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GENERAL REVIEW/REVUE GÉNÉRALE

# Chromoblastomycosis and sporotrichosis, two endemic but neglected fungal infections in Madagascar



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**Summary** Chromoblastomycosis and sporotrichosis are endemic fungal infections of tropical and subtropical regions, including Madagascar. The causal fungi develop in the soil or on plants and infect humans through wounds, either directly (wounding by the plant, through thorns, for example), or through the contact of an existing wound with contaminated soil. For this reason, the lesions predominantly occur on the limbs, and these fungi principally infect people working

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outside with bare hands and/or feet. The subcutaneous lesions of chromoblastomycosis are initially nodular, subsequently becoming warty, tumoral, cauliflower-like and pruriginous, which promotes dissemination. The chronic nature of the infection and its progression over long periods lead to highly disabling lesions in essentially rural and agricultural populations. The lesions of sporotrichosis are also nodular, but more ulcerous, and they form an extended chain following the route of the lymph vessels. Pus, squamous or skin biopsy specimens are used for the mycological examination of these mycoses. Treatment depends on the severity and form of the lesions and is based on antifungal drugs sometimes combined with physical methods. There has been no study of these infections for more than two decades in Madagascar, despite the large numbers of cases seen by doctors in all parts of the island. The nature, diversity and distribution of the plants responsible for contamination have not been described in Madagascar. In this review, we described these two endemic mycoses in terms of their epidemiological, mycological, clinical and therapeutic characteristics, focusing particularly on Madagascar, which is one of the leading foci of these two infections worldwide.

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## Introduction

Chromomycosis or chromoblastomycosis (CBM) and sporotrichosis (SPT) are chronic subcutaneous or cutaneo-lymphatic infections found mostly in tropical and subtropical regions [1–4]. Studies carried out by the Institut Pasteur of Madagascar between 1955 and 1994 provided an inventory of the number of cases of CBM and identified this country as the leading focus of this mycosis worldwide. Mean incidence was estimated at about 1/200,000 inhabitants at the time [5]. Since 1994, no further studies on CBM have been performed in Madagascar and no new data have been obtained to update the epidemiological situation [6]. CBM is usually caused by dematiaceous fungi (also known as black yeasts), principally *Fonsecaea pedrosoi* and *Cladophialophora carrionii*. The causal agent of SPT is *Sporothrix schenckii*, a dimorphic hyphomycete [4,7]. Only sporadic cases have been reported in Madagascar, due to the absence of specific surveillance. SPT may be polymorphic and disseminated, with pulmonary forms.

These fungal infections are typical of so-called “mycoses of implantation or inoculation”, because they are linked to traumatic inoculation with the fungus through wounding by the plant or through soil contamination of an existing wound [8,9]. The chronic course and long duration of lesions may result in considerable disability in the absence of treatment. Due to the large number of cases worldwide, their geographic distribution, professional origin, preponderance among the poorest populations in the world and refractory nature, these infections are candidates for inclusion in the WHO list of neglected tropical diseases. In Madagascar, it is rarely possible to confirm clinically suspected infections or to identify the fungal species responsible, because health structures are under-equipped and resources are limited. Given the large number of cases currently being seen by doctors throughout the island, the prevalence of these infections appears to be largely underestimated. In this review, we describe these two fungal infections, focusing on the most recent studies and the situation in Madagascar. We also report preliminary results for the first 28 months of a prospective study currently underway, involving the recruitment of patients

with suspect lesions. The confirmation of infection by mycological and molecular biology methods in this study suggests that these two infections remain highly prevalent in this country.

## Chromoblastomycosis

CBM is a phaeohyphomycosis, but it has a number of clinical and diagnostic features that are pathognomonic and distinguish it from the other diseases of this group, such as mycetoma. Indeed, CBM is a chronic fungal infection of the subcutaneous tissues characterized by warty hyperkeratotic plaques and the presence of fumagoid cells on microscopic examination of squamous samples. The causal fungi develop on living plants or on decomposing plant material in the soils of tropical and subtropical regions.

## Pathogenic agents

The pathogenic agents responsible for CBM are fungi from the phylum Ascomycetes, mostly from the order Chaetothyriales, and family Herpotrichiellaceae. This family includes the black yeasts of the genus *Exophiala* and dematiaceous filamentous fungi, including the causal agents of CBM: *Fonsecaea* spp., *Phialophora verrucosa*, *Cladophialophora carrionii* and *Rhinochrysiella aquaspersa* [10–12]. *F. pedrosoi* is particularly abundant in the Amazon rainforest in Brazil [13]. It was first isolated by Alexandrino Pedroso in 1911 [14] and was subsequently described as *Hormodendrum pedrosoi* by Brumpt in 1922. The genus *Fonsecaea* was established in 1936, by Negroni [15]. Several species of this genus other than *F. pedrosoi* have been implicated in CBM: *F. monophora*, *F. nubica* and *F. pugnacius*. Another species, *F. compacta*, has been reported to be a morphological variant of *F. pedrosoi* [16,17]. A recent study described two new species isolated from thorny plants: *F. erecta* and *F. minima* [18].

*P. verrucosa* was first described by Medlar in 1915 [10]. Several authors have described this fungus as a causal agent of CBM [19] and of phaeohyphomycotic cysts [20].

*C. carrionii* was first identified in the arid regions of South America, Africa and Australia. Trejos described it under the

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