarkers
- How does the microbiome impact patient outcomes in bronchiectasis?
- Why do some patients become infected with *Pseudomonas aeruginosa*?

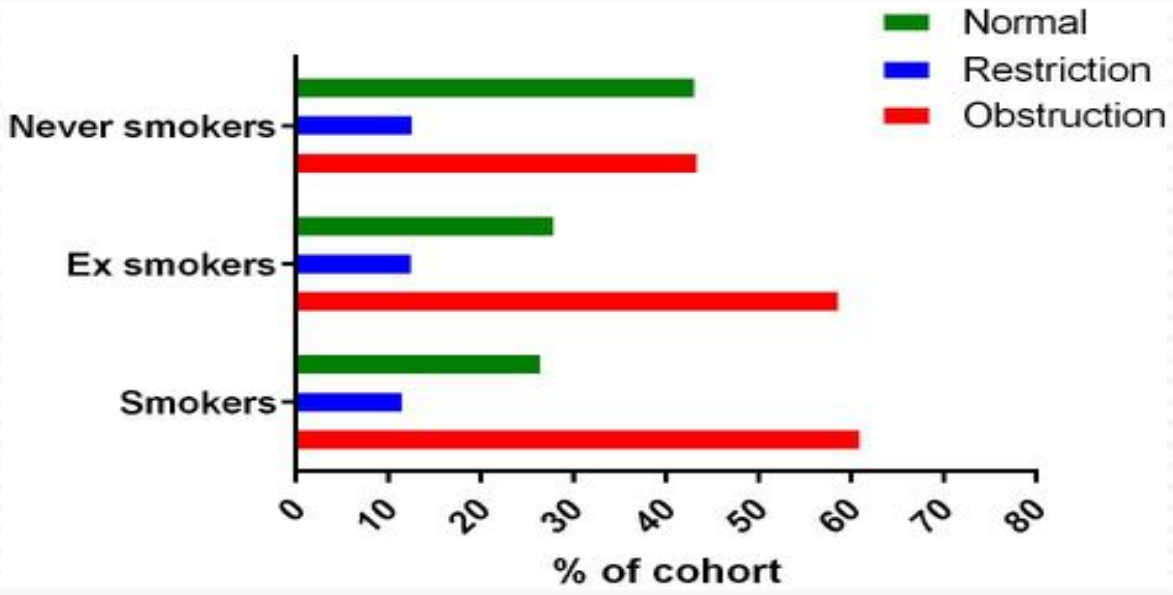
EMBARC
The European Bronchiectasis Registry

ERS EUROPEAN RESPIRATORY SOCIETY

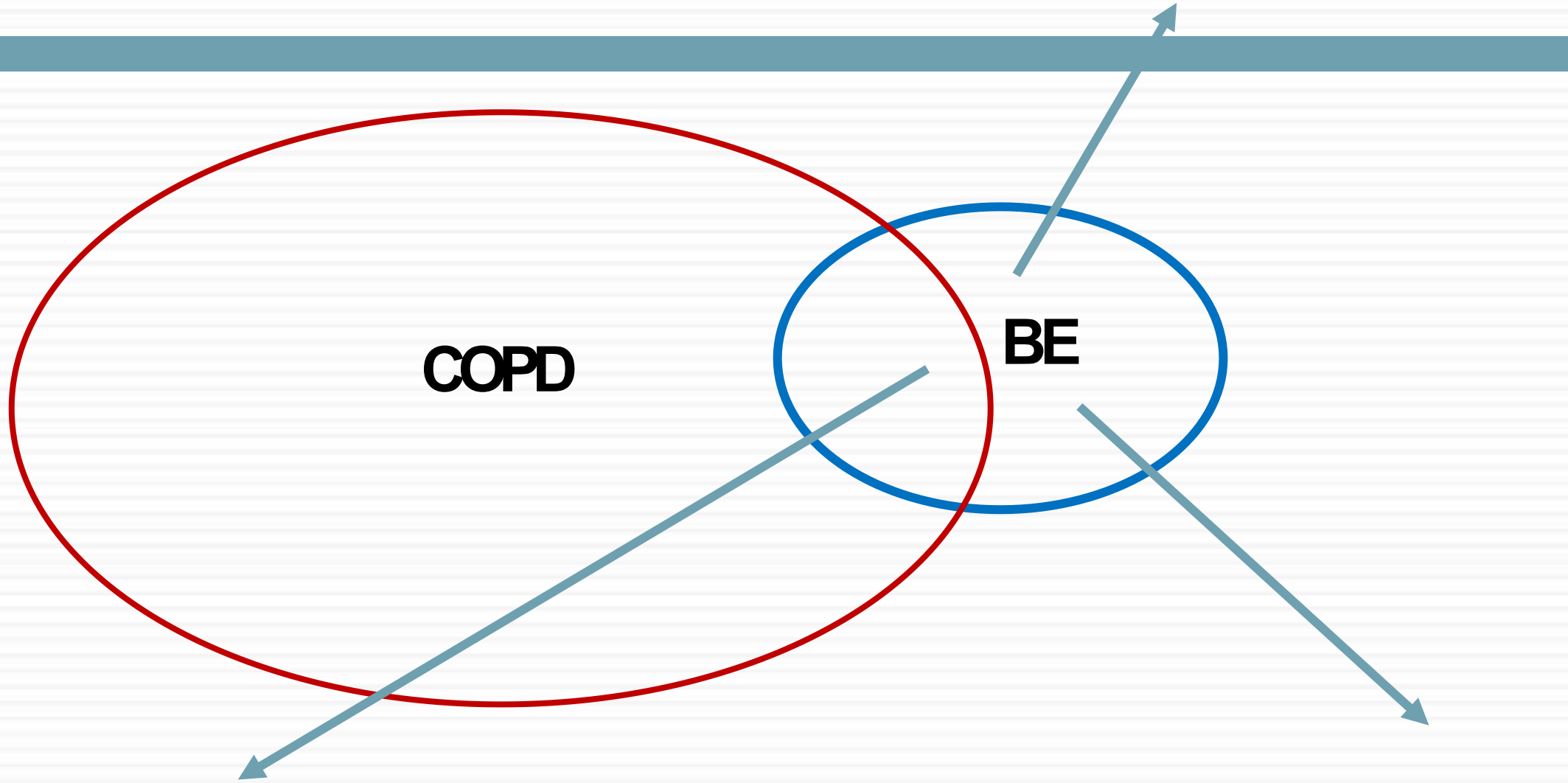
- **58% de femmes**
- Age moyen = 58 ans
- **Ex-fumeurs : 38,3%**
- Non tabagiques : 59,9%
- **Cause idiopathique : 70%**
- **Association avec un Asthme et ou une BPCO !**

8.1% des patients atteints de DDB avaient un TVO Fixe





Two or more conditions co-existing e.g RA/bronchiectasis and COPD



Smokers/ex smokers with bronchiectasis

Non-smokers with airflow obstruction

EDITORIAL
COPD–BRONCHIECTASIS OVERLAP SYNDROME

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.

Eur Respir J 2015; 45: 310–313 | DOI: 10.1183/09031936.00170014

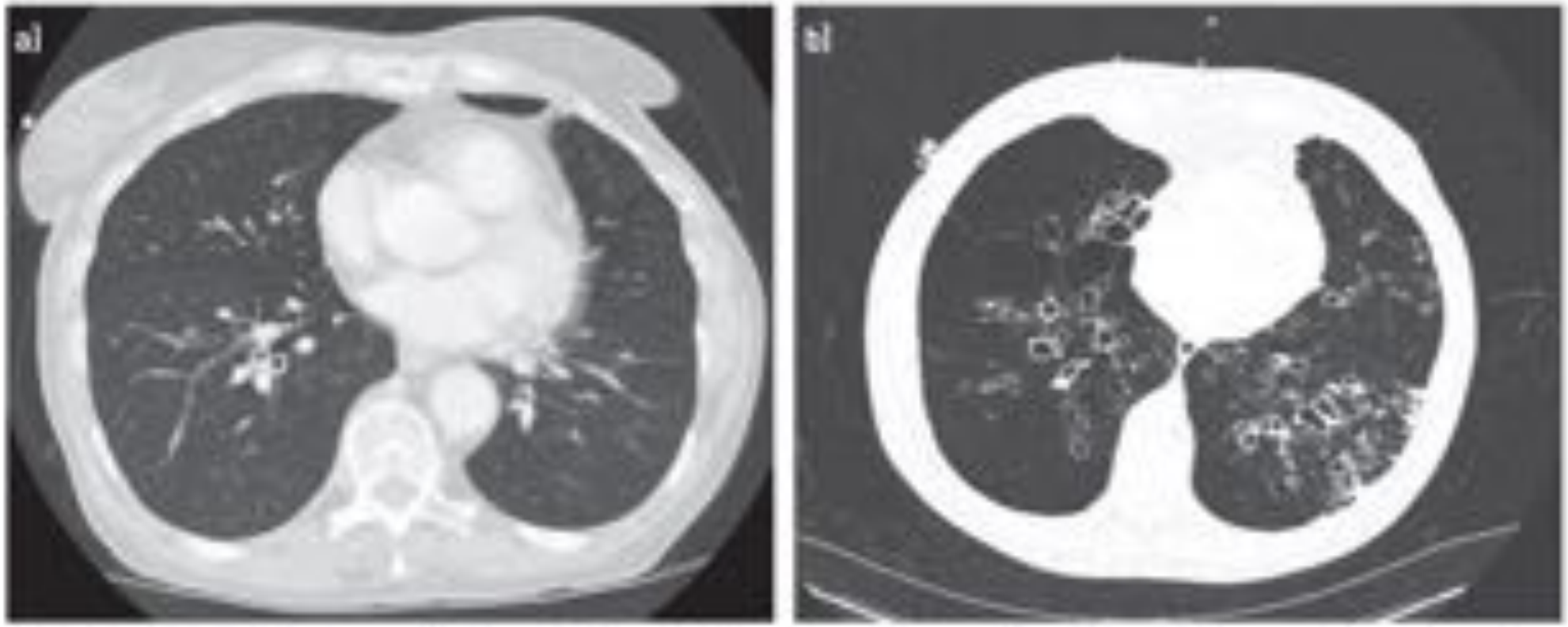


FIGURE 1 a) Typical airway wall changes in chronic obstructive pulmonary diagnosis are diffuse, and may be associated with co-existent emphysema on computed tomography. b) Airway wall changes in primary bronchiectasis may be localised or diffuse, and may be more severe resulting in cystic and/or varicose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

European Respiratory Society guidelines for the management of adult bronchiectasis

Eva Polverino[1], Pieter C. Goeminne[2,3], Melissa J. McDonnell[4,5,6], Stefano Aliberti[7], Sara E. Marshall[8], Michael R. Loebinger[9], Marlene Murris[10], Rafael Cantón[11], Antoni Torres[12], Katerina Dimakou[13], Anthony De Soyza[14,15], Adam T. Hill[16], Charles S. Haworth[17], Montserrat Vendrell[18], Felix C. Ringshausen[19], Dragan Subotic[20], Robert Wilson[9], Jordi Vilaró[21], Bjorn Stallberg[22], Tobias Welte[19], Gernot Rohde[23], Francesco Blasi[7], Stuart Elborn[9,24], Marta Almagro[25], Alan Timothy[25], Thomas Ruddy[25], Thomy Tonia[26], David Rigau[27] and James D. Chalmers[28]

@ERSpublications
The publication of the first ERS guidelines for bronchiectasis http://ow.ly/wQ8O30dU0nE

Cite this article as: Polverino E, Goeminne PC, McDonnell MJ, *et al*. European Respiratory Society guidelines for the management of adult bronchiectasis. *Eur Respir J* 2017; 50: 1700629 [https://doi.org/10.1183/13993003.00629-2017].

The Thoracic Society
of Australia & New Zealand
LEADERS IN LUNG HEALTH

Thoracic Society of Australia and New Zealand

CHRONIC SUPPURATIVE LUNG DISEASE AND BRONCHIECTASIS

IN CHILDREN AND ADULTS IN AUSTRALIA AND NEW ZEALAND

AETIOLOGY

Several causative and associated factors are described for CSLD/bronchiectasis (Table-2). Identifying aetiology (Box-2) and disease severity can influence management, including treatment intensity.[2] Investigations for specific causes of CSLD/bronchiectasis are recommended, even though many patients lack an identifiable aetiology.[2] Bronchoscopy is generally indicated in children who are unable to expectorate and adults with localised disease.[19] Given the implications of bronchiectasis for managing people with COPD[4] a new recommendation is included.

- Les étiologies des DDB sont nombreuses.
- Identifier l'étiologie et évaluer la sévérité peut influencer le traitement des DDB.
- Nouvelle recommandation : recherche de bronchectasies lors de la prise en charge de la BPCO

CO-MORBIDITIES

Patients with CSLD/bronchiectasis have increased rates of co-morbiditiy, including chronic sinusitis, gastro-oesophageal reflux, 'asthma-like' disease and depression. It is unknown whether these co-morbidities increase the frequency and/or severity of exacerbations or worsen lung injury.

Les DDB sont souvent associées à des co-morbidités /sinusites chroniques, RGO, asthme et dépression. On ne sait pas encore si ces co-morbidités augmentent la fréquence et ou la sévérité des exacerbations et ou des lésions parenchymateuses

ORIGINAL ARTICLE
ASTHMA AND BRONCHIECTASIS

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]

Affiliations:
[1]Dept of Respiratory and Critical Care Medicine, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China.
[2]Dept of Medicine, Soochow University, Suzhou, China.
[3]Both authors contributed equally.

Asthma and bronchiectasis exacerbation

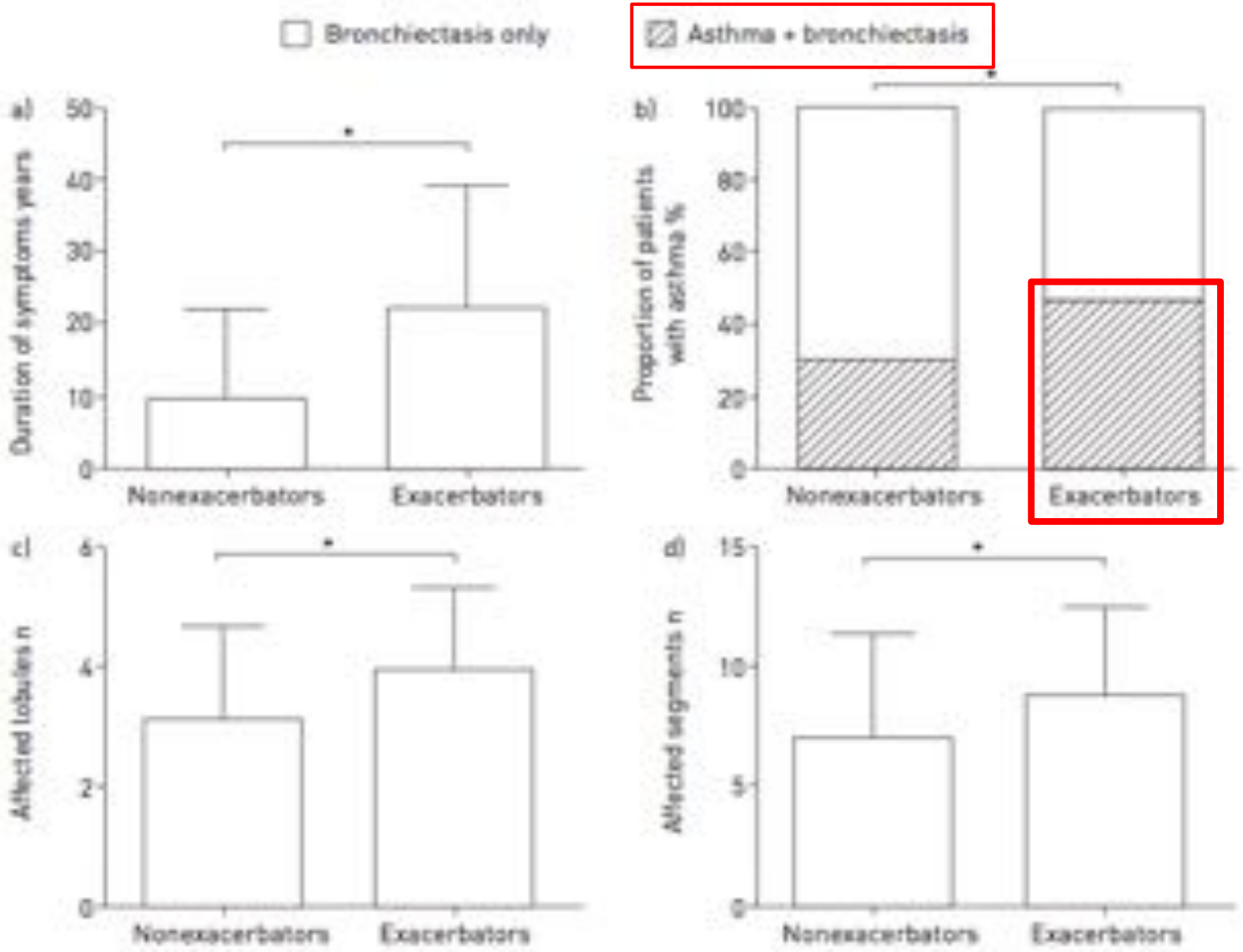
Bei Mao[1,2,3], Jia-Wei Yang[1,2,3], Hai-Wen Lu[1] and Jin-Fu Xu[1,2]

CrossMark

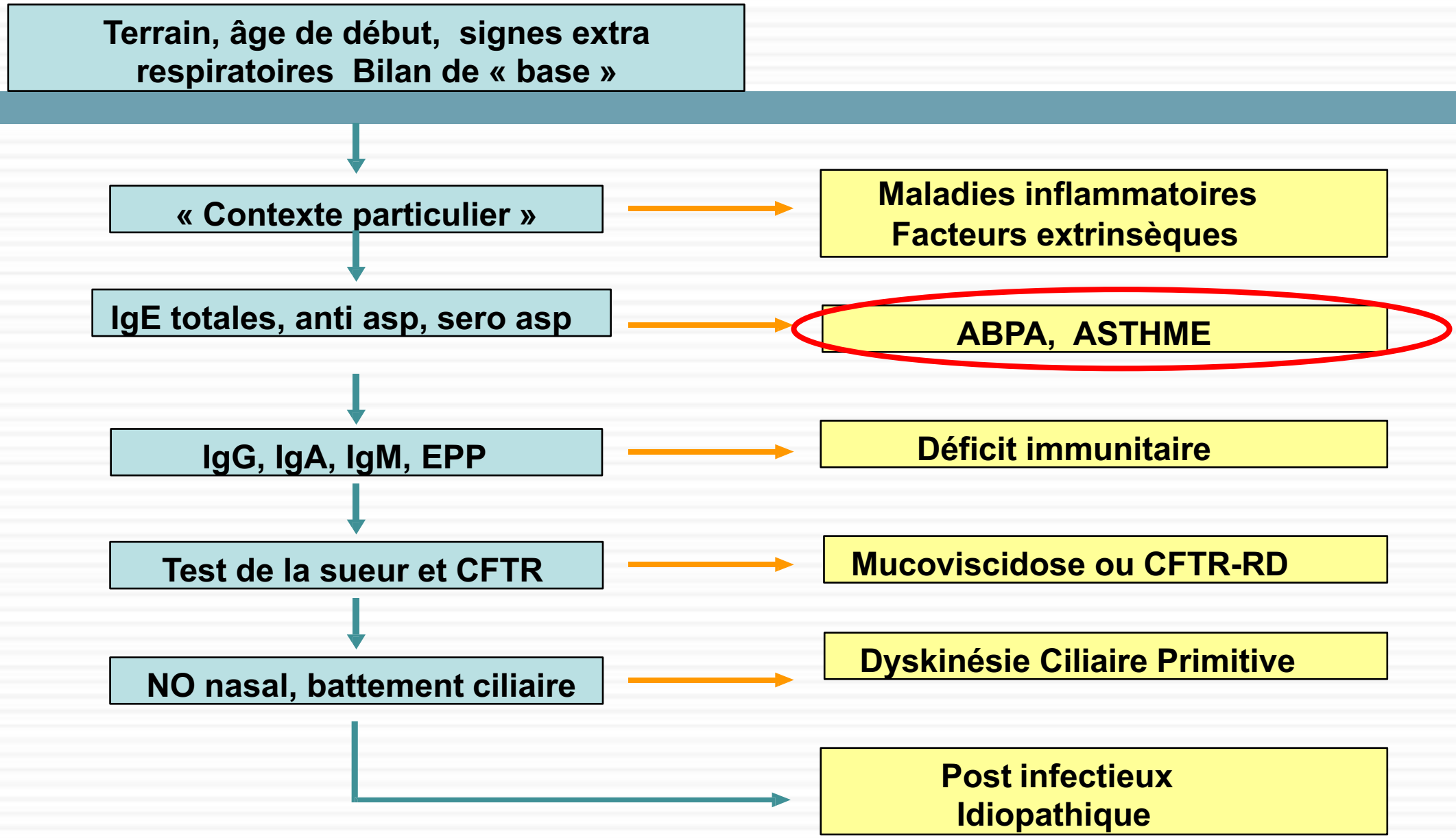
- **Objectif : analyser les effets de l'asthme sur les exacerbations des DDB**
- Janvier 2013 - Décembre 2014 - Hôpital de pneumologie – shanghai

- **249 patients : DDB isolées**
- **214 patients : DDB + Asthme**

- Variables associées (de façon indépendante) avec les exacerbations des DDB :
  - Âge
  - Durée des symptômes
  - VEMS<50%
  - Pseudomonas aeruginosa dan les crachats
  - Extension des lésions pulmonaires > 2 lobes
  - **Présence d'asthme**



L'existence d'un asthme est un facteur de risque d'exacerbation des DDB


Terrain, âge de début, signes extra respiratoires Bilan de « base »
« Contexte particulier »
Maladies inflammatoires
Facteurs extrinsèques
IgE totales, anti asp, sero asp
ABPA, ASTHME
IgG, IgA, IgM, EPP
Déficit immunitaire
Test de la sueur et CFTR
Mucoviscidose ou CFTR-RD
NO nasal, battement ciliaire
Dyskinésie Ciliaire Primitive
Post infectieux
Idiopathique

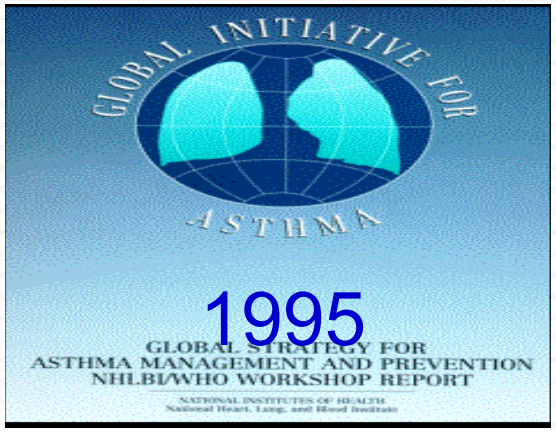
ASTHME

ASTHME

- INFLAMMATION DES VOIES AERIENNES
  - Œdème de la paroi bronchique
  - Infiltration mastocytes et polynucléaire éosinophiles
  - Sécrétion mucus
  - **Remodelage → fibrose**

- HYPERREACTIVITE BRONCHIQUE
  - **Bronchoconstriction**
  - Contraction inappropriée

GINA CONSENSUS



Global Initiative for Asthma (GINA)

What's new in GINA 2018?

GINA Global Strategy for Asthma Management and Prevention

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SYNDROME DE CHEVAUCHEMENT ASTHME - BPCO (ACO)

GINA GLOBAL STRATEGY FOR ASTHMA MANAGEMENT AND PREVENTION

GOLD GLOBAL STRATEGY FOR DIAGNOSIS, MANAGEMENT AND PREVENTION OF COPD

npj | Primary Care Respiratory Medicine

www.nature.com/npjpcrm

REVIEW ARTICLE OPEN

Raising awareness of bronchiectasis in primary care: overview of diagnosis and management strategies in adults

James D. Chalmers[1] and Sanjay Sethi[2]

npj Primary Care Respiratory Medicine (2017)27:18 ; doi:10.1038/s41533-017-0019-9

Bronchiectasis is commonly found in patients with a diagnosis of COPD and asthma. A high awareness of this overlap is needed for primary care physicians to identify patients with bronchiectasis, as symptoms can be easily dismissed as part of the underlying disorder.

Table 1. Possible causes and associated comorbid conditions of non-cystic fibrosis bronchiectasis

Causes	Frequency (%)
Primary cause	
Undetermined (idiopathic bronchiectasis)	30–53
Previous infection–bacterial or viral	33–42
Aspiration/inhalation injury	2–4
Congenital defect of large airway (e.g., Mounier-Kuhn syndrome)	<1
Immune deficiency (hypogammaglobulinaemia)	1–8
Primary ciliary dyskinesia	1–17
Connective tissue disease/rheumatoid arthritis/ Sjögren's syndrome/systemic sclerosis	3–6
Cause or comorbid condition	
COPD[a]	4–69
Asthma[a]	17.5–43.0
Allergic bronchopulmonary aspergillosis (associated with asthma)	1–7
Inflammatory bowel disease	1–2
Non-tuberculosis mycobacterial infection	0.7–34.0

CLINICS 2012;67(11):1335-1343 DOI:10.6061/clinics/2012(11)19

REVIEW

Airway disease: similarities and differences between asthma, COPD and bronchiectasis

Rodrigo Athanazio

Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Heart Institute (InCor), Pulmonary Division, São Paulo/SP, Brazil.

The objective of this review is to highlight the similarities and differences between these diseases in terms of the risk factors, pathophysiology, symptoms, diagnosis and treatment.

Table 2 - Important clinical characteristics in the differentiation of patients with asthma, COPD and bronchiectasis.

Clinical characteristic	Asthma	COPD	Bronchiectasis	Potential overlap
Risk factors	Family history Allergies	Smoking	Repeated infections Immunodeficiency	Asthmatics Smokers have an increased risk of developing COPD
Age	Children and young people	Advanced age	Variable	Asthma and bronchiectasis are misdiagnosed in the elderly and are commonly mistaken for COPD
Symptoms	Wheezing Outbreaks of dyspnea	Chronic dyspnea Productive cough	Productive cough	Patients with bronchiectasis are diagnosed late because they are first treated for COPD due to productive cough symptoms
Spirometry	Reversibility	Absence of reversibility	Absence of reversibility May present restrictive pattern	Asthmatic patients may lose reversibility over time
Computerized tomography	Bronchial thickening	Central lobular emphysema	Bronchial dilations	Bronchial thickening can occur in patients with COPD and bronchiectasis, and bronchiectasis may appear in asthmatics and individuals with COPD

La distinction entre asthme, BPCO et DDB à un stade précoce est très importante :

- Adapter le traitement, améliorer la prise en charge et le pronosctic de l'asthme et des DDB.
- Diagnostic peut être difficile ++ (similitude des symptoms et de l'existence possible de chevauchement)

Hindawi Publishing Corporation
BioMed Research International
Volume 2015, Article ID 109219, 7 pages
http://dx.doi.org/10.1155/2015/109219

Clinical Study

Prevalence of Bronchiectasis in Asthma according to Oral Steroid Requirement: Influence of Immunoglobulin Levels

Manel Luján,[1,2,3] Xavier Gallardo,[4] María José Amengual,[5] Montserrat Bosque,[6] Rosa M. Mirapeix,[7] and Christian Domingo[1,2]

Clinical Study

Prevalence of Bronchiectasis in Asthma according to Oral Steroid Requirement: Influence of Immunoglobulin Levels

- 100 patients
  - N=50 → asthme cortico-dépendant
  - N=50 → asthme non cortico-dépendant
- Dosage des IgA et IgG + spirométrie + TDM-HR
- Prévalence des DDB :
  - 20% : groupe asthme sévère corticodépendant
  - 4% : groupe asthme sévère non corticodépendant
- VEMS : diminué dans le groupe Asthme et DDB
- Taux des IG Aet IgG : pas de difference entre les 2 groupes

Les asthmes sévères cortico-dépendants sont associés à un risque plus grand de développer des DDB

Association asthme et dilatations des bronches : difficultés de prise en charge thérapeutique - 21/12/15

Doi : 10.1016/j.rmr.2015.10.064

H. Smadhi *, I. Khalfallah, H. Kammoun, C. Moussa, H. Benabdelghaffar, D. Greb, H. Hassan, I. Akrout, L. Fekih, M. Megdiche

Service de pneumologie Ibn Nafis, hôpital Abderrahman Mami, Ariana, Tunisie

Association asthme et dilatations des bronches : difficultés de prise en charge thérapeutique - 21/12/15

- **30 patients suivis pour asthme et DDB confirmés**, durant une période de 10ans.
- **90%des patients avaient un asthme persistant sévère**
- Age moyen : 40 ans [24–70 ans] , femmes (66 %), Tabagisme (10 patients).
- TDM-HR : DDB localisés (20 cas) et DDB diffuses (10 cas).
- **Sérologie aspergillaire positive chez 4 malades → Diagnostic d'ABPA**
- 6 patients avaient présenté un AAG.
- Nombre moyen d'hospitalisation pour exacerbation d'asthme = 3 fois par an
- Six patients avaient développé une insuffisance respiratoire chronique

CHEST
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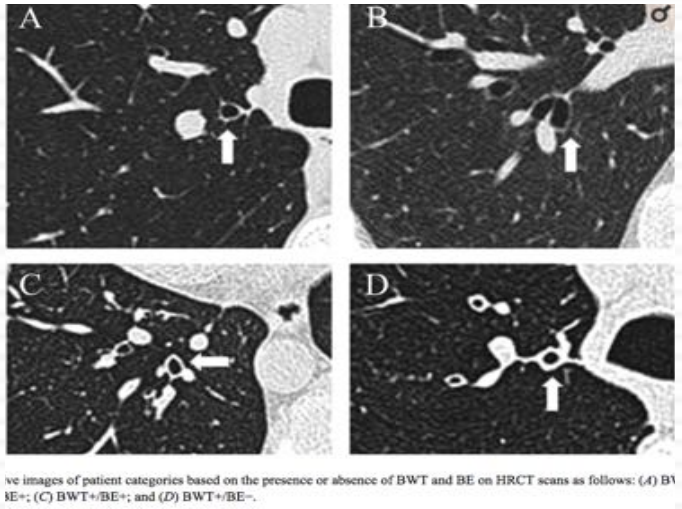
Chest. 2009 Dec; 136(6): 1521–1528.
Published online 2009 Jun 19. doi: 10.1378/chest.09-0174
PMCID: PMC2816977
PMID: 19542254

Qualitative Analysis of High-Resolution CT Scans in Severe Asthma

Sumit Gupta, MBBS, Salman Siddiqui, MBChB, Pranab Haldar, MBChB, J. Vimal Raj, MBBS, James J. Entwisle, MBBS, Andrew J. Wardlaw, PhD, Peter Bradding, DM, Ian D. Pavord, DM, Ruth H. Green, MD, and Christopher E. Brightling, PhD, FCCP



ve images of patient categories based on the presence or absence of BWT and BE on HRCT scans as follows: (*A*) BW
BE+; (*C*) BWT+/BE+; and (*D*) BWT+/BE−.

- Des anomalies TDM-HR étaient présentes chez 80% des sujets ayant un asthme sévère :
  - Bronchectasies (40%)
  - Emphysème (8%)

Devant la fréquences des anomalies scannographiques, la TDM-HR devrait faire partie du bilan de l'asthme sévère

Padilla-Galo et al. Respiratory Research (2018) 19:43
https://doi.org/10.1186/s12931-018-0746-7

Respiratory Research

RESEARCH Open Access

Factors associated with bronchiectasis in patients with uncontrolled asthma; the NOPES score: a study in 398 patients

A. Padilla-Galo[1], C. Olveira[2*], L. Fernández de Rota-García[1], I. Marco-Galve[3], A. J. Plata[4], A. Alvarez[3], F. Rivas-Ruiz[5], A. Carmona-Olveira[6], J. J. Cebrian-Gallardo[1] and M. A. Martinez-García[7]

NOPES score : varie de 0 à 4 points (0 = “pas de risqué” et 4 = “risque élevé” de DDB)

1. FeNO [cut off point 20.5 ppb]
2. Pneumonie
3. Expectorations
4. Sévérité de l’asthme

Factors associated with bronchiectasis in patients with uncontrolled asthma; the NOPES score: a study in 398 patients

Padilla-Galo et *al*. Respiratory Research (2018) 19:433

- 398 patients :
  - 60% asthme sévère
  - 40% asthme modéré
- Prévalence des bronchectasies :
  - 20,6% asthmes modérés
  - 33,6% asthmes sévères

	Points
Severity of asthma	
Moderate	0
Severe	1
Chronic bronchial expectoration	
No	0
Yes	1
Previous pneumonia	
No	0
Yes	1
FeNO	
>20.5 ppb	
≤20.5 ppb	

Score ≥ 3 (70%)

FeNO Fractional exhaled nitric oxide, ppb parts per billion

▪ **Score NOPES** est facile à utiliser et très utile pour suspecter des DDB chez les patients ayant un asthme mal contrôlé (spécificité = 95%)

Bronchiectasis Common in Patients With Severe Uncontrolled Asthma, Greek Study Finds

bronchiectasisnewstoday.com/2017/06/27/bronchiectasis-common-among-patients-with-severe-uncontrolled-asthma-greek-study-finds/

Magdalena Kegel

June 27, 2017

Bronchiectasis is common among patients with severe uncontrolled asthma and might even make their asthma worse, concludes a study by the Sotiria Chest Diseases Hospital in Athens, Greece.

Bronchiectasis Common in Patients With Severe Uncontrolled Asthma, Greek Study Finds

Magdalena Kegel Clinical Respiratory Journal June 27, 2017

- 40 patients (30 femmes- 12 hommes)
- Asthme évoluant depuis 16,5 ans
- Ttt : CI + LABA (+ antileucotriènes : 40%)
- Asthme mal contrôlé ++
- TDM-HR : DDB dans 67,5%
- Surinfection bronchiqe à *P. aeruginosa* et *H. influenzae* : 22,5%

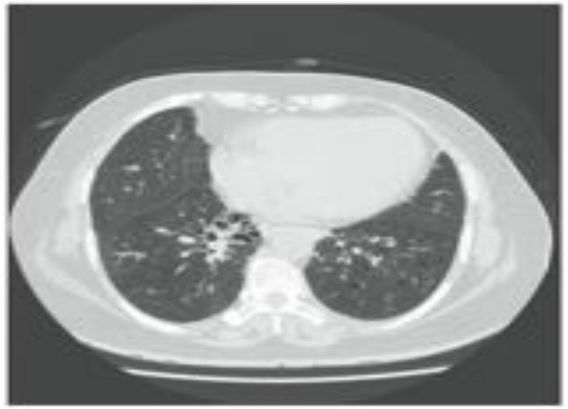


Figure 1. High-resolution computed tomography of an asthma patient with bronchiectasis.

Les DDB sont associées à des asthmes sévères difficiles à controller

Bronchiectasis Common in Patients With Severe Uncontrolled Asthma, Greek Study Finds

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June 27, 2017

The findings raise the issue of whether a subgroup of asthma patients with neutrophil- based inflammation

would respond better to treatment with antibiotics

Bronchiectasis is common among patients with severe uncontrolled asthma and might even make their asthma worse, concludes a study by the Sotiria Chest Diseases Hospital in Athens, Greece.

Aspergillose bronchopulmonaire allergique (ABPA)

- 2% des asthmatiques et **7 à 14% des asthmes cortico-dépendants** présentent une ABPA .
- La sensibilisation à l'aspergillus est estimée à 28 % chez l'asthmatique
- **la sensibilisation à l'aspergillus chez l'asthmatique augmenterait la sévérité de l'asthme**

La tomodensitométrie thoracique permet une analyse plus fine des anomalies radiologiques

Agarwal R *et al*. Chest imaging findings in ABPA

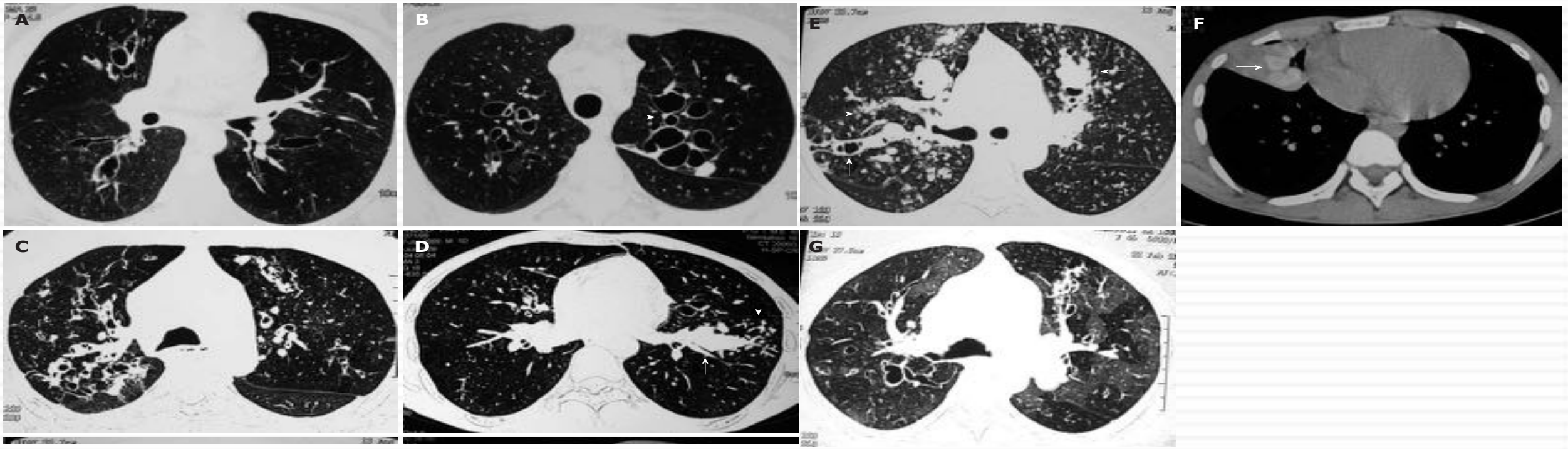

Figure 4 High resolution computed tomography chest scan. A, B: High resolution computed tomography chest scan showing typical central bronchiectasis. The upper panel shows cylindrical bronchiectasis while the lower panel shows cystic bronchiectasis; C: High resolution computed tomography chest scan showing bronchiectasis extending to the periphery. Also seen are mosaic attenuation and centrilobular nodules; D, E: High resolution computed tomography chest scan demonstrating mucus plugging of dilated bronchi (arrows) with evidence of centrilobular nodules in a tree-in-bud fashion (arrowheads); G: High resolution computed tomography chest scan showing central bronchiectasis with extensive areas of mosaic attenuation.

Aspergillose bronchopulmonaire allergique (ABPA)

Les patients porteurs de ABPA peuvent être subdivisés en 2 groupes

① Patients avec bronchectasies (ABPA-DDB)
② Patients sans bronchectasies (ABPA-antigènes)

Le retard au traitement est responsable du développement de DDB ++

Asthme et DDB : En résumé.....

- 2 affections différentes mais peuvent être associées
- Il est important de faire le diagnostic de DDB chez les patients asthmatiques

→ Modification et adaptation du traitement

- L'asthme et les DDB nécessitent une approche thérapeutique différente :
  - Asthme : inflammation causée par les éosinophiles qui répond bien aux corticoides
  - DDB : inflammation à neutrophiles peu sensible aux corticoides

Que Faut-il retenir ?

- ✓ Association asthme et DDB peu étudiée
- ✓ Impact entre les deux pathologies n'est pas clairement défini
- ✓ Pas de réciprocité de prévalence
- ✓ Pas de recommandations thérapeutiques particulières