



Available online at  
**ScienceDirect**  
www.sciencedirect.com

Elsevier Masson France  
**EM|consulte**  
www.em-consulte.com



ORIGINAL ARTICLE/ARTICLE ORIGINAL

# An estimation of burden of serious fungal infections in France



*Estimation du poids épidémiologique des infections fongiques graves en France*

J.-P. Gangneux<sup>a,\*</sup>, M.-E. Bougnoux<sup>b</sup>, C. Hennequin<sup>c</sup>,  
C. Godet<sup>d</sup>, J. Chandenier<sup>e</sup>, D.W. Denning<sup>f</sup>, B. Dupont<sup>b</sup>, for  
the LIFE program, the Société française de mycologie médicale  
SFMM-study group<sup>1</sup>

<sup>a</sup> Centre hospitalier universitaire de Rennes, laboratoire de parasitologie-mycologie, 2, rue Henri-le-Guilloux, 35033 Rennes cedex 09, France

<sup>b</sup> Centre hospitalier universitaire Necker–Enfants-Malades, Assistance publique–Hôpitaux de Paris, laboratoire de parasitologie-mycologie, 149, rue de Sévres, 75015 Paris, France

<sup>c</sup> Centre hospitalier universitaire Saint-Antoine, Assistance publique–Hôpitaux de Paris, laboratoire de parasitologie-mycologie, 184, rue du Faubourg Saint-Antoine, 75012 Paris, France

<sup>d</sup> Centre hospitalier universitaire de Poitiers, service de médecine interne, maladies infectieuses et tropicales, 2, rue de la Milétrie, 86021 Poitiers, France

<sup>e</sup> Centre hospitalier universitaire de Tours, laboratoire de parasitologie-mycologie, 2, boulevard Tonnellé, 37000 Tours, France

<sup>f</sup> The University of Manchester and National Aspergillosis Centre, University Hospital of South Manchester, Manchester, UK

Received 31 October 2016; accepted 1st November 2016

## KEYWORDS

Aspergillosis;  
Candidiasis;  
Pneumocystosis;  
Cryptococcosis;  
Mucormycosis;

## Summary

*Objective of the study.* – An estimation of burden of serious fungal diseases in France is essential data to inform public health priorities on the importance of resources and research needed on these infections. In France, precise data are available for invasive fungal diseases but estimates for several other diseases such as chronic and immunoallergic diseases are by contrast less known.

*Materials and methods.* – A systematic literature search was conducted using the Web of

\* Corresponding author.

E-mail address: Jean-pierre.gangneux@univ-rennes1.fr (J.P. Gangneux).

<sup>1</sup> In association with the LIFE program at www.LIFE-worldwide.org and the Société française de mycologie médicale SFMM-study group.

Tinea capitis;  
France

Science Platform. Published epidemiology papers reporting fungal infection rates from France were identified. Where no data existed, we used specific populations at risk and fungal infection frequencies in those populations to estimate national incidence or prevalence, depending on the condition.

**Results.** – The model predicts high prevalences of severe asthma with fungal sensitization episodes (189 cases/100,000 adults per year), of allergic bronchopulmonary aspergillosis (145/100,000) and of chronic pulmonary aspergillosis (5.24/100,000). Besides, estimated incidence for invasive aspergillosis is 1.8/100,000 annually based on classical high risk factors. Estimates for invasive mucormycosis, pneumocystosis and cryptococcosis are 0.12/100,000, 1/100,000 and 0.2/100,000, respectively. Regarding invasive candidiasis, more than 10,000 cases per year are estimated, and a much higher number of recurrent vaginal candidiasis is probable but must be confirmed. Finally, this survey was an opportunity to report a first picture of the frequency of tinea capitis in France.

**Conclusion.** – Using local and literature data of the incidence or prevalence of fungal infections, approximately 1,000,000 (1.47%) people in France are estimated to suffer from serious fungal infections each year.

© 2016 Elsevier Masson SAS. All rights reserved.

## MOTS CLÉS

Aspergillose ;  
Candidose ;  
Pneumocystose ;  
Cryptococcose ;  
Mucormycose ;  
Teigne du cuir chevelu ;  
France

## Résumé

**But de l'étude.** – L'estimation du poids épidémiologique des infections fongiques graves en France est une donnée essentielle, notamment destinée à informer les autorités de santé sur l'importance des ressources et des progrès nécessaires à la prise en charge de ces infections.

**Matériels et méthodes.** – Une revue systématique de la littérature a été effectuée grâce à la base de données Web of Science. Les publications rapportant des données d'incidence en France ont été sélectionnées. En l'absence de données d'incidence publiées, nous avons effectué une évaluation populationnelle en fonction des facteurs de risques, lorsque des fréquences étaient disponibles dans ces populations particulières.

**Résultats.** – Le modèle utilisé prédit une prévalence élevée des asthmes sévères avec sensibilisation fongique (189 cas/100 000 adultes/an), de l'aspergillose broncho-pulmonaire allergique (145/100 000) et des aspergilloses pulmonaires chroniques (5,24/100 000). Basée sur les facteurs de risque traditionnels, l'incidence de l'aspergillose invasive est estimée à 1,8/100 000, à 0,12/100 000 pour les mucormycoses invasives, 1/100 000 pour la pneumocystose et 0,2/100 000 pour la cryptococcose. Par ailleurs, il est estimé plus de 10 000 cas par an de candidoses invasives (candidémies, péritonites à *Candida*, candidoses œsophagiennes), et un nombre encore plus élevé de candidoses vaginales récurrentes est probable mais doit être confirmé. Enfin, cette étude était l'opportunité d'une photographie nationale des cas de teignes du cuir chevelu diagnostiqués dans les plus grands hôpitaux français.

**Conclusion.** – Cette approche populationnelle qui évalue à environ 1 million de cas d'infections fongiques graves par an conduit à l'estimation que 1,47 % de la population française souffre d'une maladie fongique grave.

© 2016 Elsevier Masson SAS. Tous droits réservés.

## Introduction

The burden of serious fungal diseases has only recently been considered as a health public concern worldwide [6]. Global Action Fund for Fungal Infections (GAFFI) has drawn up a 10-year global roadmap for fungal diseases. Estimates have been made for more than 5 billion of the world's population and already show that deaths due to fungal infections are similar to the number of people dying from tuberculosis ([www.LIFE-worldwide.org](http://www.LIFE-worldwide.org)).

In France, precise data are available for invasive fungal infections (IFI) such as invasive aspergillosis, candidaemia, cryptococcosis and pneumocystosis [5]. A tight network of hospitals skilled in the diagnosis of IFI and under the coordination of the French National Reference Center for invasive fungal diseases (Institut Pasteur, Paris) allows a

detailed snapshot of hospital acquired infections [4,28,29]. Epidemiology of several other significant fungal diseases are by contrast less known. In particular, chronic and immunological fungal diseases are increasingly recognised and populations at risk better identified, such as chronic obstructive pulmonary diseases, asthma or cystic fibrosis [16]. Finally, even more neglected but debilitating infections such as recurrent vulvovaginal candidiasis or tinea capitis are a cause of significant morbidity and cost (medical care, absenteeism, quality of life) and should also be considered as a burden for the health system [1,45].

Herein, we report a wide estimation of the incidence and prevalence of fungal diseases in mainland France in order to provide a basis of reflection in terms of Public Health.

## Methods

A systematic literature search was conducted using the Web of Science Platform giving access to the Medline and Academic Search Complete databases. Published epidemiology papers reporting fungal infection rates from France were identified. Where no data existed, we used specific populations at risk and fungal infection frequencies in those populations to estimate national incidence or prevalence, depending on the condition as already performed in various countries according the LIFE program [see the examples of Belgium, Germany or Spain [26,40,42]]. Population statistics were obtained from the *Institut national de la statistique et des études économiques* (INSEE-2014, [www.insee.fr](http://www.insee.fr)). Incidences of IFIs were derived from *Institut national de veille sanitaire* (InVS, [www.invs.sante.fr](http://www.invs.sante.fr), now renamed *Santé publique France*) and the National Reference Center for invasive fungal diseases (CNR-MA, Institut Pasteur, [www.pasteur.fr/fr/sante/centres-nationaux-referance/les-cnr/mycoses-invasives-et-antifongiques](http://www.pasteur.fr/fr/sante/centres-nationaux-referance/les-cnr/mycoses-invasives-et-antifongiques)) [5]. For tinea capitis epidemiology, a survey was conducted by the French Society for Medical Mycology (Société française de mycologie médicale [SFMM], [www.sfmm-mycologie-medicale.com](http://www.sfmm-mycologie-medicale.com)) in order to count all cases diagnosed in the 34 main French University hospitals during 2014 (see Acknowledgements).

## Results and discussion

Population-based estimates reported in Table 1 were calculated using the demographic report 2014 ([www.insee.fr](http://www.insee.fr)). France's population was estimated at 65.8 M of which 82% are adults and 7.3% are children < 5 years.

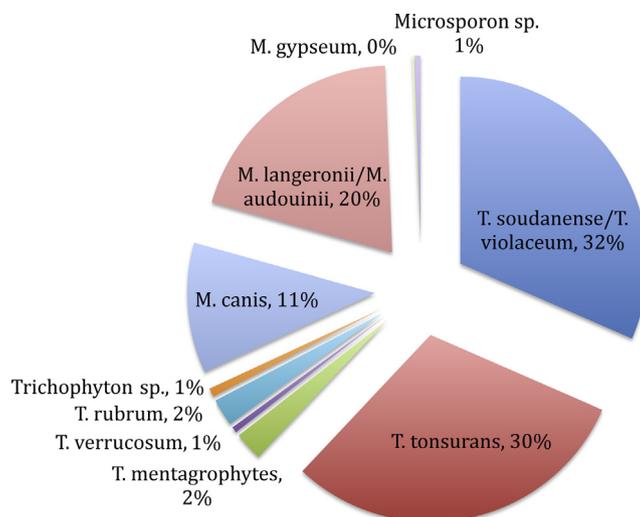
Chronic respiratory diseases are a leading cause of morbidity and mortality in France. The asthma prevalence is high worldwide and estimated in French adults at 6.7 and 7.5% of > 45 years old for chronic obstructive pulmonary diseases (COPD) [44,46,48]. Besides, pulmonary tuberculosis prevalence was as high as 7.6/100,000 in 2012 ([www.invs.sante.fr](http://www.invs.sante.fr)).

In this context, the model predicts 124,678 severe asthma with fungal sensitization (SAFS) episodes (189 cases/100,000 adults per year), 95,361 allergic bronchopulmonary aspergillosis (ABPA) episodes (145/100,000) and 3450 chronic pulmonary aspergillosis cases (5.24/100,000) (Table 1). Probably there is some overlap between SAFS and ABPA as severe asthma is a feature of a minority of ABPA cases (excluding the use of corticosteroids for ABPA treatment) and sensitisation to *A. fumigatus* is the commonest finding in SAFS patients and universal in ABPA patients [12–15]. Chronic pulmonary aspergillosis [CPA] complicates many pulmonary conditions, notably tuberculosis, non-tuberculous mycobacterial diseases, sarcoidosis, COPD and in those who have had a pneumothorax. Prior prevalence estimates of CPA complicating TB and sarcoidosis in France were and 522 and 311 cases, respectively [9,13]. The high estimated burdens of SAFS, ABPA and three times as many CPA cases as invasive aspergillosis cases suggest that these patients should be better identified and characterized in order to improve their management and prevention strategies [16,20,27,37,13]. Furthermore, the risk of severe invasive infections in such patients represents high costs due to hospitalization, diagnostic management and antifungal drug use with a persistent high mortality and emergence of resistance [24,32,38]. While a good estimate of incidence rates of documented invasive aspergillosis is available (1.8/100,000; 1185 cases/year) this is based on classical risk factors (haematological malignancies, cytotoxic chemotherapy and severe neutropenia, solid organ transplantation, long-term corticosteroid therapy and immunosuppressors) [8,10,19,23,28,35,36,43]. Our estimate of IA complicating COPD is 1300 cases per year against a smaller documented number, suggesting a major diagnostic gap. This may also be true for IA in patients with lung cancer, tuberculosis, sarcoidosis or granulomatous diseases. Mucormycosis is another life-threatening invasive fungal disease responsible for increasing morbidity and mortality [3,5]. Haematological malignancies but also diabetes mellitus or burn patients should also benefit from recent diagnostic and treatment strategies [11].

**Table 1** Burden of serious fungal infections in France.  
*Poids épidémiologique des infections fongiques graves en France.*

Infection	Number of infections per underlying disorder per year					Rate/100K	Total burden
	None/other	HIV/AIDS	Respiratory	Cancer/Tx	ICU		
ABPA	—	—	95,331	—	—	145	95,331
SAFS	—	—	124,678	—	—	189	124,678
Chronic pulmonary aspergillosis	—	—	3450	—	—	5.24	3450
Invasive aspergillosis	151	17	97	800	120	1.8	1185
Mucormycosis	10	—	—	69	—	0.12	79
<i>Pneumocystis</i> pneumonia	61	449	4	144	—	1	658
Candidaemia	533	28	85	1134	590	3.6	2370
<i>Candida</i> peritonitis	249	—	—	—	237	0.74	486
Oesophageal candidiasis	—	9075	—	?	—	13.8	9075
Recurrent vaginal candidiasis (4 × /year +)	730,690	—	—	—	—	2220 <sup>a</sup>	730,690
Cryptococcosis	32	76	2	21	—	0.2	131
Total burden estimated	731,726	9645	223,647	2168	947		968,143

<sup>a</sup> Rate for adult females only.



**Figure 1** Distribution of dermatophyte species responsible for *tinea capitis* in France ( $n = 808$ ; counts from 34 hospitals for 2014). *Distribution des espèces de dermatophytes responsables de teignes du cuir chevelu en France ( $n = 808$  ; données de 34 hôpitaux français en 2014).*

The number of opportunistic infections caused by the fungus *Pneumocystis jirovecii* may also be insufficiently documented because of changing patterns in the risk factors. AIDS-related *P. jirovecii* pneumonia is now less common than is PCP associated with other types of immunosuppression [41]. This shift must question the eligible populations for chemoprophylaxis with regards to level of risk. In particular, a monocenter study showed high incidences in patients with polyarteritis nodosa, granulomatosis with polyangiitis, polymyositis/dermatopolymyositis, acute leukemia, chronic lymphocytic leukemia, and non-Hodgkin lymphoma [17]. It is now recommended that PCP must be screened for during haematological malignancies because only prophylaxis and early treatment allow an optimal outcome [30]. The low number of estimated cases (658/year) using mainly classical diagnostic tools such as light and immunofluorescent microscopy will have to be reassessed after the implementation of the more sensitive PCR detection in most the laboratories [39].

Regarding yeasts, the management of critically ill patients has so much improved during the last decades that it yielded increased survival of patients with complex medical and surgical issues, among them *Candida* infections. Invasive candidiasis is the main cause of IFIs with various clinical presentations from intra-abdominal infections to deep-seated infections and candidaemia, particularly diagnosed in intensive care units. Invasive candidiasis affects worldwide more than 250,000 people each year with estimated incidence rates of candidaemia reported to be between 2 and 14 cases per 100,000 persons in population-based studies [25]. Between 2002 and 2010, an active hospital-based surveillance program of episodes of candidaemia in the Paris area (24 tertiary care hospitals) revealed a significantly increased incidence in the overall population and ICU [29]. The total estimation for France is more than 2000 cases/year leading to an incidence of 3.6/100,000 persons (Table 1).

*Candida peritonitis* still remains a severe disease with a mortality rate of 38%, as high as for candidaemia, without

any specific risk factors for death except those related to underlying diseases and severity of infection and the importance of early source control [33,34,47]. Using our population-based estimation model, *Candida peritonitis* affects 486 estimated cases/year (0.74/100,000 persons). Besides, *Candida* is also responsible for less severe infections which have a significant impact on the quality of life of many people [2,7,18,22,31]. Oesophageal candidiasis in HIV infection only rate is 13.8/100,000, and recurrent vaginal candidiasis incidence is estimated 2220/100,000 for adult females, a lower rate than in various European countries and USA [18]. There is however a need for adjusting such potential high burdens with additional studies that undoubtedly are lacking in France. The rate of 0.2/100,000 inhabitants in France for cryptococcosis is well documented and relies on a strong knowledge of the epidemiology with diagnostic facilities in nearly all French hospitals [5]. Incidence progressively decreased in France as in other countries for HIV co-infected patients who benefit from highly active antiretroviral therapy, but vigilance must remain for non HIV immunosuppressed patients [21].

Finally, this work was an opportunity for setting up a survey on *tinea capitis*. Dermatophyte isolation and identification is an old tradition for the network of mycology labs. The exact count of *tinea capitis* cases recorded in 2014 from 34 representative hospitals is 808 cases. The national prevalence remains to be estimated at the level of the whole population, particularly in the migrant population that can escape medical attention. Fig. 1 represents the biodiversity of dermatophytes responsible for *tinea capitis* and a huge predominance of anthropophilic dermatophytes is observed.

## Conclusion

LIFE ([www.LIFE-worldwide.org](http://www.LIFE-worldwide.org)) has launched an international initiative to estimate the burden of fungal diseases following a similar approach in many countries. Using local and literature data of the incidence or prevalence of serious fungal infections, approximately 1000,000 (1.47%) people in

France are estimated to suffer from serious fungal infections each year (with the exclusion of superficial skin and nail infections). Beside a good evaluation of 5000 cases/year of invasive fungal diseases, recurrent vaginitis and chronic and immunoallergic pulmonary diseases represent a serious impact on human health. These estimates are similar while slightly less than those from Germany and Belgium. Prospective or comprehensive registry surveys are required to accurately determine their epidemiology and improve the management of these disorders.

## Disclosure of interest

The authors declare that they have no competing interest.

## Acknowledgements

The authors want to underline the major role of the National Reference Center for invasive fungal diseases (CNR-MA, Institut Pasteur, Paris) and Institut National de Veille Sanitaire (InVS, Santé Publique France) in the surveillance of fungal infection, as well as the Société Française de Mycologie Médicale SFMM-study group for the *Tinea capitis* survey: Angers (M Pihet), Amiens (A. Totet, T. Chouaki), Besançon (F. Grenouillet), Bordeaux (I. Accoceberry), Brest (E. Moalic), Clermont-Ferrand (C. Nourrisson), Dijon (F. Dalle), Fort-de-France (N. Desbois), Grenoble (D. Maubon), Lille (E. Fréalle), Limoges (B. Bouteille), Lyon (A.L. Bienvenu), Marseille (S. Ranque), Montpellier (P. Rispaill), Nancy (M. Machouart), Nantes (P. Le Pape), Nice (M. Gary-Tous-saint), Paris area [Avicennes (S. Brun), Cochin (S. Challier), Georges Pompidou (E. Dannaoui), Henri Mondor (F. Botterel), Necker (M.E. Bounoux), Pitié-Salpêtrière (A. Fekkar), Saint-Antoine (C. Hennequin), Saint-Denis (N. Godineau), Saint-Louis (S. Bretagne)], Poitiers (C. Kauffmann-Lacroix), Reims (D. Toubas), Rennes (S. Chevrier, J.P. Gangneux), Rouen (L. Favennec), Strasbourg (V. Letscher-Bru), Tarbes (A.M. Camin-Ravenne), Toulouse (S. Cassaing), Tours (J. Chandener).

## References

- [1] Aballea S, Guelfucci F, Wagner J, Khemiri A, Dietz J-P, Sobel J, et al. Subjective health status and health-related quality of life among women with recurrent vulvovaginal candidosis (RVVC) in Europe and the USA. *Health Qual Life Outcomes* 2013;11:169-21.
- [2] Ambrosioni J, Nicolas D, Agüero F, Manzardo C, Miro JM. HIV treatment outcomes in Europe and North America: what can we learn from the differences? *Expert Rev Anti Infect Ther* 2014;12:523-6.
- [3] Bitar D, Van Cauteren D, Lanternier F, Dannaoui E, Che D, Dromer F, et al. Increasing incidence of zygomycosis (mucormycosis), France, 1997-2006. *Emerg Infect Dis* 2009;15:1395-401.
- [4] Bitar D, Morizot G, Van Cauteren D, Dannaoui E, Lanternier F, Lortholary O, et al. Estimating the burden of mucormycosis infections in France (2005-2007) through a capture-recapture method on laboratory and administrative data. *Rev Epidemiol Sante Publique* 2012;60:383-7.
- [5] Bitar D, Lortholary O, Le Strat Y, Nicolau J, Coignard B, Tattévin P, et al. Population-based analysis of invasive fungal infections, France, 2001-2010. *Emerg Infect Dis* 2014;20:1163-9.
- [6] Brown GD, Denning DW, Gow NAR, Levitz SM, Netea MG, White TC. Hidden killers: human fungal infections. *Sci Transl Med* 2012;4:165rv13.
- [7] Buchacz K, Baker RK, Palella FJ, Chmiel JS, Lichtenstein KA, Novak RM, et al. AIDS-defining opportunistic illnesses in US patients, 1994-2007: a cohort study. *AIDS* 2010;24:1549-59.
- [8] Cahill BC, Hibbs JR, Savik K, Juni BA, Dosland BM, Edin-Stibbe C, et al. *Aspergillus* airway colonization and invasive disease after lung transplantation. *Chest* 1997;112:1160-4.
- [9] Camuset J, Nunes H, Dombret MC, Bergeron A, Henno P, Philippe B, et al. Treatment of chronic pulmonary aspergillosis by voriconazole in nonimmunocompromised patients. *Chest* 2007;131:1435-41.
- [10] Chen J, Yang Q, Huang J, Li L. Risk factors for invasive pulmonary aspergillosis and hospital mortality in acute-on-chronic liver failure patients: a retrospective-cohort study. *Int J Med Sci* 2013;10:1625-31.
- [11] Cornely OA, Cuenca-Estrella M, Meis JF, Ullmann AJ. European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Fungal Infection Study Group (EFISG) and European Confederation of Medical Mycology (ECMM) 2013 joint guidelines on diagnosis and management of rare and emerging fungal diseases. *Clin Microbiol Infect* 2014;20(Suppl. 3):1-4.
- [12] Denning DW, O'Driscoll BR, Hogaboam CM, Bowyer P, Niven RM. The link between fungi and severe asthma: a summary of the evidence. *Eur Respir J* 2006;27:615-26.
- [13] Smith NL, Denning DW. Underlying conditions in chronic pulmonary aspergillosis including simple aspergilloma. *Eur Respir J* 2011;37:865-72.
- [14] Denning DW, Pleuvry A, Cole DC. Global burden of allergic bronchopulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults. *Med Mycol* 2013;51:361-70.
- [15] Denning DW, Pashley C, Hartl D, Wardlaw A, Godet C, Del Giacco S, et al. Fungal allergy in asthma-state of the art and research needs. *Clin Transl Allergy* 2014;4:14.
- [16] Denning DW, Cadranet J, Beigelman-Aubry C, Ader F, Chakraborti A, Blot S, et al. Chronic pulmonary aspergillosis: rationale and clinical guidelines for diagnosis and management. *Eur Respir J* 2016;47:45-68.
- [17] Filattre P, Decaux O, et al. Incidence of *Pneumocystis jirovecii* pneumonia among groups at risk in HIV-negative patients. *Am J Med* 2014;127:1242.e11-17.
- [18] Foxman B, Muraglia R, Dietz J-P, Sobel JD, Wagner J. Prevalence of recurrent vulvovaginal candidiasis in 5 European countries and the United States: results from an internet panel survey. *J Low Genit Tract Dis* 2013;17:340-5.
- [19] Gangneux J-P, Camus C, Philippe B. Epidemiology of invasive aspergillosis and risk factors in non neutropaenic patients. *Rev Mal Respir* 2010;27:e34-46.
- [20] Godet C, Laurent F, Béraud G, Toper C, Camara B, Philippe B, et al. Phenotyping chronic pulmonary aspergillosis by cluster analysis. *Eur Respir J* 2015;46:1509-12.
- [21] Hajjeh RA, Conn LA, Stephens DS, Baughman W, Hamill R, Graviss E, et al. Cryptococcosis: population-based multistate active surveillance and risk factors in human immunodeficiency virus-infected persons. *Cryptococcal Active Surveillance Group*. *J Infect Dis* 1999;179:449-54.
- [22] Hamers FF, Downs AM. The changing face of the HIV epidemic in western Europe: what are the implications for public health policies? *Lancet* 2004;364:83-94.
- [23] Herbrecht R, Bories P, Moulin J-C, Ledoux M-P, Letscher-Bru V. Risk stratification for invasive aspergillosis in immunocompromised patients. *Ann N Y Acad Sci* 2012;1272:23-30.
- [24] Herbrecht R, Caillot D, Cordonnier C, Auvrignon A, Thiebaut A, Baruchel A, et al. Indications and outcomes of antifungal therapy in French patients with hematologic conditions or

- recipients of hematopoietic stem cell transplantations. *J Antimicrob Chemother* 2012;67:2731–8.
- [25] Kullberg BJ, Arendrup MC. Invasive candidiasis. *N Engl J Med* 2015;373:1445–56.
- [26] Lagrou K, Maertens J, Van Even E, Denning DW. Burden of serious fungal infections in Belgium. *Mycoses* 2015;58(Suppl. S5):1–5.
- [27] Le Cann P, Paulus H, Glorennec P, Le Bot B, Frain S, Gangneux JP. Home environmental interventions for the prevention or control of allergic and respiratory diseases: what really works. *J Allergy Clin Immunol Pract* 2016 [pii : S2213-2198(16)30313-0].
- [28] Lortholary O, Gangneux J-P, Sitbon K, Lebeau B, de Monbrison F, Le Strat Y, et al. Epidemiological trends in invasive aspergillosis in France: the SAIF network (2005-2007). *Clin Microbiol Infect* 2011;17:1882–9.
- [29] Lortholary O, Renaudat C, Sitbon K, Madec Y, Denoeud-Ndam L, Wolff M, et al. Worrisome trends in incidence and mortality of candidemia in intensive care units (Paris area, 2002-2010). *Intensive Care Med* 2014;40:1303–12.
- [30] Maschmeyer G, Helweg-Larsen J, Pagano L, Robin C, Cordonnier C, Schellongowski P. 6th European Conference on Infections in Leukemia (ECIL-6), a joint venture of The European Group for Blood and Marrow Transplantation (EBMT), The European Organization for Research and Treatment of Cancer (EORTC), the International Immunocompromised Host Society (IHS) and The European LeukemiaNet (ELN). ECIL guidelines for treatment of *Pneumocystis jirovecii* pneumonia in non-HIV-infected haematology patients. *J Antimicrob Chemother* 2016;71:2405–13.
- [31] Matee M, Scheutz F, Moshy J. Occurrence of oral lesions in relation to clinical and immunological status among HIV-infected adult Tanzanians. *Oral Dis* 2000;6:106–11.
- [32] Michallet M, Gangneux JP, Lafuma A, Herbrecht R, Ribaud P, Caillot D, et al. Cost effectiveness of posaconazole in the prophylaxis of invasive fungal infections in acute leukaemia patients for the French healthcare system. *J Med Econ* 2011;14:28–35.
- [33] Montravers P, Mira J-P, Gangneux J-P, Leroy O, Lortholary O, AmarCand study group. A multicentre study of antifungal strategies and outcome of *Candida* spp. peritonitis in intensive-care units. *Clin Microbiol Infect* 2011;17:1061–7.
- [34] Montravers P, Dupont H, Eggimann P. Intra-abdominal candidiasis: the guidelines-forgotten non-candidemic invasive candidiasis. *Intensive Care Med* 2013;39:2226–30.
- [35] Pagano L, Caira M, Candoni A, Offidani M, Fianchi L, Martino B, et al. The epidemiology of fungal infections in patients with hematologic malignancies: the SEIFEM-2004 study. *Haematologica* 2006;91:1068–75.
- [36] Perkhofers S, Lass-Flörl C, Hell M, Russ G, Krause R, Hönl M, et al. The Nationwide Austrian *Aspergillus* Registry: a prospective data collection on epidemiology, therapy and outcome of invasive mould infections in immunocompromised and/or immunosuppressed patients. *Int J Antimicrob Agents* 2010;36:531–6.
- [37] Persat F, Hennequin C, Gangneux JP. *Aspergillus* antibody detection: diagnostic strategy and technical considerations from the Société Française de Mycologie Médicale (French Society for Medical Mycology) expert committee. *Med Mycol* 2016 [2016:pii:myw078].
- [38] Pfaller MA. Antifungal drug resistance: mechanisms, epidemiology, and consequences for treatment. *Am J Med* 2012;125: S3–13.
- [39] Robert-Gangneux F, Belaz S, Revest M, Tattevin P, Jouneau S, et al. Diagnosis of *Pneumocystis jirovecii* pneumonia in immunocompromised patients by real-time PCR: a 4-year prospective study. *J Clin Microbiol* 2014;52:3370–6.
- [40] Rodriguez Tudela J-L, Alastruey-Izquierdo A, Gago S, Cuenca-Estrella M, Leon C, Miro JM, et al. Burden of serious fungal infections in Spain. *Clin Microbiol Infect* 2015;21:183–9.
- [41] Roux A, Canet E, Valade S, Gangneux-Robert F, Hamane S, Lafabrie A, et al. *Pneumocystis jirovecii* pneumonia in patients with or without AIDS, France. *Emerg Infect Dis* 2014;20: 1490–7.
- [42] Ruhnke M, Groll AH, Mayser P, Ullmann AJ, Mendling W, Hof H, et al. Estimated burden of fungal infections in Germany. *Mycoses* 2015;58(Suppl. S5):22–8.
- [43] Singh N. Invasive aspergillosis in organ transplant recipients: new issues in epidemiologic characteristics, diagnosis, and management. *Med Mycol* 2005;43(Suppl. 1):S267–70.
- [44] Siroux V, Pin I, Pison C, Kauffmann F. Asthme severe en population générale : définitions et prevalence. *Rev Mal Resp* 2004;21:961–9.
- [45] Sobel JD. Recurrent vulvovaginal candidiasis. *Am J Obstet Gynecol* 2016;214:15–21.
- [46] To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health* 2012;12:204.
- [47] Vergidis P, Clancy CJ, Shields RK, Park SY, Wildfeuer BN, Simmons RL, et al. Intra-abdominal candidiasis: the importance of early source control and antifungal treatment. *Plos One* 2016;11:e0153247.
- [48] Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998;12:315–35.