Common and Emerging Dermatophytoses in Animals: Well-Known and New Threats

3

Vit Hubka, Andrea Peano, Adela Cmokova, and Jacques Guillot

Abstract

Zoophilic dermatophytes are frequently responsible for superficial mycoses in mammals worldwide. They comprise approximately ten specialized parasitic fungi belonging to genera *Trichophyton* and *Microsporum*. Due to contagious nature of the disease, the majority of species possess potential to cause outbreaks at least in their principal host(s) and at the same time have the capability to infect a wide spectrum of mammals, including humans. The purpose of this chapter is to trace the current changes in the epidemiology of animal-infecting dermatophytes that show large geographic differences and dynamically alter over time. Emphasis

V. Hubka (✉)
Department of Botany, Faculty of Science, Charles University, Prague, Czech Republic

Laboratory of Fungal Genetics and Metabolism, Institute of Microbiology of the Czech Academy of Sciences, v.v.i., Prague, Czech Republic

First Faculty of Medicine, Charles University, Prague, Czech Republic
e-mail: hubka@biomed.cas.cz

A. Peano
Department of Veterinary Sciences, University of Turin, Turin, Italy
e-mail: andrea.peano@unito.it

A. Cmokova
Department of Botany, Faculty of Science, Charles University, Prague, Czech Republic

Laboratory of Fungal Genetics and Metabolism, Institute of Microbiology of the Czech Academy of Sciences, v.v.i., Prague, Czech Republic
e-mail: cmokova@gmail.com

J. Guillot
Department of Parasitology, Mycology and Dermatology, EnvA, Ecole nationale vétérinaire d'Alfort, UPEC, Maisons-Alfort, France

Dynamyc Research Group, EnvA, Ecole nationale vétérinaire d'Alfort, UPEC, Maisons-Alfort, France
e-mail: jacques.guillot@vet-alfort.fr

S. Seyedmousavi et al. (eds.), *Emerging and Epizootic Fungal Infections in Animals*,
https://doi.org/10.1007/978-3-319-72093-7_3

is given not only to the most important and widespread dermatophyte species representing global issue for both animal and human medicine (*Microsporum canis*, *Trichophyton mentagrophytes*, and *T. verrucosum*) but also to newly emerging pathogens such as *T. benhamiae*, an agent of epidemic dermatophytosis in Europe frequently affecting guinea pigs and their breeders or owners. The methods for identification and molecular typing of dermatophytes are summarized due to their importance for outbreak detection and epidemiological surveillance. Strategies for management and prevention of outbreaks are also presented.

3.1 Introduction

Dermatophytes are the most successful pathogenic fungi causing superficial mycoses (dermatophytosis, also called ringworm) in humans and animals. They encompass ecologically and phylogenetically related fungi belonging to the family Arthrodermataceae (order Onygenales) which are able to use keratin as a sole nutrient source (Gräser et al. 1999a; Sugiyama et al. 2002). In the last several decades, the dermatophytes were usually categorized into three genera, *Trichophyton*, *Epidermophyton*, and *Microsporum*, and associated sexual state used to be classified in *Arthroderma* (Weitzman et al. 1986; Weitzman and Summerbell 1995). With complete abolition of dual nomenclature (McNeill et al. 2012) and availability of multiple gene phylogenies, the number of genera was expanded (de Hoog et al. 2017), but the most important primary pathogenic species remains in the three mentioned genera. Chronology of selected important historical events related to dermatophytosis and dermatophytes is shown in Fig. 3.1.

Dermatophytoses occur frequently in livestock, in companion animals, and also in wildlife. Infections caused by zoophilic dermatophytes are usually benign and self-limiting and respond well to treatment; they are rarely serious or manifest as systemic infection in immunocompromised host (Chermette et al. 2008; Rouzaud et al. 2016). The prevalence in animals shows large geographic differences. It seems to be influenced by trade, exchanges of animals for reproductive purposes, exhibitions (for cats and dogs), and sportive activities (e.g., horse races). Risk of zoonotic transmission depends on the local spectrum of kept animals and epidemiological situation (prevalence of pathogens in animals) but also on local relations between man and animals, hygienic standards, and socioeconomic factors. Dermatophytoses are highly contagious, and animals kept in herds or groups are threatened by the epidemic spread of infection even when one of few infected individuals are introduced into the community. The environment contaminated by arthroconidia and diseased animals (commonly with mild clinical signs or symptomless) represents a potential source of infection to humans.

High financial costs are associated worldwide with treatment, diagnosis, and prevention of dermatophytosis (Drake et al. 1996). Direct economic costs in farming and industry result from unaesthetic aspect of lesions (hide and skin industry), which

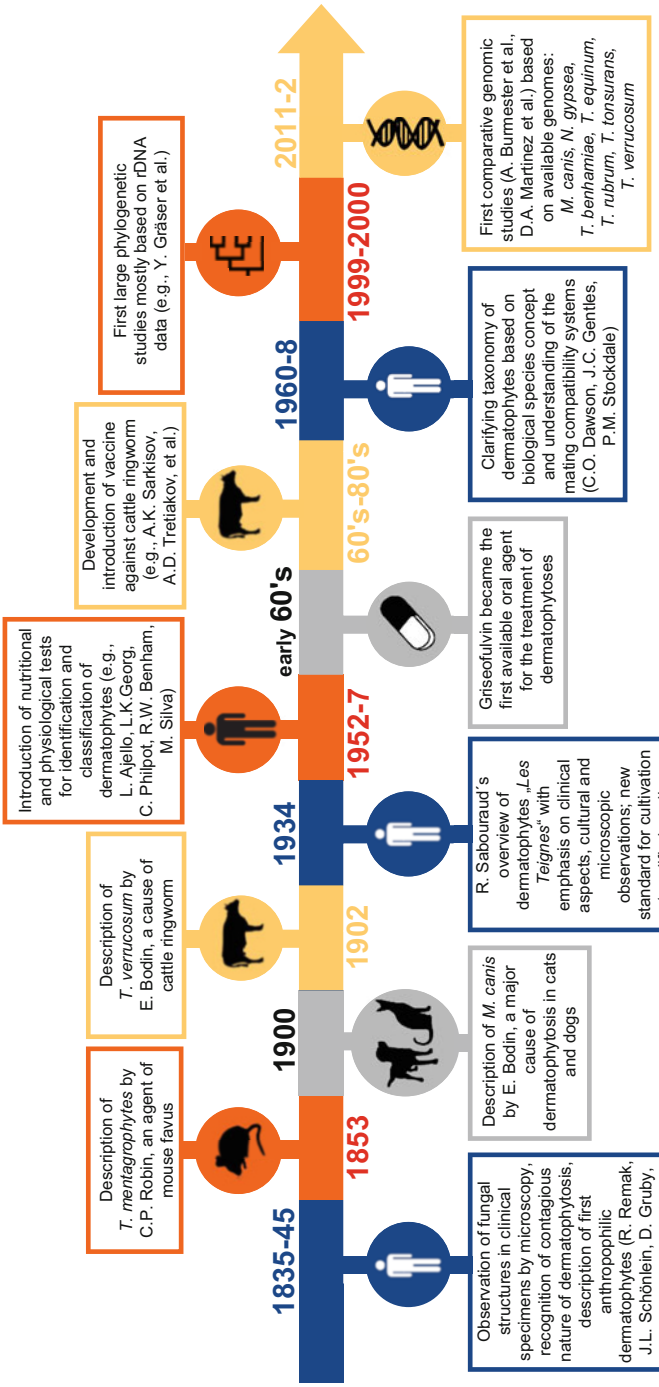

Fig. 3.1 Chronology of important events related to dermatophytosis and taxonomy of dermatophytes

hinder animal trade and are also an obstacle to attend exhibitions and sportive activities (Chermette et al. 2008).

For effective treatment and prevention of the spread of these diseases, it is important to correctly determine the causal agents at the species level, which allows prescription of suitable therapy and at the same time identification of probable source of infection. Correct species identification is an indispensable prerequisite for monitoring changes in the frequency of individual species, helps to evaluate the results of preventive measures and interventions, and is a basic requirement for the preparation of epidemiological studies. Instable taxonomy of dermatophytes, problematic species concept, and phenotypic identification limit comparability of recent epidemiological data with studies from the past. In the last two decades, the advent of molecular methods greatly contributed toward the understanding of the biodiversity of dermatophytes (Gräser et al. 1999b, 2000a, 2000b, 2008; Hubka et al. 2014a), thus challenging the previous classification based on morphology and nutritional tests. However, dermatophytosis in animals is classically based on phenotypic methods, and we have currently no systematic data supported by molecular methods worldwide on the epidemiology of dermatophytes.

3.2 Virulence Factors and Pathogenesis

The dermatophytes are transmitted by direct contact with an infected host or by contact with contaminated objects and environment. The successful initiation of infection is closely related to the capability of the pathogenic fungus to overcome the host resistance mechanisms. The adherence to the keratinized tissue, germination of the arthroconidium, and stratum corneum penetration are the first steps in this process (Hube et al. 2015; Chinnapun 2015). Mechanical disruption of the stratum corneum consequent to microtrauma of different origin (e.g., due to ectoparasites in cats and dogs) appears to be important aspect in facilitating penetration and invasion of hair follicles (Miller et al. 2013). Three crucial steps to overcome cutaneous barriers and cause infection, i.e., adhesion, germination, and invasion of the stratum corneum, are separated by variously long time periods that range from several hours to several days depending on particular species (Aljabre et al. 1993; Rashid et al. 1995; Duek et al. 2004). It has been suggested that pathogenic dermatophytes express carbohydrate-specific adhesins on conidia surface that recognize mannose and galactose on the skin surface during adhesion (Esquenazi et al. 2004). Additionally, secreted proteases are required for the adherence process and participate in invasion of epidermis (Baldo et al. 2008; Baldo et al. 2010; Shi et al. 2016). Keratin is a hard and compact protein, which is unavailable as a nutrient source to the majority of organism in the nature. Its degradation and utilization during penetration and infection are considered a major virulence attribute. The dermatophytes dispose expanded sets of endopeptidases, exopeptidases, and secreted proteases reserved for that purposes (Burmester et al. 2011; Martinez-Rossi et al. 2017). In addition, the process of keratinolysis is facilitated by sulfite efflux, a reducing agent which can cleave keratin-stabilizing cystine bonds and whose production from cystine depends on the cysteine dioxygenase (Grumbt et al. 2013).

Other tentative virulence factors comprise production of siderophores to overcome iron deficiency (Mor et al. 1992; Kröber et al. 2016), melanin with immunomodulatory properties (Youngchim et al. 2011), expression of homologues of multidrug resistance class of ABC transporters modulating susceptibility to antifungals (Fachin et al. 2006; Ghannoum 2016), or production of toxic exometabolites. Genome sequences of dermatophytes revealed a high number of secondary metabolite gene clusters, some of them are upregulated during keratinocyte infection (Burmester et al. 2011; Martinez et al. 2012; Yin et al. 2013). Toxin xanthomegnin was predicted as a virulence factor and can be extracted from infected keratinized tissues but is not detected in uninfected tissues (Gupta et al. 2000; Kandemir et al. 2015).

In general, the stepwise process of host infection is similar across the species; however, the ability to elicit a host reaction upon infection is species-specific. Different dermatophytes induce different immune responses in the host in terms of quality and intensity. They may induce a high level of tissue damage and inflammatory reaction, but in particular host species or individuals, they can manipulate the host's immune response, ensuring survival and prolonging chronic infection (Hube et al. 2015). The interaction of host cells (keratinocytes and immune cells) and dermatophyte and recognition of fungal antigens and secreted enzymes by host are basis for immune response. Cell-mediated immunity and production of various cytokines are widely considered to be involved in modulating the immune response (Achterman and White 2011; Hube et al. 2015; Chinnapun 2015; Martinez-Rossi et al. 2017).

3.3 Clinical Manifestations and Diagnosis

Dermatophytosis can be located on any part of the animal body and usually manifests as a regular and circular focus generally accompanied with alopecia and desquamation. The lesion spread centrifugally from the site of inoculation; multiple lesions can merge into large foci with irregular margins. The lesion can be erythematous over the entire surface but especially on the periphery. It can be covered by pustules and later by exudate and crusts. Other clinical signs may be present, such as pruritus accompanied by scratching and behavior change. Animal dermatophytosis has usually self-limiting nature, and spontaneous regrowth of hairs is generally observed. Infection is usually restricted to the dead cornified layers of the skin because of the inability of the dermatophytes to attack the deeper layers of the skin or organs of immunocompetent hosts. Naive, usually young, animals can be heavily infected with significant impact on health condition and growth. The increased susceptibility of young animals may also reflect differences in the biochemical properties of the skin and skin secretions (especially sebum), growth and replacement of hair, and the physiologic status of the host as related to age. Animals can exhibit subtle signs or act as "asymptomatic" carriers of dermatophytes without history of dermatophytosis as seen relatively commonly in cats infected by *M. canis* or guinea pigs infected by *T. benhamiae*. Regardless of the possibility of more virulent strain emergence, many factors related to the host play a critical role in

determining the type of clinical lesions produced and terminating the infection. More comprehensive reviews and monographs are available on this topic (Donnelly et al. 2000; Chermette et al. 2008; Miller et al. 2013; Moretti et al. 2013).

In companion animals (cats, dogs, or small mammals like rabbits, guinea pigs, and chinchillas) as well as in large animals (horses and cattle), dermatophytes are frequently responsible for skin diseases including alopecia and crusts. Dermatophytosis is a contagious disease, and cases are regularly reported in breeding facilities and farms. Human contamination is also indicative. However, experimental diagnosis is systematically required. The use of the Wood's lamp is recommended when *M. canis* infection is suspected in companion animals. The microscopic examination of hairs and scales can be performed from skin scrapings (Fig. 3.2). According to the dermatophytes species, arthroconidia have different dimensions and disposition on the hairs: *M. canis* produces clusters of very small

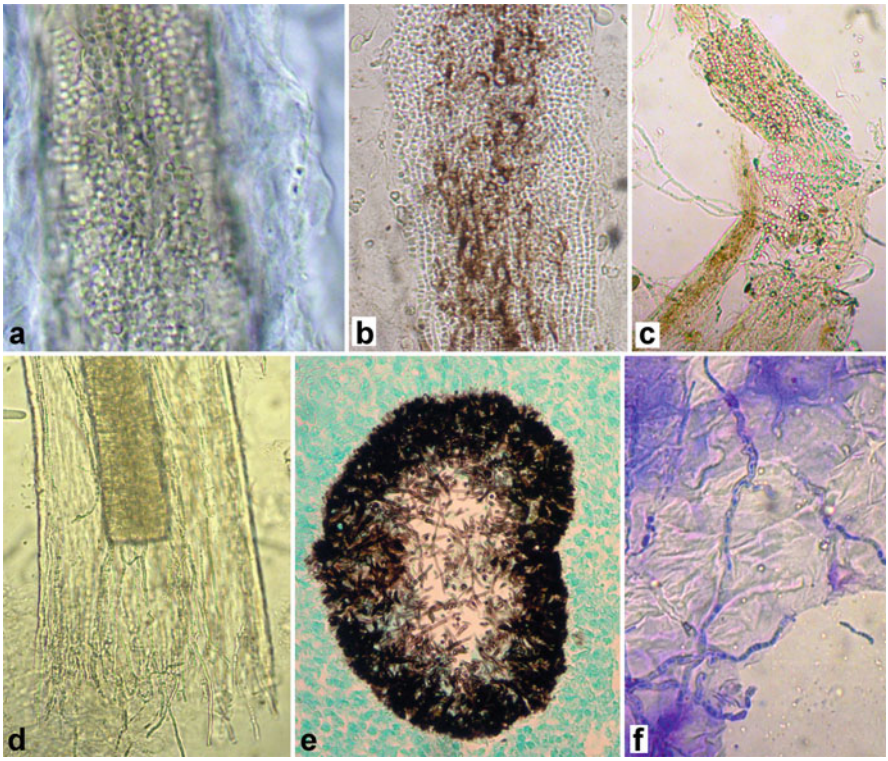

Fig. 3.2 Laboratory diagnosis of dermatophytosis by using direct microscopic examination or histology. (**a**) Arthroconidia of *Microsporum canis* at direct hair examination (digestion in 20% NaOH). (**b**) Arthroconidia of *Trichophyton benhamiae* at direct hair examination (digestion in 20% NaOH). (**c**–**d**) Arthroconidia of *Trichophyton verrucosum* at direct hair examination (digestion in 20% NaOH). (**e**) Histopathological examination (Gomori-Grocott staining) of pseudomycetoma in a cat due to *M. canis*. (**f**) Cytological examination in case of human dermatophytosis due to zoophilic *Trichophyton mentagrophytes* (scotch tape technique)

(2–4 μm) arthroconidia, whereas members of the genus *Trichophyton* form chains of arthroconidia (Chermette et al. 2008). Fungal culture is still considered as the golden standard for diagnosis. Samples of hairs, crusts, scales, or even cutaneous tissue (in the specific case of pseudomycetoma) should be collected for culture. When a large number of colonies of dermatophyte develop on the culture medium, active infection is demonstrated. When only a few colonies develop on the culture medium, subclinical infection or mechanical carriage (especially in cats or guinea pigs) should be suspected. When unusual clinical presentations are observed, histological examination is recommended (Fig. 3.2).

Sensitivity of both direct microscopic examination and cultivation depends on the combination of host and pathogen. Microscopic examination fails to provide the identification of the agent, whereas culture has usually several weeks turnaround time and the requirement of mycological expertise. The reliance on culture, which may be often unsuccessful for some dermatophyte species, can be substituted by PCR-based tests that are now available for the direct diagnosis of dermatophytosis from clinical samples and significantly reduces the time of diagnosis (hours to days). These methods can suitably supplement or even replace classical diagnostic schemes thanks to their high sensitivity and specificity. They are represented by conventional PCR, RT-PCR, or more complex methodologies (PCR-ELISA, PCR-RLB, microarrays) and usually offer opportunity to detect DNA of any dermatophyte without species identification, but some more recently developed assays are able to identify relatively broad spectrum of species including major zoophilic species (Jensen and Arendrup 2012; Cafarchia et al. 2013b; Dąbrowska et al. 2014; Mehlig et al. 2014; Kupsch et al. 2016).

3.4 Ecology of Dermatophytes and Origin of Zoophilic Species

The Mesozoic era (252–66 million years ago) was associated with a significant ecological morphological diversification of early mammals, a prerequisite for evolutionary success after extinction of the nonavian dinosaurs 66 million years ago. It was assumed based on molecular dating that dermatophytes could radiate approximately 50 million years ago (Harmsen et al. 1995) closely linked to early Cenozoic adaptive explosion of mammals. However, more recently fossil evidence of dermatophytosis in mammals was estimated to be approximately 125 million-year-old (Martin et al. 2015). Despite numerous uncertainties, it seems quite clear that dermatophytes are evolutionary young group of fungi that diverged later than other groups of pathogenic fungi (Wu et al. 2009).

Significant part of the diversity of dermatophytes is represented by geophilic species that act as uncommon causal agents of infections without significant contagious potential. They occur in soil around burrows and nests of terrestrial vertebrates and birds, can be carried in the fur, and therefore cause diagnostic doubts when they are isolated from healthy animals or animals with ambiguous symptoms. Geophilic species are characterized by relatively high intraspecies diversity, and they are all sexual and heterothallic (isolates of two opposite mating types are present in

population) with only few exceptions. The sexual process takes place in the soil on the keratinized substrates. Geophilic species are considered an ancestral ("primitive") group of dermatophytes, while "advanced" ecological groups of zoophilic and anthropophilic are derived from geophilic species. The phylogenetic grouping of anthropophilic and zoophilic species of *Trichophyton* and *Microsporum* into monophyletic clades and geophilic species from genera *Arthroderma*, *Nannizzia*, and *Paraphyton* into another monophyletic clades supports the hypothesis that ecology has been crucial driver of the evolution in dermatophytes (Gräser et al. 2008; de Hoog et al. 2017).

Specialized pathogens of animals and human, zoophilic and anthropophilic species, respectively, are primarily associated with one or few related host species but have potential to cause infection in a broad spectrum of animals (Table 3.1). They usually cause mild (chronic) or asymptomatic infections in primary host, often

Table 3.1 Ecology of zoophilic or possibly zoophilic dermatophytes

Species	Principal host(s)/ source, other hosts	Distribution	Epidemic potential in principal hosts	Zoonotic risk for human
Microsporum canis (syn. *M. equinum*)	**Cat**, **dog**, **horse**, all mammals	Worldwide	High	High
L. gallinae (syn. *M. vanbreuseghemii*)[a]	**Chicken**, **soil**, birds, mammals	Worldwide	Low	Low
T. benhamiae	**Guinea pig**, other rodents, dogs	Worldwide	High	High
T. bullosum	**Horse**, **donkey**, mole?	Syria, Sudan, Tunisia, France, Czech Republic	Insufficient data	Insufficient data
T. equinum	**Horse**	Worldwide	High	Low
T. erinacei	**Hedgehogs** (*Erinaceus europaeus, Atelerix albiventris*)	Europe, New Zealand, Africa (kept as pet worldwide)	High	Probably high
T. eriotrephon	Unknown	Netherlands, Iran	Insufficient data	Insufficient data
T. mentagrophytes	**Rabbits**, **rodents**, cats, and dogs (especially free roaming and hunting)	Worldwide	High	High
T. quinckeanum	**Rodents** (mice)	Worldwide	High	High
T. simii[a]	Soil, monkeys, chicken, dog	Worldwide	Low	Low
T. verrucosum	**Cattle**, **other ruminants**, all mammals, birds	Worldwide	High	High

[a]These species are probably geophilic—see Sect. 3.9

being widespread and epidemic/epizootic. In contrast, the infections in less common hosts tend to be acute and highly inflammatory. The population structure of many primary pathogenic species is nearly clonal, and they have unknown sexual state. It was suggested that these "species" spread clonally by asexual propagation in the population of host without having a terrestrial reservoir and thus reducing the probability of encountering a partner of the opposite sex (Summerbell 2002). Consequently, these "species" (clonal offshoots) derived from their sexual ancestors possess predominantly only strains with identical mating type across global population. Kano et al. (2014) demonstrated that strains of *T. verrucosum* have consistently only MAT1-2-1 gene corresponding to the mating type (−). Similarly, single mating is also present in anthropophilic species *T. tonsurans* (mating type −), *T. rubrum* (mating type −), and *T. violaceum* (mating type −) but also in zoophilic *T. equinum* with mating type + (Gräser et al. 2008; Metin and Heitman 2017). The intraspecies variability in these taxa is mostly generated by fixation of neutral mutations. Historically, species and populations tended to remain within limited geographic areas such as continents, a condition leading to structuration of global population. With human migration and animal trade, however, geographically restricted genotypes can be rapidly distributed over large geographic areas, leading to reduction of polymorphism within widely dispersed entities (Gräser et al. 2006).

In contrast to abovementioned species, both mating types are present in population of *T. benhamiae* (Kano et al. 2011; Symoens et al. 2013; Cmokova 2015), *T. mentagrophytes* (Symoens et al. 2011), and *M. canis* (Hironaga et al. 1980) suggesting that sexual reproduction naturally occurs in these species and probably takes place in burrows of wild animals or their close neighborhood rather than in association with dwellings of domestic animals. The distribution of mating-type genes is commonly unequal in mentioned species or at least in some subpopulations. This may be caused by clonal horizontal propagation of single or several clones in the population of the host. Assessment of species boundaries by mating experiments is in general well applicable in geophilic species (Stockdale 1964; Hubka et al. 2015). In contrast, biological compatibilities can considerably disagree with the concept of classical species of anthropophilic and zoophilic dermatophytes. These species are phylogenetically young, and prezygotic reproductive barriers are incomplete resulting in positive mating experiments even between phylogenetically distant species (Anzawa et al. 2010; Kawasaki et al. 2010; Kawasaki 2011). It is however highly unlikely that this kind of hybridization occurs naturally due to different ecological niches of species.

3.5 Phylogenetic Position of Zoophilic Dermatophytes and Their Identification

The dermatophytes have been divided into three genera by using conventional phenotypic taxonomy: *Trichophyton*, *Microsporum*, and *Epidermophyton*. This classification scheme has been widely accepted in the second half of the twentieth century and used till today. Phylogenetic relationships between dermatophytes have

been exploited by using numerous genetic loci, including mitochondrial DNA (mtDNA) (Nishio et al. 1992), small subunit of ribosomal DNA (SSU rDNA) (Harmsen et al. 1995), large subunits (LSU) of rDNA (Leclerc et al. 1994), internal transcribed spacer (ITS) region of rDNA (Gräser et al. 1999a, b, 2000b; Makimura et al. 1999; Summerbell et al. 1999; Kawasaki et al. 2011; Pchelin et al. 2016), chitin synthase (CHS) (Kano et al. 1999, 2002; Hirai et al. 2003) and DNA topoisomerase II genes (TOP II), actin, glyceraldehyde-3-phosphate dehydrogenase (GPD) (Kawasaki et al. 2011), translation elongation factor 1-α (TEF 1-α) (Mirhendi et al. 2015), β-tubulin (Rezaei-Matehkolaei et al. 2014; Pchelin et al. 2016), and calmodulin (Ahmadi et al. 2016). The topology of phylogenetic trees based on ITS region (Fig. 3.3) is congruent with those based on protein-coding loci, i.e., *TEF 1-α*, β-tubulin, and calmodulin. The studies with sufficient coverage of species across diversity of Arthrodermataceae consistently showed that both *Trichophyton* and *Microsporum* are polyphyletic prompting reevaluation of the generic concept of dermatophytes (Gräser et al. 1999a; Rezaei-Matehkolaei et al. 2014; Mirhendi et al. 2015; Ahmadi et al. 2016). The new generic concept with monophyly as a main criterion was recently introduced by de Hoog et al. (2017) who increased the number of recognized genera from three to seven. This new concept has only limited consequences for the taxonomy of human and animal pathogenic dermatophytes, while significant changes were made in the taxonomy of geophilic species.

ITS rDNA sequencing is considered a gold standard for species identification. It is still the only genetic locus available for all currently accepted species, is recommended as a barcode, and is widely used for identification in praxis (Irinyi et al. 2015). ITS region sequence has capability to discriminate even closely related species, e.g., *M. canis*, *M. audouinii*, and *M. ferrugineum*; *T. benhamiae* and *T. concentricum*; and *T. quinckeanum* and *T. schoenleinii*. Identification of all mentioned sibling species cannot be realized by amplification of any currently available protein-coding loci. When DNA sequence is available, species identification is usually obtained by comparison with the reference sequence in the database (e.g., GenBank; www.ncbi.nlm.nih.gov/genbank). Because GenBank acts primarily as an archive, many sequences have been annotated incorrectly, the reason why curated databases were established, e.g., ISHAM ITS Database (http://its.mycologylab.org) or Dermatophytes Species Database at Westerdijk Fungal Biodiversity Institute (http://www.westerdijkinstitute.nl/Dermatophytes). A plenty of PCR-based techniques were developed for identification of dermatophytes with variable discriminatory power including nested PCR, PCR-RFLP, RAPD, ISSR-PCR, AFLP, AP-PCR, etc. (Chen et al. 2011; Sharma and Gräser 2011; Cafarchia et al. 2013c). In particular PCR-RFLP targeting ITS or other regions with digestion using various restriction enzymes reached relatively broad popularity due to low financial cost and usability for identification of major pathogens (De Baere et al. 2010; Heidemann et al. 2010; Rezaei-Matehkolaei et al. 2013). Many other methods showed similar or higher potential for species identification, but they have only limited usability due to poor reproducibility or laboriousness and are now obsolete.

While DNA-based molecular methods are usually highly accurate and rapid, they are relatively costly and can be complex to implement. Matrix-assisted laser

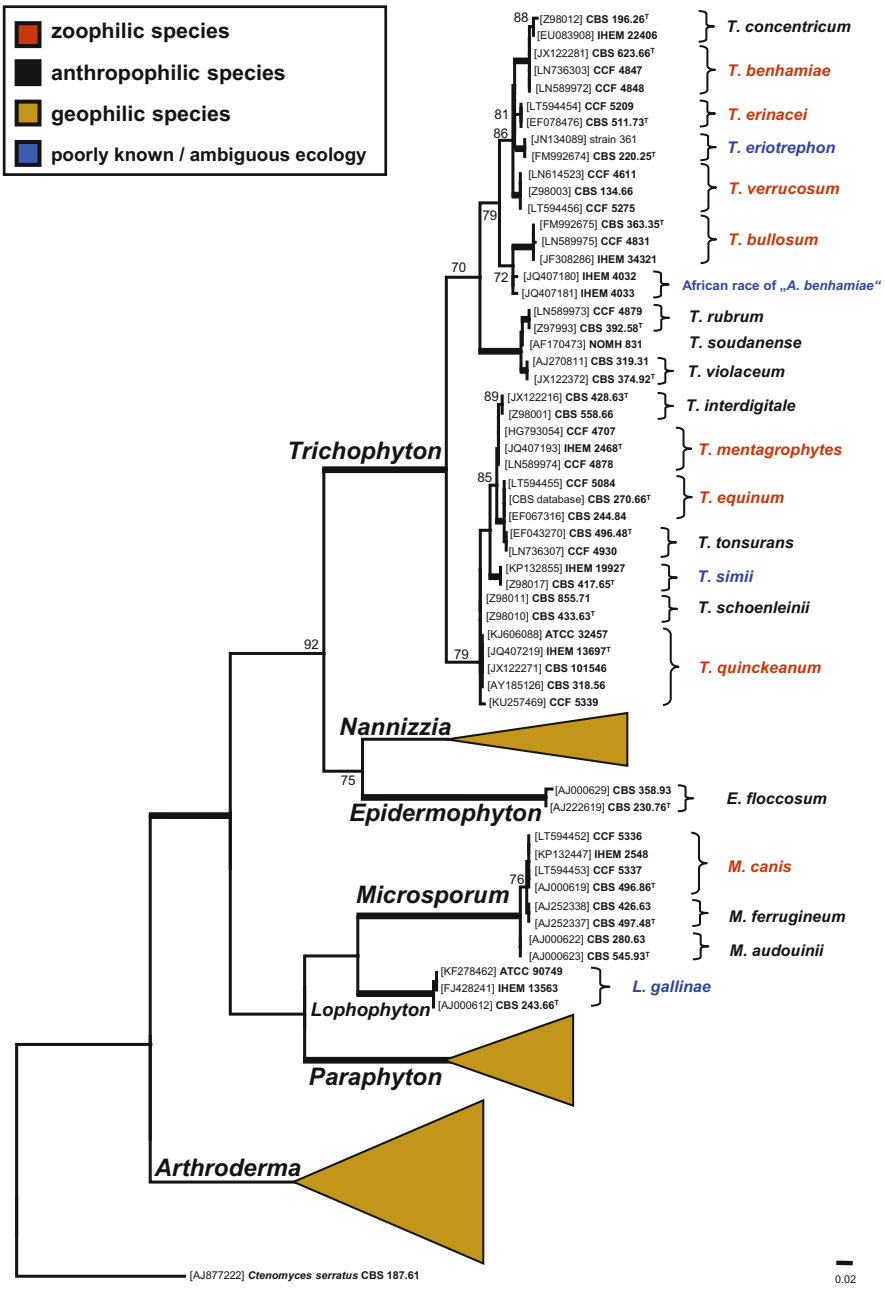

Fig. 3.3 Phylogenetic placement of zoophilic species within dermatophytes. Best scoring maximum likelihood tree-based ITS rDNA constructed with the IQ-TREE version 1.4.0 (Nguyen et al. 2015) by using GTR + I + G4 substitution model. Dataset contained 95 taxa and a total of 731 characters of which 351 were variable and 306 parsimony informative. Support values at

desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) may represent an alternative to conventional dermatophyte identification. Application of MALDI-TOF MS as an identification procedure for pathogenic dermatophytes has been increasingly used in the laboratories due to its time- and cost-effectiveness (despite the initial cost of investment for obtaining the equipment) (L'Ollivier and Ranque 2017). The method is able to distinguish all major pathogenic dermatophytes; however, the differentiation of phylogenetically closely related taxa is associated with higher level of errors, e.g., *T. quinckeanum* and *T. schoenleinii*, different races of *T. benhamiae*, or *T. interdigitale* and *T. mentagrophytes*. Thus, supplementation of the reference spectra libraries is still required for optimal dermatophyte identification (Gräser 2014).

Despite the advent of molecular methods, conventional species identification of dermatophytes is still the prevailing method of identification worldwide and consists of micro- and macromorphological examination of cultures, sometimes supplemented with various physiological and biochemical tests (e.g., nutritional tests, vitamin requirements tested on T1-T7 *Trichophyton* agars, urease activity, hair perforation test, etc.), mating experiments, etc. The Sabouraud's agar, frequently supplemented by antibiotics chloramphenicol and cycloheximide, is the most commonly used isolation medium. Strains with typical morphology can be identified directly from primary cultures, but subculturing on specific media inducing sporulation or production pigments may be necessary (Robert and Pihet 2008).

3.6 Genotyping Schemes and Population Structure of Major Zoophilic Dermatophytes

Genotyping is often employed to confirm or rule out outbreaks, gain insight into the dynamics of disease transmission, recognize virulent strains and regional and global changes in genotype pattern, determine the source and routes of infections, trace cross-transmission of healthcare-associated pathogens, and evaluate the effectiveness of control measures (Ranjbar et al. 2014). Other common issues in dermatophytes concern differentiation of relapse or reinfection, determining if the infection is caused by one or more strains, if the host can harbor different genotypes varying in their degree of virulence or potential for transmission to other hosts including human, if particular genotypes differ in clinical manifestation, etc. The success in typing of dermatophytes according to phenotype criteria has been limited. Indeed, the same strain may present with different phenotypic characteristics depending on different factors, firstly the conditions of culture (Dhieb et al. 2014).

Fig. 3.3 (continued) branches were obtained from 1000 bootstrap replicates. Only branches with bootstrap support ≥70% are shown; branches with support ≥95% are double thick; ex-type strains are designated by a superscript T. The tree is rooted with *Ctenomyces serratus*

On the other hand, strains with similar colonies may belong to different genetic types.

Because many pathogenic dermatophyte species show nearly clonal population structure and phenotype commonly do not correlate with genotype, DNA-based approaches are supposed to be tools of choice for genotyping. Although **DNA sequencing** allows species identification of dermatophytes, it lacks sufficient discriminatory power to study population structure of most clinically relevant species. Consequently, no **multilocus sequence typing schemes** (MLST) have been evaluated and developed for genotyping of dermatophytes, although MLST has found wide application in many other fungal pathogens (Meyer et al. 2009; Debourgogne et al. 2012; Bernhardt et al. 2013; Maitte et al. 2013). It is worth mentioning that certain level of intraspecies polymorphism was detected by using DNA sequencing of some genetic loci in sexual species, especially *T. mentagrophytes* and *T. benhamiae*. Four **ITS rDNA** sequence genotypes were revealed among 86 isolates of *T. mentagrophytes* sensu lato (Heidemann et al. 2010); genotyping was useful for discrimination between strains of zoophilic origin (*T. mentagrophytes* s. str.) and closely related anthropophilic *T. interdigitale* and correlated with clinical manifestation and phenotype of strains. Additional ITS rDNA genotypes in *T. mentagrophytes s. str.* were revealed by Pchelin et al. (2016) who did not confirm correlation between genotype, origin of strains, and phenotype observed by Heidemann et al. (2010). Combination of ITS rDNA and *GPD* gene revealed five genotypes in global population of *T. benhamiae* (Cmokova 2015) which corresponded with phenotype and in part with geographic origin. Apart from ITS and *GPD* genes, also *TOP II* (Kawasaki et al. 2011) and *TEF-1α* (Mirhendi et al. 2015) have potential for genotyping of *T. mentagrophytes* and *T. benhamiae* but are not available or lack discriminatory power in other pathogenic species. In conclusion, the set of four last mentioned genes has significant potential for typing of *T. mentagrophytes* and *T. benhamiae*, while population of *M. canis* and *T. verrucosum* in domestic animals and humans shows high level of clonality and resists to genotyping by currently available genetic loci. Limited variability was found in ITS region of *M. canis* (Kaneko et al. 2011); unfortunately significant part of the sequence variability in GenBank is caused by sequencing errors as demonstrated by at least four different ITS sequences deposited for the ex-type strain of *M. canis*.

Microsatellite markers are currently the most powerful and effective tool available for subtyping of dermatophytes. The typing schemes have been developed for only limited number of species, i.e., *T. rubrum*, *Nannizzia* (=*Microsporum*) *persicolor*, *M. canis*, and *T. benhamiae*. These methods will be given the most attention in the following paragraphs.

Genotyping attempts were commonly unsuccessful in *M. canis* by using various approaches including RAPD, analysis of NTS region, or PCR-RFLP targeting ITS region (Yu et al. 2004; Leibner-Ciszak et al. 2010; Dobrowolska et al. 2011; Dhieb et al. 2014). In contrast, Spesso et al. (2013) was able to reveal intraspecies variability by using RAPD method among Argentine strains without significant correlation with clinical manifestation or geographic origin. Another method,

inter-single-sequence-repeat-PCR (ISSR-PCR), revealed 21 genotypes among a total of 24 strains analyzed (Cano et al. 2005), which may indicate a good discriminatory power of the method employed. However, the stability of the markers was not assessed, and the reproducibility of the method was low. Two microsatellite loci were originally developed by Sharma et al. (2007), while more recently an extended panel of eight loci has been standardized (Pasquetti et al. 2013). By using two microsatellite loci, Sharma et al. (2007) studied genetic variation and dispersal among 101 global *M. canis* strains, distinguished three subpopulations, and found no correlation between genotype, clinical manifestation, and geographic origin. It was suggested that imbalance in the prevalence of particular genotypes among humans and animals was due to the emergence of a virulent genotype with a high potential to infect human host. Extended panel of eight loci proved to have a high discriminating power and revealed the extensive genetic diversity in global population of *M. canis* (Peano et al. 2015). Some multilocus genotypes (ML-GTs) were found with higher frequency, which leads to hypothesize the existence of clonal lines of "major success" due to a stronger parasitic aptitude. Correlation was not found between severity of clinical forms and a particular genotype. Likewise, there was no particular association between specific ML-GTs and zoonotic potential. Some ML-GTs were related to specific geographical contexts. Although it is unlikely that the loci employed for strain typing are connected with phenotypical features of interest (such as virulence, drug resistance etc.), microsatellite analysis has the potential to track these features indirectly, principally due to the clonal mode of reproduction typical of most dermatophytes (genomes are transmitted to the next generation in unaltered condition and thus associated genes – such as virulence genes and microsatellite markers are linked, which may allow tracing the feature of interest within populations of the fungus). Hence, for example, microsatellites were used to demonstrate that isolates of *M. canis* causing pseudomycetoma in cats are genetically related, if not identical, to isolates responsible for superficial ringworm lesions. These results strongly suggest that pseudomycetoma in cats is due to host factors and cannot be attributed to the specific ability of particular genotypes (Pasquetti et al. 2012). The data from two previously published studies (Sharma et al. 2007; da Costa et al. 2013) were reanalyzed here. The results (Fig. 3.4) confirmed that there is no clear association between particular haplotypes, geographical origin, and host.

Polymorphisms in population of *T. benhamiae* (American-European race) were investigated by using RFLP analysis of NTS region which produced 11 different patterns in 46 isolates; this method successfully confirmed laboratory-acquired infection as well as familial outbreaks transmitted from pets (Mochizuki et al. 2002; Takeda et al. 2012). The data indicated that *T. benhamiae* had been brought into Japan with imported animals on several occasions and spreads in Japan by transportation of animals by breeders or pet shops (Takeda et al. 2012; Hiruma et al. 2015). The global population structure of *T. benhamiae* ($n = 326$ isolates) was recently investigated by using sequences of two genetic loci (ITS rDNA and GPD) along with ten microsatellites markers (Cmokova 2015). The combined sequence analysis revealed the presence of five genotypes, while 32 unique genotypes

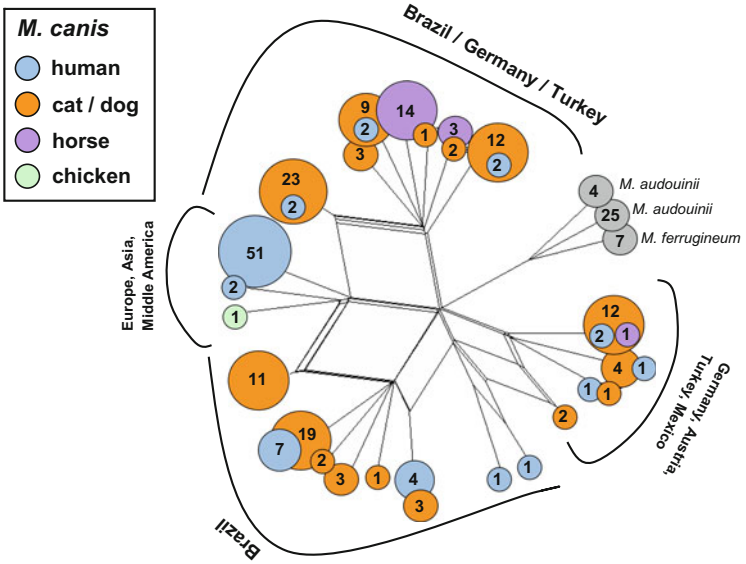

Fig. 3.4 Population structure of *Microsporum canis* complex revealed by analysis of two microsatellite loci—reanalysis of data previously published by Sharma et al. (2007) and da Costa et al. (2013). The dataset included 203 strains of *M. canis*, 29 *M. audouinii*, and 7 *M. ferrugineum*. NeighborNet phylogenetic network built using Jaccard index-based distance matrix with SplitsTree 4.13 (Huson and Bryant 2006). Colored circles correspond to different hosts; numbers in circles indicate number of isolates representing particular haplotype. No clear association between particular haplotypes, geographical origin, and host is evident. However, several haplotypes of "major success" were found in some hosts (haplotype represented by 51 human isolates; haplotype represented by 14 isolates from horses)

arranged into four subpopulations were discovered by microsatellite analysis (Fig. 3.5). The first subpopulation (S1) was most abundant in Europe and associated with guinea pigs; it was characterized by low variability in microsatellite data, yellow colonies with yellow reverse, and exclusively *MAT1-1-1* idiomorph. This clonal subpopulation is currently responsible for the outbreak of infections in the Central Europe. The second subpopulation (S2) comprised strains from North America mostly associated with dogs and typical by highly variable microsatellite data, both mating-type genes were present among strains; the colonies were mostly white, granular, and frequently with red reverse. It is probable that virulent European subpopulation has its origin in closely related subpopulation S2 in North America where the center of genetic variability of *T. benhamiae* is located and where the pathogen probably occurs on wild animals. The third subpopulation (S3) comprised strains from Europe mostly associated with guinea pigs and characterized by the presence of both mating types (predominantly *MAT1-2*). The fourth subpopulation (S4) comprised majority of strains from Japan, and some European strains that were mostly associated with rabbits; all strains had only *MAT1-1* idiomorph. Some of these subpopulations could represent separate taxonomic entities, but more research

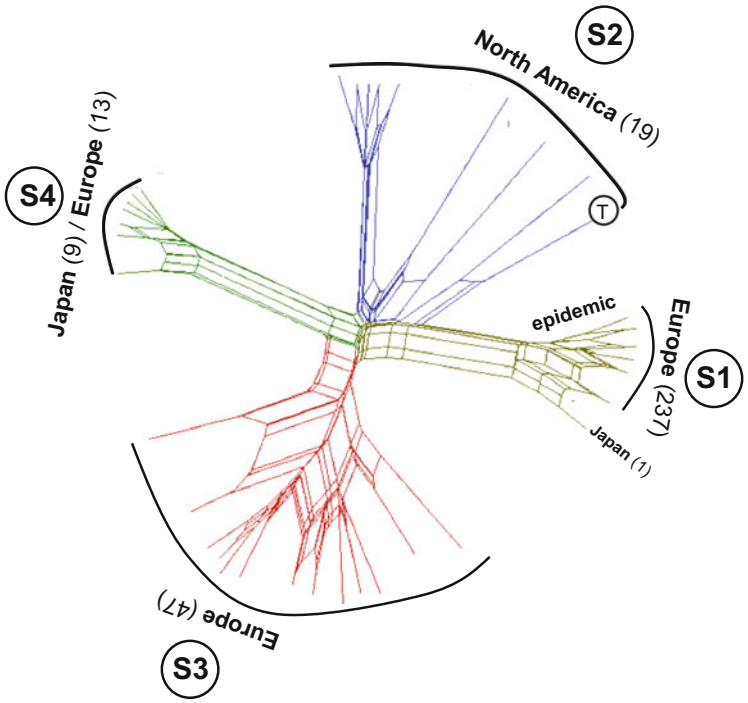

Fig. 3.5 Population structure of *Trichophyton benhamiae* ($n = 326$) revealed by analysis of ten microsatellite loci (Cmokova et al. 2017). NeighborNet phylogenetic network built using Jaccard index-based distance matrix with SplitsTree 4.13 (Huson and Bryant 2006). The data showed that the population of *T. benhamiae* is divided into four distinct subpopulations (designated S1–S4) and 32 genotypes. Numbers in parentheses indicate number of examined isolates from particular subpopulation. The subpopulation S1 was represented by highest number of isolates but at the same time had the lowest number of genotypes (clonal spreading) and is responsible for current outbreak of human and animal infections (mostly transmitted from guinea pigs) in Europe. Based on microsatellite and sequence data (not shown in figure) evidence, this clonal subpopulation is closely related to the subpopulation S2 represented exclusively by strains of North American origin (mostly infections in dogs) including the ex-type strain of *T. benhamiae* (marked with letter T)

is needed to confirm this assumption. Confusions are associated with phenotypes and genotypes recognized in the past among isolates identified as *T. benhamiae*. The isolates are usually designated as "white" or "yellow" phenotype based on macromorphology, and it was anticipated that they are connected with different genotypes (Symoens et al. 2013; Hiruma et al. 2015; Brasch et al. 2016). Apparently, the "white" phenotype which is predominant in Japan and in the USA and minority in Europe is in fact complex of several distinct taxonomic entities.

Random amplification of polymorphic DNA (RAPD) analysis (Kim et al. 2001) and PCR-RFLP targeting ITS rDNA (Heidemann et al. 2010) differentiated zoophilic *T. mentagrophytes* and anthropophilic *T. interdigitale*. Some RAPD analyses were even useful for subtle subtyping of *T. interdigitale* (Kac et al. 1999; Leibner-

Ciszak et al. 2010), but no correlation was detected between obtained profiles and geographic origin of strains. Poor reproducibility of the obtained profiles has reduced the interest in RAPD in favor of microsatellites and more reproducible methods in dermatophytes; but microsatellite markers have not been developed for *T. mentagrophytes*. PCR melting profile (PCR-MP) technique revealed seven genotypes within *T. mentagrophytes* and was able to distinguish zoophilic strains originating from Poland and Denmark (Leibner-Ciszak et al. 2010). Methods focusing on the variability in non-transcribed spacer (NTS) regions of rDNA have currently the highest discriminatory power among the methods applied on *T. mentagrophytes*. Southern blot hybridization-based RFLP analysis of NTS region was useful for subtyping of *T. mentagrophytes* and related *T. interdigitale* (23 subtypes among 60 isolates) (Mochizuki et al. 2003). Analysis of three individual subrepeat elements of the NTS identified 19 molecular types among 42 anthropophilic *T. interdigitale* strains (Jackson et al. 2006), and the method was later applied to 65 clinical strains isolated at one regional hospital in Japan with discrimination of 15 molecular types (Wakasa et al. 2010). Even higher resolution can be expected if the method was used to characterize closely related and sexually reproducing *T. mentagrophytes*.

Limited options are available for genotyping of *T. verrucosum*, *T. erinacei*, and *T. equinum*. It can be expected that at least some microsatellite markers designed for *T. benhamiae* will be useful for subtyping of *T. verrucosum* and *T. erinacei* due to close phylogenetic relatedness of these species (Fig. 3.3). Similarly, molecular subtyping based on single nucleotide polymorphisms (SNPs) developed for *T. tonsurans* (Abdel-Rahman et al. 2010) might work well in closely related *T. equinum*.

The establishment of global databases based on largely comparable data such as microsatellites, SNPs, and DNA sequences is desirable. Such databases would enable to understand global epidemiology of dermatophytes and monitor changes in genotype spectra on global and local scale. Although high throughput sequencing facilities are now widely available and increasingly used even in the epidemiology of fungal infections, this option has not yet been exploited in dermatophytes. SNP detection by using whole-genome sequence typing can be used, instead of MLST, to infer the genetic relatedness of fungal isolates. This ultimate approach will be certainly the method of choice in the future along with decreasing costs (Hadrich and Ranque 2015).

3.7 Major Zoophilic Dermatophytes: Epidemiology and Actual Concerns

3.7.1 *Microsporum canis*

Microsporum canis is the most common dermatophyte in cats and dogs (Fig. 3.6). Cats are considered to be the most important reservoir, but the species is also found regularly in rabbits and horses (Sharma et al. 2007; Cafarchia et al. 2013a; Pasquetti

Fig. 3.6 Clinical presentation of infections caused by zoophilic dermatophytes. (**a**–**c**) *Microsporum canis*: irregular areas of alopecia covered by scales and scabs in a cat (**a**), pseudomycetoma in a cat (**b**), annular area of alopecia in a dog (**c**). (**d**–**e**) *Trichophyton mentagrophytes*: annular erythematous areas of alopecia on the back, extremities, and ears of a

et al. 2013). It has been occasionally reported in a number of other domestic and wild animals, e.g., cattle, sheep, goats, ferrets, camelids, marmots, eastern cottontails, foxes, etc. (Gallo et al. 2005a, b; Chermette et al. 2008; Pignon and Mayer 2011). Isolates coming from horses were previously classified as *M. equinum*, a species later synonymized with *M. canis* based on phylogenetic and population genetic analyses (Gräser et al. 2000a; Kaszubiak et al. 2004; Sharma et al. 2007). *Microsporum canis* is known to reproduce mainly asexually, although it is also capable to produce sexual state under laboratory conditions (Hironaga et al. 1980).

Microsporum canis is diffused worldwide and plays an important zoonotic role. In some countries it tends to overpass antropophilic dermatophytes as cause of human ringworm episodes (Chermette et al. 2008; Ameen 2010). It is the most frequent agent of tinea capitis in many European countries, the Eastern Mediterranean, South America, and China; it also causes highly inflamed lesions on glabrous skin and infrequently onychomycosis (Ginter-Hanselmayer et al. 2007; Seebacher et al. 2008; Skerlev and Miklić 2010; Uhrlaß et al. 2015; Zhan et al. 2015).

Dermatophytosis by *M. canis* is a pleomorphic and usually not a localized disease in cats despite appearances to the contrary (DeBoer and Moriello 2006). In addition, many infected cats have no or only few lesions. In particular, long-haired breeds can be subclinical carriers or have only minimal clinical symptoms; sometimes lesions become evident after shaving of hair. Isolation of *M. canis* from the haircoat in the absence of obvious lesions indicates either infection or fomite carriage from exposure to a contaminated environment. Distinguishing is often impossible, and Wood's lamp can help to detect minimal lesions invisible at naked eye. A mechanical carriage will only be revealed through fungal cultures (a plate with one or few CFU is usually indicative of fomite carriage). Dogs more often exhibit the classic annular areas of peripherally expanding alopecia, scale, crust, and follicular papules and pustules, with sometimes a central area of hyperpigmentation. It is quite clear that the response to infection in cats, more often than in dogs, tends to resemble that described in human patients with chronic infection by antropophilic dermatophytes. This is illustrated by the high number of cats which develops minimal and persisting lesions, just due to a "tolerant" immune response. This is an evidence of the strong adaptation of the fungus to the feline host. It is known that Persian cats are predisposed to *M. canis* infection (DeBoer and Moriello 2006; Miller et al. 2013) and to the development of more aggressive forms such as pseudomycetoma (Zimmerman et al. 2003; Bianchi et al. 2017). Apart from a genetic predisposition, this may also reflect a less efficient grooming of the haircoat because coat length has been reported as an important factor in the carriage of *M. canis* spores (Sparkes et al. 1993). A genetic predisposition to develop a generalized form of *M. canis* infection seems to exist also in Yorkshire Terrier dogs (Sparkes et al. 1993).

Fig. 3.6 (continued) rabbit (**d**), scaling lesion on the snout and upper lip of a rabbit (**e**). (**f**–**g**) *Trichophyton verrucosum*: discrete, scaling patches of hair loss located on the head and neck of cattle (**f**) and sheep (**g**). (**h**–**i**) *Trichophyton benhamiae*: weeping lesion under the eye of a guinea pig (**h**), itchy area of alopecia behind the ear of a guinea pig (**i**)

Available data show that *M. canis* cause >90% of dermatophytoses in cats worldwide. It is generally also the most prevalent dermatophyte isolated from dogs but with greater variation. For instance, in the USA, dermatophytosis was diagnosed in 14.9% of cats and 3.8% of dogs with cutaneous lesions, and *M. canis* is accounted for 92 and 43% of feline and canine cases, respectively (Lewis et al. 1991). In Brazil, dermatophytosis was confirmed in 27.8% of cats presented with dermatological problems, with *M. canis* responsible for 100% of cases; the prevalence in dogs was 9.8%, i.e., 68.5% of all cases of dermatophytosis (Copetti et al. 2006). Similar long-term studies from Europe showed comparable or even higher prevalence of *M. canis* in animals with skin disorders. Dermatophytes were isolated from 40.7% of cats in Croatia, and *M. canis* represented 98.7% of the isolates (Pinter et al. 1999). In Italy, dermatophytosis was diagnosed in 24.7% cats and 18.7% of dogs with *M. canis* representing 97 and 83% of the isolates, respectively (Mancianti et al. 2002). Climatic conditions appear to play a significant role in the diffusion of the pathogen. The prevalence is basically higher in hot and humid climates as shown in studies from climatically different regions of the USA and Italy (Moriello et al. 1994; Romano et al. 1997; Cafarchia et al. 2004; Proverbio et al. 2014). Seasonal differences in the incidence of infection have been found in many countries in animals as well as in humans (Simpanya and Baxter 1996; Cafarchia et al. 2006; Lee et al. 2012; Uhrlaß et al. 2015). With similar climates, prevalence varies in relation to other factors, firstly the lifestyle of animals taken in consideration. In the UK, show cats were reported to have a carrier rate of 12.5%, while in household cats, the isolation rate was 2.2% (Quaife and Womar 1982; Sparkes et al. 1994). In a report from Belgium, 2.1% of pet cats were found to be asymptomatic carriers, while the prevalence in cats in shelters was 16% (Mignon and Losson 1997).

Small outbreaks (usually <20 affected individuals) in household contexts are very common and caused by infected pets adopted from the road or purchased from a breeder or a shop (Alteras and Feuerman 1979; Preiser 1991; de Mendoza et al. 2010; Pasquetti et al. 2013). Regularly, there is an important role of asymptomatic/paucisymptomatic animals and environmental contamination in the diffusion of the disease. Among episodes reported, one of the oldest stands out in terms of number of cases and length. In Montreal (Canada), an exceptionally high number of human infections by *M. canis* (>1000) was reported over an 8-year period (Strachan and Blank 1963). Circumstances that led to this outbreak were not completely clarified, but it was concluded that cats and dogs played a major role in the spread of infection. Other interesting episodes reported in literature are nosocomial epidemics, infections in schools, outbreak in a nursing home for elderly people, and veterinary clinic (Shah et al. 1988; Snider et al. 1993; Drusin et al. 2000; Yu et al. 2004; Gürtler et al. 2005; Grills et al. 2007; Kopel et al. 2012; Pasquetti et al. 2012; Hillary and Suys 2014; Šubelj et al. 2014). In all these contexts, the infection spreads without an animal intervention, which shows that human-to-human transfer of *M. canis*, although considered rare and self-limiting, can be occasionally very efficient. Rarely, *M. canis* causes outbreaks in rabbit farms, and their origin usually came from animals imported from abroad and integrated into the local farms (Gonzalez et al.

1988; Cabañes et al. 1997); outbreaks in laboratory mice (Difonzo et al. 1986) and a porcine farm have also been described (Cabo et al. 1995).

In general, studies of the fungal flora of asymptomatic cats and dogs highlight a very important point. Although many animals have been found to act as healthy carrier of *M. canis*, this fungus should not be considered part of the normal fungal flora. If it was, it would have been isolated routinely from healthy animals regardless of geographical region, lifestyle (indoor or outdoor), or status (pet or stray) (DeBoer and Moriello 2006).

3.7.2 *Trichophyton mentagrophytes, T. quinckeanum,* and *T. interdigitale*

In the past, *T. mentagrophytes* complex was divided into numerous anthropophilic or zoophilic varieties associated with multiple sexual states (*A. vanbreuseghemii*, *A. benhamiae*, and *A. simii*) (Takashio 1977; Hironaga and Watanabe 1980; Hejtmánek and Hejtmánková 1989). Phylogenetic analyses resolved the status of these varieties, some of them were elevated to a species level, others became superfluous (Gräser et al. 1999b; de Hoog et al. 2017). The data also confirmed that three sexual states attributed in the past to *T. mentagrophytes* represent separate species complexes. The concept of *T. interdigitale* (former *T. mentagrophytes* var. *interdigitale*) and *T. mentagrophytes s. str*. has changed significantly during the last two decades especially in connection with their neotypification by Gräser et al. (1999b). The selection of neotype (closely phylogenetically related to *T. schoenleinii*) changed significantly the practical use of the well-known name *T. mentagrophytes* that became rare species in clinical practice. The concept of "anthropophilic and zoophilic strains of *T. interdigitale*" was used instead for a transitional period (Nenoff et al. 2007; Heidemann et al. 2010), and consequently, the majority of isolates previously identified as *T. mentagrophytes* were relabeled as zoophilic strains of *T. interdigitale*. The selection of neotype of *T. mentagrophytes* was subsequently disputed by several authors (Sun et al. 2010; Beguin et al. 2012; Chollet et al. 2015a), and in the light of new arguments, an alternative neotype was designated by de Hoog et al. (2017). Although the validity of this neotype may be subject of future nomenclature debate, we follow here the recently designated neotype that returns the name *T. mentagrophytes* back to common use together with the name *T. quinckeanum*, an agent of mouse favus. In contrast to Heidemann et al. (2010), no clear relationship between origin, morphology of the strains, genotype, and clinical manifestation was found in isolates of *T. interdigitale/T. mentagrophytes* from Tunisia (Dhib et al. 2017). These conclusions are in agreement with our observation in strains from Czech patients and may suggest that *T. interdigitale* and *T. mentagrophytes* sensu de Hoog et al. (2017) are conspecific.

The reservoir of *T. mentagrophytes* are rodents, hunting cats (rather than indoor cats), dogs, and less commonly other animals such as ruminants and horses. When transmitted to human, infection usually manifest as inflammatory tinea of glabrous skin (tinea corporis, faciei, barbae), less frequently as tinea capitis (Frealle et al.

2007; Cafarchia et al. 2013c). The isolates are usually typical by colonies in shades of beige and granular/powdery colony texture; numerous microconidia, macroconidia, and spiral hyphae can be usually observed in microscope slides. Mating of isolates with opposite mating types leads to production of a sexual state corresponding to former *A. vanbreuseghemii*. In contrast, anthropophilic *T. interdigitale* represent a clonal lineage (only single mating type) derived from sexual zoophilic lineage that lost the ability to mate with them. The colonies of anthropophilic strains are usually white and cottony; micromorphology is typical by the presence of microconidia and the absence of macroconidia and spiral hyphae. These strains are almost exclusively associated with onychomycosis and tinea pedis in human and absent in animals (Nenoff et al. 2007; Heidemann et al. 2010).

Trichophyton mentagrophytes is distributed worldwide. It is currently a major cause of dermatophytosis in rabbits (Fig. 3.6) and other rodents (except guinea pigs) followed by much less frequent *M. canis*, *T. benhamiae*, and others (Hoppmann and Barron 2007; Cafarchia et al. 2010, 2012; Kraemer et al. 2012). The transmission from pet rabbits to humans (mostly children) is well known, and the individual cases manifest usually as tinea capitis or corporis (Van Rooij et al. 2016; Zhang et al. 2009). Rabbitries constitute an important reservoir of the disease, and their environment can be heavily contaminated. Widespread dermatophytosis in young rabbits impacts profoundly on animal health along with bacterial superinfections (caused mostly by staphylococci). The infected animals have lower indices in prolificacy and growth, and the severely infected individuals usually have to be discarded, thus reducing productivity and causing financial loss (Moretti et al. 2013). Recurring disease is reported in rabbit farm workers (Torres-Rodriguez et al. 1992; Van Rooij et al. 2016). Significant outbreaks due to *T. mentagrophytes* in animals have been infrequently reported (Alteras and Cojocaru 1969; Mesquita et al. 2016) or are underreported. The prevalence in animals is frequently very high and may be neglected due to high percentage of asymptomatic animals. For instance, a study was conducted on 220 Spanish rabbit farms, and 79.5% of the examined animals were positive for *T. mentagrophytes* that corresponds to 98% of all isolated dermatophytes (Torres-Rodriguez et al. 1992). In another study from Spain, dermatophytes were cultured from 83% of rabbits with suspected dermatophytosis, and *T. mentagrophytes* (69.2%) was the most abundant pathogen (Cabañes et al. 1997). Similar situation has been found in Italy, where dermatophytosis was found in ~60–87% rabbit farms and *T. mentagrophytes* represented ~92–93% of isolated dermatophytes. Higher temperature and relative humidity or inadequate and infrequent disinfection practices were identified as the most significant risk factors for dermatophytosis in rabbit farms (Cafarchia et al. 2010). Young animals or animals in fattening and finishing stages are the most frequently infected (Cafarchia et al. 2010; Moretti et al. 2013). It has been shown that the ITS sequences of *T. mentagrophytes* isolates from rabbits from southern Europe countries were identical, but different from those isolated from dogs and cats or rabbits from Asia. These results may suggest that a particular genotype could be prevalent in rabbits in southern Europe (Mesquita et al. 2016). Several outbreaks involving up to dozens of human patients have also been described and transmitted from rabbits (Alteras and Cojocaru 1969;

Veraldi et al. 2012; Mesquita et al. 2016) and horse (Chollet et al. 2015b). Chinchillas are also vulnerable to infection, and *T. mentagrophytes* is isolated from ~5 to 10% of asymptomatic fur-ranched or pet chinchillas and 30% of animals with fur damage (Donnelly et al. 2000; Moretti et al. 2013). The infections in dogs and cats occur regularly through the world, but the infection counts are usually relatively low compared to *M. canis* (Lewis et al. 1991; Mancianti et al. 2002; Khosravi and Mahmoudi 2003; Cafarchia et al. 2004; Seker and Dogan 2011). Significantly higher infection rates are detected in free roaming, feral, and hunting dogs and cats in which *T. mentagrophytes* can even prevail over *M. canis* (Drouot et al. 2009; Duarte et al. 2010).

Trichophyton quinckeanum is a species historically associated with favus in rodents and rarely isolated from human infections (mostly tinea of glabrous skin). It is reasonable that this fungus is even rarer today because of improved living conditions. Its closest relatives are anthropophilic *T. schoenleinii* (an agent of tinea capitis typical by scutula formation) and probably geophilic *T. simii*. The morphology of *T. quinckeanum* is nearly indistinguishable from *T. mentagrophytes*, although the species are phylogenetically distinct (Fig. 3.3). *Trichophyton quinckeanum* has not been detected at all in majority of published epidemiological studies on human and animal dermatophytoses supported by molecular data. The exception is a recent report of 62 infections in human patients in Germany (tinea of glabrous skin and tinea capitis) (Uhrlaß et al. 2018). Interestingly, all cases were diagnosed during a 3-year period (2013–2017) in a single laboratory, and no cases were detected during previous years despite molecular verification of identification. Cats were identified as a source of infection in several patients, and all isolates had a unique ITS genotype that was different from all previously examined European and Asian strains. This suggests a clonal spread of a new genotype.

3.7.3 *Trichophyton verrucosum*

Trichophyton verrucosum is a clonal (Kano et al. 2014), slow-growing species with global distribution. It is typically found in cattle and other ruminants (Fig. 3.6), but it can easily spread to humans and animals, including horses, donkeys, camels, rabbits, dogs, cats, pigs, and even birds (Baudet 1932; Blank 1955; Georg 1960; Dvorak et al. 1965; Ali-Shtayeh et al. 1988; Khosravi and Mahmoudi 2003; Chermette et al. 2008). Modern intensive battery farms are the main reservoir of *T. verrucosum* in developed countries as conditions favor its proliferation. It is mainly transmitted through direct contact with infected animals or contaminated environment, and therefore high prevalence levels often occur in overcrowded stables where the fungus can spread easily among subjects confined in small areas. In cattle, ringworm is usually more widespread in young animals because of their lack of specific immunity against the fungus. The infection is often clearly evident, with alopecic areas covered with thin farinaceous desquamations or with thick crusty lamellar scales difficult to pull off the skin. Lesions are mainly distributed on the head and neck (Fig. 3.6), but in most severe cases, the whole body can be affected. Although

frequently considered as a benign self-healing infection, ringworm in cattle may be responsible for economic losses due to the negative impact on milk and meat production. Ringworm also leads to impairments in the hide and skin industries, as lesion scars are evident on leather following tawing and tanning (Chermette et al. 2008; Bond 2010; Hameed et al. 2017).

Trichophyton verrucosum infection can be considered as a cosmopolitan disease as, over time, it has been reported in livestock and people in different countries from all continents. Infection rates in cattle appear variable depending primarily on the geographical and social context. For example, low infection rates (around 2%) were detected in rural areas of Pakistan (Hameed et al. 2017) and Iran (around 5%) (Aghamirian and Ghiasian 2011). In such contexts the fungus probably does not find the conditions which are known to promote its spread, such as overcrowding of animals and high humidity, which are more typically encountered in intensive breeding. Indeed, some surveys, performed instead in intensive and semi-intensive farms in Central Italy, detected much higher infection rates, i.e., 19, 60, and 88% (Moretti et al. 1998; Papini et al. 2009; Agnetti et al. 2014). In particular, the survey which reported the highest prevalence (Papini et al. 2009) was based on the analysis of only young animals living in crowded environments; the authors found high prevalence even in asymptomatic animals (80.4%). In addition, the investigation was carried out during winter months when skin lesions are in general more common because stabled animals are in close contact. A high infection rate (31%) was also found in a study in Jordan which took into account ten large dairy farms (Al-Ani et al. 2002). Other studies reporting high infection rates describe actually outbreak episodes on a limited scale, e.g., study of Dalis et al. (2014) from Nigeria. Likewise, the infection rate reported in a Chinese study (20%) reflects the prevalence within an outbreak in a single farm, with 200 animals infected out of a total of 1000 (Ming et al. 2006). The infections are less frequent in small ruminants (Chermette et al. 2008; Bond 2010), perhaps due to a stronger inherited immune response against the fungus compared with that of cattle or to other factors linked to the breeding systems. An increasing prevalence of the disease and the existence of extensive outbreaks were documented in sheep (Fig. 3.6) in the UK, USA, and Morocco (Pandey et al. 1979; Power and Malone 1987; Sargison et al. 2002). It cannot be excluded that dermatophytosis in sheep and goats is actually an under-diagnosed disease.

The incidence of infections in cattle was decreased in many regions by specific fighting measures, especially by vaccination programs or changes in the agricultural systems, such as reduction of the number of cattle in breeding units; the infections in humans decreases proportionally (Seebacher et al. 2008; Lund et al. 2014). Lack of prophylaxis with *T. verrucosum* vaccination accounts for the high infection rates in Italy (Moretti et al. 2013); in contrast cattle ringworm due to *T. verrucosum* was eradicated in Norway (Lund et al. 2014).

Trichophyton verrucosum is characterized by a high zoonotic potential. People at higher risk of infection are farmers and their families, and veterinaries and technicians involved in animal management. Several week-long sick leaves of employees further increase financial costs (Moretti et al. 2013). Human patients usually develop aggressive inflammatory skin lesions (usually on extremities and

head), which may be accompanied by constitutional symptoms, such as fever and lymphadenopathy (Silver et al. 2008; Courtellemont et al. 2017). Tinea barbae and capitis are relatively common clinical forms which can result in irreversible scarring and alopecia. The incidence of human infection among other dermatophyte species is very high in some regions of Africa and Middle East (up to dozen percent) and relatively low in European countries and the USA (usually 0–2%, but up to 4%) (Havlickova et al. 2008; Seebacher et al. 2008; Moretti et al. 2013; Courtellemont et al. 2017).

Zoophilic variety *T. verrucosum* var. *autotrophicum* (described from Karakul sheep, goat, and cattle) and *T. immergens* (from ruminants) have morphology resembling that of *T. verrucosum*, but based on molecular genetic data, they are closely related or identical to *T. mentagrophytes* and *T. tonsurans*, respectively (Gräser et al. 1999b; de Hoog et al. 2017). Infections in horses and donkeys due to *T. verrucosum*-like strains are relatively rare but occur worldwide (Lyskova et al. 2015). It is probable that at least part of these infections is caused by phenotypically similar *T. bullosum* that has been confirmed by molecular data from North Africa, from Middle East, and recently from Europe (Sitterle et al. 2012; Lyskova et al. 2015; Sabou et al. 2018). Large-scale and comprehensive studies have not been performed worldwide on the epidemiology of dermatophytosis in cattle, other ruminants, horses, and donkeys using DNA-based methods for identification of dermatophytes. *Trichophyton verrucosum* was confirmed by DNA sequencing as an agent of infection in recent studies examining *T. verrucosum*-like isolates from cattle and patients infected by cattle from Japan, Czech Republic, and Tunisia (Hubka et al. 2014b; Kano et al. 2014; Neji et al. 2016). In contrast, *T. bullosum* has been confirmed only from horses, donkey and a patient who was likely infected from a donkey. Host specificity of *T. bullosum*, but also the real etiology of infections in uncommon hosts, should be verified in future studies.

3.7.4 *Trichophyton equinum*

Trichophyton equinum is a species strongly associated with horses. It is generally reported as the most common cause of dermatophytosis in horses worldwide and occasionally causes outbreaks in horse farms (English 1961; Connole and Pascoe 1984; Pereira et al. 2006). The infections prevail in young animals, and additional risk factors for dermatophytosis include poor grooming practice, moist conditions, and a high number of animals in the herd (Ahdy et al. 2016). Available data from Italy, Jordan, and Egypt found prevalence of dermatophytosis in horses 9, 18, and 16.8%, respectively, and *T. equinum* represented 66.7, 24 and 58.4% of all isolated dermatophytes (Moretti et al. 1998; Al-Ani et al. 2002; Ahdy et al. 2016). Similarly, the studies on horses with skin lesion from Egypt and Nigeria reported *T. equinum* as a main causal agent of dermatophytosis that was confirmed in 49.2 and 44% culture-positive cases, respectively (Mahmoud 1995; Nweze 2011). Exceptionally, other species were found with higher frequencies in horses such as *M. canis* (Al-Ani et al. 2002) and *T. verrucosum* (Maurice et al. 2016; Balogun et al. 2017). The latter species is usually found when horses are pastured with cattle (Weiss et al. 1984).

Occupational infections in breeders, riders and veterinarians are relatively rare (less than 30 cases reported in the literature) and usually manifest as tinea corporis and tinea capitis, exceptionally as onychomycosis (Veraldi et al. 2018).

The differentiation of *T. equinum* from closely related anthropophilic *T. tonsurans* is possible based on ecological preferences, nutritional requirements, and mating behavior (Woodgyer 2004; Summerbell et al. 2007), while distinguishing based on DNA sequence data may be problematic (de Hoog et al. 2017).

3.8 Emerging Dermatophytes

3.8.1 *Trichophyton benhamiae*: An Emerging Pathogen in Europe

Abandoning the previously accepted nomenclature of an asexual state, i.e., *T. mentagrophytes*, and a sexual state, i.e., *Arthroderma benhamiae* (see above), resulted in situation that no name combined in *Trichophyton* was available for *A. benhamiae* despite its clear phylogenetic position within *Trichophyton* clade (Fig. 3.3). This combination was introduced recently (de Hoog et al. 2017), but during the last decade, the species was usually designated *A. benhamiae* or "*Trichophyton* sp. anamorph of *A. benhamiae*" in the literature. Originally, the sexual state of this species was induced by crossing of two isolates designated by authors as "*T. mentagrophytes* var. *granulosum*" which originated from a dog and a man with dermatophytosis in the USA (Ajello and Cheng 1967). Consequently, the identification of isolates designated as *A. benhamiae* before the molecular era is commonly doubtful and can comprise quite broad spectrum of currently accepted species, i.e., *T. benhamiae s. str.*, *T. erinacei*, *T. mentagrophytes*, and some less common related species (Fig. 3.3). Isolates designated as "African race of *A. benhamiae*" represent an independent monophyletic entity related to *T. bullosum* rather than to *T. benhamiae* (Fig. 3.3). However, mating compatibility between "African race of *A. benhamiae*" and *T. benhamiae* (also called American-European race) was observed in vitro (Takashio 1974). The mating groups were indicated as "races" because no morphological differences could be observed between strains from different continents.

Guinea pigs represent the main host reservoir (Fig. 3.6) in Europe (Drouot et al. 2009; Kraemer et al. 2013; Hubka et al. 2014b); infections occasionally occur also in dogs (mostly USA), pigs (USA), and cats (Belgium) or various rodents (rabbits, chinchilla, mouse, rat, porcupine, degus) (Ajello and Cheng 1967; Takahashi et al. 2008; Takeda et al. 2012; Symoens et al. 2013; Sieklucki et al. 2014; Hiruma et al. 2015; Overgaauw et al. 2017). Our knowledge on spectrum of hosts worldwide supported by molecular data is still insufficient. Based on sequence data, it seems that the majority of infections in guinea pigs is caused by *T. benhamiae*, to a less

extent by *T. mentagrophytes* and rarely by *M. canis*; in contrast *T. mentagrophytes* is a frequent pathogen in rabbits followed by *M. canis* and *T. benhamiae* (Arabatzis et al. 2006; Frealle et al. 2007; Drouot et al. 2009; Heidemann et al. 2010; Sun et al. 2010; Cafarchia et al. 2012; Symoens et al. 2013). The prevalence of *T. benhamiae* in various animals probably differs significantly in different geographic areas, and these infections seem to be associated with different genotypes or subpopulations, respectively (Cmokova 2015). A small outbreak of dermatophytosis due to *T. benhamiae* was reported in Canadian porcupines (*Erethizon dorsatum*), a close relative of the guinea pig, housed in a Japanese zoo (Takahashi et al. 2008). A case of infection in Cape porcupine (*Hystrix africaeaustralis*) and a man who handled animals (Marais and Olivier 1965) were reported from Southern Africa.

Trichophyton benhamiae has been reported and confirmed by molecular methods in many European countries, the USA, and Japan. The prevalence and distribution in rodents is largely unknown due to fact that the pathogens were usually identified as *T. mentagrophytes* across published studies. It was determined that the prevalence of dermatophytosis in guinea pigs in Germany was 38.1% of which 91.6% infections were caused by species from *T. mentagrophytes* complex (Kraemer et al. 2012; Kraemer et al. 2013) in agreement with an older study which found prevalence 37% (Weiß et al. 1979). A recent study revealed more than 90% prevalence of *T. benhamiae* in guinea pigs from pet shops in Germany, 9% of which showed visible symptoms (Kupsch et al. 2017). The prevalence in Switzerland was 38.1%, and *T. benhamiae* was confirmed in all mycologically positive samples (Drouot et al. 2009); the prevalence of dermatophytosis in guinea pigs across pet shops in the Netherlands was 16.8% (88% of cases were caused by *T. benhamiae*) that corresponds to 27.3% of pet shops which sell infected but mostly asymptomatic animals (Overgaauw et al. 2017). The retrospective analysis of the activity of a veterinary laboratory from 2010 to 2012 in France demonstrated that dermatophytes were isolated from 41.2% of 148 pet rodents (guinea pigs, rats, mice, hamsters, and chinchillas) and 38.2% of 76 pet rabbits (Guillot et al. 2016). In guinea pigs, *T. benhamiae* was predominant, whereas *T. mentagrophytes* was most frequently isolated from other rodents and from rabbits. In contrast, low prevalence (3.5%) of *T. mentagrophytes* was detected among guinea pigs in Belgium (Vangeel et al. 2000), and no *Trichophyton* spp. were isolated among 200 pet guinea pigs in Italy (d'Ovidio et al. 2014). The lack of reports of *T. benhamiae* from guinea pigs in the USA (a country of origin) is obvious, and guinea pig was determined as a source of infection only in one human case of dermatophytosis (Ajello and Cheng 1967). Although epizootic episodes in guinea pigs colonies and laboratory guinea pigs attributed to *T. mentagrophytes* have been described in the USA (Menges and Georg 1956; Pombier and Kim 1975) and other countries (Rush-Munro et al. 1977; McAller 1980), the identity of the pathogen is unclear in the context of recent taxonomic changes. More recently *T. benhamiae* was confirmed by molecular data in Iran at relatively low frequencies (Abastabar et al. 2013; Ansari et al. 2016; Rezaei-Matehkolaei et al. 2016) contrasting to its absence in the past studies.

Trichophyton benhamiae causes 2.9% of all human dermatophytoses in Germany (Uhrlaß et al. 2015) and 7.2% in the Czech Republic (Hubka et al. 2014b).

Consequently, it is the most important agent of dermatophytosis transmitted from animals in the Czech Republic and causes 22.9% of all infections on glabrous skin and 29.2% of tinea capitis infections; median age of all patients was 12, and women comprised 71% of patients (Hubka et al. 2014b; Hamal et al. 2016). Current status of *T. benhamiae* infection in Japan, the USA, and other countries is almost unknown due to insufficient surveillance and lack of epidemiological studies supported by molecular-based identification. In contrast to Europe, rabbits seem to be a major reservoir of *T. benhamiae* in Japan; 78% of published Japanese cases were reported in women; median age of patients was 26 (Kimura et al. 2015). The infection in guinea pigs does not show any gender predisposition, but the young individuals are more frequently affected and symptomatic, whereas adult animals are mostly symptomless. In symptomatic guinea pigs, the infection manifests as alopecia with scaling and crusting located predominantly on the head, less frequently on the other body parts (Drouot et al. 2009; Kraemer et al. 2012, 2013; Overgaauw et al. 2017).

With respect to the current epidemiological situation, it is clear that *T. benhamiae* is a new emerging pathogen in human clinical material in Europe and Japan. This fact is surprising because guinea pig breeding has a long tradition in these regions, and *T. benhamiae* has been documented among guinea pigs in the past, but the clinical cases in human were absent or very rare. Before widespread dispersal of *T. benhamiae* in Europe, sporadic cases of human and guinea pig infections caused usually by "yellow-pigmented isolates" which macroscopically resembled *M. canis* were reported from different countries. First cases due to *T. benhamiae* in Switzerland were dated in 2002 (Fumeaux et al. 2004), and similarly, first isolates from French cases were collected between 2002 and 2008 (Frealle et al. 2007; Contet-Audonneau and Leyer 2010; Charlent 2011; Khettar and Contet-Audonneau 2012). The first cases were observed in Germany and Czech Republic before 2010, and the pathogen became rapidly epidemic during following years (Hubka et al. 2014b; Nenoff et al. 2014; Skořepová et al. 2014; Uhrlaß et al. 2015). In Japan, the species was first isolated in 1996 from an infected rabbit (Kano et al. 1998); the human cases were reported in following years (Nakamura et al. 2002) and summarized by Kimura et al. (2015). Because *T. benhamiae* became common in companion animals of Japan, increasing number of infections can be expected there.

3.8.2 *Trichophyton erinacei*: An Emerging Pathogen Introduced into New Regions Along with Hedgehogs

Smith and Marples (1964) gave a status of variety *T. mentagrophytes* var. *erinacei* to a "hedgehog fungus" based on morphological and physiological differences from other varieties of *T. mentagrophytes*. It was elevated to a species level by Quaife (1966), and the species rank was supported by phylogeny (Gräser et al. 1999b) (Fig. 3.3).

European hedgehog (*Erinaceus europaeus*) was first reported as a host along with infection of humans who were in contact with animals (Smith and Marples 1964). The four-toed hedgehog (*Atelerix albiventris*) is another host of *T. erinacei* as

verified by sequence data and mating experiments (Takahashi et al. 2002). *Trichophyton erinacei* has been recorded also from dogs (Piérard-Franchimont et al. 2008; Kurtdede et al. 2014), wood mice (*Apodemus sylvaticus*) (English 1969), house mice, and rats in New Zealand (Marples 1967); it was suggested that the animals were directly or indirectly infected from hedgehogs living in the same habitat.

The activities associated with direct contact between individuals such as fighting and mating probably represent the main source of cross infection between hedgehogs (Morris and English 1973). The hedgehog mites may act as a vector in the transmission due to common coinfection and presence in the nests and soil. *Trichophyton erinacei* has never been isolated from soil, but it remains viable for up to 1 year in nests. The nests are therefore potential source of infection for other animals and humans (English and Morris 1969).

The presentation in hedgehog ranges from asymptomatic infection to extensive involvement of the body surface. The infection is predominantly located on the head and usually spreads slowly (Morris and English 1973; Takahashi et al. 2002; Schauder et al. 2007). In human, cases of dermatophytosis are localized on contact sites with hedgehog, i.e., extremities (palm, fingers, wrist) are affected in ca 70–80% of reported cases, although tinea corporis, barbae, faciei, capitis, and onychomycosis have been also reported (English et al. 1962; Piérard-Franchimont et al. 2008; Concha et al. 2012).

The natural habitats of the main animal hosts are the UK and Northern and Western Europe (*Erinaceus europaeus*), and the species was introduced into New Zealand with the human immigration. It has been confirmed that Western European hedgehogs became wild in Japan after 1987 or even earlier (Takahashi et al. 2003). The four-toed hedgehog (*Atelerix albiventris*) is widely encountered in savanna and steppe zones of equatorial Africa from Senegal across to Ethiopia and south to the Zambezi River (sporadic in other regions of Africa). It is smaller than the Western European hedgehog, has a white abdomen, and is characterized by lacking the first toe of the hind leg. *Atelerix albiventris* has spread all over the world as a pet animal, most of them are domesticated with wild populations reported to be few (Takahashi et al. 2002; Santana et al. 2010).

Since the description of *T. erinacei*, hundreds of zoonotic infections due to *T. erinacei* have been reported from hedgehogs and humans across many European countries, Middle East, New Zealand, Australia (humans who handled animals in New Zealand), Africa, Japan, Korea, Taiwan, the USA, and Chile (English et al. 1962; Connole and Johnston 1967; Rosen 2000; Schauder et al. 2007; Piérard-Franchimont et al. 2008; Hsieh et al. 2010; Sun et al. 2010; Concha et al. 2012; Rezaei-Matehkolaei et al. 2013; Sieklucki et al. 2014; Drira et al. 2015; Jang et al. 2016). In an epidemiological survey, *T. erinacei* was reported in 44.7% of wild hedgehogs in New Zealand (Smith and Marples 1964), 20–25% of wild hedgehogs in Britain (Morris and English 1969) and 29.5% of hedgehogs in France (Le-Barzic et al. 2017). Skin lesions suggestive of dermatophytosis were observed only in ~6% of infected animals (Le-Barzic et al. 2017). The prevalence in household hedgehogs in Japan was 39% (Takahashi et al. 2003) and 50% in Spain (Abarca

et al. 2017). The incidence of human dermatophytosis due to contact with hedgehogs is difficult to estimate. When molecular methods are used for species identification, *T. erinacei* is regularly detected at low frequencies (Sun et al. 2010; Rezaei-Matehkolaei et al. 2013; Hubka et al. 2014b).

Because the hedgehogs are increasingly popular as pets, global prevalence and spread of *T. erinacei* requires close monitoring. The high infection rate in household hedgehogs predicts that the number of patients will have increasing tendency along with growing popularity of hedgehogs as pets.

3.9 Species with Doubtful Ecology and Often Referred to As Zoophilic

Insufficient data are available on distribution of *T. eriotrephon* which is known from four cases of dermatophytosis in man (tinea corporis, Netherlands; tinea manuum and tinea faciei, Iran; tinea barbae, France) (Papegaay 1925; Rezaei-Matehkolaei et al. 2013; Sabou et al. 2018) and a dog (isolate IHEM 24340 from Belgium). Two isolates of unnamed species usually called "African race of *Arthroderma benhamiae*" are known from dermatomycosis in man (Takashio 1974). It is anticipated that both species are zoophilic based on clinical manifestation of infection and their close phylogenetic relationships to pathogenic *Trichophyton* species (Fig. 3.3).

Occasionally, cases of infections in various animals and human are attributed to species from geophilic *Nannizzia* (formerly *Microsporum*) species (*N. gypsea*, *N. fulva*, *N. persicolor*, *N. praecox*, *N. incurvata*, *N. nana*, etc.). Some of these species (mainly *N. persicolor* and *N. nana*) are commonly designated as zoophilic in the medical literature solely based on the evidence of previous clinical cases. Indeed, the boundaries between zoophilic and geophilic species are not always sharp, and this is usually due to insufficient ecological data. Epidemiological features typical for geophilic species involve low host specificity (infections are reported from broad range of animals), clinical cases occur separately without clear connection between themselves (except of contact with soil), geographic origin of clinical isolates do not correlates with distribution of any host, and the dermatophyte species have very limited potential to cause significant outbreaks even if they occur in animals kept in large numbers in a limited space (low contagiousness). Geophilic species *N. persicolor*, relatively commonly associated with infections in dogs (Carlotti and Bensignor 1999; Muller et al. 2011) and humans (Chen et al. 2012; Hubka et al. 2014b) but frequently misidentified with *T. mentagrophytes*, can serve as a good example. The species was considered to be zoophilic in the past with probable reservoir in rodents (Kane et al. 1987). Its geophilic nature was confirmed by subsequent investigations of soil samples that revealed widespread dispersal of *N. persicolor* in soil (Sharma et al. 2008). In addition, poor growth at 37 °C and significant intraspecies variability revealed by using molecular data are typical for geophilic species rather than primarily pathogenic ones (Sharma et al. 2008). Phylogenetic position of *N. persicolor* within geophilic species from *N. gypsea*

complex is in agreement with such conclusion because related dermatophytes have usually similar ecology (Gräser et al. 2008).

Similar doubts on ecology exist in *Trichophyton simii* and *Lophophyton* (=*Microsporum*) *gallinae* which were traditionally considered zoophilic species with reservoir in monkeys or chickens, respectively. Both species fulfill many criteria typical for geophiles listed above. *Trichophyton simii* is known from sporadic cases of animal and human mycoses without specific predilection sites. The majority of case reports were summarized by Beguin et al. (2013), and they were described worldwide and involved monkeys, poultry, man, and dog (Okoshi et al. 1966; Clayton 1978; Constantino and Torre Mendoza 1979; Beguin et al. 2013; Yamaguchi et al. 2014). The species is known from soil or sand in India (Padhye and Thirumalachar 1967; Gugnani et al. 1968; Padhye and Carmichael 1968; Jain and Sharma 2011), France (Visset 1973), and Ivory Coast (Beguin et al. 2013) and was also recovered abundantly from asymptomatic small mammals in India, Africa, and Czech Republic (Gugnani et al. 1968, 1975; Ditrich and Otcenasek 1982; Hubálek 2000), from the fur of baboon in Guinea (Mariat and Tapia 1966) and poultry feather (Hubálek 2000) bringing another evidence of probable geophilic origin. No outbreaks were reported except of local epizootic in poultry (Gugnani and Randhawa 1973).

Lophophyton gallinae is well known as a causative agent of avian dermatophytosis (favus) that predominantly manifests in chicks and roosters as white to yellow scales or thick crusts on the comb and wattle; hens are less commonly affected. In severe cases, the infection spread on the other parts of the face, head, and neck with feather loss. The majority of infections was summarized previously by Murata et al. (2013) and older reports by Londero et al. (1969). These cases are again distributed worldwide and involved chickens but also ducks, dogs, monkeys, cats, squirrels, mouse, canary, pigeon, turkey, and man (no apparent predilection site in humans); outbreaks were rarely reported (Londero et al. 1969; Bradley et al. 1993). It is worth noting that some animals were healthy without any signs of infection, and no contact with birds was revealed in history of some patients. The fungus is known also from birds' nests of blue tit (*Cyanistes caeruleus*) and great tit (*Parus major*) (Goodenough and Stallwood 2010). Kawasaki et al. (1995) revealed close relationships between *M. gallinae*, geophilic *M. vanbreuseghemii*, and its sexual state *Arthroderma grubyi*. The conspecificity of these was subsequently supported by analysis of ITS rDNA region (Gräser et al. 1999a, 2008; de Hoog et al. 2017). The synonymization of these taxa was surprising due to different morphology and mating behavior. The ecology of former *M. vanbreuseghemii* is ambiguous (soil, asymptomatic as well as symptomatic animals and humans), similar to *L. gallinae*.

3.10 Outbreaks and Epidemics

Notable epidemic and outbreak episodes due to dermatophytes are considered to be rare, especially compared with other pathogens, such as bacteria and viruses. For instance, GIDEON (Global Infectious Disease and Epidemiology Network) database

(http://www.gideononline.com/) reports 1267 outbreaks (with approximately 275,000 patients involved) of diarrhea by *Escherichia coli* in an 82-year period (1934–2016) and 140 outbreaks (with approximately 9600 patients involved) of dermatophytosis in a 133-year period (1882–2015). Of these latter, 25 episodes (18%) were due to *M. canis* and distributed worldwide. This discrepancy between the number of reported outbreaks and real significance of dermatophytes is due to many factors. The episodes occur in different contexts and usually with a limited number (less than 20) of people/animals involved, but in some occasions numbers are much higher. Outbreaks in households and animal communities are frequent worldwide, although they are hardly reported in the literature because dermatophytosis, both in humans and animals, is not a notifiable disease in most countries. Among factors that contribute to the occurrence of such episodes, one of the most important is the poor awareness of people about the role of animals, especially pets, as carriers of dermatophytes. Indeed, in most cases, infected animals are introduced and manipulated without any precaution (e.g., a quarantine period, a veterinary visit, etc.) and left free to stay with animals already present in the house, breeding, pet shop, etc. Significant changes in epidemiological patterns on the large geographic areas take place on relatively long time scale (years and decades) and are detectable only when long-term epidemiological data are available what is an uncommon condition in veterinary dermatology. Additionally, changes in the prevalence of dermatophytosis can be easily neglected in principal hosts of particular pathogens because infections are commonly asymptomatic in high percentage of infected animals. The screening should therefore include ostensibly healthy animals as well.

Exceptionally, extensive changes in the epidemiology happen very quickly. For instance, the emergence and rapid spread of *T. benhamiae* in Europe have been one of major public health events in the field of zoonotic superficial mycoses in recent years that underscored the need for closer collaboration between the veterinary profession, dermatologists, epidemiologists, and public health personnel. Zoonotic infections associated with pet shops are likely to result in individual cases or small familial outbreaks. On the other hand, an infected animal kept in a group in a pet shop can potentially transmit the illness to other animals, and subsequently to a large number of pet owners, who may be geographically dispersed (Halsby et al. 2014). Because of this, pet shops can be the focus of large outbreaks, such as in the case of recent epidemics of *T. benhamiae* infections in pediatric patients. Epidemiological surveys in different European countries showed that ~17–90% of guinea pigs (commonly asymptomatic) in pet shops are infected. This resulted in high incidence of tinea corporis and capitis in children and young adults in affected countries. The first human infections started to occur in different European countries between 2000 and 2010, and it seems that the incidence has not yet reached its peak. For instance, in Germany and Czech Republic, *T. benhamiae* became within several years the most important agent of zoonotic dermatomycoses at all (Hubka et al. 2014b; Uhrlaß et al. 2015).

3.11 Changing Etiology of Zoonotic Dermatophytosis: Perspective of Human Medicine

Dermatophytes are still an important public health problem in both "developed" and "developing" countries, and their prevalence remains high. Zoophilic dermatophytes remain frequent causative agents and should be considered especially in children and adolescents with tinea capitis and tinea of glabrous skin. Changes in epidemiological patterns and prevalence of dermatophytosis in domestic animals are commonly detected secondarily from epidemiological studies on human population because of better surveillance and more complex epidemiological data.

Tinea capitis is a typical clinical entity caused predominantly by zoophilic species in majority of developed countries. *Microsporum canis* is a prevalent causal agent, and this could be related to close association between humans and companion animals and mass tourism to endemic regions (such as the Mediterranean area). Exceptional situation is currently in Germany, where *T. benhamiae* prevails over *M. canis*. Studies in Europe, Asia, and Africa indicate that anthropophilic agents of scalp infections are being almost eradicated and are now more typical of countries with low socioeconomic status. The exception is tinea capitis due to *T. tonsurans* in North America. A shift toward tinea capitis due to anthropophilic dermatophytes (*T. tonsurans*, *T. soudanense*, and *M. audouinii*) is obvious in some urban areas in Europe, e.g., from the UK, France, Sweden, and Switzerland. This pattern seems to be linked to ethnic groups originating from Africa or from the Caribbean. Various anthropophilic species remain major causal agents of tinea capitis in many Asian and African countries, although significant shift toward zoophilic etiology (similar to situation in Europe) was observed in numerous more developed regions during last decades as described in detail, e.g., from China (Havlickova et al. 2008; Seebacher et al. 2008; Nweze 2010; Hayette and Sacheli 2015; Kieliger et al. 2015; Uhrlaß et al. 2015; Zhan et al. 2015; Nweze and Eke 2016). Exceptionally, other zoophilic species such as *T. mentagrophytes* or *T. verrucosum* may represent the major agents of tinea capitis as reported, e.g., from some region of China, Middle East, or Africa (Al-Duboon et al. 1999; Metin et al. 2002; Nweze 2010; Oudaina et al. 2011; Zhan et al. 2015).

Epidemiologic changes in the prevalence and etiology of inflammatory dermatophytoses on bare skin have been less extensively studied. Their prevalence and pathogens responsible for causing them usually reflect local trends in tinea capitis and tinea pedis. In general, broad spectrum of anthropophilic, zoophilic, and geophilic species can be responsible for similar clinical manifestation. Various anthropophilic species cause majority of infections in developed as well as in developing countries, and zoophilic species such as *M. canis*, *T. mentagrophytes*, and *T. verrucosum* supplement the spectrum of the most important causative agents worldwide. *Microsporum canis* still prevails over anthropophilic species in South European countries, although increase of anthropophilic species was observed in the most recent studies. *Trichophyton verrucosum* and *T. mentagrophytes* remain predominant dermatophytes in rural regions of the Middle East (Naseri et al. 2013; Hayette and Sacheli 2015; Chadeganipour et al. 2016).

Zoophilic dermatophytes also importantly contribute to a number of occupational infections in farmers, workers in livestock production, laboratory workers, pet shop workers, and other professions that require contact with animals (McAller 1980; Cafarchia et al. 2013c; Halsby et al. 2014). Incidence of dermatophytosis in farm workers can be strikingly high (Torres-Rodriguez et al. 1992; Agnetti et al. 2014).

3.12 Management of Outbreaks and Their Prevention

In most cases, animal dermatophytoses are self-limiting diseases because innate and/or acquired immunity is strong enough to control the spread of infection. Nevertheless, specific treatment is required to obtain a more rapid clinical cure, to minimize contamination to other hosts (including humans) and to reduce the dissemination of infective arthroconidia in the environment. Recommendations for the treatment are based on both in vivo and in vitro investigations (Moriello et al. 2017). These recommendations systematically include the disinfection of the environment and the limitation of contact between infected animals and healthy ones.

The transmission of zoophilic dermatophyte is through direct contact with infected animals or through contaminated environments, and limiting this kind of contact is a simple way for the prevention of transmission (Chermette et al. 2008). Sometimes prevention is difficult to perform. In case of subclinical infection or mechanical carriage, animals have no cutaneous lesions but may be responsible for contamination. Such a situation is frequently reported in some animal populations (e.g., cats infected by *M. canis* or guinea pigs infected by *T. benhamiae*).

The use of antifungals has been proposed for the prevention of animal dermatophytosis. However, investigations showed that the oral administration of griseofulvin did not allow the prevention of infection in humans. Topical administration of antifungal drugs seems to be more appropriate. When an animal has been in contact with an infected animal or area, it could be useful to use an antifungal shampoo.

Efforts in developing fungal vaccines to prevent dermatophytosis in different animal species are going on (Lund and DeBoer 2008; Mignon et al. 2008; Moriello et al. 2017). Immunoprophylaxis is particularly valuable in large breeding units or when pastures are shared by herds of different origins. Vaccination of animals has become the rule in some countries where bovine dermatophytosis is a notifiable disease (Gudding and Lund 1995). Anti-dermatophyte vaccines have been developed against dermatophytosis in cattle, horses, and less frequently sheep, but they are not available worldwide (Chermette et al. 2008). Both inactivated and live-attenuated vaccines, monovalent or multivalent, have been developed against animal ringworm. Ribosomal fractions of *T. verrucosum* have demonstrated promising immunogenic properties in cattle (Elad and Segal 1995). Recombinant protein and DNA vaccines derived from the heat-shock protein hsp60 of *T. mentagrophytes* allowed to control the clinical course of ringworm in guinea pigs and cattle (Milan et al. 2004). Other studies in horses using an inactivated preparation containing conidia and hyphae of *T. equinum* with adjuvant demonstrated a 75–87% relative

protection of vaccinated horses against an infective contact (Pier and Zancanella 1993). Live vaccine against dermatophytes has been developed in the former USSR. A particular strain of *T. verrucosum* (the LTF 130 strain, with abundant production of microconidia in culture) was selected because of a high immunogenicity and attenuated pathogenicity. LTF live vaccines are currently used or have been used for several years in different countries, especially in Europe and on other continents (Canada, Cuba, Kenya, or Mongolia). To obtain optimal results, the vaccination program must concern all the animals of the cattle herd; then only the young calves between 2 weeks and 4 months of age and the newly introduced cattle will be vaccinated. In countries that have achieved successful control and eradication of cattle ringworm, a mass and systematic vaccination of cattle were undertaken. Failure of immunoprophylaxis can be explained by the non-respect of vaccination procedures, the reintroduction of infected cattle, the development of dermatophytes different from *T. verrucosum* and lack of crossed immunity, and the absence of hygienic and disinfection measures in farms. A dramatic reduction of dermatophytosis incidence in cattle, an improvement of the quality of leather and skins, and a decrease in case number of human contaminations have been observed when vaccination is correctly applied (Chermette et al. 2008; Seebacher et al. 2008).

To date, there is no vaccine (with high level of efficacy and safety) for companion animals exposed to *M. canis* infection (Moriello et al. 2017). The vaccine licensed for use in cats in the USA in 1994 provided disappointing results and is not commercialized anymore. Broad-spectrum dermatophyte vaccines (for instance, against *T. mentagrophytes* and *M. canis*) are currently available in some European countries. They have been used in different species including pet carnivores and fur animals.

3.13 Conclusion

Zoophilic dermatophytes remain an important public health concern in both developed and developing countries. *Microsporum canis* is a major cause of dermatophytosis in plenty of domestic animals and tinea capitis in developed countries and urban region of developing ones. Together with other zoophilic species *M. canis* contributes significantly to a number of glabrous skin dermatophytosis worldwide. *Trichophyton verrucosum* and *T. mentagrophytes* cause considerable morbidity and economic losses in rabbit and cattle farms, respectively. Strict compliance with the recommended preventive measures can effectively eliminate these problems. In contrast, *T. benhamiae* and *T. erinacei* are typical emerging zoonotic pathogens associated with pets and small wild mammals. The prevalence and spread of these species require close monitoring, particularly because the infection rates in the principal hosts, guinea pigs, and hedgehogs, respectively, are high, and the hedgehogs are increasingly popular as pets worldwide. There are still numerous questions to resolve in basic research on dermatophytes concerning pathogenesis, species concept, and ecology of some species. Additionally, reproducible and effective genotyping methods are not

available for all major zoophilic dermatophytes what limits our understanding of global epidemiological trends, monitoring of changes on the level of genotypes and detecting outbreaks.

Acknowledgments VH was supported by the Charles University Grant Agency (GAUK 8615), Charles University Research Centre program No. 204069, Czech Ministry of Health (AZV 17-31269A), and the project BIOCEV (CZ.1.05/1.1.00/02.0109) provided by the Ministry of Education, Youth and Sports of CR, and ERDF. The contribution of AC was supported by the project of Charles University Grant Agency (GAUK 600217). Vit Hubka is grateful for the support from the Czechoslovak Microscopy Society (CSMS scholarship 2016).

References

Abarca M, Castellá G, Martorell J et al (2017) *Trichophyton erinacei* in pet hedgehogs in Spain: occurrence and revision of its taxonomic status. Med Mycol 55:164–172

Abastabar M, Rezaei-Matehkolaei A, Shidfar MR et al (2013) A molecular epidemiological survey of clinically important dermatophytes in Iran based on specific RFLP profiles of beta-tubulin gene. Iran J Public Health 42:1049–1057

Abdel-Rahman SM, Sugita T, González GM et al (2010) Divergence among an international population of *Trichophyton tonsurans* isolates. Mycopathologia 169:1–13

Achterman RR, White TC (2011) Dermatophyte virulence factors: identifying and analyzing genes that may contribute to chronic or acute skin infections. Int J Microbiol 2012:358305

Aghamirian MR, Ghiasian SA (2011) Dermatophytes as a cause of epizoonoses in dairy cattle and humans in Iran: epidemiological and clinical aspects. Mycoses 54:e52–e56

Agnetti F, Righi C, Scoccia E et al (2014) *Trichophyton verrucosum* infection in cattle farms of Umbria (Central Italy) and transmission to humans. Mycoses 57:400–405

Ahdy AM, Sayed-Ahmed MZ, Younis EE et al (2016) Prevalence and potential risk factors of dermatophytosis in Arabian horses in Egypt. J Equine Vet Sci 37:71–76

Ahmadi B, Mirhendi H, Makimura K et al (2016) Phylogenetic analysis of dermatophyte species using DNA sequence polymorphism in calmodulin gene. Med Mycol 54:500–514

Ajello L, Cheng S-L (1967) The perfect state of *Trichophyton mentagrophytes*. Sabouraudia 5:230–234

Al-Ani F, Younes F, Al-Rawashdeh O (2002) Ringworm infection of cattle and horses in Jordan. Acta Vet Brno 71:55–60

Al-Duboon A, Muhsin T, Al-Rubaiy K (1999) Tinea capitis in Basrah, Iraq. Mycoses 42:331–333

Ali-Shtayeh M, Arda H, Hassouna M et al (1988) Keratinophilic fungi on the hair of cows, donkeys, rabbits, cats, and dogs from the West Bank of Jordan. Mycopathologia 104:109–121

Aljabre S, Richardson M, Scott E et al (1993) Adherence of arthroconidia and germlings of anthropophilic and zoophilic varieties of *Trichophyton mentagrophytes* to human corneocytes as an early event in the pathogenesis of dermatophytosis. Clin Exp Dermatol 18:231–235

Alteras I, Cojocaru I (1969) Human infection by *Trichophyton mentagrophytes* from rabbits. Mycoses 12:543–544

Alteras I, Feuerman EJ (1979) Two outbreaks of *Microsporum canis* ringworm in Israel. Mycopathologia 67:169–172

Ameen M (2010) Epidemiology of superficial fungal infections. Clin Dermatol 28:197–201

Ansari S, Hedayati MT, Zomorodian K et al (2016) Molecular characterization and in vitro antifungal susceptibility of 316 clinical isolates of dermatophytes in Iran. Mycopathologia 181:89–95

Anzawa K, Kawasaki M, Mochizuki T et al (2010) Successful mating of *Trichophyton rubrum* with *Arthroderma simii*. Med Mycol 48:629–634

Arabatzis M, Xylouri E, Frangiadaki I et al (2006) Rapid detection of *Arthroderma vanbreuseghemii i*n rabbit skin specimens by PCR–RFLP. Vet Dermatol 17:322–326
Baldo A, Tabart J, Vermout S et al (2008) Secreted subtilisins of *Microsporum canis* are involved in adherence of arthroconidia to feline corneocytes. J Med Microbiol 57:1152–1156
Baldo A, Mathy A, Tabart J et al (2010) Secreted subtilisin Sub3 from *Microsporum canis* is required for adherence to but not for invasion of the epidermis. Br J Dermatol 162:990–997
Balogun R, Jegede H, Jibril A, Kwanashie C, Kazeem H (2017) Prevalence and distribution of dermatophytes among domestic horses in Kwara state, Nigeria. Sokoto J Vet Sci 15:1–6
Baudet EARF (1932) Recherches experimentales sur les *Trichophyton* animaux a cultures faviformes. Ann Parasitol Hum Comp 10:520–541
Beguin H, Pyck N, Hendrickx M et al (2012) The taxonomic status of *Trichophyton quinckeanum* and *T. interdigitale* revisited: a multigene phylogenetic approach. Med Mycol 50:871–882
Beguin H, Goens K, Hendrickx M et al (2013) Is *Trichophyton simii* endemic to the Indian subcontinent? Med Mycol 51:444–448
Bernhardt A, Sedlacek L, Wagner S et al (2013) Multilocus sequence typing of *Scedosporium apiospermum* and *Pseudallescheria boydii* isolates from cystic fibrosis patients. J Cyst Fibros 12:592–598
Bianchi MV, Laisse CJ, Vargas TP et al (2017) Intra-abdominal fungal pseudomycetoma in two cats. Rev Iberoam Micol 34:112–115
Blank F (1955) Dermatophytes of animal origin transmissible to man. Am J Med Sci 229:302–316
Bond R (2010) Superficial veterinary mycoses. Clin Dermatol 28:226–236
Bradley FA, Bickford A, Walker RL (1993) Diagnosis of favus (avian dermatophytosis) in Oriental breed chickens. Avian Dis 37:1147–1150
Brasch J, Beck-Jendroschek V, Voss K et al (2016) *Arthroderma benhamiae* strains in Germany. Morphological and physiological characteristics of the anamorphs. Hautarzt 67:700–705
Burmester A, Shelest E, Glöckner G et al (2011) Comparative and functional genomics provide insights into the pathogenicity of dermatophytic fungi. Genome Biol 12:R7
Cabañes F, Abarca ML, Bragulat MR (1997) Dermatophytes isolated from domestic animals in Barcelona, Spain. Mycopathologia 137:107–113
Cabo JG, Asensio MB, Rodriguez FG et al (1995) An outbreak of dermatophytosis in pigs caused by *Microsporum canis*. Mycopathologia 129:79–80
Cafarchia C, Romito D, Sasanelli M et al (2004) The epidemiology of canine and feline dermatophytoses in southern Italy. Mycoses 47:508–513
Cafarchia C, Romito D, Capelli G et al (2006) Isolation of *Microsporum canis* from the hair coat of pet dogs and cats belonging to owners diagnosed with *M. canis* tinea corporis. Vet Dermatol 17:327–331
Cafarchia C, Camarda A, Coccioli C et al (2010) Epidemiology and risk factors for dermatophytoses in rabbit farms. Med Mycol 48:975–980
Cafarchia C, Weigl S, Figueredo LA et al (2012) Molecular identification and phylogenesis of dermatophytes isolated from rabbit farms and rabbit farm workers. Vet Microbiol 154:395–402
Cafarchia C, Figueredo LA, Otranto D (2013a) Fungal diseases of horses. Vet Microbiol 167:215–234
Cafarchia C, Gasser RB, Figueredo LA et al (2013b) An improved molecular diagnostic assay for canine and feline dermatophytosis. Med Mycol 51:136–143
Cafarchia C, Iatta R, Latrofa MS et al (2013c) Molecular epidemiology, phylogeny and evolution of dermatophytes. Infect Genet Evol 20:336–351
Cano J, Rezusta A, Solé M et al (2005) Inter-single-sequence-repeat-PCR typing as a new tool for identification of *Microsporum canis* strains. J Dermatol Sci 39:17–21
Carlotti D, Bensignor E (1999) Dermatophytosis due to *Microsporum persicolor* (13 cases) or *Microsporum gypseum* (20 cases) in dogs. Vet Dermatol 10:17–27
Chadeganipour M, Mohammadi R, Shadzi S (2016) A 10-year study of dermatophytoses in Isfahan, Iran. J Clin Lab Anal 30:103–107

Charlent A-L (2011) Le complexe *Trichophyton mentagrophytes*, caractérisation mycologique et moléculaire d'un nouveau variant: *Trichophyton mentagrophytes* var. *porcellae*. Master Thesis. Université Henri Poincaré, Nancy

Chen SCA, Ellis D, Sorrell TC et al (2011) *Trichophyton*. In: Liu D (ed) Molecular detection of human fungal pathogens. CRC Press, Boca Raton, pp 357–375

Chen W, Seidl HP, Ring J et al (2012) Two pediatric cases of *Microsporum persicolor* infection. Int J Dermatol 51:204–206

Chermette R, Ferreiro L, Guillot J (2008) Dermatophytoses in animals. Mycopathologia 166:385–405

Chinnapun D (2015) Virulence factors involved in pathogenicity of dermatophytes. Walailak J Sci Tech 12:573–580

Chollet A, Cattin V, Fratti M et al (2015a) Which fungus originally was *Trichophyton mentagrophytes*? Historical review and illustration by a clinical case. Mycopathologia 180:1–5

Chollet A, Wespi B, Roosje P et al (2015b) An outbreak of *Arthroderma vanbreuseghemii* dermatophytosis at a veterinary school associated with an infected horse. Mycoses 58:233–238

Clayton Y (1978) The changing pattern of tinea capitis in London schoolchildren. Mykosen Suppl 1:104–107

Cmokova A (2015) Molecular typization of isolates from *Arthroderma benhamiae* complex, a zoonotic agent of epidemic dermatophytosis in Europe. Master Thesis. Charles University, Prague

Cmokova A, Kolarik M, Dobiasova S et al (2017) Outbreak of children's dermatophytosis due to highly virulent population of *Trichophyton benhamiae*. Mycoses 60(Suppl. 2):134

Concha M, Nicklas C, Balcells E et al (2012) The first case of tinea faciei caused by *Trichophyton mentagrophytes* var. *erinacei* isolated in Chile. Int J Dermatol 51:283–285

Connole M, Johnston L (1967) A review of animal mycoses in Australia. Vet Bull Weybridge 37:145–153

Connole M, Pascoe R (1984) Recognition of *Trichophyton equinum* var. *equinum* infection of horses. Aust Vet J 61:94–94

Constantino MFH, Torre Mendoza C (1979) Isolation of dermatophytes from clinical cases of dermatomycosis in the game fowl. Philipp J Vet Med 18:79–91

Contet-Audonneau N, Leyer C (2010) Émergence d'un dermatophyte transmis par le cochon d'Inde et proche de *Trichophyton mentagrophytes* var. *erinacei: T. mentagrophytes* var. *porcellae*. J Mycol Med 20:321–325

Copetti MV, Santurio JM, Cavalheiro AS et al (2006) Dermatophytes isolated from dogs and cats suspected of dermatophytosis in southern Brazil. Acta Sci Vet 34:119–124

Courtellemont L, Chevrier S, Degeilh B et al (2017) Epidemiology of *Trichophyton verrucosum* infection in Rennes University Hospital, France: a 12-year retrospective study. Med Mycol 55:720–724

d'Ovidio D, Grable S, Ferrara M et al (2014) Prevalence of dermatophytes and other superficial fungal organisms in asymptomatic guinea pigs in Southern Italy. J Small Anim Pract 55:355–358

da Costa FV, Farias MR, Bier D et al (2013) Genetic variability in *Microsporum canis* isolated from cats, dogs and humans in Brazil. Mycoses 56:582–588

Dąbrowska I, Dworecka-Kaszak B, Brillowska-Dąbrowska A (2014) The use of a one-step PCR method for the identification of *Microsporum canis* and *Trichophyton mentagrophytes* infection of pets. Acta Biochim Pol 61:375–378

Dalis J, Kazeem H, Kwaga J et al (2014) An outbreak of ringworm caused by *Trichophyton verrucosum* in a group of calves in Vom, Nigeria. Afr J Microbiol Res 8:783–787

De Baere T, Summerbell R, Theelen B et al (2010) Evaluation of internal transcribed spacer 2-RFLP analysis for the identification of dermatophytes. J Med Microbiol 59:48–54

de Hoog GS, Dukik K, Monod M et al (2017) Toward a novel multilocus phylogenetic taxonomy for the dermatophytes. Mycopathologia 182:5–31

de Mendoza MH, de Mendoza JH, Alonso JM et al (2010) A zoonotic ringworm outbreak caused by a dysgonic strain of *Microsporum canis* from stray cats. Rev Iberoam Micol 27:62–65

DeBoer D, Moriello K (2006) Dermatophytosis. In: Greene C (ed) Infectious diseases of the dog and cat, 3rd edn. Elsevier, St. Louis, pp 550–565

Debourgogne A, Gueidan C, de Hoog S et al (2012) Comparison of two DNA sequence-based typing schemes for the *Fusarium solani* species complex and proposal of a new consensus method. J Microbiol Methods 91:65–72

Dhib I, Khammari I, Yaacoub A et al (2017) Relationship between phenotypic and genotypic characteristics of *Trichophyton mentagrophytes* strains isolated from patients with dermatophytosis. Mycopathologia 182:487–493

Dhieb C, Essghaier B, El Euch D et al (2014) Phenotypical and molecular characterization of *Microsporum canis* strains in North-Tunisia. Pol J Microbiol 63:307–315

Difonzo E, Palleschi G, Vannini P et al (1986) *Microsporum canis* epidemic in laboratory mice. Mycoses 29:591–595

Ditrich O, Otcenasek M (1982) *Microsporum vanbreuseghemii* and *Trichophyton simii* in Czechoslovakia. Ces Mykol 36:236–242

Dobrowolska A, Dębska J, Kozłowska M et al (2011) Strains differentiation of *Microsporum canis* by RAPD analysis using $(GACA)_4$ and $(ACA)_5$ primers. Pol J Microbiol 60:145–148

Donnelly TM, Rush EM, Lackner PA (2000) Ringworm in small exotic pets. Semin Avian Exotic Pet Med 9:82–93

Drake LA, Dinehart SM, Farmer ER et al (1996) Guidelines of care for superficial mycotic infections of the skin: tinea corporis, tinea cruris, tinea faciei, tinea manuum, and tinea pedis. J Am Acad Dermatol 34:282–286

Drira I, Neji S, Hadrich I et al (2015) Tinea manuum due to *Trichophyton erinacei* from Tunisia. J Mycol Med 25:200–203

Drouot S, Mignon B, Fratti M et al (2009) Pets as the main source of two zoonotic species of the *Trichophyton mentagrophytes* complex in Switzerland, *Arthroderma vanbreuseghemii* and *Arthroderma benhamiae*. Vet Dermatol 20:13–18

Drusin LM, Ross BG, Rhodes KH et al (2000) Nosocomial ringworm in a neonatal intensive care unit: a nurse and her cat. Infect Control Hosp Epidemiol 21:605–607

Duarte A, Castro I, da Fonseca IMP et al (2010) Survey of infectious and parasitic diseases in stray cats at the Lisbon Metropolitan Area, Portugal. J Feline Med Surg 12:441–446

Duek L, Kaufman G, Ulman Y et al (2004) The pathogenesis of dermatophyte infections in human skin sections. J Infect 48:175–180

Dvorak J, Otcenasek M, Komarek J (1965) Das Spektrum der aus Tierläsionen in Ostböhmen in den Jahren 1962–1964 isolierten Dermatophyten. Mycoses 8:126–127

Elad D, Segal E (1995) Immunogenicity in calves of a crude ribosomal fraction of *Trichophyton verrucosum*: a field trial. Vaccine 13:83–87

English M (1961) An outbreak of equine ringworm due to *Trichophyton equinum*. Vet Rec 73:578–580

English MP (1969) Ringworm in wild mammals: further investigations. J Zool 159:515–522

English MP, Morris P (1969) *Trichophyton mentagrophytes* var. *erinacei* in hedgehog nests. Sabouraudia 7:118–121

English MP, Evans CD, Hewitt M et al (1962) Hedgehog ringworm. Br Med J 1:149–151

Esquenazi D, Alviano CS, de Souza W et al (2004) The influence of surface carbohydrates during in vitro infection of mammalian cells by the dermatophyte *Trichophyton rubrum*. Res Microbiol 155:144–153

Fachin AL, Ferreira-Nozawa MS, Maccheroni W Jr et al (2006) Role of the ABC transporter TruMDR2 in terbinafine, 4-nitroquinoline N-oxide and ethidium bromide susceptibility in *Trichophyton rubrum*. J Med Microbiol 55:1093–1099

Frealle E, Rodrigue M, Gantois N et al (2007) Phylogenetic analysis of *Trichophyton mentagrophytes* human and animal isolates based on MnSOD and ITS sequence comparison. Microbiology 153:3466–3477

Fumeaux J, Mock M, Ninet B et al (2004) First report of *Arthroderma benhamiae* in Switzerland. Dermatology 208:244–250
Gallo M, Lanfranchi P, Poglayen G et al (2005a) Seasonal 4-year investigation into the role of the alpine marmot (*Marmota marmota*) as a carrier of zoophilic dermatophytes. Med Mycol 43:373–379
Gallo M, Tizzani P, Peano A et al (2005b) Eastern cottontail (*Sylvilagus floridanus*) as carrier of dermatophyte fungi. Mycopathologia 160:163–166
Georg LK (1960) Animal ringworm in public health: diagnosis and nature. US Government Printing Office, Washington, DC
Ghannoum M (2016) Azole resistance in dermatophytes: prevalence and mechanism of action. J Am Podiatr Med Assoc 106:79–86
Ginter-Hanselmayer G, Weger W, Ilkit M et al (2007) Epidemiology of tinea capitis in Europe: current state and changing patterns. Mycoses 50(Suppl. 2):6–13
Gonzalez J, Solans C, Latre M (1988) *Microsporum canis* productor de dermatofitosis en conejos. Rev Iberoam Micol 5:84–89
Goodenough AE, Stallwood B (2010) Intraspecific variation and interspecific differences in the bacterial and fungal assemblages of blue tit (*Cyanistes caeruleus*) and great tit (*Parus major*) nests. Microb Ecol 59:221–232
Gräser Y (2014) Species identification of dermatophytes by MALDI-TOF MS. Curr Fungal Infect Rep 8:193–197
Gräser Y, El Fari M, Vilgalys R et al (1999a) Phylogeny and taxonomy of the family Arthrodermataceae (dermatophytes) using sequence analysis of the ribosomal ITS region. Med Mycol 37:105–114
Gräser Y, Kuijpers AFA, Presber W et al (1999b) Molecular taxonomy of *Trichophyton mentagrophytes* and *T. tonsurans*. Med Mycol 37:315–330
Gräser Y, Kuijpers AFA, El Fari M et al (2000a) Molecular and conventional taxonomy of the *Microsporum canis* complex. Med Mycol 38:143–153
Gräser Y, Kuijpers AFA, Presber W et al (2000b) Molecular taxonomy of the *Trichophyton rubrum* complex. J Clin Microbiol 38:3329–3336
Gräser Y, De Hoog S, Summerbell R (2006) Dermatophytes: recognizing species of clonal fungi. Med Mycol 44:199–209
Gräser Y, Scott J, Summerbell R (2008) The new species concept in dermatophytes—a polyphasic approach. Mycopathologia 166:239–256
Grills CE, Bryan PL, O'Moore E et al (2007) *Microsporum canis*: Report of a primary school outbreak. Australas J Dermatol 48:88–90
Grumbt M, Monod M, Yamada T et al (2013) Keratin degradation by dermatophytes relies on cysteine dioxygenase and a sulfite efflux pump. J Investig Dermatol 133:1550–1555
Gudding R, Lund A (1995) Immunoprophylaxis of bovine dermatophytosis. Can Vet J 36:302–306
Gugnani H, Randhawa H (1973) An epizootic of dermatophytosis caused by *Trichophyton simii* in poultry. Sabouraudia 11:1–3
Gugnani H, Shrivastav J, Gupta N (1968) Occurrence of *Arthroderma simii* in soil and on hair of small mammals. Sabouraudia 6:77–80
Gugnani H, Wattal B, Sandhu R (1975) Dermatophytes and other keratinophilic fungi recovered from small mammals in India. Mycoses 18:529–538
Guillot J, Johannsen C, Guechi R et al (2016) Dermatophytes species isolated from companion animals in France. In: Proceedings of the 8th world congress of veterinary dermatology, Bordeaux, France
Gupta AK, Ahmad I, Borst I et al (2000) Detection of xanthomegnin in epidermal materials infected with *Trichophyton rubrum*. J Investig Dermatol 115:901–905
Gürtler TGR, Diniz LM, Nicchio L (2005) Tinea capitis micro-epidemic by *Microsporum canis* in a day care center of Vitória-Espírito. An Bras Dermatol 80:267–272
Hadrich I, Ranque S (2015) Typing of fungi in an outbreak setting: lessons learned. Curr Fungal Infect Rep 9:314–323

Halsby KD, Walsh AL, Campbell C et al (2014) Healthy animals, healthy people: zoonosis risk from animal contact in pet shops, a systematic review of the literature. PLoS One 9:e89309

Hamal P, Hubka V, Cmokova A et al (2016) Molecular epidemiology of dermatophytosis: results of a three year multicentric survey in the Czech Republic. Mycoses 59(Suppl. 1):14

Hameed K, Riaz FC, Nawaz MA et al (2017) *Trichophyton verrucosum* infection in livestock in the Chitral District (Pakistan). J Infect Dev Ctries 11:326–333

Harmsen D, Schwinn A, Weig M et al (1995) Phylogeny and dating of some pathogenic keratinophilic fungi using small subunit ribosomal RNA. J Med Vet Mycol 33:299–303

Havlickova B, Czaika V, Friedrich M (2008) Epidemiological trends in skin mycoses worldwide. Mycoses 51(Suppl. 4):2–15

Hayette M-P, Sacheli R (2015) Dermatophytosis, trends in epidemiology and diagnostic approach. Curr Fungal Infect Rep 9:164–179

Heidemann S, Monod M, Gräser Y (2010) Signature polymorphisms in the internal transcribed spacer region relevant for the differentiation of zoophilic and anthropophilic strains of *Trichophyton interdigitale* and other species of *T. mentagrophytes* sensu lato. Br J Dermatol 162:282–295

Hejtmánek M, Hejtmánková N (1989) Hybridization and sexual stimulation in *Trichophyton mentagrophytes*. Folia Microbiol 34:77–79

Hillary T, Suys E (2014) An outbreak of tinea capitis in elderly patients. Int J Dermatol 53:e101–e103

Hirai A, Kano R, Nakamura Y et al (2003) Molecular taxonomy of dermatophytes and related fungi by chitin synthase 1 (CHS1) gene sequences. Antonie Leeuwenhoek 83:11–20

Hironaga M, Watanabe S (1980) Mating behavior of 334 Japanese isolates of *Trichophyton mentagrophytes* in relation to their ecological status. Mycologia 72:1159–1170

Hironaga M, Nozaki K, Watanabe S (1980) Ascocarp production by *Nannizzia otae* on keratinous and non-keratinous agar media and mating behavior of *N. otae* and 123 Japanese isolates of *Microsporum canis*. Mycopathologia 72:135–141

Hiruma J, Kano R, Harada K et al (2015) Occurrence of *Arthroderma benhamiae* genotype in Japan. Mycopathologia 179:219–223

Hoppmann E, Barron HW (2007) Rodent dermatology. J Exot Pet Med 16:238–255

Hsieh C-W, Sun P-L, Wu Y-H (2010) *Trichophyton erinacei* infection from a hedgehog: a case report from Taiwan. Mycopathologia 170:417–421

Hubálek Z (2000) Keratinophilic fungi associated with free-living mammals and birds. In: Kushwaha RKS, Guarro J (eds) Biology of dermatophytes. Revista Iberoamericana de Micología, Bilbao, pp 93–103

Hube B, Hay R, Brasch J et al (2015) Dermatomycoses and inflammation: the adaptive balance between growth, damage, and survival. J Mycol Med 25:e44–e58

Hubka V, Dobiasova S, Dobias R et al (2014a) *Microsporum aenigmaticum* sp. nov. from *M. gypseum* complex, isolated as a cause of tinea corporis. Med Mycol 52:387–396

Hubka V, Větrovský T, Dobiášová S et al (2014b) Molecular epidemiology of dermatophytoses in the Czech Republic – two-year-study results. Čes-Slov Dermotol 89:167–174

Hubka V, Nissen C, Jensen R et al (2015) Discovery of a sexual stage in *Trichophyton onychocola*, a presumed geophilic dermatophyte isolated from toenails of patients with a history of *T. rubrum* onychomycosis. Med Mycol 53:798–809

Huson DH, Bryant D (2006) Application of phylogenetic networks in evolutionary studies. Mol Biol Evol 23:254–267

Irinyi L, Serena C, Garcia-Hermoso D et al (2015) International Society of Human and Animal Mycology (ISHAM)-ITS reference DNA barcoding database—the quality controlled standard tool for routine identification of human and animal pathogenic fungi. Med Mycol 53:313–337

Jackson CJ, Mochizuki T, Barton RC (2006) PCR fingerprinting of *Trichophyton mentagrophytes* var. *interdigitale* using polymorphic subrepeat loci in the rDNA nontranscribed spacer. J Med Microbiol 55:1349–1355

Jain N, Sharma M (2011) Distribution of dermatophytes and other related fungi in Jaipur city, with particular reference to soil pH. Mycoses 54:52–58

Jang MS, Park JB, Jang JY et al (2016) Kerion celsi caused by *Trichophyton erinacei* from a hedgehog treated with terbinafine. J Dermatol 44(9):1070–1071.

Jensen RH, Arendrup MC (2012) Molecular diagnosis of dermatophyte infections. Curr Opin Infect Dis 25:126–134

Kac G, Bougnoux M, Feuilhade De Chauvin M et al (1999) Genetic diversity among *Trichophyton mentagrophytes* isolates using random amplified polymorphic DNA method. Br J Dermatol 140:839–844

Kandemir H, Ilkit M, Çürük A (2015) Xanthomegnin detection does not discriminate between *Trichophyton rubrum* and *T. mentagrophytes* complexes. J Microbiol Methods 111:122–126

Kane J, Sigler L, Summerbell R (1987) Improved procedures for differentiating *Microsporum persicolor* from *Trichophyton mentagrophytes*. J Clin Microbiol 25:2449–2452

Kaneko T, Kaneko M, Makimura K (2011) Cluster analysis of *Microsporum canis* isolated from a patient with tinea corporis and an infected cat based on the DNA sequences of nuclear ribosomal internal transcribed spacer 1. Mycoses 54:e867–e869

Kano R, Nakamura Y, Yasuda K et al (1998) The first isolation of *Arthroderma benhamiae* in Japan. Microbiol Immunol 42:575–578

Kano R, Nakamura Y, Watanabe S et al (1999) Phylogenetic relation of *Epidermophyton floccosum* to the species of *Microsporum* and *Trichophyton* in chitin synthase 1 (CHS1) gene sequences. Mycopathologia 146:111–113

Kano R, Nakamura Y, Watanabe S et al (2002) Chitin synthase 1 and 2 genes of dermatophytes. Stud Mycol 47:49–55

Kano R, Yamada T, Makimura K et al (2011) *Arthroderma benhamiae* (the teleomorph of *Trichophyton mentagrophytes*) mating type-specific genes. Mycopathologia 171:333–337

Kano R, Yoshida E, Yaguchi T et al (2014) Mating type gene (MAT1-2) of *Trichophyton verrucosum*. Mycopathologia 177:103–112

Kaszubiak A, Klein S, de Hoog GS et al (2004) Population structure and evolutionary origins of *Microsporum canis*, *M. ferrugineum* and *M. audouinii*. Infect Genet Evol 4:179–186

Kawasaki M (2011) Verification of a taxonomy of dermatophytes based on mating results and phylogenetic analyses. Med Mycol J 52:291–295

Kawasaki M, Aoki M, Ishizaki H (1995) Phylogenetic relationships of some *Microsporum* and *Arthroderma* species inferred from mitochondrial DNA analysis. Mycopathologia 130:11–21

Kawasaki M, Anzawa K, Wakasa A et al (2010) Matings among three teleomorphs of *Trichophyton mentagrophytes*. Jpn J Med Mycol 51:143–152

Kawasaki M, Anzawa K, Ushigami T et al (2011) Multiple gene analyses are necessary to understand accurate phylogenetic relationships among *Trichophyton* species. Med Mycol J 52:245–254

Khettar L, Contet-Audonneau N (2012) Cochon d'Inde et dermatophytose. Ann Dermatol Venereol 139:631–635

Khosravi A, Mahmoudi M (2003) Dermatophytes isolated from domestic animals in Iran. Mycoses 46:222–225

Kieliger S, Glatz M, Cozzio A et al (2015) Tinea capitis and tinea faciei in the Zurich area–an 8-year survey of trends in the epidemiology and treatment patterns. J Eur Acad Dermatol Venereol 29:1524–1529

Kim J, Takahashi Y, Tanaka R et al (2001) Identification and subtyping of *Trichophyton mentagrophytes* by random amplified polymorphic DNA. Mycoses 44:157–165

Kimura U, Yokoyama K, Hiruma M et al (2015) Tinea faciei caused by *Trichophyton mentagrophytes* (molecular type *Arthroderma benhamiae*) mimics impetigo: a case report and literature review of cases in Japan. Med Mycol J 56:E1–E5

Kopel E, Amitai Z, Sprecher H et al (2012) Tinea capitis outbreak in a paediatric refugee population, Tel Aviv, Israel. Mycoses 55:e36–e39

Kraemer A, Mueller R, Werckenthin C et al (2012) Dermatophytes in pet guinea pigs and rabbits. Vet Microbiol 157:208–213

Kraemer A, Hein J, Heusinger A et al (2013) Clinical signs, therapy and zoonotic risk of pet guinea pigs with dermatophytosis. Mycoses 56:168–172

Kröber A, Scherlach K, Hortschansky P et al (2016) HapX mediates iron homeostasis in the pathogenic dermatophyte *Arthroderma benhamiae* but is dispensable for virulence. PLoS One 11:e0150701

Kupsch C, Ohst T, Pankewitz F et al (2016) The agony of choice in dermatophyte diagnostics–performance of different molecular tests and culture in the detection of *T. rubrum* and *T. interdigitale*. Clin Microbiol Infect 22:735.e711–735.e717

Kupsch C, Berlin M, Gräser Y (2017) Dermophytes and guinea pigs: an underestimated danger? Hautarzt 68:827–830

Kurtdede A, Haydardedeoglu A, Alihosseini H et al (2014) Dermatophytosis caused by *Trichophyton mentagrophytes* var. *erinacei* in a dog: a case report. Vet Med (Praha) 59:349–351

L'Ollivier C, Ranque S (2017) MALDI-TOF-based dermatophyte identification. Mycopathologia 182:183–192

Le-Barzic C, Denaes C, Arné P et al (2017) *Trichophyton erinacei*, un incontournable compagnon des hérissons… Résultats d'une enquête épidémiologique dans un centre de soins en Île-de-France. J Mycol Med 27:e39

Leclerc M, Philippe H, Guého E (1994) Phylogeny of dermatophytes and dimorphic fungi based on large subunit ribosomal RNA sequence comparisons. J Med Vet Mycol 32:331–341

Lee WJ, Song CH, Lee S-J et al (2012) Decreasing prevalence of *Microsporum canis* infection in Korea: through analysis of 944 cases (1993–2009) and review of our previous data (1975–1992). Mycopathologia 173:235–239

Leibner-Ciszak J, Dobrowolska A, Krawczyk B et al (2010) Evaluation of a PCR melting profile method for intraspecies differentiation of *Trichophyton rubrum* and *Trichophyton interdigitale*. J Med Microbiol 59:185–192

Lewis DT, Foil CS, Hosgood G (1991) Epidemiology and clinical features of dermatophytosis in dogs and cats at Louisiana State University: 1981–1990. Vet Dermatol 2:53–58

Londero A, Ramos CD, Fischman O (1969) Four epizooties of *Trichophyton gallinae* infection on chickens in Brasil. Mycoses 12:31–38

Lund A, DeBoer DJ (2008) Immunoprophylaxis of dermatophytosis in animals. Mycopathologia 166:407–424

Lund A, Bratberg AM, Næss B et al (2014) Control of bovine ringworm by vaccination in Norway. Vet Immunol Immunopathol 158:37–45

Lyskova P, Hubka V, Petricakova A et al (2015) Equine dermatophytosis due to *Trichophyton bullosum*, a poorly known zoophilic dermatophyte masquerading as *T. verrucosum*. Mycopathologia 180:407–419

Mahmoud A-L (1995) Dermatophytes and other keratinophilic fungi causing ringworm of horses. Folia Microbiol 40:293–296

Maitte C, Leterrier M, Le Pape P et al (2013) Multilocus sequence typing of *Pneumocystis jirovecii* from clinical samples: how many and which loci should be used? J Clin Microbiol 51:2843–2849

Makimura K, Tamura Y, Mochizuki T et al (1999) Phylogenetic classification and species identification of dermatophyte strains based on DNA sequences of nuclear ribosomal internal transcribed spacer 1 regions. J Clin Microbiol 37:920–924

Mancianti F, Nardoni S, Cecchi S et al (2002) Dermatophytes isolated from symptomatic dogs and cats in Tuscany, Italy during a 15-year-period. Mycopathologia 156:13–18

Marais V, Olivier DL (1965) Isolation of *Trichophyton mentagrophytes* from a porcupine. Sabouraudia 4:49–52

Mariat F, Tapia G (1966) Denombrement des champignons keratinophiles d'une population de cynocephales (*Papio papio*). Ann Parasitol Hum Comp 41:627–634

Marples MJ (1967) Non-domestic animals in New Zealand and in Rarotonga as reservoir of the agents of ringworm. N Z Med J 66:299–302
Martin T, Marugán-Lobón J, Vullo R et al (2015) A Cretaceous eutriconodont and integument evolution in early mammals. Nature 526:380–384
Martinez DA, Oliver BG, Gräser Y et al (2012) Comparative genome analysis of *Trichophyton rubrum* and related dermatophytes reveals candidate genes involved in infection. MBio 3: e00259–e00212
Martinez-Rossi NM, Peres NT, Rossi A (2017) Pathogenesis of dermatophytosis: sensing the host tissue. Mycopathologia 182:215–227
Maurice MN, Kazeem HM, Kwanashie CN et al (2016) Equine dermatophytosis: a survey of its occurrence and species distribution among horses in Kaduna State, Nigeria. Scientifica 2016:8309253
McAller R (1980) An epizootic in laboratory guinea pigs due to *Trichophyton mentagrophytes*. Aust Vet J 56:234–236
McNeill J, Barrie FR, Buck WR et al (2012) International code of nomenclature for algae, fungi, and plants (Melbourne code) adopted by the eighteenth international botanical congress, Melbourne, Australia, July 2011. Regnum vegetabile 154. Koeltz Scientific Books, Königstein
Mehlig L, Garve C, Ritschel A et al (2014) Clinical evaluation of a novel commercial multiplex-based PCR diagnostic test for differential diagnosis of dermatomycoses. Mycoses 57:27–34
Menges RW, Georg LK (1956) An epizootic of ringworm among guinea pigs caused by *Trichophyton mentagrophytes*. J Am Vet Med Assoc 128:395–398
Mesquita JR, Vasconcelos-Nóbrega C, Oliveira J et al (2016) Epizootic and epidemic dermatophytose outbreaks caused by *Trichophyton mentagrophytes* from rabbits in Portugal, 2015. Mycoses 59:668–673
Metin B, Heitman J (2017) Sexual reproduction in dermatophytes. Mycopathologia 182:45–55
Metin A, Subaşi Ş, Bozkurt H et al (2002) Tinea capitis in Van, Turkey. Mycoses 45:492–495
Meyer W, Aanensen DM, Boekhout T et al (2009) Consensus multi-locus sequence typing scheme for *Cryptococcus neoformans* and *Cryptococcus gattii*. Med Mycol 47:561–570
Mignon B, Losson B (1997) Prevalence and characterization of *Microsporum canis* carriage in cats. J Med Vet Mycol 35:249–256
Mignon B, Tabart J, Baldo A et al (2008) Immunization and dermatophytes. Curr Opin Infect Dis 21:134–140
Milan R, Alois R, Josef C et al (2004) Recombinant protein and DNA vaccines derived from hsp60 *Trichophyton mentagrophytes* control the clinical course of trichophytosis in bovine species and guinea-pigs. Mycoses 47:407–417
Miller WH, Griffin CE, Campbell KL (2013) Fungal and algal skin diseases: dermatophytosis. In: Miller WH et al (eds) Muller and Kirk's small animal dermatology, 7th edn. Elsevier, St. Louis, pp 231–243
Ming PX, Ti YLX, Bulmer GS (2006) Outbreak of *Trichophyton verrucosum* in China transmitted from cows to humans. Mycopathologia 161:225–228
Mirhendi H, Makimura K, de Hoog GS et al (2015) Translation elongation factor 1-α gene as a potential taxonomic and identification marker in dermatophytes. Med Mycol 53:215–224
Mochizuki T, Watanabe S, Kawasaki M et al (2002) A Japanese case of tinea corporis caused by *Arthroderma benhamiae*. J Dermatol 29:221–225
Mochizuki T, Ishizaki H, Barton RC et al (2003) Restriction fragment length polymorphism analysis of ribosomal DNA intergenic regions is useful for differentiating strains of *Trichophyton mentagrophytes*. J Clin Microbiol 41:4583–4588
Mor H, Kashman Y, Winkelmann G et al (1992) Characterization of siderophores produced by different species of the dermatophytic fungi *Microsporum* and *Trichophyton*. Biometals 5:213–216
Moretti A, Boncio L, Pasquali P et al (1998) Epidemiological aspects of dermatophyte infections in horses and cattle. J Vet Med Ser B 45:205–208

Moretti A, Agnetti F, Mancianti F et al (2013) Dermatophytosis in animals: epidemiological, clinical and zoonotic aspects. G Ital Dermatol Venereol 148:563–572
Moriello KA, Coyner K, Paterson S, Mignon B (2017) Diagnosis and treatment of dermatophytosis in dogs and cats. Vet Dermatol 28:266–268
Moriello KA, Kunkle G, Deboer DJ (1994) Isolation of dermatophytes from the haircoats of stray cats from selected animal shelters in two different geographic regions in the United States. Vet Dermatol 5:57–62
Morris P, English MP (1969) *Trichophyton mentagrophytes* var. *erinacei* in British hedgehogs. Sabouraudia 7:122–128
Morris P, English MP (1973) Transmission and course of *Trichophyton erinacei* infections in British hedgehogs. Sabouraudia 11:42–47
Muller A, Guaguère E, Degorce-Rubiales F et al (2011) Dermatophytosis due to *Microsporum persicolor*: a retrospective study of 16 cases. Can Vet J 52:385–388
Murata M, Takahashi H, Takahashi S et al (2013) Isolation of *Microsporum gallinae* from a fighting cock (*Gallus gallus domesticus*) in Japan. Med Mycol 51:144–149
Nakamura Y, Kano R, Nakamura E et al (2002) Case report. First report on human ringworm caused by *Arthroderma benhamiae* in Japan transmitted from a rabbit. Mycoses 45:129–131
Naseri A, Fata A, Najafzadeh MJ et al (2013) Surveillance of dermatophytosis in northeast of Iran (Mashhad) and review of published studies. Mycopathologia 176:247–253
Neji S, Trabelsi H, Hadrich I et al (2016) Molecular characterization of strains of the *Trichophyton verrucosum* complex from Tunisia. Med Mycol 54:787–793
Nenoff P, Herrmann J, Gräser Y (2007) *Trichophyton mentagrophytes sive interdigitale?* A dermatophyte in the course of time. J Dtsch Dermatol Ges 5:198–202
Nenoff P, Uhrlaß S, Krüger C et al (2014) *Trichophyton* species von *Arthroderma benhamiae* – a new infectious agent in dermatology. J Dtsch Dermatol Ges 12:571–582
Nguyen L-T, Schmidt HA, von Haeseler A et al (2015) IQ-TREE: a fast and effective stochastic algorithm for estimating maximum-likelihood phylogenies. Mol Biol Evol 32:268–274
Nishio K, Kawasaki M, Ishizaki H (1992) Phylogeny of the genera *Trichophyton* using mitochondrial DNA analysis. Mycopathologia 117:127–132
Nweze E (2010) Dermatophytosis in Western Africa: a review. Pak J Biol Sci 13:649–656
Nweze EI (2011) Dermatophytoses in domesticated animals. Rev Inst Med Trop Sao Paulo 53:94–99
Nweze I, Eke I (2016) Dermatophytosis in northern Africa. Mycoses 59:137–144
Okoshi S, Takashio M, Hasegawa A (1966) Ringworm caused by *Trichophyton simii* in a captive Chimpanzee. Jpn J Med Mycol 7:204–207
Oudaina W, Biougnach H, Riane S et al (2011) Epidemiology of tinea capitis in outpatients at the Children's Hospital in Rabat (Morocco). J Mycol Med 21:1–5
Overgaauw P, van Avermaete K, Mertens C, Meijer M, Schoemaker N (2017) Prevalence and zoonotic risks of *Trichophyton mentagrophytes* and *Cheyletiella* spp. in guinea pigs and rabbits in Dutch pet shops. Vet Microbiol 205:106–109
Padhye A, Carmichael J (1968) Mating reactions of *Trichophyton simii* and *T. mentagrophytes* strains from poultry farm soil in India. Sabouraudia 6:238–240
Padhye A, Thirumalachar M (1967) Isolation of *Trichophyton simii* and *Cryptococcus neoformans* from soil in India. Hindustan Antibiot Bull 9:155–157
Pandey V, Makin L, Vanbreusegham R (1979) Prevalence and distribution of ringworm by *Trichophyton verrucosum* in sheep in the high atlas of Moracco. Ann Soc Belg Med Trop 54:385–389
Papegaay J (1925) Over pathogene huidschimmels in Amsterdam voorkomend bij den mensch. Ned Tijdschr Geneeskd 69:879–890
Papini R, Nardoni S, Fanelli A et al (2009) High infection rate of *Trichophyton verrucosum* in calves from Central Italy. Zoonoses Public Health 56:59–64
Pasquetti M, Gräser Y, Mialot M et al (2012) Use of microsatellite markers for typing of *Microsporum canis* isolates causing pseudomycetoma in cats. Mycoses 55(Suppl. 4):152–153

Pasquetti M, Peano A, Soglia D et al (2013) Development and validation of a microsatellite marker-based method for tracing infections by *Microsporum canis*. J Dermatol Sci 70:123–129
Pchelin IM, Zlatogursky VV, Rudneva MV et al (2016) Reconstruction of phylogenetic relationships in dermatomycete genus *Trichophyton* Malmsten 1848 based on ribosomal internal transcribed spacer region, partial 28S rRNA and beta-tubulin genes sequences. Mycoses 59:566–575
Peano A, Pasquetti M, Guillot J et al (2015) Use of eight microsatellite markers to reveal the genetic variability of *Microsporum canis* from different hosts and different geographic origins. In: Proceedings of the 19th congress of the international society for human and animal mycology, Sydney, Australia
Pereira DIB, Oliveira LSS, Bueno A et al (2006) Outbreak of *Trichophyton equinum* var. *equinum* in horses in the south of Brazil. Cienc Rural 36:1849–1853
Pier A, Zancanella P (1993) Immunization of horses against dermatophytosis caused by *Trichophyton equinum*. Equine Pract 15:23–27
Piérard-Franchimont C, Hermanns J-F, Collette C et al (2008) Hedgehog ringworm in humans and a dog. Acta Clin Belg 63:322–324
Pignon C, Mayer J (2011) Zoonoses of ferrets, hedgehogs, and sugar gliders. Vet Clin North Am Exot Anim Pract 14:533–549
Pinter L, Jurak Z, Ukalovic M et al (1999) Epidemiological and clinical features of dermatophytoses in dogs and cats in Croatia between 1990 and 1998. Vet Arh 69:261–270
Pombier E, Kim J (1975) An epizootic outbreak of ringworm in a guinea-pig colony caused by *Trichophyton mentagrophytes*. Lab Anim 9:215–221
Power S, Malone A (1987) An outbreak of ringworm in sheep in Ireland caused by *Trichophyton verrucosum*. Vet Rec 121:218–220
Preiser G (1991) An outbreak of tinea corporis among schoolgirls. Pediatrics 88:327–328
Proverbio D, Perego R, Spada E et al (2014) Survey of dermatophytes in stray cats with and without skin lesions in Northern Italy. Vet Med Int 2014:565470
Quaife R (1966) Human infection due to the hedgehog fungus, *Trichophyton mentagrophytes* var. *erinacei*. J Clin Pathol 19:177–178
Quaife R, Womar S (1982) *Microsporum canis* isolations from show cats. Vet Rec 110:333–334
Ranjbar R, Karami A, Farshad S et al (2014) Typing methods used in the molecular epidemiology of microbial pathogens: a how-to guide. New Microbiol 37:1–15
Rashid A, Scott E, Richardson M (1995) Early events in the invasion of the human nail plate by *Trichophyton mentagrophytes*. Br J Dermatol 133:932–940
Rezaei-Matehkolaei A, Makimura K, de Hoog S et al (2013) Molecular epidemiology of dermatophytosis in Tehran, Iran, a clinical and microbial survey. Med Mycol 51:203–207
Rezaei-Matehkolaei A, Mirhendi H, Makimura K et al (2014) Nucleotide sequence analysis of beta tubulin gene in a wide range of dermatophytes. Med Mycol 52:674–688
Rezaei-Matehkolaei A, Rafiei A, Makimura K et al (2016) Epidemiological aspects of dermatophytosis in Khuzestan, southwestern Iran, an update. Mycopathologia 181:547–553
Robert R, Pihet M (2008) Conventional methods for the diagnosis of dermatophytosis. Mycopathologia 166:295–306
Romano C, Valenti L, Barbara R (1997) Dermatophytes isolated from asymptomatic stray cats. Mycoses 40:471–472
Rosen T (2000) Hazardous hedgehogs. South Med J 93:936–938
Rouzaud C, Hay R, Chosidow O et al (2016) Severe dermatophytosis and acquired or innate immunodeficiency: a review. J Fungi 2:4
Rush-Munro F, Woodgyer A, Hayter M (1977) Ringworm in guinea-pigs. Mycoses 20:292–296
Sabou M, Denis J, Boulanger N et al (2018) Molecular identification of *Trichophyton benhamiae* in Strasbourg, France: a 9-year retrospective study. Med Mycol 56, https://doi.org/10.1093/mmy/myx100
Santana EM, Jantz HE, Best TL (2010) *Atelerix albiventris* (Erinaceomorpha: Erinaceidae). Mamm Species 42:99–110

Sargison N, Thomson J, Scott P et al (2002) Ringworm caused by *Trichophyton verrucosum*-an emerging problem in sheep flocks. Vet Rec 150:755–756
Schauder S, Kirsch-Nietzki M, Wegener S et al (2007) Von Igeln auf Menschen: Zoophile Dermatomykose durch *Trichophyton erinacei* bei 8 Patienten. Hautarzt 58:62–67
Seebacher C, Bouchara J-P, Mignon B (2008) Updates on the epidemiology of dermatophyte infections. Mycopathologia 166:335–352
Seker E, Dogan N (2011) Isolation of dermatophytes from dogs and cats with suspected dermatophytosis in Western Turkey. Prev Vet Med 98:46–51
Shah P, Krajden S, Kane J et al (1988) Tinea corporis caused by *Microsporum canis*: report of a nosocomial outbreak. Eur J Epidemiol 4:33–38
Sharma R, Gräser Y (2011) Microsporum. In: Liu D (ed) Molecular detection of human fungal pathogens. CRC Press, Boca Raton, pp 285–298
Sharma R, De Hoog S, Presber W et al (2007) A virulent genotype of *Microsporum canis* is responsible for the majority of human infections. J Med Microbiol 56:1377–1385
Sharma R, Presber W, Rajak RC et al (2008) Molecular detection of *Microsporum persicolor* in soil suggesting widespread dispersal in central India. Med Mycol 46:67–73
Shi Y, Niu Q, Yu X et al (2016) Assessment of the function of SUB6 in the pathogenic dermatophyte *Trichophyton mentagrophytes*. Med Mycol 54:59–71
Sieklucki U, Oh SH, Hoyer LL (2014) Frequent isolation of *Arthroderma benhamiae* from dogs with dermatophytosis. Vet Dermatol 25:39–41
Silver S, Vinh DC, Embil JM (2008) The man who got too close to his cows. Diagn Microbiol Infect Dis 60:419–420
Simpanya M, Baxter M (1996) Isolation of fungi from the pelage of cats and dogs using the hairbrush technique. Mycopathologia 134:129–133
Sitterle E, Frealle E, Foulet F et al (2012) *Trichophyton bullosum*: a new zoonotic dermatophyte species. Med Mycol 50:305–309
Skerlev M, Miklić P (2010) The changing face of *Microsporum* spp infections. Clin Dermatol 28:146–150
Skořepová M, Hubka V, Polášková S et al (2014) Our first experiences with Infections caused by *Arthroderma benhamiae* (*Trichophyton* sp.) Čes-Slov Dermatol 89:192–198
Smith J, Marples MJ (1964) *Trichophyton mentagrophytes* var. *erinacei*. Sabouraudia 3:1–10
Snider R, Landers S, Levy ML (1993) The ringworm riddle: an outbreak of *Microsporum canis* in the nursery. Pediatr Infect Dis J 12:145–148
Sparkes A, Gruffydd-Jones T, Shaw S et al (1993) Epidemiological and diagnostic features of canine and feline dermatophytosis in the United Kingdom from 1956 to 1991. Vet Rec 133:57–61
Sparkes A, Werrett G, Stokes C et al (1994) *Microsporum canis*: inapparent carriage by cats and the viability of arthrospores. J Small Anim Pract 35:397–401
Spesso M, Nuncira C, Burstein V et al (2013) Microsatellite-primed PCR and random primer amplification polymorphic DNA for the identification and epidemiology of dermatophytes. Eur J Clin Microbiol Infect Dis 32:1009–1015
Stockdale PM (1964) The *Microsporum gypseum* complex (*Nannizzia incurvata* Stockd., *N. gypsea* (Nann.) comb. nov., *N. fulva* sp. nov.) Sabouraudia 3:114–126
Strachan A, Blank F (1963) On 1117 *Microsporum canis* infections in Montreal (1954–1961). Dermatology 126:271–290
Šubelj M, Marinko JS, Učakar V (2014) An outbreak of *Microsporum canis* in two elementary schools in a rural area around the capital city of Slovenia, 2012. Epidemiol Infect 142:2662–2666
Sugiyama M, Summerbell R, Mikawa T (2002) Molecular phylogeny of onygenalean fungi based on small subunit (SSU) and large subunit (LSU) ribosomal DNA sequences. Stud Mycol 47:5–23
Summerbell R (2002) What is the evolutionary and taxonomic status of asexual lineages in the dermatophytes? Stud Mycol 47:97–101

Summerbell R, Haugland R, Li A et al (1999) rRNA gene internal transcribed spacer 1 and 2 sequences of asexual, anthropophilic dermatophytes related to *Trichophyton rubrum*. J Clin Microbiol 37:4005–4011

Summerbell RC, Moore MK, Starink-Willemse M et al (2007) ITS barcodes for *Trichophyton tonsurans* and *T. equinum*. Med Mycol 45:193–200

Sun PL, Hsieh HM, Ju YM et al (2010) Molecular characterization of dermatophytes of the *Trichophyton mentagrophytes* complex found in Taiwan with emphasis on their correlation with clinical observations. Br J Dermatol 163:1312–1318

Symoens F, Jousson O, Planard C et al (2011) Molecular analysis and mating behaviour of the *Trichophyton mentagrophytes* species complex. Int J Med Microbiol 301:260–266

Symoens F, Jousson O, Packeu A et al (2013) The dermatophyte species *Arthroderma benhamiae*: intraspecies variability and mating behaviour. J Med Microbiol 62:377–385

Takahashi Y, Haritani K, Sano A et al (2002) An isolate of *Arthroderma benhamiae* with *Trichophyton mentagrophytes* var. *erinacei* anamorph isolated from a four-toed hedgehog (*Atelerix albiventris*) in Japan. Jpn J Med Mycol 43:249–255

Takahashi Y, Sano A, Takizawa K et al (2003) The epidemiology and mating behavior of *Arthroderma benhamiae* var. *erinacei* in household four-toed hedgehogs (*Atelerix albiventris*) in Japan. Jpn J Med Mycol 44:31–38

Takahashi H, Takahashi-Kyuhachi H, Takahashi Y et al (2008) An intrafamilial transmission of *Arthroderma benhamiae* in Canadian porcupines (*Erethizon dorsatum*) in a Japanese zoo. Med Mycol 46:465–473

Takashio M (1974) Observations on African and European strains of *Arthroderma benhamiae*. Int J Dermatol 13:94–101

Takashio M (1977) The *Trichophyton mentagrophytes* complex. In: Iwata K (ed) Recent advances in medical and veterinary mycology. University of Tokyo Press, Tokyo, pp 271–276

Takeda K, Nishibu A, Anzawa K et al (2012) Molecular epidemiology of a major subgroup of *Arthroderma benhamiae* isolated in Japan by restriction fragment length polymorphism analysis of the non-transcribed spacer region of ribosomal RNA gene. Jpn J Infect Dis 65:233–239

Torres-Rodriguez J, Dronda M, Rossell J et al (1992) Incidence of dermatophytoses in rabbit farms in Catalonia, Spain, and its repercussion on human health. Eur J Epidemiol 8:326–329

Uhrlaß S, Krüger C, Nenoff P (2015) *Microsporum canis*: Aktuelle Daten zur Prävalenz des zoophilen Dermatophyten im mitteldeutschen Raum. Hautarzt 66:855–862

Uhrlaß S, Schroedl W, Mehlhorn C et al (2018) Molecular epidemiology of *Trichophyton quinckeanum* – a zoophilic dermatophyte on the rise. J Dtsch Dermatol Ges 16:21–32

Vangeel I, Pasmans F, Vanrobaeys M et al (2000) Prevalence of dermatophytes in asymptomatic guinea pigs and rabbits. Vet Rec 146:440–441

Van Rooij P, Detandt M, Nolard N (2016) *Trichophyton mentagrophytes* of rabbit origin causing family incidence of kerion: an environmental study. Mycoses 49:426–430

Veraldi S, Genovese G, Peano A (2018) Tinea corporis caused by *Trichophyton equinum* in a rider and review of the literature Infection 46:135–137

Veraldi S, Guanziroli E, Schianchi R (2012) Epidemic of tinea corporis due to *Trichophyton mentagrophytes* of rabbit origin. Pediatr Dermatol 29:392–393

Visset M (1973) *Arthroderma simii* dans les sables de La Baule, premier isolement en Europe. Bull Soc Mycol Fr 11:151–152

Wakasa A, Anzawa K, Kawasaki M et al (2010) Molecular typing of *Trichophyton mentagrophytes* var. *interdigitale* isolated in a university hospital in Japan based on the non-transcribed spacer region of the ribosomal RNA gene. J Dermatol 37:431–440

Weiß R, Böhm KH, Mumme J et al (1979) 13 Jahre Veterinärmedizinische Mykologische Routinediagnostik. Dermatophytennachweise in den Jahren 1965 Bis 1977. Sabouraudia 17:345–353

Weiss R, Földy I, Christoph H (1984) Trichophyton-verrucosum-Infektion bei Pferden. Tierarztl Prax 12:49–53

Weitzman I, Summerbell RC (1995) The dermatophytes. Clin Microbiol Rev 8:240–259

Weitzman I, McGinnis M, Padhye A et al (1986) The genus *Arthroderma* and its later synonym *Nannizzia*. Mycotaxon 25:505–518

Woodgyer A (2004) The curious adventures of *Trichophyton equinum* in the realm of molecular biology: a modern fairy tale. Med Mycol 42:397–403

Wu Y, Yang J, Yang F et al (2009) Recent dermatophyte divergence revealed by comparative and phylogenetic analysis of mitochondrial genomes. BMC Genomics 10:238

Yamaguchi S, Sano A, Hiruma M et al (2014) Isolation of dermatophytes and related species from domestic dowl (*Gallus gallus domesticus*). Mycopathologia 178:135–143

Yin W-B, Chooi YH, Smith AR et al (2013) Discovery of cryptic polyketide metabolites from dermatophytes using heterologous expression in *Aspergillus nidulans*. ACS Synth Biol 2:629–634

Youngchim S, Pornsuwan S, Nosanchuk JD et al (2011) Melanogenesis in dermatophyte species in vitro and during infection. Microbiology 157:2348–2356

Yu J, Wan Z, Chen W et al (2004) Molecular typing study of the *Microsporum canis* strains isolated from an outbreak of tinea capitis in school. Mycopathologia 157:37–41

Zhan P, Li D, Wang C et al (2015) Epidemiological changes in tinea capitis over the sixty years of economic growth in China. Med Mycol 53:691–698

Zhang H, Ran Y, Liu Y et al (2009) *Arthroderma vanbreuseghemii* infection in three family members with kerion and tinea corporis. Med Mycol 47:539–544

Zimmerman K, Feldman B, Robertson J et al (2003) Dermal mass aspirate from a Persian cat. Vet Clin Pathol 32:213–217