Jean-Philippe Bouchara Pietro Nenoff · Aditya K. Gupta Vishnu Chaturvedi *Editors* 

# Dermatophytes and Dermatophytoses



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ISBN 978-3-030-67420-5 ISBN 978-3-030-67421-2 (eBook) https://doi.org/10.1007/978-3-030-67421-2

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#### **Preface**

The study of dermatophytes and dermatophytoses is continually evolving. This edited volume provides an up-to-date snapshot of the basic and translational research and contemporary approaches in use in the dermatology clinics and diagnostic laboratories. Both clinical researchers and physicians will find valuable information about the molecular, genetic, and epidemiological aspects. The diagnosis and treatment of dermatophytoses are discussed in detail, which is increasingly challenging due to resistance to current antifungal drugs. The spectrum of pathogens causing dermatophytoses has expanded in recent years. The reasons for this include the direct migration from Africa and Asia to Europe and North America. In addition, the increased travel and trade due to globalization have brought old and new dermatophytes to new geographic locations. Molecular methods for direct detection of fungi or fungal DNA are increasingly part of diagnosing dermatophytoses alongside conventional techniques. Similarly, many dermatophyte species require exact identification by DNA sequencing or mass spectrometry.

The future of dermatophytosis treatment will probably involve innovative treatment regimens and novel pharmaceuticals to fight the acquired mutations in fungal pathogens. The increase in mixed infections and geographic distribution also poses barriers to successful treatment, demonstrating the necessity for more effective diagnostic methods. Similar concerns exist about the increase in the incidence of chronic recurrent and treatment-recalcitrant dermatophytoses. As a result of the "globalization of people and fungi," the first isolates of terbinafine-resistant dermatophyte are now known from India, the Middle East, Iran, Germany, Finland, and the USA. In vitro resistance testing of dermatophytes, including mutation analysis of squalene epoxidase, has experienced an unexpected boom in the last few years. It is likely to become a mainstay of clinical management of dermatophytoses.

The Part I "Current Taxonomy of Dermatophytes" is a formal introduction to fungal pathogens classified as "dermatophytes." The focus is on a current understanding of their evolution with human and animal hosts, changing epidemiology, recommended identification methods, and a list of valid species in genera *Trichophyton*, *Epidermophyton*, *Nannizzia*, *Microsporum*, *Paraphyton*, *Lophophyton*, and *Arthroderma*.

The Part II "Clinical Aspects" includes five contributions. "Dermatophytes and Dermatophytic Infections Worldwide" is a sweeping overview of dermatophytes and

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dermatophytic infections worldwide. Many maps are provided to highlight geographic distribution and to postulate future trends. "Onychomycosis in the Twenty-First Century: An Update on Epidemiology and Diagnosis" focuses on the global prevalence of fungal nail infections (onychomycosis), epidemiological factors, and contemporary laboratory diagnosis methods. "Invasive Dermatophytoses: Clinical Presentations, Diagnosis, and Treatment" introduces invasive or dermatophytoses, relatively rare but serious conditions, which afflict humans with underlying immune dysfunctions. An excellent overview is presented about the combined medical and surgical management of deep dermatophytoses. "Unusual Dermatophytosis Presentations and New Emerging Dermatophytes Species" describes newly emerging species of dermatophytes and unusual presentations of dermatophytosis. Chapter "Non-dermatophyte Dermatoses Dermatophytoses in Animals" includes dermatopytoses in animals, dermatoses that mimic dermatophytoses, and the fungal species involved. The scope is inclusive of pets, domestic animals, and wildlife with an enhanced focus on differential diagnosis.

The Part III focuses on the pathogenesis of dermatophytosis. The three contributions, "Experimental Models of Dermatophytosis", "Transcriptome of Host-Dermatophyte Interactions Using Infection Models" and "Genetic Predictors of Susceptibility to Dermatophytosis" highlight contemporary experimental approaches to study pathogenic potential, host responses, and antifungal efficacy. "Experimental Models of Dermatophytosis" provides a comprehensive overview of in vitro, in vivo, and ex vivo models to study dermatophytoses and evaluation of new antifungal agents. The complexity of infectious propagules, pathogen recognition, immune responses, histopathology, and antifungal effects are explained with exquisite illustrations. "Transcriptome of Host-Dermatophyte Interactions Using Infection Models" introduces experimental approaches to understand host-pathogen interplay in dermatophytoses. Novel gene expression studies in experimental animal models are applied to gain insights into pathogenic factors and host defense mechanisms in dermatophytoses. "Genetic Predictors of Susceptibility to Dermatophytosis" covers genetic factors that predispose humans to infections with dermatophytes. A critical analysis of existing data is presented to summarize putative underlying host mechanisms that determine susceptibility to dermatophytosis.

The Part IV highlights epidemiology of dermatophytes and dermatophytosis. "The *Trichophyton rubrum* Complex" focuses on the *Trichophyton rubrum* complex, which includes agents of nail, skin, and hair infections. An elaborate polyphasic scheme with morphological, physiological, and DNA methods is highlighted as "gold standard" for *T. rubrum* complex. "*Microsporum ferrugineum*: The Renaissance of a Forgotten Dermatophyte" details unusual findings of *Microsporum ferrugineum* in Germany, an anthropophilic dermatophyte not seen in the country for nearly 50 years. Clinical workup, enhanced laboratory diagnostic tools, and treatment approaches are detailed. "*Trichophyton mentagrophytes* ITS Genotype VII from Thailand" highlights emerging European cases of *T. mentagrophytes* ITS-genotype VII, which causes inflammatory and abscessing dermatophytoses. The unusual geographic emergence is linked with human-to-human transmission. "Trends in Epidemiology of Dermatophytes in Iran" is a comprehensive review of

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epidemiology of dermatophytes in Iran in the last 70 years. It details changes in species spectrum, antifungal treatment, emergence of resistance, and improved laboratory diagnosis. "Onychomycosis in Adults: A Clinical Perspective from Mexico" summarizes onychomycosis with emphasis on South America and Latin America. "*Tinea capitis* in School Children: Current Status" is about *Tinea capitis* with emphasis on epidemiology, clinical presentations and complications, treatment, and community management.

Part V "Laboratory and Molecular Diagnosis of Dermatophytosis" includes three contributions. "The Potential of Molecular Diagnostics in Routine Dermatology" widens the traditional mycological examination of clinical specimens to molecular diagnostics. In-house PCR and hybridization tests are compared to commercial kits, and challenges and strategies for their implementation. "Laboratory Diagnosis of Dermatophytosis" summarizes the traditional mycological examination of clinical specimens to confirm dermatophytoses. "MALDI-TOF-Based Identification of Dermatophytes" focuses on the application of mass spectrometry for the identification of dermatophytes. It presents a useful comparison of the commercial systems, their databases, and relative performances.

Parts VI and VII describe antifungal resistance of dermatophytes and treatment of dermatophytoses. "Antifungal Susceptibility Testing of Dermatophytes" deals with antifungal susceptibility testing of dermatophytes. The description includes broth microdilution and other testing formats, endpoint reading, clinical breakpoints, and the diagnosis of terbinafine resistance. "Terbinafine and Itraconazole Resistance in Dermatophytes" widens the perspective on antifungal susceptibility testing with a focus on terbinafine and itraconazole resistance. "New Antifungal Agents and New Formulations Against Dermatophytes" introduces new antifungal drugs and new formulations of existing drugs for the treatment of onychomycosis. The value of clinical management, combined with patient education, is emphasized. "Are Natural Products an Alternative Therapy for Dermatophytosis?" involves the potential of natural products used in traditional methods for dermatophytoses treatment. As scientific evidence accumulates for their efficacy, it is expected that these plant-based products and their derivatives would be valuable sources of new drugs to treat dermatophytoses.

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