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REVIEW

# Talaromycosis (Penicilliosis) Due to *Talaromyces* (*Penicillium*) *marneffei*: Insights into the Clinical Trends of a Major Fungal Disease 60 Years After the Discovery of the Pathogen

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**Abstract** Talaromycosis (penicilliosis) is a major fungal disease endemic across a narrow band of tropical countries of South and Southeast Asia. The etiologic agent is a thermally dimorphic fungus *Talaromyces* (*Penicillium*) *marneffei*, which was first isolated from a bamboo rat in Vietnam in 1956, but no formal description was published. In 1959, Professor Gabriel Segretain formally described it as a novel species *Talaromyces* (*Penicillium*) *marneffei*, and the human pathogenic potential of the fungus in *Mycopathologia*. The first natural human case of talaromycosis (penicillosis) was reported in 1973 and involved an American minister with Hodgkin's disease who lived in Southeast Asia. Sixty years after the discovery of the pathogen, talaromycosis caused by *T. marneffei* is recognized as an important human disease with the potential to cause high mortality in the absence of proper diagnosis and prompt treatment. Talaromycosis remains a significant infectious complication in HIV/AIDS patients and in patients with other immune defects. The disease is being recognized with an increasing frequency well beyond the traditional endemic areas. The natural reservoirs of *T. marneffei* in wild rodents are well-defined, which links the ecology with the epidemiology of talaromycosis in endemic areas. There is an urgent unmet need for rapid and affordable point-of-care diagnostic tests. We also

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need more clinical studies to define the best therapeutic options for the management of talaromycosis patients.

**Keywords** Talaromycosis · Talaromyces marneffei · Clinical trends · Sixty years · Anniversary

## Introduction

*Talaromyces* (*Penicillium*) *marneffei* is an important thermally dimorphic fungus endemic across a narrow band of tropical South and Southeast Asia [1–5]. The fungus was first isolated from the swollen liver of a bamboo rat (*Rhizomys sinensis*) in Vietnam in 1956, which died spontaneously from the infection [6]. Professor Gabriel Segretain first described the mycology characteristic of *T. marneffei*, and its pathogenesis to a human when he accidentally pricked his finger with a needle filled with *T. marneffei* and developed a small nodule at the site of inoculation in 1959 [7, 8]. In 1959, Prof. Segretain formally described the mycology characteristic of *T. marneffei* and identified it as a novel species. To memory of Hubert Marneffe, director of Pasteur Institute in Indochinae, the fungus was named *Penicillium marneffei*. His important research was published in *Mycopathologia* in 1959. Taxonomically, it was classified into the *Deuteromycotina*, *Hyphomycetes*, subgenus *Penicillium*, and Subgen *Biverticillium* of *Halomycetes* according to its morphology characteristic [7]. Based on phylogenetic analysis and phenotypic analysis, *T. marneffei* was re-classified as a member of the family *Trichocomaceae*, order *Eurotiales*, class *Eurotiomycetes*, division *Ascomycota* in 2011 [9]. This microorganism is the only thermally dimorphic pathogen in over 200 species of *Talaromyces*. When cultured on SDA medium at 25 °C, the colony is velvety yellow–green or gray–green and producing diffusible red pigment in the culture medium. Microscopic morphology shows septate hyphae with branched or unbranched conidiophores with secondary branches. Phialides grouped in brush-like clusters (penicilli) at the end of conidiophores are arranged in whorls; flask-shaped phialides bearing unbranched chains of smooth or rough, and round to ovoid conidia (2–3 µm diameter) are also seen. When cultured at 37 °C or upon entering the human body, conidia convert to the pathogenic yeast phase and divide by fission [10] (Fig. 1).

## Epidemiology and Ecology

### Endemic Regions

*Talaromyces marneffei* is an AIDS-defining illness in South and Southeast Asia, ranking just after tuberculosis and cryptococcosis [1, 11]. The endemic regions of the fungal disease include Northern Thailand, Southern China, Vietnam, Northern India, Hong Kong, and Taiwan [3–5, 12–17]. Travel-related talaromycosis is being increasingly recognized in non-endemic areas such as Australia, Belgium, France, Germany, Japan, the Netherlands, Oman, Sweden, Switzerland, Togo, the United Kingdom, and the USA [18–24]. In China, the highest incidence areas of *T. marneffei* are Guangxi, Guangdong [3, 25]. As the floating population number increases year by year, the disease has traveled far beyond the original epidemic area, and the other 21 provinces and cities have reported cases successively in China [26–28] (Fig. 2). Thus, the prevailing evidence strongly indicates an expansion of the known endemic region.

### Host Susceptibility Risk Factors

HIV-infected individuals with CD4 cell count $< 100$ cells/µL are at particular risk and make up most infections in regions of endemicity [29]. Talaromycosis also has a higher mortality rate than most HIV-associated complications in Southern China [30]. In recent decades, improved treatment of HIV infection with highly active antiretroviral therapy and control of the HIV/AIDS epidemic with other measures has led to a decline in the incidence of *T. marneffei* infection among HIV-infected patients. An increasing number of *T. marneffei* infections have been reported among non-HIV-infected patients with impaired cell-mediated immunity [31]. Immunodeficiency due to anti-IFN-γ autoantibodies is an emerging adult-onset immunodeficiency syndrome associated with severe or persistent infections caused by *T. marneffei* in adult non-HIV-infected patients [32, 33]. The affected patients have high-titer serum neutralizing anti-IFN-γ autoantibodies that inhibit STAT1 phosphorylation and IL-12 production, leading to a severely compromised Th1 response [34]. Talaromycosis was also reported in other secondary immunodeficiency conditions, including autoimmune diseases (systemic lupus erythematosus, connective tissue diseases), cancers, hematological

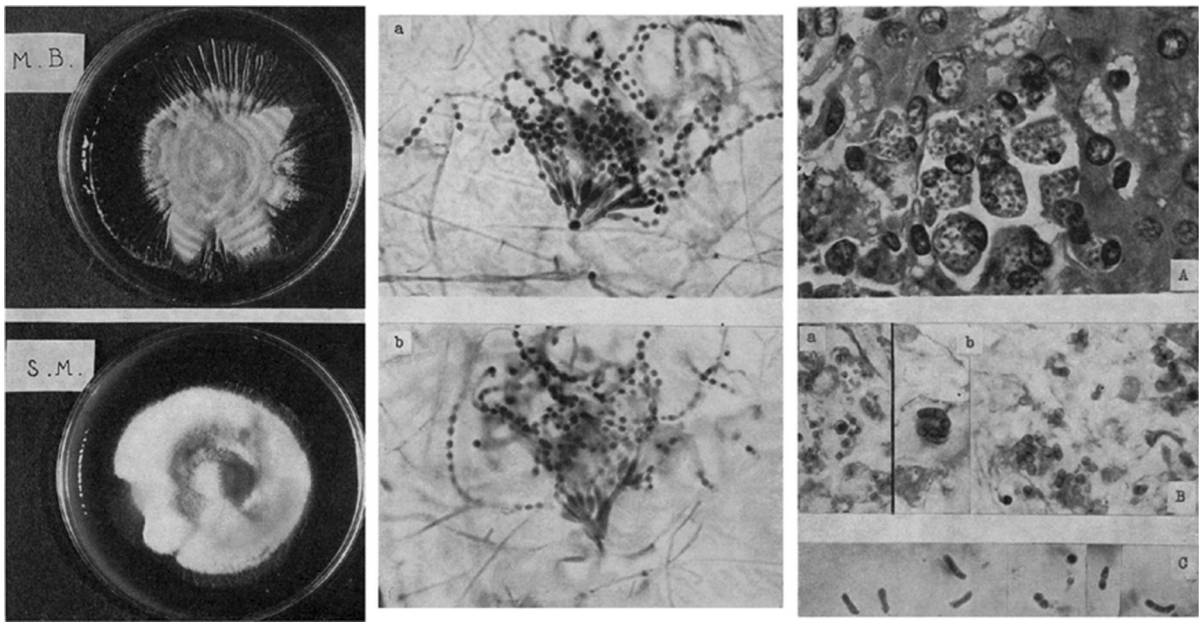


**Fig. 1** Formal characterization of *Penicillium marneffei*, Segretain, *Mycopathologia et Mycologia Applicata*, 1959

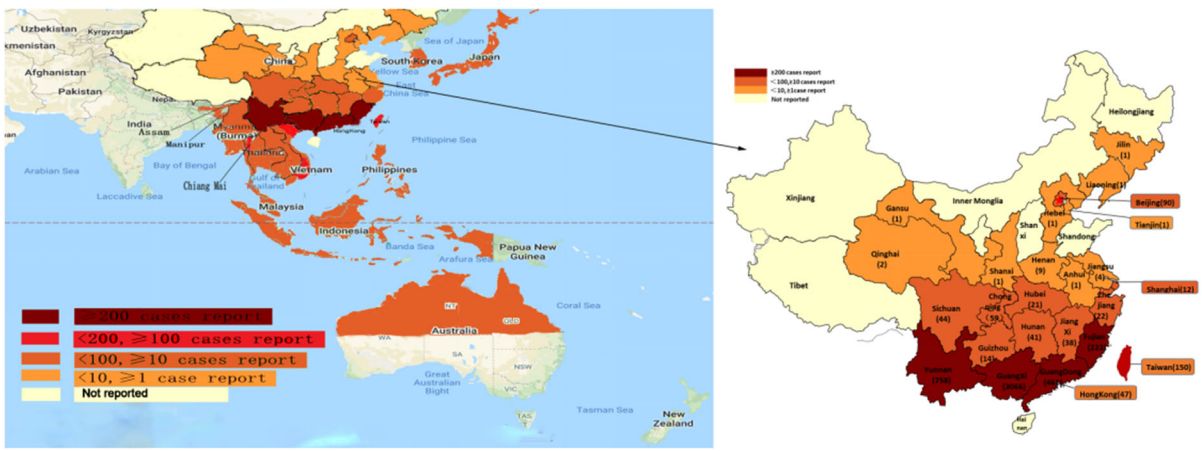


**Fig. 2** Geographical distribution of *Talaromyces marneffei* infection

malignancies, solid organ or hematopoietic stem cell transplantation, and use of novel target therapy such as monoclonal antibodies against CD20 and kinase inhibitors [3, 29, 35–43] (Fig. 3).

The proportion of *T. marneffei* infection is about 6–7.5% in reported cases of talaromycosis in which patient's age ranged from 3 months to 16 years [25, 44]. Unlike the previous reports with most HIV-infected pediatric cases, recent studies showed most pediatric patients were HIV negative [45]. In recent years, improved immunological investigation and genetic studies identified various forms of immune-related underlying diseases and primary immunodeficiency (PIDs) associated with *T. marneffei* infection in children, including leukemia, hyper-IgM syndrome, hyper-IgE syndrome, mutations in *CYBB*, *CD40L*, or gain-of-function mutation in *STAT1/STAT3* pathway, resulting in a functional defect of the IFN-gamma and IL-17 immune response [44, 46–49]. Hence, the epidemiology of *T. marneffei* infection transformed in the past three decades. *T. marneffei* infection is not limited to HIV-infected patients. This suggests that

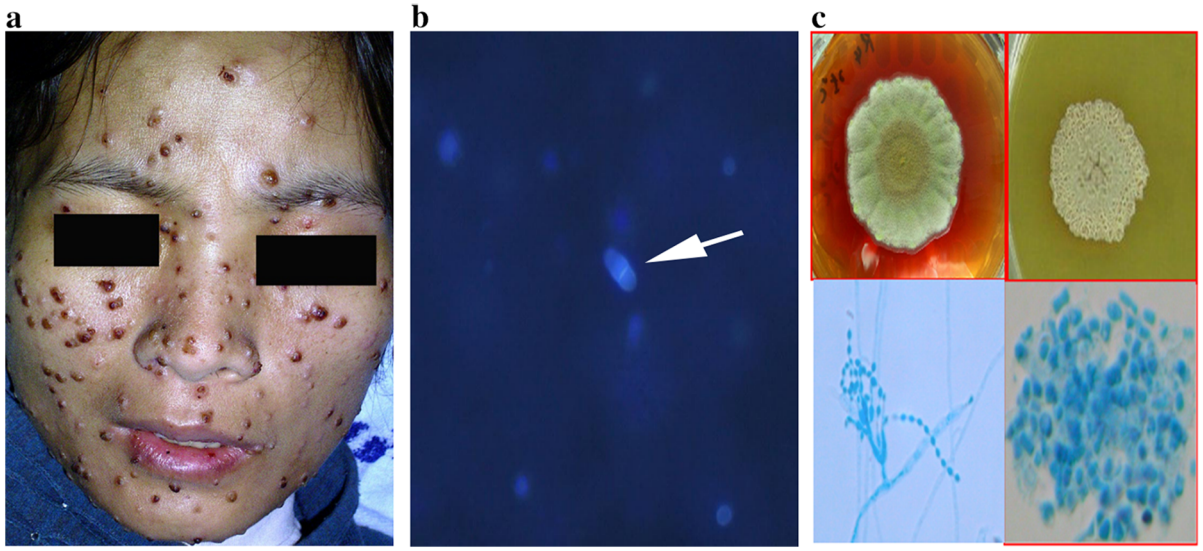


**Fig. 3** Features of talaromycosis in patients with HIV. Photograph of skin lesions in a patient with talaromycosis (**a**). Fluorescence-stained touch skin smear showing sausage-like shapes yeast organisms. The arrowhead highlights the midline septum in a dividing yeast cell characteristic of *Talaromyces marneffei* (**b**). Morphology of *T. marneffei* colonies and *T. marneffei* cells grown at 25 °C and at 37 °C on Sabouraud agar medium (**c**)

disseminated talaromycosis should be an indicator to look for underlying primary immunodeficiency after excluding secondary causes.

Ecology and Transmission

Subsequent studies showed that four species of bamboo rats (*Rhizomys sinensis*, *R. pruinosis*, *R. sumatrensis*, and *Cannomys badius*) were important enzootic reservoirs of *T. marneffei* [7, 8, 50–53]. 100% of the *R. pruinosus* rats captured in Guangxi and Guangdong Provinces in Southern China were positive for *T. marneffei* [54, 55]. Multi-locus genotypes show that *T. marneffei* isolates from humans are similar or identical to those infecting bamboo rats [55]. *T. marneffei* DNA has also been detected by PCR in nasal swabs of 13% of outdoor dogs in Thailand [56]. However, there is no evidence of direct animal-to-human transmission. *T. marneffei* has been isolated from bamboo rat feces and soil samples within or surrounding wild bamboo rat's burrow, while no detection in the artificial farm of bamboo rats. Collectively, these epidemiological data suggest humans and bamboo rats are exposed to an as-yet-undiscovered common environment reservoir of infection, in which bamboo rats may be exploited by *T. marneffei* to expand its biomass and biogeography [54, 55].

History of exposure to or consumption of bamboo rats was not a risk factor for infection; instead, agricultural exposure to the soil during the rainy season [57, 58] serves as an important risk factor for *T. marneffei* infection and can be predicted by humidity levels [59]. So, infections in people probably occur through inhalation of *T. marneffei* conidia. According to the literature, the incubation periods of infection with *T. marneffei* are highly variable, which could be 1–3 weeks in acute disease or reactivation of a latent infection several years after exposure [21, 59].

## Clinical Manifestations

Patients infected with *T. marneffei* would present various degrees of severity depending on the underlying immunocompromising condition and the timing of diagnosis. Generally, talaromycosis presented either as a local or disseminated infection. Local infections were rare, only involving single organs, such as corneas or lungs [21, 60]. Clinically, they only show local symptoms without systemic involvement. Disseminated infections were usually associated with HIV/AIDS patients or immunosuppressed HIV-negative patients with the pathogen isolated from more than one body site (noncontiguous) or from blood or

bone marrow. The symptoms and signs of disseminated *T. marneffei* infection are atypical, including fever, weight loss, fatigue, hepatosplenomegaly, lymphadenopathy, respiratory, and gastrointestinal abnormalities. Central nervous system involvement is an emerging syndrome in *T. marneffei* infected HIV-positive patients, presented with an acute onset of altered mental status with confusion, agitation, or depressed consciousness [61, 62].

Skin lesions can be a single or first-episode symptom of *T. marneffei* infection [3, 31]. It often becomes the first sign to attract attention in disseminated cases and has a strong suggestive role in the diagnosis of this disease. Characteristic lesions are papules with central necrosis, predominantly on the head and upper chest, which presented in 70% of HIV-infected and 40% of non-HIV-infected patients and aid in the rapid diagnosis [3, 31]. In addition, papules, pustules, nodules, subcutaneous abscesses, cysts or ulcers can also occur. Reactive rashes, such as Sweet's syndrome, can occur in non-HIV patients who suffered from adult-onset immunodeficiency syndrome due to anti-interferon-gamma autoantibodies. *T. marneffei*-associated immune reconstitution inflammatory syndrome (IRIS) has been reported as unmasking IRIS in patients starting ART. Skin lesions can be atypical, including erythematous nodules, verrucous lesions, or erythematous plaques [63].

In the literature, compared to HIV-infected patients, HIV-negative patients with *T. marneffei* infection have a longer diagnostic interval, a higher percentage of dyspnea and were significantly older, less likely to have fever, splenomegaly, and umbilicated skin lesions, and more likely to have Sweet's syndrome and osteoarticular lesions. The non-HIV-infected patients also had higher leukocyte, CD4 lymphocyte and platelet counts, and lower alanine transaminase level and blood culture-positive rate [27, 29].

## Diagnosis

Traditionally, the diagnosis of *T. marneffei* infection depends on identifying the fungus in clinical specimens by microscopy and culture. Microscopic examination of a direct smear of bone marrow aspirates, touch smear of skin biopsy, or lymph node biopsy specimens can lead to rapid presumptive diagnosis [1, 10, 64]. In patients with heavy fungemia, the organisms may be seen on the peripheral blood smear [65]. *T. marneffei* can be observed in histopathological sections [13, 66–68], preferably stained by Grocott methenamine silver or periodic acid-Schiff stain. *T. marneffei* yeast-like cells distributed within and outside macrophages and histiocytes, 2–3 μm in diameter with oval, round, elongated, sausage-like shapes, and divided by fission. The cross-wall formation can differentiate yeast cells of *T. marneffei* from those of *Histoplasma capsulatum*, which also appear as intracellular yeasts. The histopathological characteristic of *T. marneffei* infected tissues manifested as granulomatous, suppurative reaction, and non-reactive necrosis.

Mycological culture of all tissues or body fluids is the gold standard method for the diagnosis of *T. marneffei* infection. The high sensitivity samples are bone marrow (100%), skin biopsy (90%), and blood (76%), respectively [69]. Identification of *T. marneffei* is based upon the morphology of the colony, the organism's microscopic morphology, and its mold-to-yeast conversion when moved from 25 °C (to) 37 °C [70]. Culture can be slow (3–14 days), resulting in diagnostic delay and raised mortality, particularly in patients without skin lesions [71].

The development of non-culture-based assays for rapid detection of *T. marneffei* infection has the potential to improve treatment outcomes. The commercial β-D-glucan assays or GM test (*Aspergillus* galactomannan antigen detection test) can be useful as a screening tool and adjunct to diagnosis [72, 73]. PCR-based assays such as nested PCR, TaqMan real-time PCR, targeting the ribosomal DNA (ITS1-5.8S-ITS2, 18S), or *MP1* gene have been developed to detect *T. marneffei* in clinical samples including whole blood, plasma or paraffin-embedded tissue [74–77]. Evaluation of the tests revealed a high diagnostic specificity of the assay (100%), while diagnostic sensitivity ranged from 67 to 77%, respectively. These assays provide useful tools for the rapid diagnosis of *T. marneffei* infection. Recently, a monoclonal-based immunoassay has been used to detected *T. marneffei* Mp1p antigen in patient plasma with a sensitivity of 75% (15/20) and specificity of 99.4% (537/540). The assay detected Mp1p antigenemia in 9.4% of over 8000 HIV-infected patients in outpatient clinics, offering another tool for rapid diagnosis of *T. marneffei* infection [78, 79]. However, these methods require the physician to suspect the pathogen before examination, which might limit the application

clinically. Recently, the next generation sequencing (NGS) based on metagenomics has been successfully applied in the diagnosis of disseminated *T.marneffei* infection, which does not depend upon prior assumptions from the physicians and provides a new technique for rapid etiological diagnosis [80]. NGS availability is limited especially in the resource-limited settings. Overall, it might be prudent to use a combination of several methods to achieve the highest diagnostic yield [81].

## In Vitro Drug Susceptibility, Therapeutics Strategies, and Prevention

### In Vitro Drug Susceptibility

At present, no existing guidelines were available for susceptibility testing of *Talaromyces marneffei* in vitro. However, studies using different methods showed that posaconazole, voriconazole, itraconazole, and other azole drugs had high activity against *T. marneffei* (except fluconazole), Amphotericin B showed intermediate antifungal activity, whereas echinocandins showed intermediate to resistance [82–85]. Besides, traditional herb, berberine had antifungal activity against *T. marneffei*, especially in combination with antifungal agents in vitro [86].

### Therapeutic Strategies in Talaromycosis With or Without HIV-Infected

Amphotericin B deoxycholate (D-AmB) is still the first-line initial antifungal treatment for severe *T. marneffei* infection. International guidelines recommend for talaromycosis in HIV-infected patients is: D-AmB; 0.6–1.0 mg/kg per day for 2 weeks, followed by itraconazole 400 mg per day for 10 weeks, then with itraconazole 200 mg per day as secondary prophylaxis until CD4 counts are higher than 100 cells per μL for at least 6 months [87, 88]. Liposomal amphotericin B (L-AmB) at 3–5 mg/kg per day is effective and better tolerated than D-AmB. However, the drug is not available in a resource-limited situation [89]. Voriconazole is an effective therapeutic option for disseminated talaromycosis, given 6 mg/kg BID for one day, 4 mg/kg BID for 10–14 days, followed by oral voriconazole 200 mg BID for 12 weeks in HIV patients. It has been reported that voriconazole is effective in the treatment of patients who did not respond to amphotericin B initial therapy [90, 91]. Considering it can be administered by the oral route or by using intravenous-to-oral step-down therapy, voriconazole has the potential to be more convenient than the currently recommended treatment regimen.

In a multicenter open-label, non-inferiority trial comparing itraconazole (600 mg per day for 3 days, followed by 400 mg per day, for 11 days) with standard D-AmB initial therapy in HIV-infected talaromycosis patients reported mortality after 6 months is 11.3% and 21.0%, respectively. The study indicated D-AmB was superior to itraconazole as initial treatment for talaromycosis [92].

For prevention, HIV-infected people living or traveling in endemic areas, primary prophylactic treatment with itraconazole is recommended when the CD4 cell count is less than 100 $mm^3$. Itraconazole can be taken orally for 200 mg once a day until CD4 cell count $> 100$ $mm^3$ and more than 6 months [86].

At present, the standard recommendation regarding the appropriate duration of treatment and prophylaxis of *T. marneffei* among HIV-uninfected patients is unavailable. In the literature, the duration of treatment was significantly longer in HIV-uninfected patients compared to HIV-infected patients, and some cases may require lifelong treatment.

### Special Population: Treatment of Non-HIV *T. marneffei* Infection in Children

Clinical experience in the treatment of non-HIV *T. marneffei* pediatric patients is limited. Studies showed when treated with voriconazole 7 mg/kg twice per day, for at least 12 days, followed by oral for at least 13 weeks, 70–80% children had a complete response to therapy at primary and long-term follow-up assessment [90, 93]. No adverse events were recorded during and after the treatment. D-AmB 1 mg/kg/d has been used for *T. marneffei* infected children, but the nephrotoxic side effects are significant. Regarding the dose-dependent nephrotoxicity, and electrolyte imbalance related to D-AmB treatment, pharmacokinetics and pharmacodynamics study has been used to evaluate the association between D-AmB exposure and response in the treatment of talaromycosis [94].

Despite antifungal therapy, case fatality rates among adult patients with or without HIV-infected are 20%, 29.4%, respectively. Whereas, mortality in

**Table 1** Well-cited clinical articles on *Penicillium marneffei*

| Title | Authors | Citations (Google Scholar/Scopus/ Web of science) | Refs. |
|---|---|---|---|
| Disseminated *Penicillium marneffei* infection in Southeast Asia | Supparatpinyo, K., Khamwan, C., Baosoung, V., Sirisanthana, T., Nelson, K.E. | 609/424/343 | [69] |
| Infection due to *Penicillium marneffei*, an emerging pathogen: Review of 155 reported cases | Duong, T.A. | 363/236/187 | [96] |
| Amphotericin B and itraconazole for treatment of disseminated *Penicillium marneffei* infection in human immunodeficiency virus-infected patients | Sirisanthana, T., Supparatpinyo, K., Perriens, J., Nelson, K.E. | 193/146/102 | [107] |
| Infection caused by *Penicillium marneffei*: description of first natural infection in man | DiSalvo, A.F., Fickling, A.M., Ajello, L. | 250/139/124 | [35] |
| *Penicillium marneffei* Infection in Patients Infected with Human Immunodeficiency Virus | Supparatpinyo, K., Chiewchanvit, S., Hirunsri, P., Uthammachai, C., Nelson, K.E., Sirisanthana, T. | 187/136/133 | [97] |
| A controlled trial of itraconazole to prevent relapse of *Penicillium marneffei* infection in patients infected with the human immunodeficiency virus | Supparatpinyo, K., Perriens, J., Nelson, K.E., Sirisanthana, T. | 193/135/99 | [88] |
| Progressive disseminated penicilliosis caused by *Penicillium marneffei*. Report of eight cases and differentiation of the causative organism from *Histoplasma capsulatum* | Deng, Z., Connor, D.H. | 159/110/110 | [13] |
| Penicilliosis marneffei in Thailand: Report of five human cases | Jayanetra, P., Nitiyanant, P., Ajello, L., Padhye, A.A., Lolekha, S., Atichartakarn, V., Vathesatogit, P., Sathaphatayavongs, B., Prajaktam, R. | 159/106/108 | [12] |
| Serodiagnosis of *Penicillium marneffei* infection | Yuen, K., Wong, S.S., Chau, P., Tsang, D.N. | 104/81/70 | [11] |
| Seasonal variation of disseminated *Penicillium marneffei* infections in northern Thailand: A clue to the reservoir? | Chariyalertsak, S., Sirisanthana, T., Supparatpinyo, K., Nelson, K.E. | 111/76/59 | [58] |

the pediatric patients with talaromycosis could be up to 55% [42], higher than the adult patients, due to underlying immunodeficiency and delated treatment.

## Bibliometrics of Talaromycosis and *T. marneffei*

We used a bibliometric analysis to highlight clinical and research trends and provide an impetus for future investigations [95]. Since the first description of experimental infection from France, the scientific literature on talaromycosis and *T. marneffei* has grown substantially with most contributions originating from investigators working in the endemic areas. With the search term "marneffei," we found ~ 1000 articles in Google Scholar, 1070 articles in Scopus, and 942 articles in Web of Science (last accessed on November 19, 2019). We highlight well-cited articles on clinical disease, diagnosis and provide a summary of the highest-cited articles published in *Mycopathologia* since the original discovery by Prof. Segraetain (Tables 1 and 2). Late eighties–early nineties saw rapid advances in defining the clinical spectrum of talaromycosis (penicilliosis) especially in settings of HIV-positive patients [12, 13, 35, 58, 69, 96, 97]. The state-of-the-art serodiagnostic tests and clinical trials of amphotericin B and itraconazole were reported [11, 88, 98]. After Prof. Segretain' initial description, *Mycopathologia* coverage described improved serological tests for the detection of *P. marneffei* antigenemia, antibodies, and exoantigens [7, 99, 100]. The test innovations also included antifungal susceptibility testing and PCR from paraffin-embedded tissues

**Table 2** Well-cited *Mycopathologia* articles on *Penicillium marneffei*

| Title | Authors | Citations (Google Scholar/Scopus/Web of science) | Refs. |
|---|---|---|---|
| [*Penicillium marneffei n.sp*., agent of a mycosis of the reticuloendothelial system] | Segretain G | 141/89/93 | [7] |
| *Penicillosis marneffei*: serological and exoantigen studies | Sekhon AS, Li JS, Garg AK | 66/48/39 | [99] |
| Pulmonary penicillosis marneffei: report of the first imported case in Canada. | Sekhon AS, Stein L, Garg AK, Black WA, Glezos JD, Wong C | 25/23/17 | [103] |
| Update of *Penicillosis marneffei* in Thailand | Imwidthaya P | 46/34/32 | [4] |
| Occurrence of *Penicillium marneffei* infections among wild bamboo rats in Thailand | Ajello L, Padhye AA, Sukroongreung S, Nilakul CH, Tantimavanic S | 71/47/40 | [52] |
| Usefulness of a microimmunodiffusion test for the detection of *Penicillium marneffei* antigenemia, antibodies, and exoantigens | Imwidthaya P, Sekhon AS, Mastro TD, Garg AK, Ambrosie E | 14/10/8 | [100] |
| *Penicillium marneffei*: types and drug susceptibility | Imwidthaya P, Thipsuvan K, Chaiprasert A, Danchaivijitra S, Sutthent R, Jearanaisilavong J | 45/27/31 | [101] |
| *Penicillium marneffei* SKN7, a novel gene, could complement the hypersensitivity of *S. cerevisiae* skn7 Disruptant strain to oxidative stress | Cao C, Liu W, Li R | 16/13/13 | [105] |
| Identification of *Penicillium marneffei* in Paraffin-Embedded Tissue Using Nested PCR | Zeng H, Li X, Chen X, Zhang J, Sun J, Xie Z, Xi L | 21/12/10 | [76] |
| Disseminated *Penicillium marneffei* infection in an SLE patient: a case report and literature review | Luo DQ, Chen MC, Liu JH, Li Z, Li HT | 20/16/14 | [104] |
| Isolation of *Penicillium marneffei* from soil and wild rodents in Guangdong, SE China | Li X, Yang Y, Zhang X, Zhou X, Lu S, Ma L, Lu C, Xi L | 20/7/7 | [102] |
| Development of in vitro macrophage system to evaluate phagocytosis and intracellular fate of Penicillium marneffei conidia | Lu S, Hu Y, Lu C, Zhang J, Li X, Xi L | 14/10/10 | [106] |
| *Penicillium marneffei* infection: an emerging disease in mainland China | Hu Y, Zhang J, Li X, Yang Y, Zhang Y, Ma J, Xi L | 111/74/71 | [3] |
| Retrospective analysis of 15 cases of *Penicilliosis marneffei* in a southern China hospital | Zhou F, Bi X, Zou X, Xu Z, Zhang T | 21/10/14 | [37] |

[76, 101]. *Mycopathologia* remained an important source of publications on the natural reservoir of the pathogen in wild rodents, and endemic and travel-related penicillosis [3, 4, 37, 52, 102–104]. Two notable contributions described an ex vivo host–pathogen interaction model and a novel gene that mediates oxidative stress in *P. marneffei* [105, 106].

## Summary and Conclusions

Talaromycosis remains a significant infectious complication for patients with HIV/AIDS and other immune defects. The disease is being recognized with an increasing frequency well beyond the original endemic areas. Therefore, there is an urgent need for the development of rapid and affordable point-of-care diagnostic tests. More clinical studies are also needed to define the best therapeutic options for the management of talaromycosis patients.

## References

1. Vanittanakom N, Cooper CR Jr, Fisher MC, Sirisanthana T. *Penicillium marneffei* infection and recent advances in the epidemiology and molecular biology aspects. Clin Microbiol Rev. 2006;19(1):95–110.

2. Ustianowski AP, Sieu TP, Day JN. *Penicillium marneffei* infection in HIV. Curr Opin Infect Dis. 2008;21(1):31–6.
3. Hu YX, Zhang JM, Li XQ, Yang YB, Zhang Y, Ma JC, et al. *Penicillium marneffei* infection: an emerging disease in Mainland China. Mycopathologia. 2013;175(1–2):57–67.
4. Imwidthaya P. Update of penicillosis marneffei in Thailand: review article. Mycopathologia. 1994;127(3):135–7.
5. Tsang CC, Lau SKP, Woo PCY. Sixty years from Segretain's description: what have we learned and should learn about the basic mycology of *Talaromyces marneffei*? Mycopathologia. 2019. https://doi.org/10.1007/s11046-019-00395-y.
6. Capponi M, Sureau P, Segretain G. Penicillosis of *Rhizomys sinensis*. Bull Soc Pathol Exot. 1956;49(3):418–21.
7. Segretain G. *Penicillium marneffei* N. Sp., Agent D'une Mycose Du Système Réticulo-Endothélial. Mycopathologia et Mycologia Applicata. 1959;11(4):327–53.
8. Segretain G. Description d'une nouvelle especе de *Penicillium*: *Penicillium marneffei n. sp*. Bull Soc Mycol Fr. 1959;75:412–6.
9. Samson R, Yilmaz N, Houbraken J, Spierenburg H, Seifert K, Peterson S, et al. Phylogeny and nomenclature of the genus *Talaromyces* and taxa accommodated in *Penicillium* subgenus *Biverticillium*. Stud Mycol. 2011;70:159–83.
10. Liyan X, Changming L, Xianyi Z, Luxia W, Suisheng X. Fifteen cases of penicilliosis in Guangdong, China. Mycopathologia. 2004;158(2):151–5.
11. Yuen K-Y, Wong SS-Y, Chau P, Tsang D. Serodiagnosis of *Penicillium marneffei* infection. Lancet. 1994;344(8920):444–5.
12. Jayanetra P, Nitiyanant P, Ajello L, Padhye AA, Lolekha S, Atichartakarn V, et al. Penicilliosis marneffei in Thailand: report of five human cases. Am J Trop Med Hyg. 1984;33(4):637–44.
13. Deng Z, Connor DH. Progressive disseminated penicilliosis caused by *Penicillium marneffei*. Report of eight cases and differentiation of the causative organism from *Histoplasma capsulatum*. Am J Clin Pathol. 1985;84(3):323–7.
14. Cao CW, Bulmer G, Li JS, Liang L, Lin YK, Xu YJ, et al. Indigenous case of disseminated histoplasmosis from the *Penicillium marneffei* endemic area of China. Mycopathologia. 2010;170(1):47–50.
15. Ranjana K, Priyokumar K, Singh TJ, Gupta CC, Sharmila L, Singh P, et al. Disseminated *Penicillium marneffei* infection among HIV-infected patients in Manipur state, India. J Infect. 2002;45(4):268–71.
16. Tsui W, Ma K, Tsang D. Disseminated *Penicillium marneffei* infection in HIV-infected subject. Histopathology. 1992;20(4):287–93.
17. Liu MT, Wong CK, Fung CP. Disseminated *Penicillium marneffei* infection with cutaneous lesions in an HIV-positive patient. Br J Dermatol. 1994;131(2):280–3.
18. Antinori S, Gianelli E, Bonaccorso C, Ridolfo AL, Croce F, Sollima S, et al. Disseminated *Penicillium marneffei* infection in an HIV-positive Italian patient and a review of cases reported outside endemic regions. J Travel Med. 2006;13(3):181–8.
19. Castro-Lainez MT, Sierra-Hoffman M, Lompart-Zeno J, Adams R, Howell A, Hoffman-Roberts H, et al. *Talaromyces marneffei* infection in a non-HIV non-endemic population. IDCases. 2018;12:21–4.
20. Julander I, Petrini B. *Penicillium marneffei* infection in a Swedish HIV-infected immunodeficient narcotic addict. Scand J Infect Dis. 1997;29(3):320–2.
21. De Monte A, Risso K, Normand AC, Boyer G, L'Ollivier C, Marty P, et al. Chronic pulmonary penicilliosis due to *Penicillium marneffei*: late presentation in a french traveler. J Travel Med. 2014;21(4):292–4.
22. Patassi AA, Saka B, Landoh DE, Kotosso A, Mawu K, Halatoko WA, et al. First observation in a non-endemic country (Togo) of *Penicillium marneffei* infection in a human immunodeficiency virus-infected patient: a case report. BMC Res Notes. 2013;6(1):506.
23. Pautler K, Padhye AA, Ajello L. Imported penicilliosis marneffei in the United States: report of a second human infection. Sabouraudia. 1984;22(5):433–8.
24. Li L, Chen K, Dhungana N, Jang Y, Chaturvedi V, Desmond E. Characterization of clinical isolates of *Talaromyces marneffei* and related species, California, USA. Emerg Infect Dis. 2019;25(9):1765–8.
25. Guo J, Li BK, Li TM, Wei FL, Fu YJ, Zheng YQ, et al. Characteristics and prognosis of *Talaromyces marneffei* infection in non-HIV-infected children in Southern China. Mycopathologia. 2019. https://doi.org/10.1007/s11046-019-00373-4.
26. Zheng J, Gui X, Cao Q, Yang R, Yan Y, Deng L, et al. A clinical study of acquired immunodeficiency syndrome associated *Penicillium marneffei* infection from a non-endemic area in China. PLoS ONE. 2015;10(6):e0130376.
27. Li H-R, Cai S-X, Chen Y-S, Yu M-E, Xu N-L, Xie B-S, et al. Comparison of *Talaromyces marneffei* infection in human immunodeficiency virus-positive and human immunodeficiency virus-negative patients from Fujian, China. Chin Med J. 2016;129(9):1059.
28. Li H, Sang J, Li R, Liu Y, Zhang J. Disseminated *Penicillium marneffei* infection with verrucoid lesions in an AIDS patient in Beijing, a non-endemic region. Eur J Dermatol. 2010;20(3):378–80.
29. Kawila R, Chaiwarith R, Supparatpinyo K. Clinical and laboratory characteristics of penicilliosis marneffei among patients with and without HIV infection in Northern Thailand: a retrospective study. BMC Infect Dis. 2013;13(1):464.
30. Jiang J, Meng S, Huang S, Ruan Y, Lu X, Li JZ, et al. Effects of *Talaromyces marneffei* infection on mortality of HIV/AIDS patients in southern China: a retrospective cohort study. Clin Microbiol Infect. 2019;25(2):233–41.
31. Chan JF, Lau SK, Yuen K-Y, Woo PC. *Talaromyces* (*Penicillium*) marneffei infection in non-HIV-infected patients. Emerg Microbes Infect. 2016;5(1):1–9.
32. Tang BS-F, Chan JF-W, Chen M, Tsang OT-Y, Mok M-Y, Lai RW-M, et al. Disseminated penicilliosis, recurrent bacteremic nontyphoidal salmonellosis, and burkholderiosis associated with acquired immunodeficiency due to autoantibody against gamma interferon. Clin Vaccine Immunol. 2010;17(7):1132–8.
33. Shi N, Kong J, Wang K, Cao C. Coinfection with Talaromyces marneffei and other pathogens associated with acquired immunodeficiency. JAMA Dermatol. 2019;. https://doi.org/10.1001/jamadermatol.2019.1532.

34. Browne SK, Burbelo PD, Chetchotisakd P, Suputtamongkol Y, Kiertiburanakul S, Shaw PA, et al. Adult-onset immunodeficiency in Thailand and Taiwan. N Engl J Med. 2012;367(8):725–34.
35. DiSalvo AF, Fickling AM, Ajello L. Infection caused by *Penicillium marneffei*: description of first natural infection in man. Am J Clin Pathol. 1973;60(2):259–63.
36. Lam K, Cheung F, Yam L, Lee C, Fung K. Atypical manifestations in a patient with systemic lupus erythematosus. J Clin Pathol. 1997;50(2):174–6.
37. Zhou F, Bi X, Zou X, Xu Z, Zhang T. Retrospective analysis of 15 cases of *Penicilliosis marneffei* in a southern China hospital. Mycopathologia. 2014;177(5–6):271–9.
38. Hart J, Dyer J, Clark B, McLellan D, Perera S, Ferrari P. Travel-related disseminated *Penicillium marneffei* infection in a renal transplant patient. Transpl Infect Dis. 2012;14(4):434–9.
39. Woo P, Lau S, Lau C, Chong K, Hui W, Wong S, et al. *Penicillium marneffei* fungaemia in an allogeneic bone marrow transplant recipient. Bone Marrow Transpl. 2005;35(8):831.
40. Stathakis A, Lim K, Boan P, Lavender M, Wrobel J, Musk M, et al. *Penicillium marneffei* infection in a lung transplant recipient. Transpl Infect Dis. 2015;17(3):429–34.
41. Seo JY, Ma YE, Lee JH, Lee S-T, Ki C-S, Lee NY. A case of disseminated *Penicillium marneffei* infection in a liver transplant recipient. Korean J Lab Med. 2010;30(4):400–5.
42. Chan JF, Chan TS, Gill H, Lam FY, Trendell-Smith NJ, Sridhar S, et al. Disseminated infections with *Talaromyces marneffei* in non-AIDS patients given monoclonal antibodies against CD20 and kinase inhibitors. Emerg Infect Dis. 2015;21(7):1101.
43. Ramírez I, Hidrón A, Cardona R. Successful treatment of pulmonary invasive fungal infection by Penicillium non-marneffei in lymphoblastic lymphoma: case report and literature review. Clin Case Rep. 2018;6(6):1153.
44. Lee PP, Chan K-W, Lee T-L, Ho MH-K, Chen X-Y, Li C-H, et al. Penicilliosis in children without HIV infection—are they immunodeficient? Clin Infect Dis. 2011;54(2):e8–19.
45. Sirisanthana V, Sirisanthana T. Disseminated *Penicillium marneffei* infection in human immunodeficiency virus-infected children. Pediatr Infect Dis J. 1995;14(11):935–9.
46. Han XJ, Su DH, Yi JY, Zou YW, Shi YL. A literature review of blood-disseminated *P. marneffei* infection and a case study of this infection in an HIV-negative child with comorbid eosinophilia. Mycopathologia. 2019;184(1):129–39.
47. Lin W, Dai Y-S, Tsai M, Huang L, Chiang B. Systemic *Penicillium marneffei* infection in a child with common variable immunodeficiency. J Formos Med Assoc. 1998;97(11):780–3.
48. Fan H, Huang L, Yang D, Lin Y, Lu G, Xie Y, et al. Pediatric hyperimmunoglobulin E syndrome: a case series of 4 children in China. Medicine (Baltimore). 2018;97(14):e0215.
49. Lee PP, Mao H, Yang W, Chan K-W, Ho MH, Lee T-L, et al. *Penicillium marneffei* infection and impaired IFN-γ immunity in humans with autosomal-dominant gain-of-phosphorylation STAT1 mutations. J Allergy Clin Immunol. 2014;133(3):894.
50. Deng Z, Yun M, Ajello L. Human penicilliosis marneffei and its relation to the bamboo rat (*Rhizomys pruinosus*). J Med Vet Mycol. 1986;24(5):383–9.
51. Gugnani H, Fisher MC, Paliwal-Johsi A, Vanittanakom N, Singh I, Yadav PS. Role of *Cannomys badius* as a natural animal host of *Penicillium marneffei* in India. J Clin Microbiol. 2004;42(11):5070–5.
52. Ajello L, Padhye A, Sukroongreung S, Nilakul C, Tantimavanic S. Occurrence of *Penicillium marneffei* infections among wild bamboo rats in Thailand. Mycopathologia. 1995;131(1):1–8.
53. Chariyalertsak S, Vanittanakom P, Nelson KE, Sirisanthana T, Vanittanakom N. *Rhizomys sumatrensis* and *Cannomys badius*, new natural animal hosts of *Penicillium marneffei*. J Med Vet Mycol. 1996;34(2):105–10.
54. Huang X, He G, Lu S, Liang Y, Xi L. Role of *Rhizomys pruinosus* as a natural animal host of *Penicillium marneffei* in Guangdong, China. Microb Biotechnol. 2015;8(4):659–64.
55. Cao C, Liang L, Wang W, Luo H, Huang S, Liu D, et al. Common reservoirs for *Penicillium marneffei* infection in humans and rodents, China. Emerg Infect Dis. 2011;17(2):209.
56. Chaiwun B, Vanittanakom N, Jiviriyawat Y, Rojanasthien S, Thorner P. Investigation of dogs as a reservoir of *Penicillium marneffei* in northern Thailand. Int J Infect Dis. 2011;15(4):e236–9.
57. Chariyalertsak S, Sirisanthana T, Khuanchai S, Praparattanapan J, Nelson KE. Case-control study of risk factors for *Penicillium marneffei* infection in human immunodeficiency virus-infected patients in northern Thailand. Clin Infect Dis. 1997;24(6):1080–6.
58. Chariyalertsak S, Sirisanthana T, Supparatpinyo K, Nelson KE. Seasonal variation of disseminated *Penicillium marneffei* infections in northern Thailand: a clue to the reservoir? J Infect Dis. 1996;173(6):1490–3.
59. Bulterys PL, Le T, Quang VM, Nelson KE, Lloyd-Smith JO. Environmental predictors and incubation period of AIDS-associated *Penicillium marneffei* infection in Ho Chi Minh City, Vietnam. Clin Infect Dis. 2013;56(9):1273–9.
60. Anutarapongpan O, Thanathanee O, Suwan-Apichon O. *Penicillium* keratitis in a HIV-infected patient. BMJ Case Rep. 2016;2016:bcr2016216139.
61. Le T, Huu Chi N, Kim Cuc NT, Sieu TPM, Shikuma CM, Farrar J, et al. AIDS-associated *Penicillium marneffei* infection of the central nervous system. Clin Infect Dis. 2010;51(12):1458–62.
62. Noritomi DT, Bub GL, Beer I, da Silva ASF, de Cleva R, Gama-Rodrigues JJ. Multiple brain abscesses due to *Penicillium* spp. infection. Crit Care. 2005;9(2):65.
63. Sudjaritruk T, Sirisanthana T, Sirisanthana V. Immune reconstitution inflammatory syndrome from *Penicillium marneffei* in an HIV-infected child: a case report and review of literature. BMC Infect Dis. 2012;12(1):28.
64. Chaiwun B, Khunamornpong S, Sirivanichai C, Rangdaeng S, Supparatpinyo K, Settakorn J, et al. Lymphadenopathy due to *Penicillium marneffei* infection:

diagnosis by fine needle aspiration cytology. Mod Pathol. 2002;15(9):939.
65. Othman J, Brown CM. *Talaromyces marneffei* and dysplastic neutrophils on blood smear in newly diagnosed HIV. Blood. 2018;131(2):269.
66. Deng Z, Ribas JL, Gibson DW, Connor DH. Infections caused by *Penicillium marneffei* in China and Southeast Asia: review of eighteen published cases and report of four more Chinese cases. Rev Infect Dis. 1988;10(3):640–52.
67. Cooper CR Jr, McGinnis MR. Pathology of *Penicillium marneffei*. Arch Pathol Lab Med. 1997;121(8):798.
68. Yousukh A, Jutavijittum P, Pisetpongsa P, Chitapanarux T, Thongsawat S, Senba M, et al. Clinicopathologic study of hepatic *Penicillium marneffei* in Northern Thailand. Arch Pathol Lab Med. 2004;128(2):191–4.
69. Supparatpinyo K, Khamwan C, Baosoung V, Sirisanthana T, Nelson KE. Disseminated *Penicillium marneffei* infection in southeast Asia. Lancet. 1994;344(8915):110–3.
70. Cao C, Li R, Wan Z, Liu W, Wang X, Qiao J, et al. The effects of temperature, pH, and salinity on the growth and dimorphism of *Penicillium marneffei*. Sabouraudia. 2007;45(5):401–7.
71. Le T, Wolbers M, Chi NH, Quang VM, Chinh NT, Huong Lan NP, et al. Epidemiology, seasonality, and predictors of outcome of AIDS-associated *Penicillium marneffei* infection in Ho Chi Minh City, Viet Nam. Clin Infect Dis. 2011;52(7):945–52.
72. Yoshimura Y, Sakamoto Y, Lee K, Amano Y, Tachikawa N. *Penicillium marneffei* infection with β-D-glucan elevation: a case report and literature review. Intern Med. 2016;55(17):2503–6.
73. Huang Y-T, Hung C-C, Liao C-H, Sun H-Y, Chang S-C, Chen Y-C. Detection of circulating galactomannan in serum samples for diagnosis of *Penicillium marneffei* infection and cryptococcosis among patients infected with human immunodeficiency virus. J Clin Microbiol. 2007;45(9):2858–62.
74. Hien HTA, Thanh TT, Thu NTM, Nguyen A, Thanh NT, Lan NPH, et al. Development and evaluation of a real-time polymerase chain reaction assay for the rapid detection of *Talaromyces marneffei* MP 1 gene in human plasma. Mycoses. 2016;59(12):773–80.
75. Lu S, Li X, Calderone R, Zhang J, Ma J, Cai W, et al. Whole blood nested PCR and real-time PCR amplification of *Talaromyces marneffei* specific DNA for diagnosis. Sabouraudia. 2015;54(2):162–8.
76. Zeng H, Li X, Chen X, Zhang J, Sun J, Xie Z, et al. Identification of *Penicillium marneffei* in paraffin-embedded tissue using nested PCR. Mycopathologia. 2009;168(1):31–5.
77. Zhang J-M, Sun J-F, Feng P-Y, Li X-Q, Lu C-M, Lu S, et al. Rapid identification and characterization of *Penicillium marneffei* using multiplex ligation-dependent probe amplification (MLPA) in paraffin-embedded tissue samples. J Microbiol Methods. 2011;85(1):33–9.
78. Wang Y-F, Cai J-P, Wang Y-D, Dong H, Hao W, Jiang L-X, et al. Immunoassays based on *Penicillium marneffei* Mp1p derived from *Pichia pastoris* expression system for diagnosis of penicilliosis. PLoS ONE. 2011;6(12):e28796.
79. Wang Y-F, Xu H-F, Han Z-G, Zeng L, Liang C-Y, Chen X-J, et al. Serological surveillance for *Penicillium marneffei* infection in HIV-infected patients during 2004–2011 in Guangzhou, China. Clin Microbiol Infect. 2015;21(5):484–9.
80. Li X, Zheng Y, Wu F, Mo D, Liang G, Yan R, et al. Evaluation of quantitative real-time PCR and Platelia galactomannan assays for the diagnosis of disseminated *Talaromyces marneffei* infection. Med Mycol. 2019.
81. Zhu Y-M, Ai J-W, Xu B, Cui P, Cheng Q, Wu H, et al. Rapid and precise diagnosis of disseminated *T. marneffei* infection assisted by high-throughput sequencing of multifarious specimens in a HIV-negative patient: a case report. BMC Infect Dis. 2018;18(1):379. https://doi.org/10.1186/s12879-018-3276-5.
82. Lei H-L, Li L-H, Chen W-S, Song W-N, He Y, Hu F-Y, et al. Susceptibility profile of echinocandins, azoles and amphotericin B against yeast phase of *Talaromyces marneffei* isolated from HIV-infected patients in Guangdong, China. Eur J Clin Microbiol Infect Dis. 2018;37(6):1099–102.
83. Lau SK, Lo GC, Lam CS, Chow W-N, Ngan AH, Wu AK, et al. In vitro activity of posaconazole against *Talaromyces marneffei* by broth microdilution and Etest methods and comparison to itraconazole, voriconazole, and anidulafungin. Antimicrob Agents Chemother. 2017;61(3):e01480-16.
84. Liu D, Liang L, Chen J. In vitro antifungal drug susceptibilities of *Penicillium marneffei* from China. J Infect Chemother. 2013;19(4):776–8.
85. Sekhon A, Garg A, Padhye A, Hamir Z. In vitro susceptibility of mycelial and yeast forms of *Penicillium marneffei* to amphotericin B, fluconazole, 5-fluorocytosine and itraconazole. Eur J Epidemiol. 1993;9(5):553–8.
86. Luo H, Pan K-S, Luo X-L, Zheng D-Y, Andrianopoulos A, Wen L-M, et al. In vitro susceptibility of berberine combined with antifungal agents against the yeast form of *Talaromyces marneffei*. Mycopathologia. 2019;184(2):295–301.
87. Benson CA, Brooks JT, Holmes KK, Kaplan JE, Masur H, Pau A. Guidelines for prevention and treatment opportunistic infections in HIV-infected adults and adolescents; recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association/Infectious Diseases Society of America. 2009.
88. Supparatpinyo K, Perriens J, Nelson KE, Sirisanthana T. A controlled trial of itraconazole to prevent relapse of *Penicillium marneffei* infection in patients infected with the human immunodeficiency virus. N Engl J Med. 1998;339(24):1739–43. https://doi.org/10.1056/NEJM199812103392403.
89. Iribarren JA, Rubio R, Aguirrebengoa K, Arribas JR, Baraia-Etxaburu J, Gutiérrez F, et al. Prevention and treatment of opportunistic infections and other coinfections in HIV-infected patients: May 2015. Enfermedades infecciosas y microbiologia clinica. 2016;34(8):516.e1–18.
90. Ouyang YY, Cai SQ, Liang H, Cao CW. Administration of voriconazole in disseminated *Talaromyces* (penicillium) marneffei infection: a retrospective study. Mycopathologia. 2017;182(5–6):569–75.

91. Supparatpinyo K, Schlamm HT. Voriconazole as therapy for systemic *Penicillium marneffei* infections in AIDS patients. Am J Trop Med Hyg. 2007;77(2):350–3.
92. Le T, Kinh NV, Cuc NT, Tung NL, Lam NT, Thuy PT, et al. A trial of itraconazole or amphotericin B for HIV-associated talaromycosis. N Engl J Med. 2017;376(24):2329–40.
93. Zeng W, Qiu Y, Lu D, Zhang J, Zhong X, Liu G. A retrospective analysis of 7 human immunodeficiency virus-negative infants infected by *Penicillium marneffei*. Medicine (Baltimore). 2015;94(34):e1439.
94. Le T, Ly VT, Thu NTM, Nguyen A, Thanh NT, Chau NVV, et al. Population pharmacodynamics of amphotericin B deoxycholate for disseminated infection caused by *Talaromyces marneffei*. Antimicrob Agents Chemother. 2019;63(2):e01739-18.
95. Thompson DF, Walker CK. A Descriptive and Historical Review of Bibliometrics with Applications to Medical Sciences. Pharmacother J Hum Pharmacol Drug Therapy. 2015;35(6):551–9.
96. Duong TA. Infection due to *Penicillium marneffei*, an emerging pathogen: review of 155 reported cases. Clin Infect Dis. 1996;23(1):125–30.
97. Supparatpinyo K, Chiewchanvit S, Hirunsri P, Uthammachai C, Nelson KE, Sirisanthana T. *Penicillium marneffei* infection in patients infected with human immunodeficiency virus. Clin Infect Dis. 1992;14(4):871–4.
98. Sirisanthana T, Supparatpinyo K, Perriens J, Nelson KE. Amphotericin B and itraconazole for treatment of disseminated *Penicillium marneffei* infection in human immunodeficiency virus-infected patients. Rev Infect Dis. 1998;26(5):1107–10.
99. Sekhon A, Li J, Garg A. Penicillosis marneffei: serological and exoantigen studies. Mycopathologia. 1982;77(1):51–7.
100. Imwidthaya P, Sekhon A, Mastro T, Garg A, Ambrosie E. Usefulness of a microimmunodiffusion test for the detection of *Penicillium marneffei* antigenemia, antibodies, and exoantigens. Mycopathologia. 1997;138(2):51–5.
101. Imwidthaya P, Thipsuvan K, Chaiprasert A, Danchaivijitra S, Sutthent R, Jearanaisilavong J. *Penicillium marneffei*: types and drug susceptibility. Mycopathologia. 2001;149(3):109–15.
102. Li X, Yang Y, Zhang X, Zhou X, Lu S, Ma L, et al. Isolation of *Penicillium marneffei* from soil and wild rodents in Guangdong, SE China. Mycopathologia. 2011;172(6):447–51.
103. Sekhon A, Stein L, Garg A, Black W, Glezos J, Wong C. Pulmonary penicillosis marneffei: report of the first imported case in Canada. Mycopathologia. 1994;128(1):3–7.
104. Luo D-Q, Chen M-C, Liu J-H, Li Z, Li H-T. Disseminated *Penicillium marneffei* infection in an SLE patient: a case report and literature review. Mycopathologia. 2011;171(3):191–6.
105. Cao C, Liu W, Li R. *Penicillium marneffei* SKN7, a novel gene, could complement the hypersensitivity of *S. cerevisiae* skn7 disruptant strain to oxidative stress. Mycopathologia. 2009;168(1):23–30.
106. Lu S, Hu Y, Lu C, Zhang J, Li X, Xi L. Development of in vitro macrophage system to evaluate phagocytosis and intracellular fate of *Penicillium marneffei* conidia. Mycopathologia. 2013;176(1–2):11–22.
107. Sirisanthana T, Supparatpinyo K, Perriens J, Nelson KE. Amphotericin B and itraconazole for treatment of disseminated *Penicillium marneffei* infection in human immunodeficiency virus-infected patients. Clin Infect Dis. 1998;26(5):1107–10.