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Diagnosis, Therapy and Prophylaxis of Fungal Diseases

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ABSTRACTS

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different groups of microorganisms involved in respiratory diseases (fungi, bacteria, dust mites).

Material and methods In our study, ten specific qPCR targets (six fungal species, one family and two genera of bacteria, one house dust mite) were used to analyze the microorganism composition of electrostatic dust fall collector (EDC) (Scherer E *et al.*, 2014) from 3193 dwellings of the Elfe French cohort study (Etude Longitudinale Française depuis l'Enfance). Multivariate analyses allowed us to show that the microbial composition of dwellings, assessed with simultaneous analysis of 10 microorganisms, can be characterized by four entities: three bacteria, house dust mite *Dermatophagoides pteronyssinus*, fungi *Alternaria alternata*, and five other molds.

Results Some dwellings' intrinsic characteristics (occupational ratio, type of dwelling and presence of pets) clearly influence microorganism distribution, and six different profiles of dwellings, characterized by their composition in microorganisms, have been described across France: Clean profile (cluster 1); Bacteria only profile (cluster 2); Bacteria and *A. alternata* profile (cluster 3); Bacteria and mite profile (cluster 4); High level of all microorganisms profile (cluster 5); High bacteria and *A. alternata* levels profile (cluster 6).

Although all clusters were present in each French region, their occurrence differed greatly. A dominant cluster was identified in each region.

A map of distribution of dominant cluster was made (Rocchi *et al.*, 2015) and compared to the distribution of wheezing in nursery school children (Delmas *et al.*, 2012), a single study conducted throughout France and dealing with a large number of children (>20 000 children). The recovery rate between the two most contaminated clusters (clusters 4 and 5) on our map and the highest wheezing prevalence on Delmas' map (>9.8%) is 85% of the undivided regional area (western France). In the same way, the recovery rate between the two less contaminated clusters (clusters 1 and 3) on our map and the lowest wheezing prevalence on Delmas' map ($\leq 9.8\%$) is 88% of the undivided regional area (eastern France).

Conclusion The use of these clusters seems promising in the evaluation of allergic risk. Allergic respiratory diseases will develop in the near future in some children of the Elfe cohort and will indicate to what extent our approach can be predictive of respiratory disease.

References Scherer E *et al.* Dust sampling and QPCR standard operating procedure for measuring Microorganisms in dwellings in the Elfe study. *Sc Tot Environ* 2014.

Rocchi S *et al.* Microbiological characterization of 3193 French dwellings of Elfe cohort children. *Sc Tot Environ* 2015.

Delmas MC *et al.* Prévalence et contrôle de l'asthme chez le jeune enfant en France. *Rev Mal Respir* 2012.

EORTC/MSG Definitions of invasive fungal diseases - updates & revisions

S14

EORTC/MSG Definitions of invasive fungal diseases - updates & revisions

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Background Even before the revised EORTC/MSG definitions of invasive fungal disease were published in *Clinical Infectious Diseases* in 2008 (De Pauw *et al.* 2008 *Clin Infect Dis* 46:1813–21) the consensus group acknowledged that there were remaining gaps in these definitions that needed to be filled.

Methods Rather than attempt a full revision of the definitions we decided to establish working groups to examine 10 areas needing further clarification. These were: diagnosis (imaging, updates on galactomannan, PCR and beta-D-glucan, tissue diagnosis), special populations (ICU patients and paediatrics) and other disease entities (pneumocystosis, cryptococcosis and endemic mycoses). Some topics were handled jointly, in part or wholly, by other scientific groups. Volunteers from the EORTC IDG and MSG were sought to attain an

equal balance between Europe and other parts of the world and chairs were appointed. Each group was assigned the task of reviewing the literature since the appearance of the revised definitions to see whether or not there was sufficient evidence to justify updating or revising the definitions. Their findings were presented via a web meeting to members of the EORTC IDG and MSG to comment.

Results During this symposium, after a brief introduction each group chair will present the recommendations of its group to the community at large. Audience participation will be encouraged and there will be time for short questions and comments. A general summary will be presented at the end of the meeting.

The clinical and treatment challenges of dermatophytes

S15.1

Onychomycosis: is it possible to increase the cure rate?

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Onychomycosis represent about 50% of nails disorders in the world with a very variable prevalence depending of the countries considered. Dermatophytes, non-dermatophyte molds and *Candida sp.* are the main causing agents. A rapid and accurate diagnosis is essential in order to give an adequate treatment to the patient. Generally, a combination of microscopy and culture is used for laboratory diagnosis. However, microscopy does not always allow the distinction between yeasts or filamentous fungi, culture takes generally about a week before identification and the result is compromised if there is contamination by not relevant fungi. Therefore commercially available PCR-based methods have been developed in order to provide a rapid and accurate identification of dermatophytes and yeasts in nails samples. Combination of microscopy and PCR may provide a rapid and specific diagnosis in 2 working days. However this methodology is still not widely used by laboratories because of the high cost. Furthermore, this technology can detect DNA from dead fungi and therefore is not suitable for assessment of treatment efficacy.

Onychomycosis therapy depends on different factors such as the causative agent, the number of nails and degree of nail involvement, the type of onychomycosis, potential drug interactions or drug intolerance and a failure to previous treatments. Oral and topical antifungals are mostly used separately or in combination. Oral therapy includes azoles (itraconazole, fluconazole) and/or allylamine (terbinafin), this latter being the most frequently prescribed antifungal for treatment of onychomycosis in North America and Europe. Topical amorolfine and ciclopirox formulations can be used alone in mild cases or in case of intolerance to oral antifungals. However, one of the biggest problems of therapy for onychomycosis is the high frequency of relapse which concerns about 20 to 40% of the patients treated by oral antifungals. Different strategies have been developed to overcome this problem amongst which are: optimization of the dosing regimens (continuous vs pulse therapy) or therapy duration, combination therapy (nail debridement + antifungals, oral + topical drugs, 2 oral drugs), improving drug delivery (use of physical or chemical enhancers, and modification of the pharmacological formulation for increasing drug uptake). Some strategies such as combination therapy (oral + topical) have demonstrated enhanced efficacy and should be recommended in case of poor efficacy of the initial treatment or in case of extended infection. Prophylactic topical therapy implemented after completion of oral treatment has been shown to delay relapse. Preventive measures such as treatment of concurrent tinea pedis and/or infected family members and regular cleaning of bathroom and shower floors can help to reduce the risk of reinfection particularly when a dermatophyte is the causative agent.

In conclusion, treatment for onychomycosis is associated with frequent relapse. Consequently, follow-up is mandatory and combination therapy can be necessary in case of relapse or resistance to treatment. Patients should also be aware of the preventive hygiene

measures to apply in order to decrease the risk of reinfection. New strategies improving treatment efficacy are promising but their efficacy have still to be demonstrated in comparative clinical trials before their implementation in therapy.

S15.2

Tinea capitis: import, export and epidemics?

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The predominant etiologic pathogen of tinea capitis, a dermatophyte infection of the hair, differs between geographical regions and may change over time. The anthropophilic dermatophytes such as e.g. *Trichophyton* (*T.*) *violaceum*, *T. tonsurans*, and *Microsporum* (*M.*) *audouinii* may cause epidemics especially among children, whereas zoophilic dermatophytes, such as *M. canis*, are transferred sporadically from animals to humans. Anthropophilic infections may also be 'exported' from an area with a high prevalence to an area with low prevalence due to tourism or family visits. As the clinical picture of an anthropophilic infection is less inflammatory than a zoophilic infection, this may cause a diagnostic delay until the local physician recognizes the 'import' of an anthropophilic dermatophyte. This presentation will focus on trends in epidemiology and the diagnostic challenges and the clinical impact.

S15.3

Tinea incognita

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Tinea incognita is a fungal infection in which topical or systemic steroids as well as topical application of calcineurin inhibitors, have modified the clinical appearance of the mycosis and mimicking other skin diseases.

Clinical entity could be presented in various clinical forms ranging from lupus erythematosus discoid-like, eczema-like, rosacea-like, impetigo-like dermatitis, but it can resemble psoriasis, purpura, seborrhoeic dermatitis and lichen planus. Physical examination usually revealed plaques with erythema and papules on the treated area, along with pruritus.

The diagnosis is confirmed by direct microscopic examination of the skin scrapings with 10% potassium hydroxide preparation including culture.

Complete clinical resolutions is observed with oral and topical antimycotic treatment.

Tinea incognita is not a rare clinical entity. Atypical erythematous plaques should be investigated in terms of presence of fungi and treated accordingly to establish total clinical and mycological cure.

S15.4*

Increase of *Trichophyton tonsurans* in the urban area of Paris: a 4-year long study

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Objectives Tinea capitis (TC) is due to different keratinophilic fungi and remains a major public health concern in pediatric population in

urban areas. The dermatophytes responsible for TC can be divided into three major groups according to their reservoir and transmission: anthropophilic, zoophilic, and geophilic species. Our objective was to analyze the epidemiology of TC in Paris, France.

Methods We included all the patients seen from January 2011 to December 2014 in our laboratory for suspicion of TC. Suspected lesions were sampled and epidemiological data (age, gender, geographical origin, and familial links) were recorded. After a direct microscopic examination, hair samples were seeded on Sabouraud medium agar slant and kept 3 weeks at 26 °C. The species identification was based on macroscopic and microscopic examination.

Results We obtained 2739 samples from 2522 patients (sex ratio 0.95; median age: 7 years, range: 1 month to 89 years). We observed a positive direct examination and/or a positive culture for 1084 patients (43%) with an overrepresentation of boys (75.4 %) between 5 and 6 years. The anthropophilic species were predominant (96%) with three major species: *Trichophyton soudanense*, *Trichophyton tonsurans*, and *Microsporum audouinii* var *langeronii* (39.1%, 31%, 29.9% in 2011; 41.2%, 30.7%, 28.1% in 2012; 40.2%, 28.4%, 31.4% in 2013; and 36%, 39.2%, 25.8% in 2014, respectively). Therefore, *T. tonsurans* was the first species isolated in 2014 in the global population. For a given family ($n = 246$, 2 to 6 members), the same species was identified when several TCs were diagnosed. Therefore, we considered one family as one case to analyze the evolution over time. The main striking result was the increase of *T. tonsurans* in the sub-Saharan African cases ($n = 522$ cases), mainly at the expense of *M. langeronii*, *T. soudanense* remaining stable (Figure 1). For the Caribbean cases ($n = 84$ cases), *T. tonsurans* was the main agent of TC and stable over the studied period, although *T. soudanense* was present, suggesting transmission between communities.

This increase of *T. tonsurans* in the sub-Saharan patients could be due to a better fitness of this species for transmission between individuals through community contacts or by common hairdressers. Another explanation could be the less susceptibility of *T. tonsurans* to griseofulvin, the main agent used in the pediatric population to treat TC.

Conclusion This 4-year comprehensive observation showed that *T. tonsurans* became in 2014 the major agent of TC in the urban area of Paris, as already reported in London. Although British and American guidelines support terbinafine as the first choice to treat *Trichophyton* TCs, the French recommendation is griseofulvin since terbinafine does not have governmental approval in children. These recommendations could be challenged in case of continuous increase of *T. tonsurans* in TC.

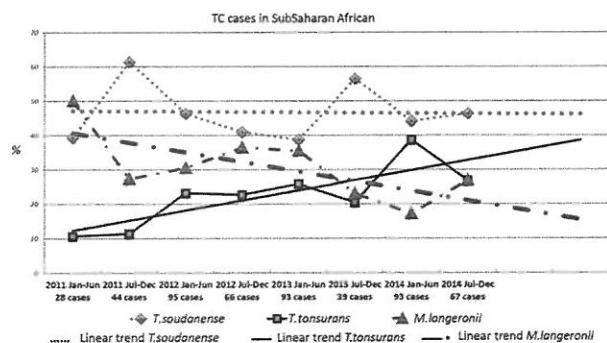


Figure 2 Evolution over time and trends of the three main anthropophilic dermatophytes in sub-Saharan African cases. When multiple members of one fam.