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► To cite this version:

Jean-Pierre Gangneux, Sophie Brun, Jean Menotti, Françoise Botterel. Role of the mycological diagnosis in the management of tinea capitis: French recommendations in the post-griseofulvin era. *Journal of Medical Mycology = Journal de Mycologie Médicale*, 2023, 33 (3), pp.101379. 10.1016/j.mycmed.2023.101379 . hal-04099840

HAL Id: hal-04099840

<https://hal.science/hal-04099840>

Submitted on 23 May 2023

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Role of the mycological diagnosis in the management of *tinea capitis*: French recommendations in the post-griseofulvin era

Jean-Pierre Gangneux^{a,b}, Sophie Brun^{c,d}, Jean Menotti^e, Françoise Botterel^{f,g}, Présidente of French Society of Medical Mycology

^a Laboratoire de Parasitologie et Mycologie Médicale, LA-AspC Centre National de Référence des Mycoses et Antifongiques, European Excellence Center for Medical Mycology (ECMM), Centre hospitalier Universitaire de Rennes, F-35000 Rennes, France

^b Univ Rennes, CHU Rennes, Inserm, EHESP, Irset (Institut de recherche en santé environnement et Travail) – UMR_S 1085, F-35000 Rennes, France

^c Service de Parasitologie-Mycologie, Hôpital Avicenne, AP-HP, 93009 Bobigny, France.

^d Faculté de Médecine, Université Sorbonne Paris Nord, 93009 Bobigny, France

^e Service de Parasitologie-Mycologie, Institut des Agents Infectieux, Hospices civils de Lyon, 69004 Lyon, France

^f Unité de Parasitologie-Mycologie, Département de Prévention, Diagnostic et Traitement des Infections, CHU Henri Mondor, Assistance Publique des Hôpitaux de Paris (APHP), France

^g UR DYNAMYC 7380, Faculté de Santé, Univ Paris-Est Créteil (UPEC), EnvA, USC ANSES, Créteil, France

Corresponding author: Françoise Botterel, francoise.botterel@aphp.fr

Key-words: *tinea capitis*, mycology diagnosis, griseofulvin, terbinafin, itraconazole

The management of *tinea capitis* has significantly evolved since 2021. Indeed, on that date, the griseofulvin, the only systemic treatment marketed in France for this indication, was withdrawn from the French market due to manufacturing issues. Strategies with other

molecules had to be analyzed and mycological diagnosis became essential at different stages of management (1).

In this context, a multidisciplinary task force composed of dermatologists, mycologists, pediatricians, and infectious disease specialists proposed an algorithm for the management and follow up of *tinea capitis* after a review of the literature and of international guidelines and based on their own expertise. The algorithm (Figure 1) and its supplemental pieces of information were approved by the French Agency called Agence nationale de sécurité du médicament et des produits de santé (ANSM) in July 9, 2021 (<https://ansm.sante.fr/actualites/traitement-de-la-teigne-de-lenfant-et-indisponibilite-de-la-griseofulvine-lansm-precise-la-conduite-a-tenir>) (2).

Treatment of *tinea capitis* in children ≥ 10 kgs now relies on two drugs: (i) terbinafine is preferred for *tinea capitis* due to *Trichophyton* spp. and (ii) itraconazole for *Microsporum* spp. infection. For children weighing ≥ 10 kg, the oral terbinafine regimen (once daily with a meal) for 4 weeks should be adapted to the child's weight with 62.5 mg/d for 10 to 20 kg; 125 mg/d for 21 to 40 kg and 250 mg/d for > 40 kg. If oral itraconazole (once daily without food) was chosen, the dosing regimen is 50 mg/d for 10 to 20 kg; 100 mg/d for > 20 kg for 6 weeks. Most often, terbinafine is given as a probabilistic treatment even if mycologists prefer to have the result of the hair parasitism to prescribe itraconazole when *tinea capitis* is microsporic (30% of the cases in France) (3). In addition to systemic treatment, topical antifungal drugs as well as complementary measures (screening of parents, siblings, and animals; bed linen in contact with the head washed at 60°C, ...) are highly recommended (4). Most often, terbinafine is given as a probabilistic treatment even if mycologists prefer to have a direct hair examination to decide between microsporic and trichophytic *tinea capitis* and prescribe itraconazole when the *tinea capitis* is microsporic.

Access to mycological diagnosis may be difficult and must not delay the initiation of treatment. Because French epidemiological data show that *Trichophyton* species represent more than 70% of *tinea capitis* cases, especially with *T. soudanense*/*T. violaceum* and *T. tonsurans* (2), the algorithm proposes the possibility of a probabilistic treatment with terbinafine as the first-line.

However, identification of the causal dermatophyte is essential to drive the choice of the drug and the mycological diagnosis is also fundamental to reevaluate the prescription and for the follow up :

- *Identification of the causal dermatophyte.* Clinical examination and Wood light can orient towards a trichophytic, a microsporic, or an inflammatory *tinea capitis* but without intangible result. Only direct examination of the hair parasitism combined with culture and/or molecular identification will allow the exact identification of the genus and species in most of cases. In addition to prescription assistance, these epidemiological data are important to know the species of dermatophytes circulating in a region or country. Indeed, these data may be evolutive, depending on the environment of the fungus, whether for humans (anthropophilic contamination), for the environment (telluric contamination) and for animals (zoophilic contamination) and must therefore be analysed to adapt prevention.

- *Reevaluation of the drug choice after 4 weeks of antifungal treatment.* If *Trichophyton* spp. is confirmed by the culture, terbinafine is stopped after 4 weeks. When a probabilistic treatment with terbinafine for four weeks has been initiated and a *Microsporum* species has been obtained in culture, then it is proposed to switch to itraconazole for 2 weeks or to continue terbinafine for 2 weeks if the evolution is favorable.

- *Management of failure.* After checking the correct dosage, duration, and intake of oral treatments, it is essential to examine a microbiological cause of failure: identification of the

unavailable dermatophyte and/or search for intrinsic resistance. The resistance of dermatophytes to terbinafine and itraconazole is now well documented worldwide and methods for *in vitro* determination of antifungal sensitivity are now proposed (5, 6). In parallel, molecular tools to detect mutations in squalene epoxidase gene for terbinafine and in 14-alpha-demethylase gene for itraconazole that are associated with *in vitro* resistance are now available (4,5). However, such analyzes can only be carried out in expert mycology laboratories in university hospitals.

Tinea capitis is still a common contagious dermatophyte infection of the scalp and hair that predominantly occurs in children. Cases frequently spread in an epidemic mode within families or schools or kinder gardens. The withdraw of griseofulvin previously used in all forms of *tinea capitis* has made its management significantly more complex. This difficulty is especially notable in infants under 10 kgs where itraconazole and terbinafin are difficult to use in terms of marketing authorization, galenic, dosage, However, *tinea capitis* predominates in healthy preadolescent children aged 6-10 years; infants are less frequently affected. A survey by the French Society of Medical Mycology conducted in July 2022 asked mycology laboratories in French university hospitals caring for children under 1 year of age and/or under 10 kgs, whether they had been involved in the management of *tinea capitis* between June 1, 2021 and June 30, 2022. Out of eight French centres (Bobigny, Grenoble, Lyon, Nantes, Nice, Montpellier, Rennes, Tours) that treated *tinea capitis* in children, only one centre (Rennes) took care of children under 1 year of age (n = 3) who were treated with topical antifungals (n = 2) and fluconazole (n = 1). These very small children are therefore rarely affected by *tinea capitis* and it is essential to collect them for an accurate diagnosis and probably to use a biological monitoring.

Because of this paradigm shift in the management of *tinea capitis* in children in France, various prospective studies need to be undertaken between paediatricians, dermatologists, and

mycologists, especially to know how to manage difficult cases, low weight < 10 kgs, terbinafine and itraconazole resistance.

Acknowledgments to the French Society of Dermatology (S. Barbarot, M. Beylot-Barry, O. Chosidow, B. Guillot, N. Dupin, A. Maruani), the French Paediatric Society (M. Caseris, J. Toubiana) and the French Society of Pharmacology and Therapeutics (L. Chouchana).

Disclosure of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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7. Legend of figure

Figure 1. Algorithm for the management of *tinea capitis* in children proposed in the post-griseofulvin era validated by the French agency “Agence nationale de sécurité du médicament et des produits de santé” and published in *Ann Dermatol Venereol* in 2022 thanks to the work of several French Societies: French Society of Dermatology (S. Barborot, M. Beylot-Barry, O. Chosidow, B. Guillot, N. Dupin, A. Maruani); French Society of Medical Mycology (F. Botterel, S. Brun, J.P. Gangneux, J. Menotti), French Paediatric Society (M. Caseris, J. Toubiana), French Society of Pharmacology and Therapeutics (L. Chouchana).

2021

Appendices

- (1) Clinical characteristics of tinea
- (2) Recommendations for children under 10 kg
- (3) Guide for treatment with terbinafine and itraconazole
- (4) Associated measures
- (5) Recommendations in case of treatment failure at 4 weeks

