# Aspergillus : les différentes formes

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# Aspergillus et Mucoviscidose

| Pathogènes conventionnels | Pathogènes émergents |
|---|---|
| Pseudomonas aeruginosa | Stenotrophomonas maltophilia |
| Staphylococcus aureus | Methicillin-resistant staphylococcus aureus (MRSA) |
| Haemophilus influenzae | Achromobacter spp |
| Burkholderia cepacia complex | Streptococcus milleri/anginosus group |
| | Aspergillus fumigatus |
| | Mycobacterium abscessus |

Centre Hospitalier Régional Universitaire de Lille

# Evaluation of the risk of fungal colonisation/infection in patients with cystic fibrosis: an international prospective study comparing the performances of mycological culture media - MycoFong International Project (mfip)

Acronym : « **mfip** »


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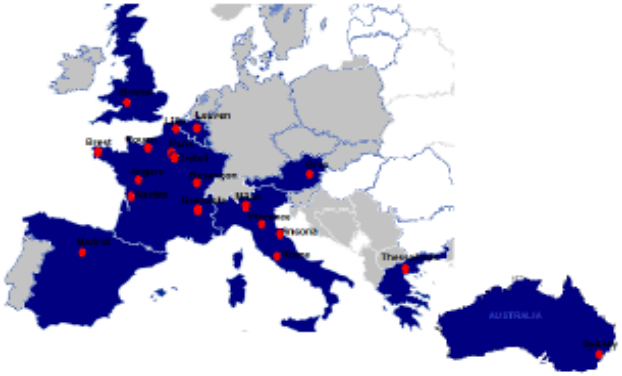

**Fig. 1:** Map of the partipating centers

# Evaluation of the risk of fungal colonization/infection in patients with cystic fibrosis: an international prospective study comparing the performance of media for mycological culturing – MucoFong International Project (MFIP)


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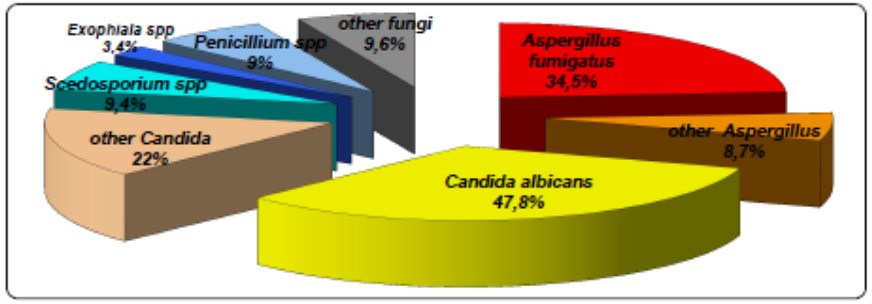


**Fig.4:** Frequency of fungal species isolated (n=680)

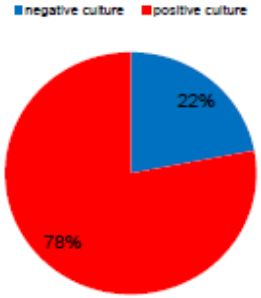


**Fig 2:** Positive or negative culture

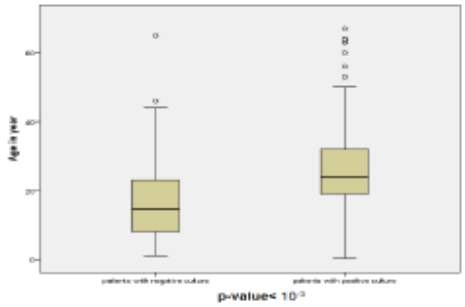


**Fig.3**: Mean age of CF patient (n=452) with and without positive culture

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# Cohort Study of Airway Mycobiome in Adult Cystic Fibrosis Patients: Differences in Community Structure between Fungi and Bacteria Reveal Predominance of Transient Fungal Elements

**Rolf Kramer,[a] Annette Sauer-Heilborn,[b] Tobias Welte,[b,c] Carlos A. Guzman,[a] Wolf-Rainer Abraham,[a] Manfred G. Höfle[a]**

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TABLE 1 Prevalence of major fungal OTUs identified by their ITS sequences in 72 CF sputum samples from 56 patients

| Phylum | Class[a] (no. of incidences) | Major species | % Positive samples |
|---|---|---|---|
| *Ascomycota* | *Saccharomycetes*(101) | *Candida albicans* | 44.4 |
| | | *Candida dubliniensis* | 23.6 |
| | | *Saccharomyces cerevisiae* | 19.4 |
| | | *Candida parapsilosis* | 13.8 |
| | | *Candida glabrata* | 12.5 |
| | | *Candida tropicalis* | 4.1 |
| | | *Cyberlindnera jadinii* | 4.1 |
| | | *Candida sake* | 2.7 |
| | *Dothideomycetes*(24) | *Cladosporium cladosporioides* | 11.1 |
| | | *Cladosporium herbarum* | 9.7 |
| | | *Lewia infectoria* | 2.7 |
| | *Eurotiomycetes* (9) | *Exophiala dermatitidis*[b] | 4.1 |
| | | *Aspergillus fumigatus*[b] | 2.7 |
| | *Sordariomycetes*(5) | *Scedosporium apiospermum*[b] | 4.1 |
| | *Leotiomycetes*(3) | *Blumeria graminis* | 2.7 |
| *Basidiomycota* | *Pucciniomycetes*(12) | *Sporobolomyces roseus* | 11.1 |
| | | *Sporobolomyces ruberrimus* | 5.5 |
| | *Microbotryomycetes*(3) | *Rhodotorula glutinis* | 2.7 |

[a] Table includes only fungal OTUs detected more than once. Fungal OTUs are grouped according to taxonomic classification and ranked according to number of positive samples. The absolute number of detected incidences for each class is given in parentheses (considering all detected OTUs, including unique species). The following classes of *Basidiomycetes* were represented by unique OTUs only and are therefore not considered in this table: *Agaricomycetes*, *Tremellomycetes*, *Exobasidiomycetes*.

[b] Emerging or acknowledged pathogenic species for CF patients.

**Rolf Kramer et al. J. Clin. Microbiol. 2015;53:2900-2907**

Pediatric Pulmonology 50:S31–S38 (2015)

# Cystic Fibrosis Lung Microbiome: Opportunities to Reconsider Management of Airway Infection

Lindsay J. Caverly, MD, Jiangchao Zhao, PhD, and John J. LiPuma, MD

ELSEVIER

Journal of Cystic Fibrosis 12 (2013) 187–193

Journal of Cystic Fibrosis

www.elsevier.com/locate/jcf

Review

# What is the clinical significance of filamentous fungi positive sputum cultures in patients with cystic fibrosis? ☆

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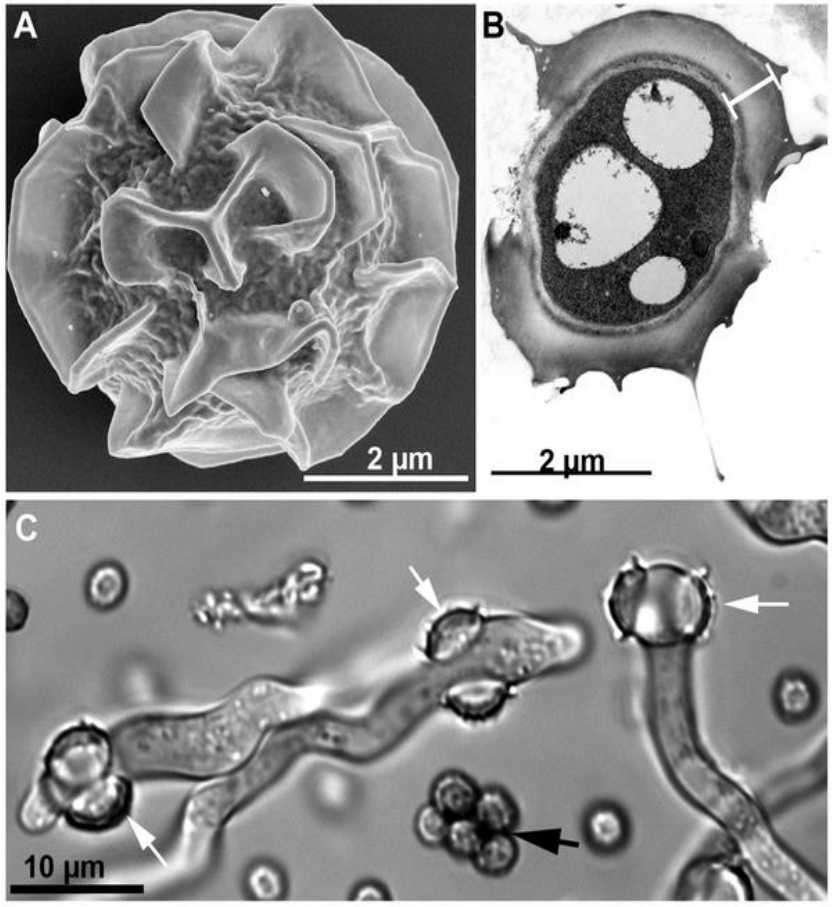
Available online 13 March 2013

| *Aspergillus* spp. colonisation | *Aspergillus* spp. infection |
|---|---|
| • Isolation of *Aspergillus* spp. from 50% or more sputum samples over six months to one year<br>• No deterioration in lung function<br>• No increase in respiratory symptoms like cough | • Isolation of *Aspergillus* spp. from 50% or more sputum samples over six months to one year<br>• Decline in lung function parameters<br>• Respiratory exacerbation with (increased) cough<br>• *Aspergillus* spp. the only organism isolated from repeated sputum samples<br>• No, or incomplete response to a two to four week course of appropriate broad spectrum antibiotics |

## Figure 1. Aspergillus fumigatus ascospores.

**Infection**




**Sensibilisation**

Kwon-Chung KJ, Sugui JA (2013) Aspergillus fumigatus—What Makes the Species a Ubiquitous Human Fungal Pathogen?. PLoS Pathog 9(12): e1003743. doi:10.1371/journal.ppat.1003743
http://journals.plos.org/plospathogens/article?id=info:doi/10.1371/journal.ppat.1003743

**From: The Effect of Chronic Infection With Aspergillus fumigatus on Lung Function and Hospitalization in Patients With Cystic Fibrosis**

Chest. 2010;137(1):171-176. doi:10.1378/chest.09-1103

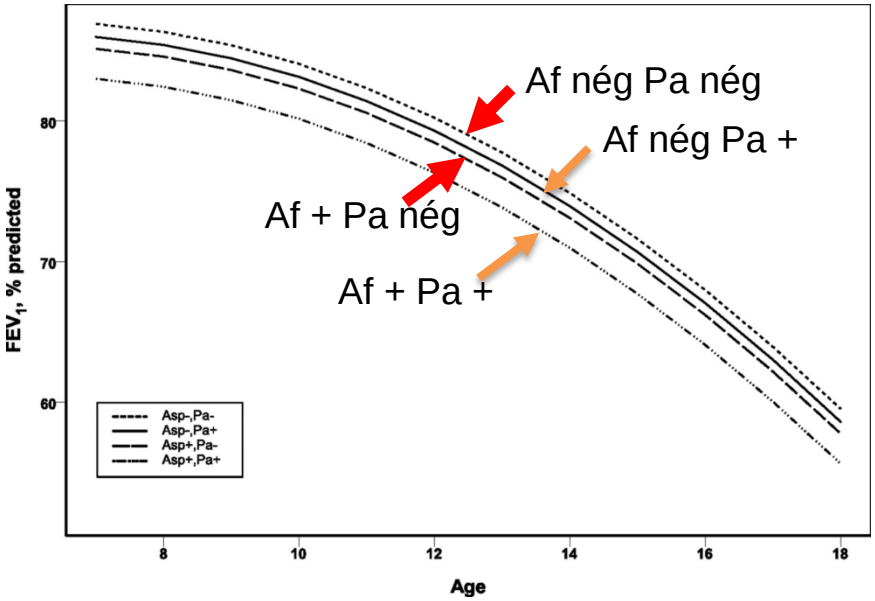



Figure Legend:

**Decline in $FEV_1$% predicted over time for the Aspergillus fumigatus and Pseudomonas aeruginosa interaction (baseline $FEV_1$ of 85% predicted and starting age of 7 years). Asp=Aspergillus fumigatus; Pa=Pseudomonas aeruginosa.**

# Conséquences de la colonisation à Aspergillus et de la sensibilisation à Aspergillus chez adultes avec mucoviscidose

**Table 4—*Lung Function and Antibiotics Days With Colonization***

| Characteristic | All Patients (N = 55) | *Candida* Colonization | | | *Aspergillus* Colonization | | |
|---|---|---|---|---|---|---|---|
| | | Yes (n = 38) | No (n = 17) | *P* Value[a] | Yes (n = 33) | No (n = 22) | *P* Value[a] |
| 2-y IV antibiotics days | 42 (14-96) | 67 (16-108) | 29 (9-80) | .17 | 38 (15-93) | 42 (14-96) | .70 |
| 2-y change $FEV_1$ % predicted | 3.0 (3.0-8.0) | 2.5 (0.0-11.3) | 3.0 (1.5-6.0) | .90 | 3.0 (1.0-10.0) | 2.0 (0.0-6.5) | .41 |
| 2-y change FVC % predicted | 2.0 (2.0-8.0) | 2.0 (2.0-9.0) | 3.0 (0.0-5.5) | .37 | 3.0 (0.0-8.5) | 2.0 (0.0-5.0) | .87 |

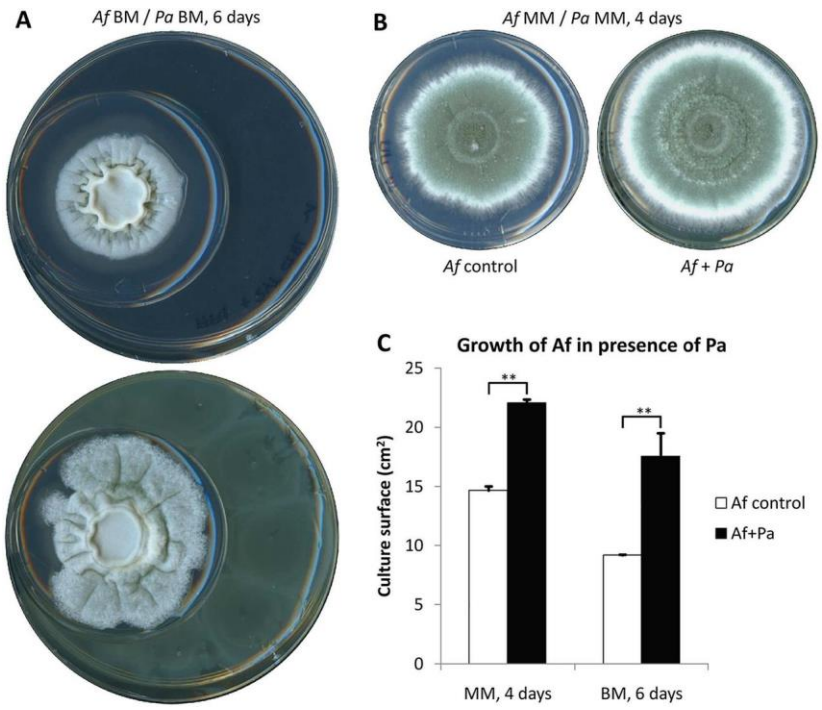
Data are presented as median (interquartile range).
[a]*P* values were calculated using Mann-Whitney *U* tests.

**Table 5—*Lung Function and Antibiotics Days With Sensitization***

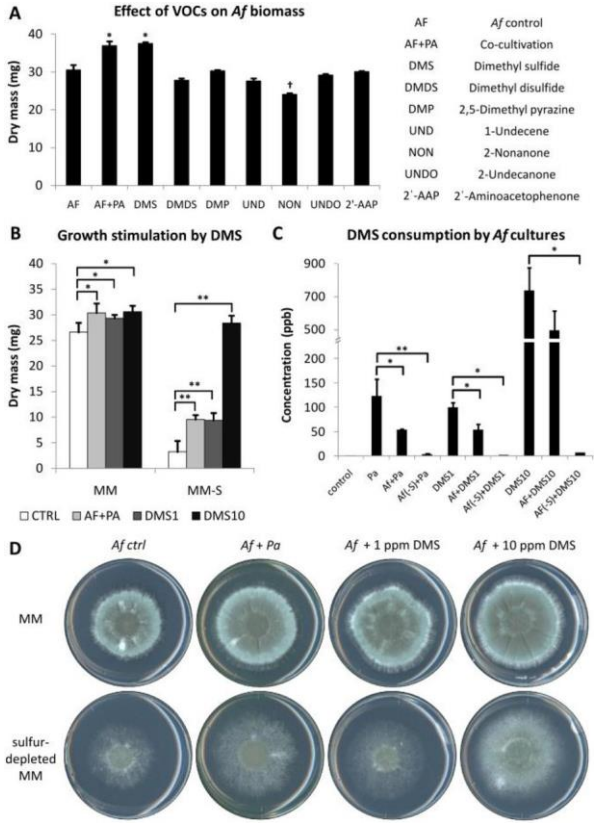
| Characteristic | All Patients (N = 55) | *Candida* Sensitization | | | *Aspergillus* Sensitization | | |
|---|---|---|---|---|---|---|---|
| | | Yes (n = 9) | No (n = 46) | *P* Value[a] | Yes (n = 33) | No (n = 22) | *P* Value[a] |
| Baseline $FEV_1$ % predicted | 58 (37-75) | 50 (34-76) | 61 (40-76) | .408 | 50 (35-72) | 62 (41-79) | .196 |
| Baseline FVC % predicted | 75 (59-89) | 65 (56-80) | 77 (59-88) | .224 | 70 (57-87) | 76 (61-91) | .555 |
| 2-y change $FEV_1$ % predicted | 3.0 (3.0-8.0) | 2.0 (2.0-10.5) | 3.0 (1.0-8.8) | .517 | 4.0 (3.0-12.0) | 2.0 (2.0-6.0) | .027[b] |
| 2-y change FVC % predicted | 2.0 (2.0-8.0) | 2.0 (2.0-6.5) | 3.0 (0.0-8.8) | .366 | 3.5 (1.5-9.0) | 2.0 (2.0-6.5) | .086 |
| 2-y change in $FEV_1$, mL | 100 (50-300) | 100 (0-350) | 100 (50-300) | .638 | 175 (100-462) | 100 (0-175) | .019[b] |
| 2-y change in FVC, mL | 100 (0-350) | 50 (0-320) | 100 (0-300) | .468 | 187 (100-425) | 50 (0-295) | .028[b] |
| 2-y IV antibiotics days | 42 (14-96) | 38 (15-89) | 49 (23-104) | .567 | 63 (28-109) | 34 (14-93) | .034[b] |

Baxter C et al, Chest 2013;143:1351-7

## Growth characteristics of A. fumigatus in a plate-in-plate (PIP) coculture assay.




## Effects of VOCs on the growth of A. fumigatus.

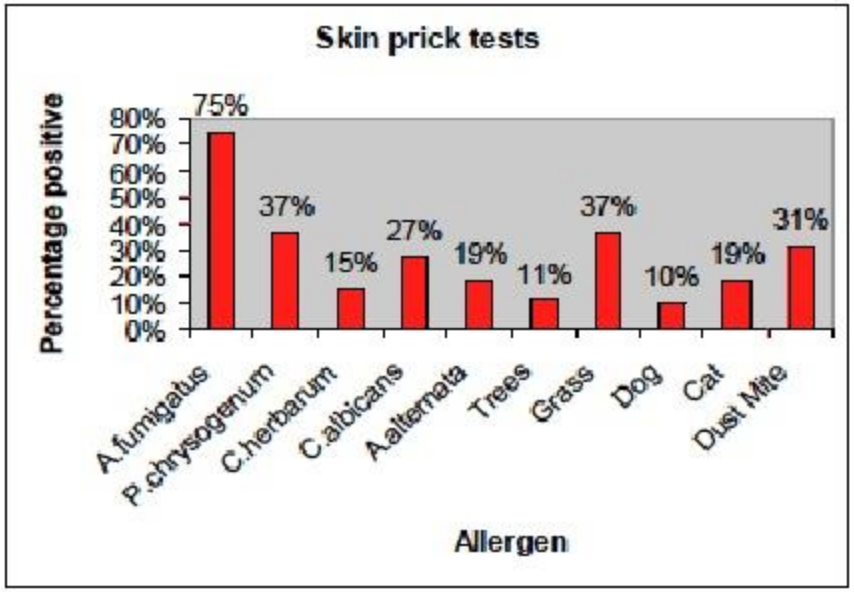



Benoit Briard et al. mBio 2016; doi:10.1128/mBio.00219-16

# Fungal allergy - SPTs

- Atopie à Aspergillus la plus fréquente : 75%
- 52% ont plus d'un test positif vis-à-vis de champignons
- Patients ayant une atopie aux allergènes communs sont plus susceptibles d'être sensibilisés aux allergènes fongiques

Manchester UK CF center 54 adultes




C Baxter, ISHAM 2009

# Quelle est l'étendue du problème ?

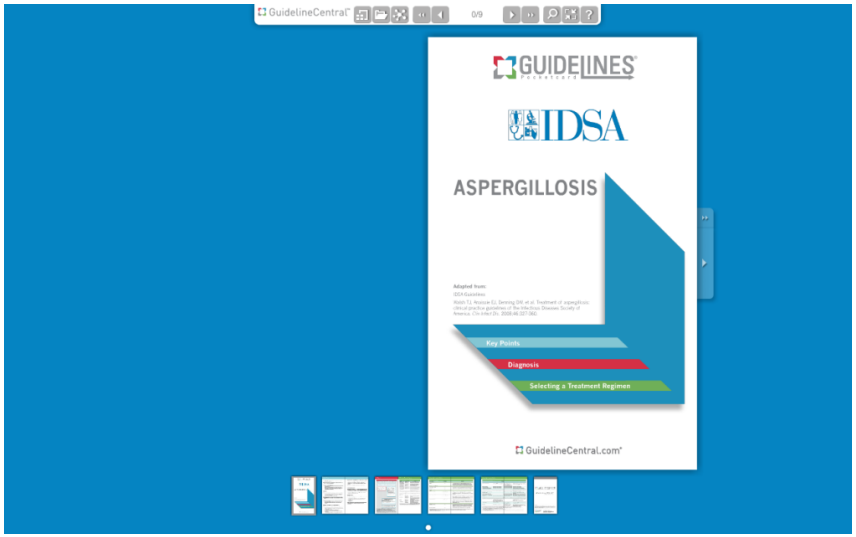
| References | Country (total no. of patients) | *A. fumigatus* positive patients (%) | ABPA positive patients (%) |
|---|---|---|---|
| Nelson *et al.* [6] | USA (46) | 21/37 (56.7) | 5 (10.8) |
| Laufer *et al.* [7] | USA (100) | 5/55 (9) | 10 (10) |
| Bauernfeind *et al.* [8] | Germany (102) | 6 (5.9) | Not specified |
| Simmonds *et al.* [9] | UK (137) | Not specified | 8 (5.8) |
| Marchant *et al.* [10] | UK (160) | Not specified | 11 (6.8) |
| Mroueh and Spock [11] | USA (236) | 60 (25.4) | 15 (6.4) |
| Becker *et al.* [12] | USA (49) | 8 (16) | 1 (1.9) |
| Milla *et al.* [13] | USA (212) | 45 (21.2) | Not specified |
| Hutcheson *et al.* [14] | USA (118) | Not specified | 6 (5.1) |
| Cimon *et al.* [15] | France (210) | 45 (21.4) | 2 (0.95) |
| Cimon *et al.* [16] | France (128) | 59 (46.1) | 5 (3.9) |
| Skov *et al.* [17] | Denmark (238) | 61 (25.6) | 26 (10.9) |
| Bakare *et al.* [18] | Germany (94) | 43 (45.7) | Not specified |
| Taccetti *et al.* [19] | Italy (3089) | Not specified | 191 (6.18) |
| Skov *et al.* [20] | Australia (270) | 22 in 1998 (7.4)<br>52 in 2002 (18.8) | 13 (4.7) |
| Valenza *et al.* [21] | Germany (60) | 35 (58.3) | Not specified |

| | Prevalence rate (%) | |
|---|---|---|
| Fungal species | Transversal study [15] (210 patients) | Longitudinal study [41] (128 patients) |
| *Aspergillus fumigatus* | 21.4 | 46.1 |
| *Scedosporium apiospermum* | 3.3 | 8.6 |
| *Aspergillus terreus* | 1.9 | 6.2 |

Pihet M et al, Med Myc 2009;47:387

# Aspergilloses : recommandations

UPDATE IN PROGRESS*




- Aspergillus
- Share this Guideline

- Published: Clinical Infectious Diseases ; 2008 ; 46 : 327 -360
- "Treatment of Aspergillosis"

- Aspergillus species have emerged as an important cause of life-threatening infections in immunocompromised patients. This expanding population is composed of patients with prolonged neutropenia, advanced HIV infection, and inherited immunodeficiency and patients who have undergone allogeneic hematopoietic stem cell transplantation (HSCT) and/or lung transplantation. This document constitutes the guidelines of the Infectious Diseases Society of America for treatment of aspergillosis and replaces the practice guidelines for Aspergillus published in 2000. Link to full text guideline

- *Projected Publication, Spring 2016
- - See more at: http://www.idsociety.org/Organism/#sthash.mPlQIQx0.dpuf

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Fédération des C.R.C.M
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# Aspergilloses pulmonaires

Editorial

## Chronic pulmonary aspergillosis: help is on the way

Chronic pulmonary aspergillosis (CPA) is an oft overlooked threat to life in patients with respiratory disease. It is an umbrella term that includes simple aspergilloma (presence of a fungal ball in a single lung cavity), chronic cavitary pulmonary aspergillosis (the most common variant that presents with formation of lung cavities with or without an aspergilloma or nodules), and chronic fibrosing pulmonary aspergillosis (the advanced disease state with chronic scarring of the lungs).

CPA affects about 3 million people worldwide, and almost always presents in people with underlying pulmonary disease such as tuberculosis, bullous disease in COPD, and sarcoidosis. As such, early symptoms of the infection are frequently missed. If left untreated, 80% of people with the infection will die within 5 years. Yet despite this, the best diagnostic technique remains undefined and there is no approved treatment specifically listed for CPA by the European Medicine's Agency.

On Dec 23, 2015, the European Respiratory Society and the European Society of Clinical Microbiology and Infectious Diseases released the world's first clinical guidelines for diagnosis and management of CPA, with the aim of increasing recognition of the disease and improving early detection. The guidelines stipulate that diagnosis of CPA requires imaging confirmation of at least one cavity, with or without a fungal ball or nodule (with features present for at least 3 months), direct evidence of *Aspergillus* infection or an immunological response to *Aspergillus* spp, and absence of an alternative diagnosis.

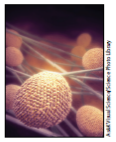
Treatment aims for CPA are the resolution of patient symptoms (primarily haemoptysis) and prevention of disease progression and further fibrosis. For simple aspergilloma, the gold standard treatment is surgical resection, ideally with video-assisted thoracic surgery. In chronic cavitary pulmonary aspergillosis, a surgical approach is more complex because of the multicavity nature of the disease, but resection should still be considered in patients with life-threatening haemoptysis. Standard treatment for patients with chronic cavitary pulmonary aspergillosis should be prescription of an oral triazole (eg, itraconazole or voriconazole), which are successful in preventing haemoptysis, stabilising disease, and are well tolerated by patients. However, treatment response is often slow (minimum 4–6 months) and relapse is common in patients who discontinue treatment. Patients showing no response within 6 months should be deemed treatment failures and should progress to the second-line approach of intravenous antifungal treatment (eg, amphotericin B). A final treatment option, when others have failed, is local cavity therapy, where an antifungal drug is surgically installed in an aspergilloma cavity via an endobronchial catheter.

Although these recommendations are hugely valuable to treating physicians, they are based on low-quality evidence from cohort studies—only two phase 2 trials have been published so far. Stronger evidence from high-quality randomised controlled trials of antifungals, with standardised criteria to define treatment response, are urgently needed to guide future practice.

All patients with CPA require long-term surveillance because relapse is common and cure is rare. As with use of many long-term drugs, azole resistance threatens treatment progress. The meagre discovery pipeline at present emphasises an urgent need for identification of new classes of antifungals. Additionally, vigilant management of comorbidities such as COPD is essential as some chronic lung disorder drugs such as inhaled corticosteroids confer an independent risk of aspergillosis lung infection.

One important area not expounded on by the guidelines is the critical burden of CPA in the developing world; more than a third of cases are in patients with tuberculosis. There is an urgent unmet need for low-cost diagnostics, as an alternative to CT scanning, and for the development of effective screening techniques to identify people most at risk of infection, such as those living with tuberculosis. Furthermore, with restricted access to drugs, physicians in resource-limited areas are forced to consider surgery in cases that are better suited to medical treatment. The Global Action Fund for Fungal Infections' application for itraconazole to be added to WHO's essential medicines list failed, meaning that many vulnerable people remain without access to life-saving diagnostics and antifungal drugs.

We hope these guidelines will serve as a catalyst to publicise the heavy burden of CPA across all global economic regions, and to encourage research to fill current knowledge gaps so we can effectively combat this indiscriminate and resilient infection. ■ *The Lancet Respiratory Medicine*



For the guidelines see http://erj.ersjournals.com/content/47/1/45

For the Global Action Fund for Fungal Infections see http://www.gaffi.org/



TASK FORCE REPORT
ESCMID/ERS GUIDELINES

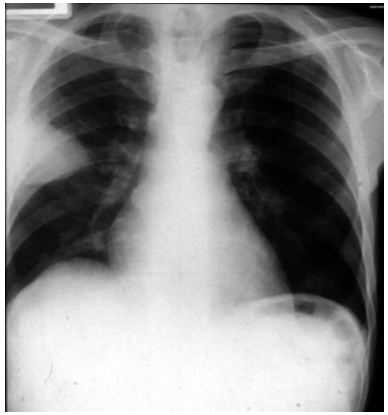
## Chronic pulmonary aspergillosis: rationale and clinical guidelines for diagnosis and management

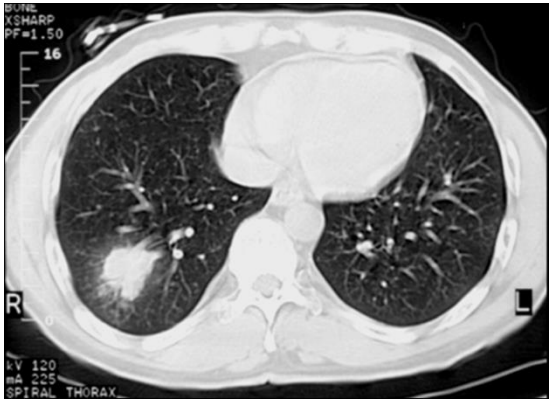
David W. Denning[1], Jacques Cadranel[2], Catherine Beigelman-Aubry[3], Florence Ader[4,5], Arunaloke Chakrabarti[6], Stijn Blot[7,8], Andrew J. Ullmann[9], George Dimopoulos[10] and Christoph Lange[11–14] on behalf of the European Society for Clinical Microbiology and Infectious Diseases and European Respiratory Society

Eur Respir J 2016; 47: 45–68 | DOI: 10.1183/13993003.00583-2015

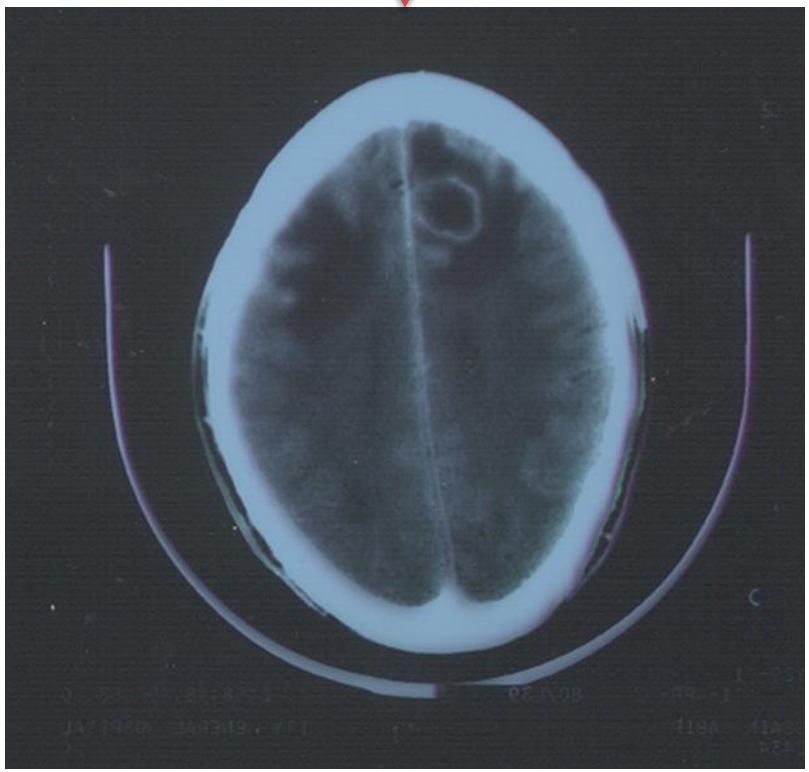
# Aspergilloses pulmonaires aiguës

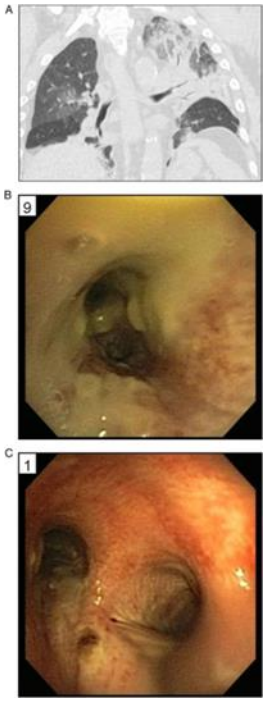
- Invasion du tissu pulmonaire par des hyphes (histologie)
- Évolution rapide : quelques jours à quelques semaines
- circonstances favorables
  - ✓ Neutropénie > 10 jours
  - ✓ Allogreffe cellules souches hématopoïétiques
  - ✓ Agents anti-Ly T, inhibiteurs calcineurine et TNFα
  - ✓ Transplantation d'organe solide : poumon; cœur-poumons
  - ✓ SIDA, BPCO, diabète, cirrhose
  - ✓ Corticothérapie > 3 semaines
  - ✓ séjour en USIR
  - ✓ Exposition aérique massive





# Aspergilloses pulmonaires aiguës





**Trachéo-bronchite invasive**

Ulcérée
Pseudo-membraneuse
Obstructive

Atélectasie

Neutropénie
Transplantation pulmonaire

BPCO
VIH
USIR

# Aspergilloses pulmonaires chroniques

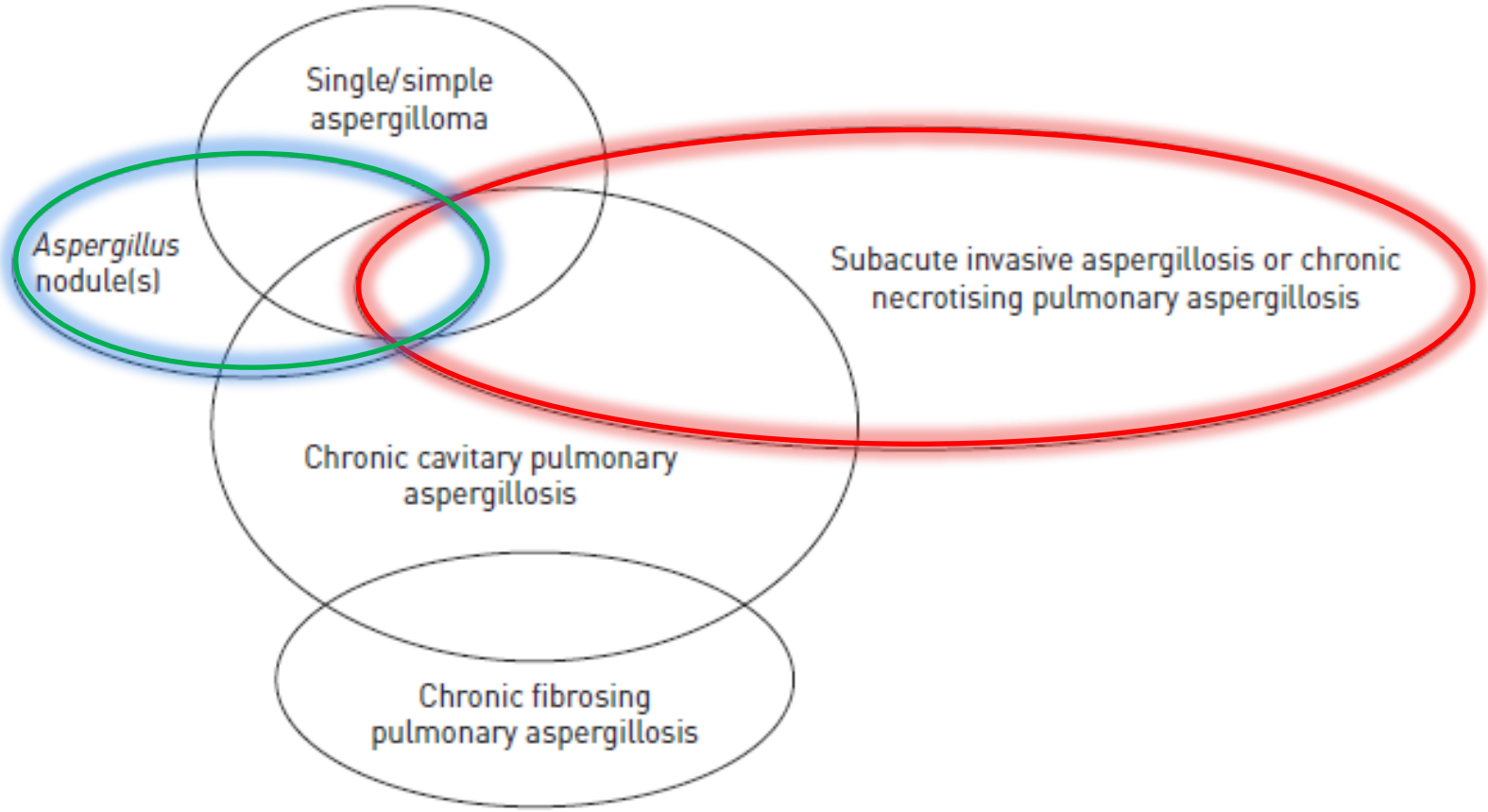



FIGURE 1 A schematic to illustrate the different forms of chronic pulmonary aspergillosis, in particular the overlap that is often seen.

# Aspergilloses pulmonaires chroniques

## Aspergillome simple

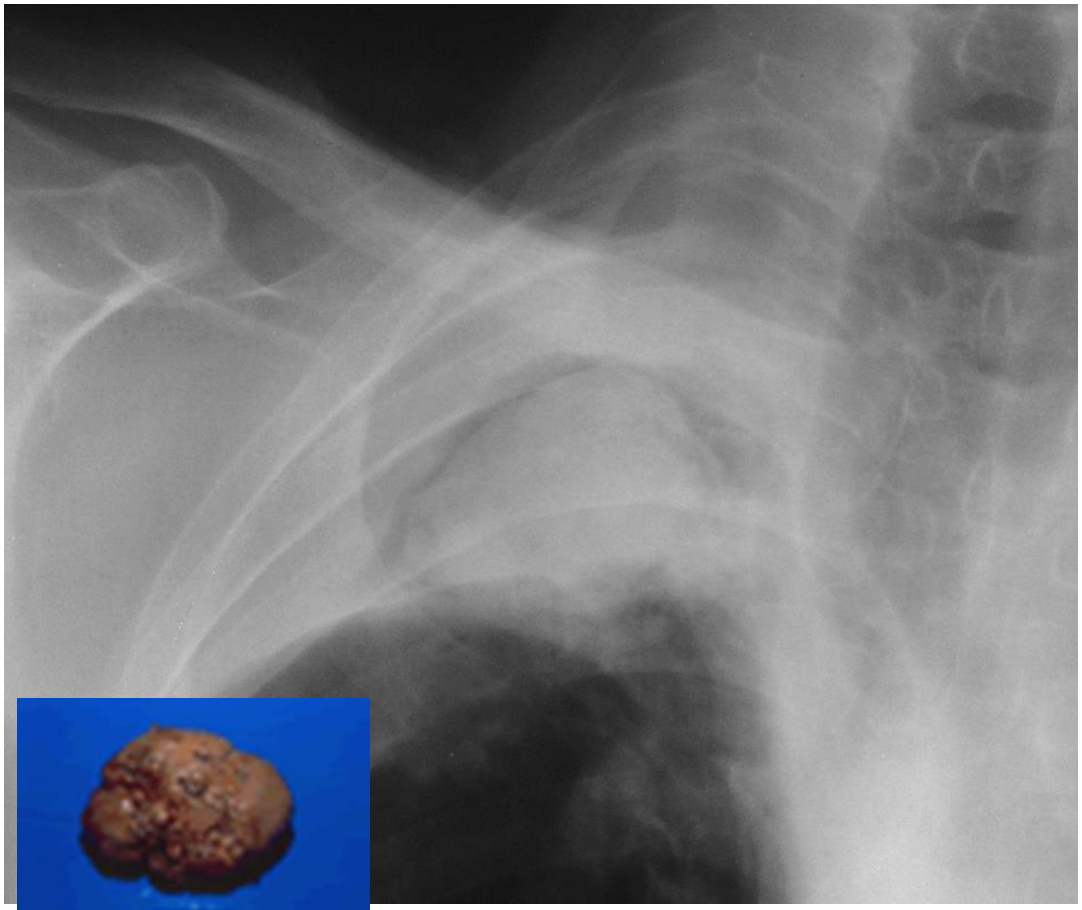
Cavité unique contenant une truffe aspergillaire

Sérologie ou prélèvement confirmant la présence d'aspergillus spp.

Patient immuno-compétent

Symptômes absents ou minimes

Absence de progression radiologiques sur trois mois au moins





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# Aspergilloses pulmonaires chroniques

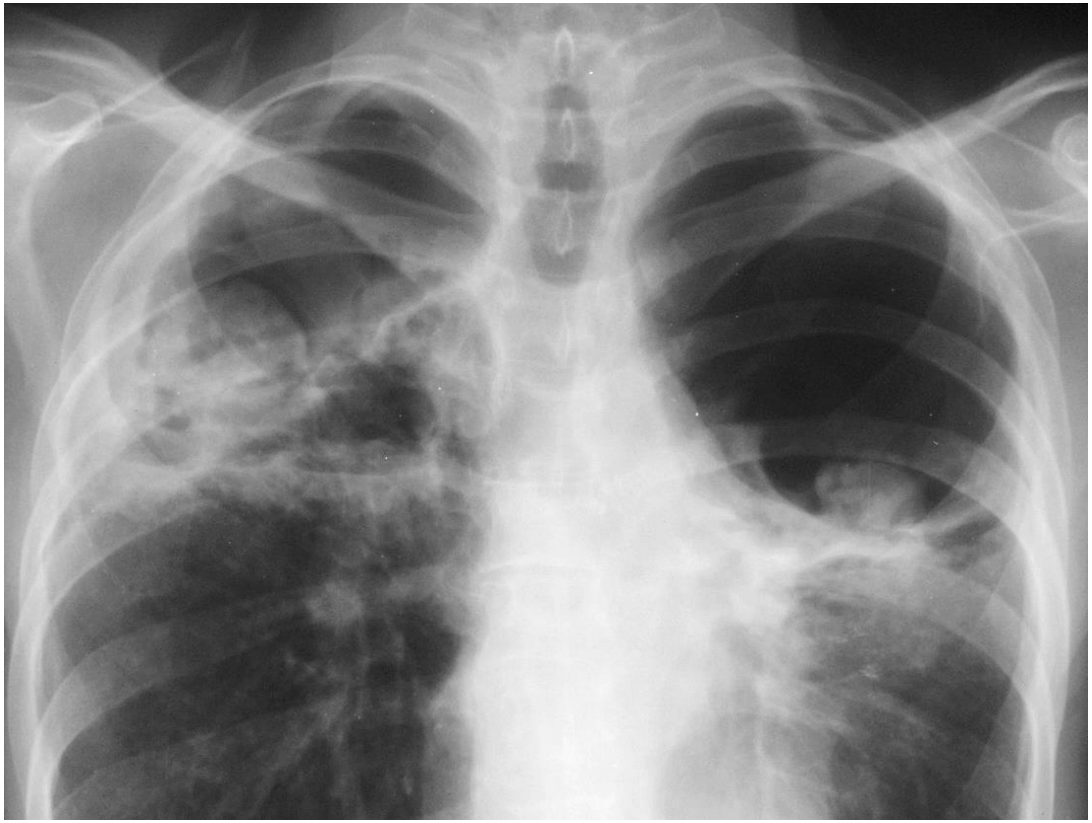
## Aspergillose pulmonaire chronique cavitaire

**Une ou plusieurs cavités à parois fines ou épaisses pouvant contenir un ou plusieurs aspergillomes ou du matériel séquestré**

**Preuve sérologique ou microbiologique de la présence d'Aspergillus spp.**

**Présence de signes cliniques respiratoires et/ou généraux**

**Progression sur trois mois ou plus : cavités, infiltrat, fibrose**



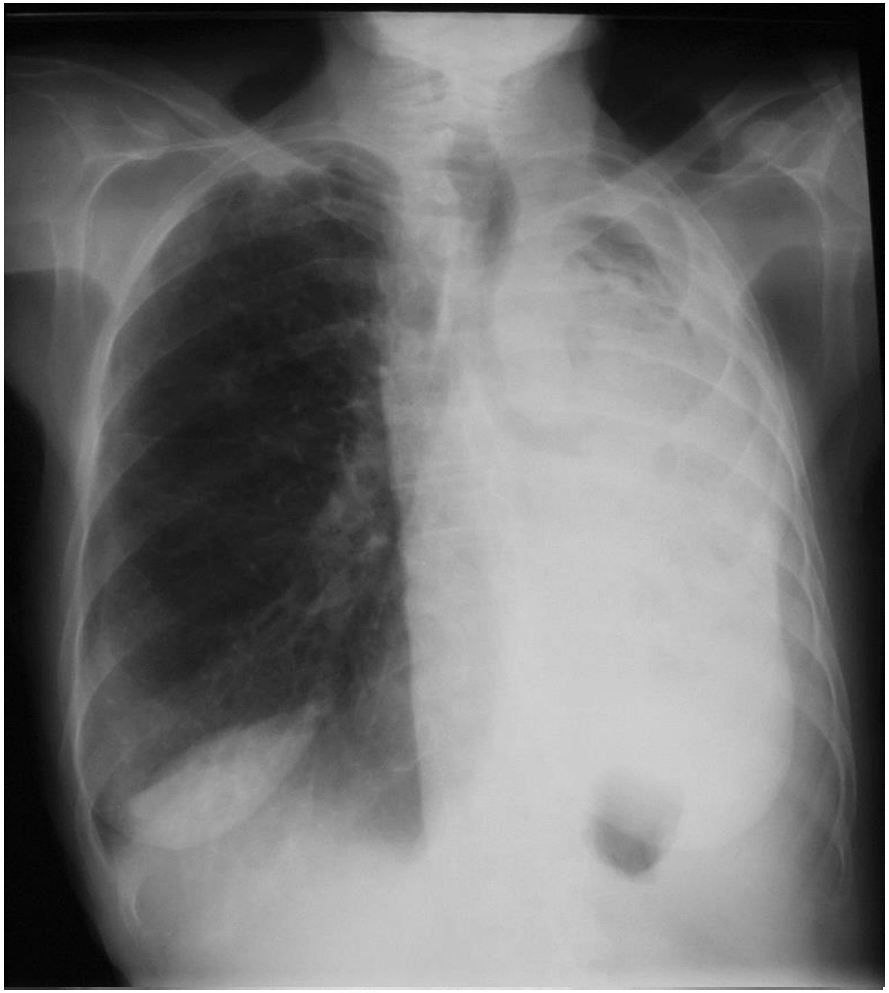
# Aspergilloses pulmonaires chroniques

**Aspergillose pulmonaire chronique fibrosante**

**Destruction fibreuse sévère d'au moins deux lobes compliquant une APCC avec perte fonctionnelle majeure.**

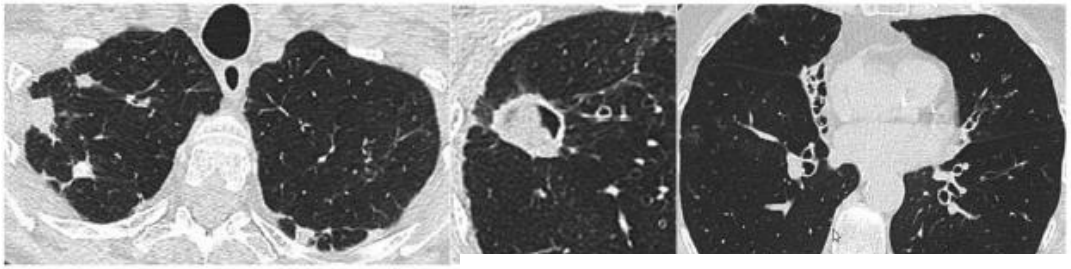
**Opacité entourée ou non de cavités**

**La destruction d'un seul lobe reste une APCC**



# Aspergilloses pulmonaires chroniques

**Nodule aspergillaire**



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**Un ou plusieurs nodules avec ou sans cavitation**

**Forme atypique d'aspergillose chronique**

**Absence d'invasion tissulaire**

# Aspergilloses pulmonaires chroniques

**Aspergillose invasive subaiguë**

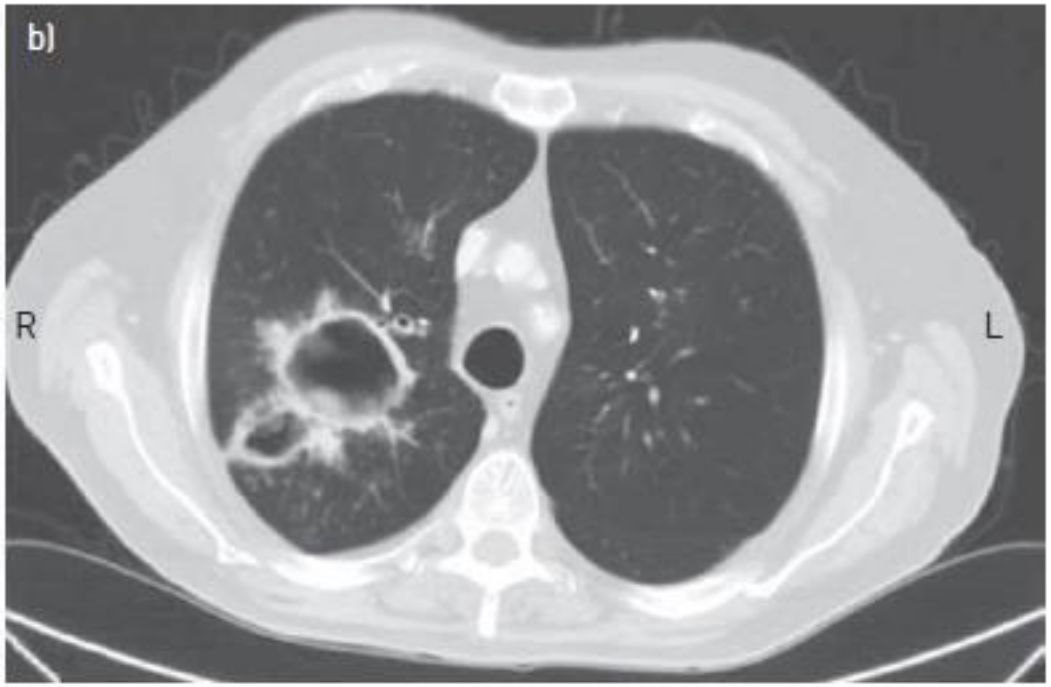
Aspergillose semi-invasive

Évoluant sur 1 à 3 mois

Cavitation, nodules, condensation avec abcès

Invasion tissulaire par des hyphes

Signes biologiques compatibles avec une forme invasive (galactomanne positif)

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# Aspergilloses pulmonaires

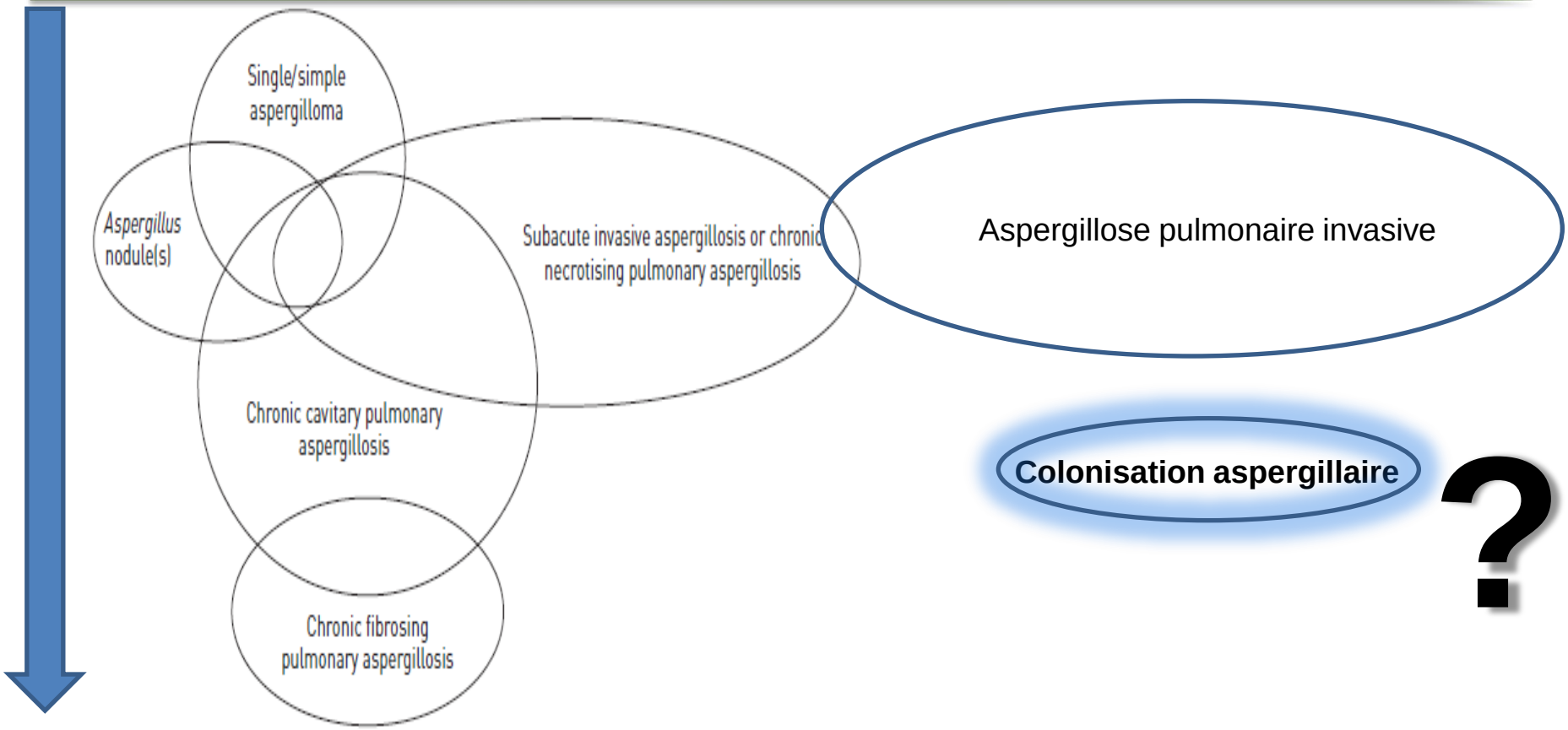
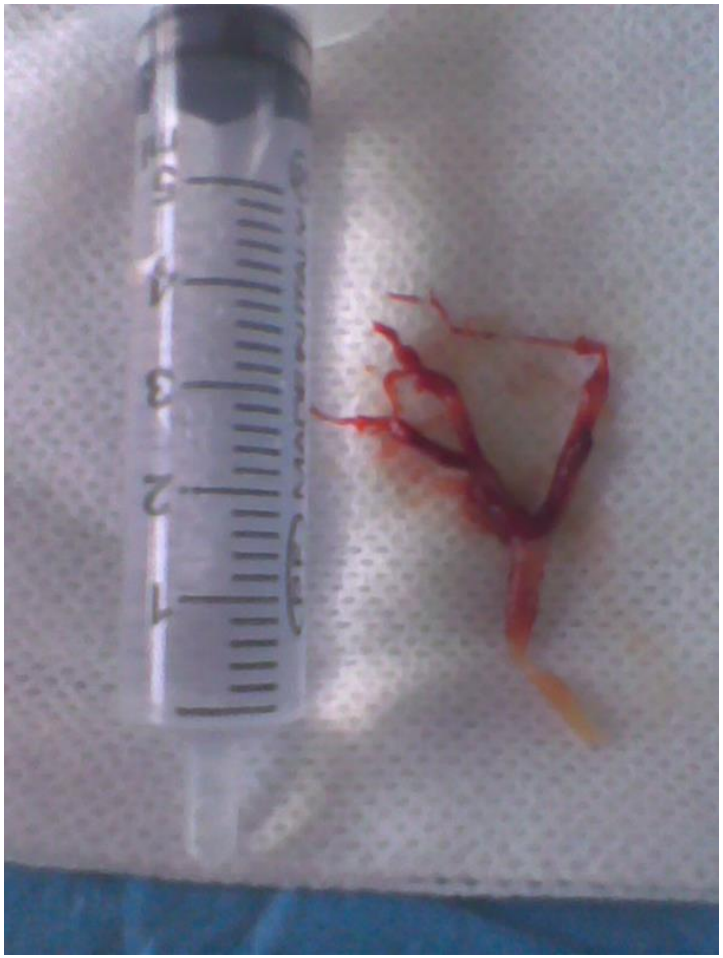
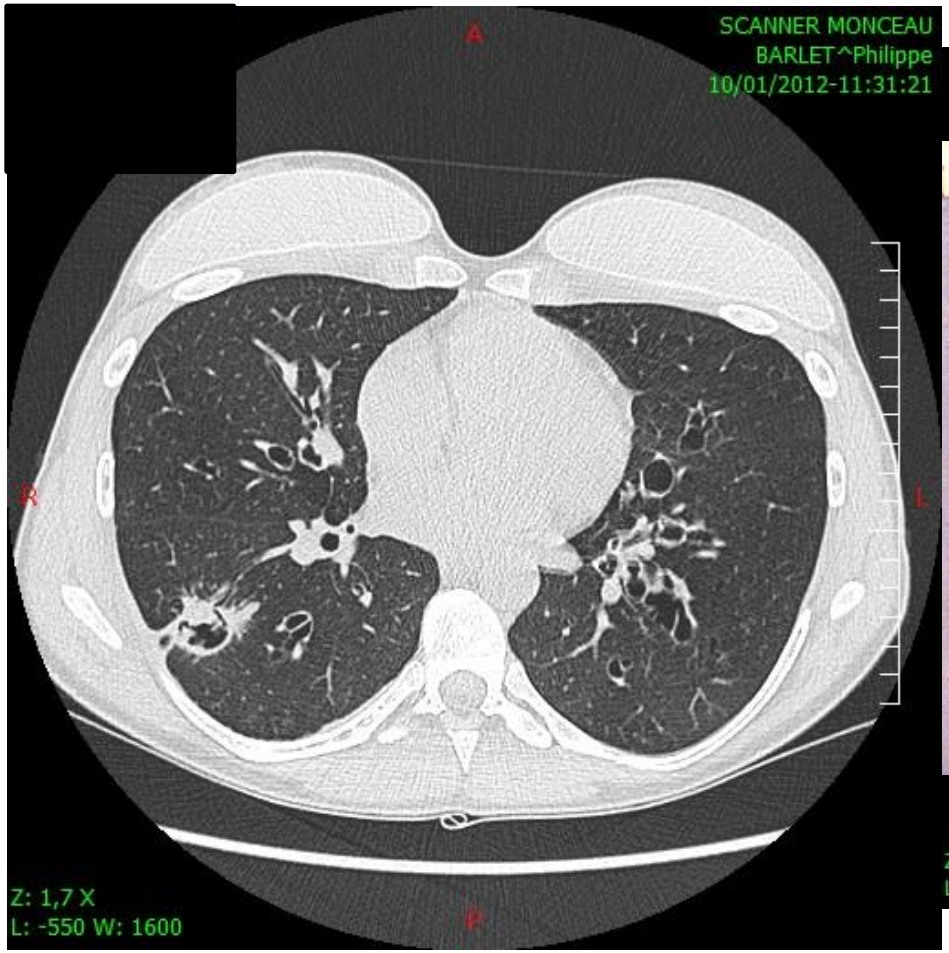


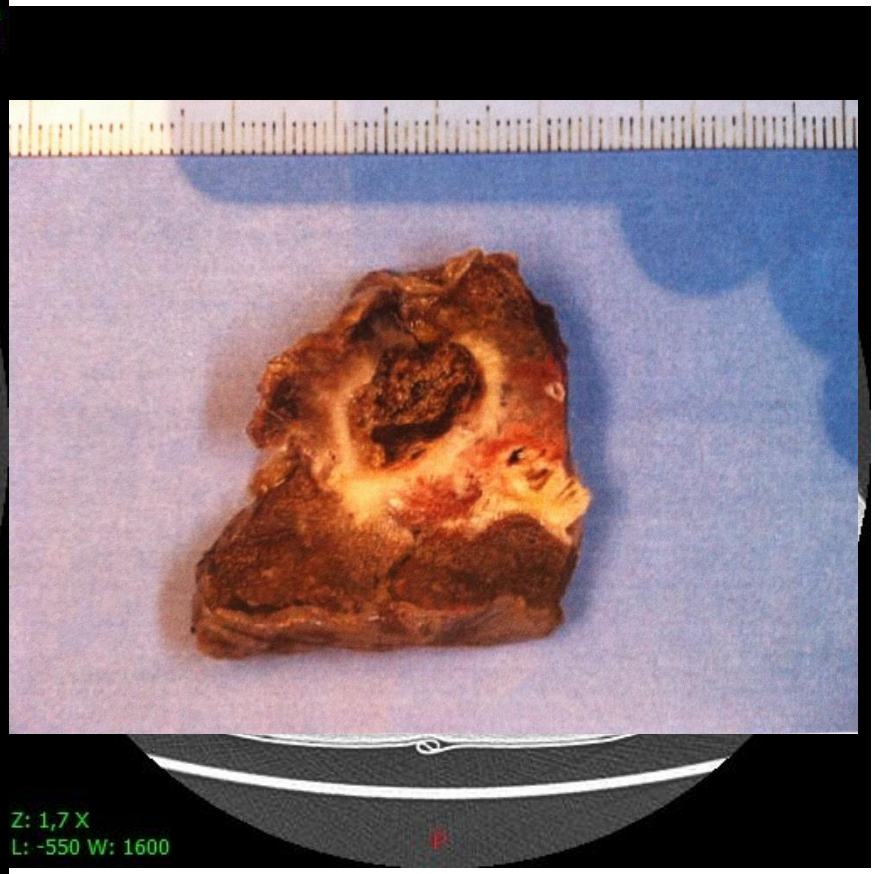

FIGURE 1 A schematic to illustrate the different forms of chronic pulmonary aspergillosis, in particular the overlap that is often seen.

# Aspergillus et Hypersensibilité

- Asthme aspergillaire
- Asthme sévère associé à une sensibilisation fongique
- Aspergillose broncho-pulmonaire allergique
- Alvéolite allergique extrinsèque



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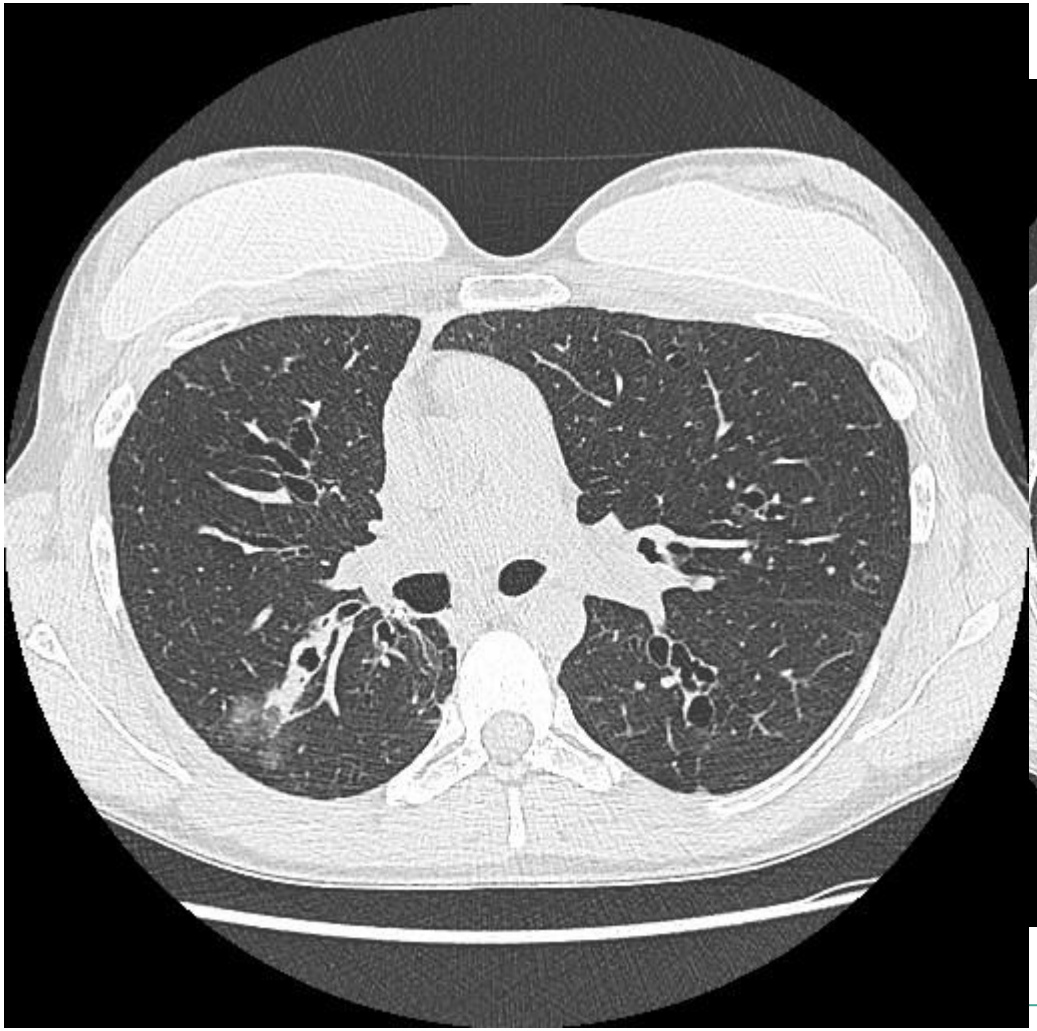

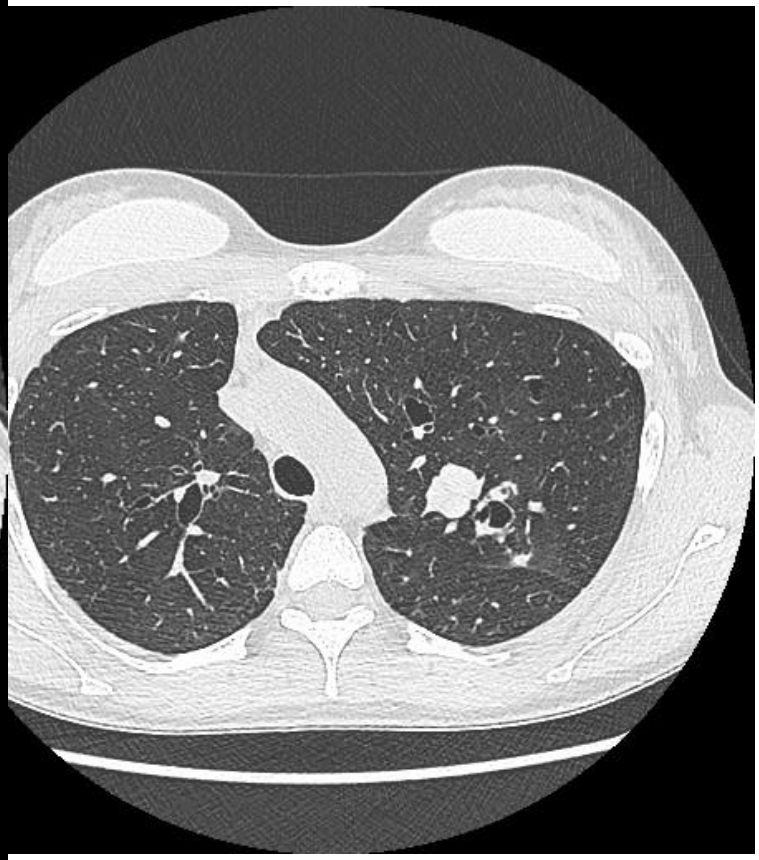

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# Critères ABPA : Patterson - Rosenberg

| Major Criteria<br>« ARTEPICS » | Minor criteria |
|---|---|
| - Asthma<br>- Roentgenographic fleeting pulmonary opacities<br>- Skin test positive for *Aspergillus* (HS type I)<br>- Eosinophilia<br>- Precipiting antibodies (IgG) in serum<br>- IgE in serum > 1.000 IU/mL<br>- Central bronchiectasis<br>- Serums *A. fumigatus*-specific IgG and IgE | - *Aspergillus* in sputum<br>- Expectoration of brownish black mucus plugs<br>- Skin reaction type III to *Aspergillus* antigen |

*Rosenberg Ann Int Med 1977 ; Patterson Arch Int Med 1986*

# New diagnostic criteria for ABPA

- Predisposing conditions
  - Bronchial asthma, cystic fibrosis
- Obligatory criteria (both should be present)
  - Type I *Af* skin test positive or elevated *Af* IgE (>0.35 kUA/L)
  - Elevated total IgE levels (>1000 IU/mL)*
- Other criteria (at least two of three)
  - Presence of *Af* precipitating (or IgG) antibodies in serum
  - Radiographic pulmonary opacities consistent with ABPA†
  - Total eosinophil count >500 cells/µL in steroid naïve patients (may be historical)



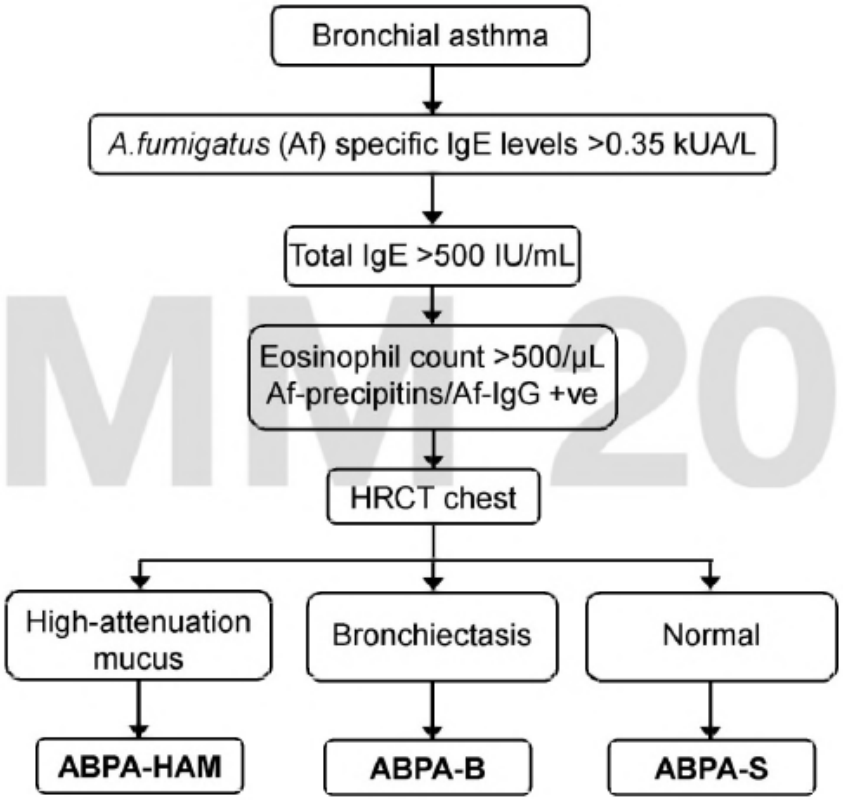
*If the patient meets all other criteria, an IgE value < 1000 IU/mL may be acceptable
†Chest radiographic features consistent with ABPA may be transient or permanent

*Agarwal R, et al. Clin Exp Allergy 2013;43:850-873*

# Critères de l'ABPA au cours de la mucoviscidose

| Critères classiques | Critères minimaux |
|---|---|
| Détérioration aiguë ou subaiguë et déclin de VEMS sans autre cause | Détérioration aiguë ou subaiguë et déclin de VEMS sans autre cause |
| IgE > 1000 IU/ml | IgE > 500 UI/L |
| Réactivité cutanée immédiate prick test<br>Ou<br>IgE spécifiques anti-aspergillaires | Réactivité cutanée immédiate prick test<br>Ou<br>IgE spécifiques anti-aspergillaires |
| Précipitines à A.fumigatus<br>Ou<br>IgG anti-A.fumigatus | Précipitines à A fumigatus<br>Ou<br>IgG anti-A fumigatus<br>Ou<br>Infiltrat pulmonaire nouveau ou récent |
| Infiltrat pulmonaire nouveau ou récent | |

# Screening protocol at Chest Clinic






*Agarwal R, et al. In: Fungal Infections in Asia: Eastern frontier of Mycology: Elsevier, 2013; 173-193*

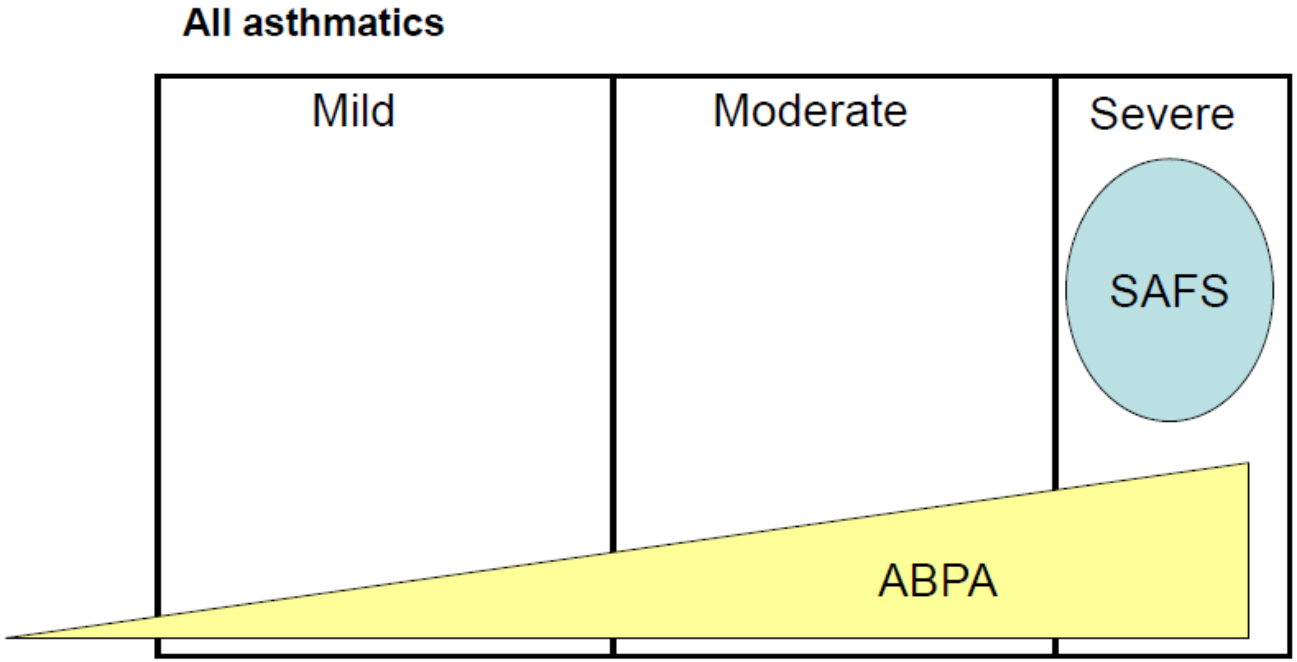
# Critères de l'ABPA

**TABLE 4** Diagnosing ABPA

| Diagnostic Criteria | Historically Included | Recent Modifications Highlight |
|---|---|---|
| Predisposing condition | Asthma | Cystic fibrosis |
| Demonstration of fungal sensitization | Sensitization to *Aspergillus* fumigatus<br>Positive *Aspergillus* skin test or elevated IgE levels against *Aspergillus* fumigatus | Sensitization can be to a variety of *Aspergillus* species or other fungal organisms<br>Intradermal testing is more sensitive than skin prick<br>The combination of serum *Aspergillus* IgE and skin testing is most sensitive |
| Elevated total serum IgE | Levels >1,000 IU/mL | Levels may be lower for patients on corticosteroids or in a less active phase of disease |
| Positive *Aspergillus*-specific serologies | Elevated serum *Aspergillus* IgE and positive precipitins | Quantitative *Aspergillus* IgG titers often replace precipitins testing |
| Radiographic changes | Opacities from mucous plugging<br>Central bronchiectasis | High attenuation mucous plugging is pathognomonic<br>Not all patients have bronchiectasis, particularly early in disease |

See Table 1 for expansion of abbreviation.

# ABPA, SAFS and asthma



# Bronchite aspergillaire

**Table 2.** Underlying pulmonary disease, comorbid conditions, and mannose binding lectin levels in patients with *Aspergillus* bronchitis

| Underlying diseases | Number affected (%) |
|---|---|
| Pulmonary disease | $n = 17$ |
| COPD[a] | 6 (35) |
| Asthma[a] | 4 (23) |
| Bronchiectasis[b] | 12/14 (86) |
| Mucus impaction[b] | 2 (12) |
| Lung cancer | 1 (6) |
| Oral corticosteroids >10 mg/day | 3 (18%) |
| Oral corticosteroids <10 mg/day | 3 (18%) |
| Infliximab | 1 (6%) |
| Inhaled corticosteroids | 12 (70%) |
| Breast cancer radiotherapy | 2 (12%) |
| Hyperthyroidism | 2 (12%) |
| Gamma-IFN production low | 1 (6%) |
| Alpha1 antitrypsin deficiency | 1 (6%) |
| Type II diabetes mellitus | 1 (6%) |
| Hypogammaglobulinemia | 1 (6%) |
| Fibromyalgia | 1 (6%) |
| Irritable bowel syndrome | 1 (6%) |
| No comorbidity | 2 (12%) |
| Mannose binding lectin levels (mg/L) | $N = 16$ |
| >1 (normal) | 7 (44%) |
| >0.5–< 1 (possibly low) | 3 (18%) |
| >0.1–< 0.5 (low) | 4 (24%) |
| <0.1 (undetectable) | 2 (12%) |

[a]COPD and asthma noted if severe and long established, otherwise probably underestimated.
[b]Bronchiectasis and mucus impaction as determined by HRCT.
COPD, chronic obstructive pulmonary disease; IFN, interferon.

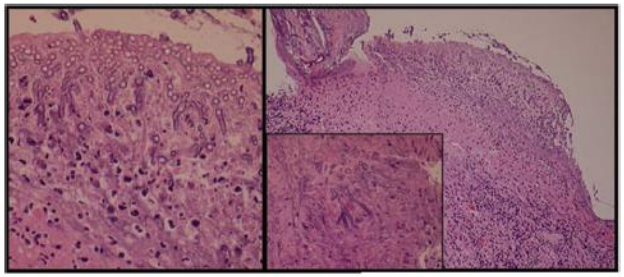


**Figure 2.** Transbronchial biopsy of patient 2 stained with H&E showing focal squamous metaplasia in the superficial layers of the bronchial epithelium (left panel). An area of ulceration covered by granulation tissue, with a superficial layer of fungal hyphae is seen from 12–3:00 o'clock. Deeper in the biopsy there is a chronic inflammatory cell infiltrate without eosinophilia. The inset shows septate branching hyphae typical of Aspergillus superficially within bronchial tissue.

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# Catégorisation

**TABLE II.** Average values of latent class variables for 130 triazole-naive patients

| | Class 1 (n = 49) | Class 2 (n = 23) | Class 3 (n = 19) | Class 4 (n = 39) |
|---|---|---|---|---|
| Average class probability | 0.981 | 0.996 | 0.921 | 0.992 |
| Median sIgG (mg/L) (SD) | 36 (20) | 112 (132) | 47 (24) | 98 (29) |
| Median sIgE (kUa/L) (SD) | 0 (0.6) | 13.2 (19.0) | 5.2 (3.9) | 0 (1.0) |
| Median tIgE (kUI/L) (SD) | 28 (28) | 690 (1230) | 170 (98) | 35 (157) |
| Mean RT-PCR $C_t$ value $(38 - C_t)^* \pm$ SD | 2.6 ± 3.3 | 8.2 ± 4.0 | 3.7 ± 3.3 | 7.1 ± 4.0 |
| Probability of positive PCR | 0.497 | 1.000 | 0.778 | 1.000 |
| Mean GM index ± SD | 0.161 ± 0.19 | 2.544 ± 2.04 | 0.135 ± 0.17 | 2.960 ± 2.11 |
| Probability of positive GM | 0.004 | 0.946 | 0.000 | 1.000 |

*sIgG*, Specific *Aspergillus* IgG; *tIgE*, total IgE.

*The RT-PCR $C_t$ limit of blank is 38. To facilitate comparisons between GM and RT-PCR, the actual $C_t$ value is shown as $38 - C_t$ and so higher numbers reflect increasing *Aspergillus* DNA concentrations.

**Af négatif 38%**

**ABPA 18%**

**Af Allergie 15%**

**Af bronchitis 30%**

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# Aspergilloses pulmonaires

UPDATE IN PROGRESS*

**Colonisation aspergillaire**

**Bronchite aspergillaire**

**ABPA**

**asthme aspergillaire**

**Asthme sévère avec sensibilisation aspergillaire**

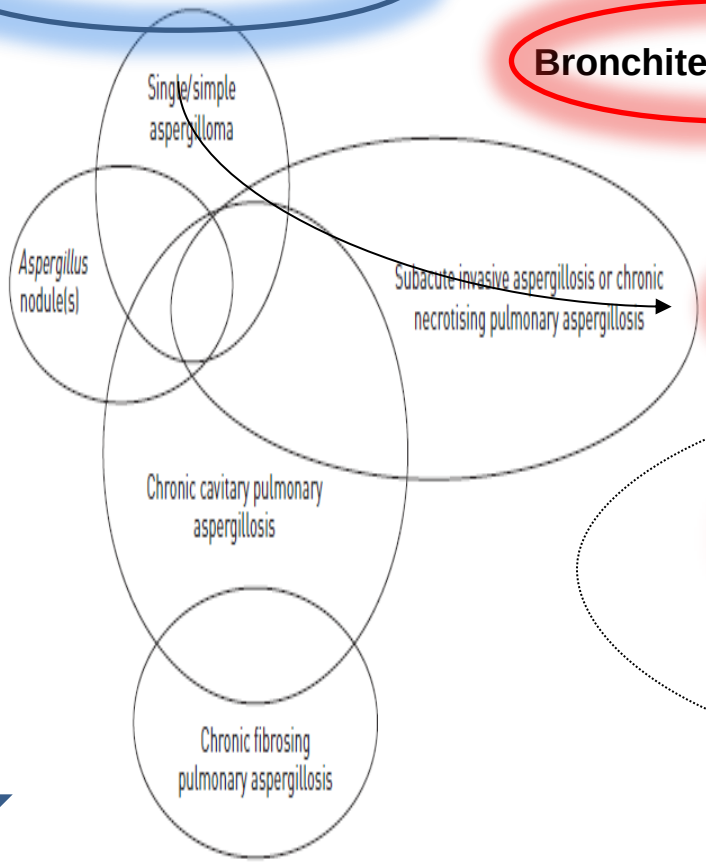


FIGURE 1 A schematic to illustrate the different forms of chronic pulmonary aspergillosis, in particular the overlap that is often seen.

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INSTITUTE FOR LUNG HEALTH
LEICESTER

# Culture and sensitisation in asthma, CF and COPD – what does it tell us?

Catherine Pashley

maara
Midlands Asthma & Allergy Research Association

University of Leicester

- L’étendue du spectre de l’aspergillose reste à définir en partie parce que les moyens standards de détection sont encore insuffisants