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# *Aspergillus fumigatus* and cystic fibrosis: a 12-year observational cohort

J. Fillaux, F. Brémont, S. Cassaing, M. Murriss, M.D. Linas, M.H.  
Bessières, J.L. Rittié, L. Tétu, C. Segonds, E. Bieth, M. Abbal, A. Berry,  
B. Pipy, J.F. Magnaval

Service de Parasitologie – Mycologie, Hôpital Rangueil, Toulouse, France




# Aspergillus and cystic fibrosis

- Wide range of pulmonary diseases
- Not sufficient evidence to generally recommend treatment of an *Aspergillus*-positive sputum culture in the absence of ABPA






# Objectives

- To determine the impact of the different *Af*-induced pulmonary states on the FEV<sub>1</sub> of CF patients
  - To study the relationship between these different states and the presence of *Pa*
  - To search for associated factors with these different pulmonary states
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# Population and variables

- Prospective observational cohort
  - January, 1995 - July, 2007
  - Demographic data
    - date of birth, gender, diagnosis date, CF gene mutation
  - Medical data
    - sputum production, FEV<sub>1</sub>, BMI
  - Microbiological findings
    - presence of Pa in sputum (culture), presence of Af in sputum (direct examination and culture)
  - Immune parameters
    - IgEt, IgE-*Af* and IgG-*Af*, precipitin-*Af*
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# *Af*-related pulmonary states

- “ABPA susceptibility” group:
    - positive IgE-*Af*
    - precipitin-*Af*  $\geq 3$  lines
    - IgEt  $\geq 500$  IU/mL
  - “Sensitized” group:
    - non-ABPA group
    - positive IgE-*Af*
  - “Colonized” group:
    - non-ABPA group
    - negative IgE-*Af*
    - colonization with *Af* or precipitin-*Af*  $\geq 3$  lines
  - “Control” group: excluded from the precedent groups
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# Patients' description (1)

- 271 patients evaluated 6314 times
  - Sex ratio: 1.2
  - Median age at the CF diagnosis date: 8.2 m [1.6 m-3.2 y].
  - Severe mutation: 85%.
  - 4826 sputum to identify bacteria
    - *Pa*-positive culture: 39%
    - At least one *Pa*-positive sputum: 177 (65%) patients
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## Patients' description (2)

- 3214 sputum for fungi identification
    - *Af*-positive culture: 30%
    - At least one *Af*-positive sputum: 158 (58%) patients
  - Groups
    - “ABPA susceptibility” group: 40 (15%) patients
    - “Sensitized” group: 66 (24%)
    - “Colonized” group: 39 (14%)
  - 3704 spirometric tests
    - Clinical worsening: 30% of the visits
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# Impact of *Af* on FEV<sub>1</sub>

		FEV <sub>1</sub> Med [IQR]	OR [95% CI]
<b>Groupe</b>	control	91.5 [58-108]	1
	colonized	73 [51-96]	10.9 [0.4-21.3]
	sensitized	77 [51-101]	14.8 [5.4-24.3]
	ABPA suscept.	76 [57-94]	18.5 [8.4-28.6]
<b>Age at the visit</b>		2.5 [2.2-2.7]	
<b>BMI</b>	normal weight	87 [63-103]	1
	underweight	54 [38-71]	9.1 [7.2-11.1]
	overweight	80 [59-96]	10.8 [4.8-16.9]
<b><i>Pa</i> colonization</b>	absence	89 [63-105]	1
	presence	62 [41-83]	3.8 [1.4-6.3]





# Relationship between *Af* and *Pa*


- *Pa* +ve sputum associated with *Af* +ve sputum
  - 81% *Pa*+ & *Af*+ versus 38% *Pa*- & *Af*+,  $p < 0.001$
- Patients *Pa*+ and *Af*+
  - Age of *Pa* 1<sup>st</sup> detection < Age of *Af* 1<sup>st</sup> detection
  - 5.3 years [3.4-8.9] versus 7.3 years [5.1-11.7],  
 $p = 0.04$





## Associated factors to *Af*-related pulmonary states

	Control	Colonized	Sensitized	ABPA suscept.	p
<b><i>Pa</i> col.</b>	3 (10)	2 (15)	6 (20)	9 (50)	0.003
<b>Age of <i>Pa</i> colonization</b>	25.1 [6.8-33.6]	24.1 [18.0-30.1]	10.4 [4.9-15.4]	7.9 [5.9-11.0]	0.027
<b>Severe mutation</b>	31 (73.8)	6 (85.7)	25 (96.1)	16 (100)	0.002
<b>IgG-<i>Af</i> antibodies</b>	3.9 [2.1-8.9]	6.5 [4.9-9.2]	6.4 [3.5-25.9]	23.9 [8.5-55.1]	< 0.001





# Conclusion

- *Af* sensitization harmful and more than *Af* colonization
  - Concomitance of sensitization and 1<sup>st</sup> *Af* detection
  - *Pa* colonization associated with “ABPA susceptibility”  
group
  - IgG-*Af* useful in ABPA diagnostic ?
  - Interest of early treatment of positive *Af* sputum by  
antifungal molecule ?
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