Medical Mycology, 2018, 56, S165–S187
doi: 10.1093/mmy/myx104
Review Article

Review Article

Fungal infections in animals: a patchwork of different situations

Seyedmojtaba Seyedmousavi[1,*], Sandra de M. G. Bosco[2], Sybren de Hoog[3], Frank Ebel[4], Daniel Elad[5], Renata R. Gomes[6], Ilse D. Jacobsen[7], Henrik E. Jensen[8], An Martel[9], Bernard Mignon[10], Frank Pasmans[9], Elena Piecková[11], Anderson Messias Rodrigues[12], Karuna Singh[13], Vania A. Vicente[6], Gudrun Wibbelt[14], Nathan P. Wiederhold[15] and Jacques Guillot[16,*]

[1]Molecular Microbiology Section, Laboratory of Clinical Immunology and Microbiology (LCIM), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), Bethesda, MD, USA, [2]Department of Microbiology and Immunology, Institute of Biosciences-UNESP Univ Estadual Paulista Botucatu, São Paulo, Brazil, [3]Westerdijk Fungal Biodiversity Institute, Utrecht, and Center of Expertise in Mycology of Radboudumc/CWZ, Nijmegen, The Netherlands, [4]Institut für Infektionsmedizin und Zoonosen, Munich, Germany, [5]Department of Clinical Bacteriology and Mycology, Kimron Veterinary Institute, Veterinary Services, Ministry of Agriculture, Beit Dagan, Israel, [6]Microbiology, Parasitology and Pathology Graduate Programme, Curitiba Department of Basic Pathology, Federal University of Paraná, Curitiba, Brazil, [7]Research Group Microbial Immunology, Hans Knöll Institute, Jena, Germany, [8]Department of Veterinary and Animal Science, University of Copenhagen, Denmark, [9]Department of Pathology, Bacteriology and Avian Diseases. Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium, [10]Department of Infectious and Parasitic Diseases, Faculty of Veterinary Medicine, FARAH (Fundamental and Applied Research for Animals & Health), University of Liège, Liège, Belgium, [11]Faculty of Medicine, Slovak Medical University, Faculty of Chemical and Food Technology, Slovak University of Technology, Bratislava, Slovakia, [12]Department of Microbiology, Immunology and Parasitology, Federal University of São Paulo, São Paulo, Brazil, [13]Department of Zoology, Mahila Mahavidyalaya, Banaras Hindu University, Varanasi, India, [14]Leibniz Institute for Zoo and Wildlife Research, Berlin, Germany, [15]Fungus Testing Laboratory, Department of Pathology and Laboratory Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas, USA and [16]Department of Parasitology, Mycology and Dermatology, EA Dynamyc UPEC, EnvA, Ecole nationale vétérinaire d'Alfort, Maisons-Alfort, France

*To whom correspondence should be addressed. Seyedmojtaba Seyedmousavi, MSc, DVM, PhD. Molecular Microbiology Section, Laboratory of Clinical Microbiology and Immunology (LCMI), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), Bethesda, MD, USA. Tel: 31623417380. E-mail: Seyedmousavi@nih.gov. Jacques Guillot, DVM, PhD. Department of Parasitology, Mycology and Dermatology, EA Dynamyc UPEC, EnvA, Ecole nationale vétérinaire d'Alfort, Maisons-Alfort, France. Tel: 33143967157; E-mail: jacques.guillot@vet-alfort.fr

Received 19 June 2017; Revised 9 August 2017; Accepted 27 September 2017; Editorial Decision 31 August 2017

Abstract

The importance of fungal infections in both human and animals has increased over the last decades. This article represents an overview of the different categories of fungal infections that can be encountered in animals originating from environmental sources without transmission to humans. In addition, the endemic infections with indirect transmission from the environment, the zoophilic fungal pathogens with near-direct transmission, the zoonotic fungi that can be directly transmitted from animals to humans, mycotoxicoses and antifungal resistance in animals will also be discussed. Opportunistic mycoses are responsible for a wide range of diseases from localized infections to fatal disseminated diseases, such as aspergillosis, mucormycosis, candidiasis, cryptococcosis and infections caused by melanized fungi. The amphibian fungal disease chytridiomycosis and the Bat White-nose syndrome are due to obligatory fungal pathogens. Zoonotic agents are naturally transmitted from vertebrate animals to humans and vice versa. The list of zoonotic fungal agents is limited but some species, like *Microsporum canis* and *Sporothrix brasiliensis* from cats, have a strong public health impact. Mycotoxins are defined as the chemicals of fungal origin being toxic for warm-blooded vertebrates. Intoxications by aflatoxins and ochratoxins represent a threat for both human and animal health. Resistance to antifungals can occur in different animal species that receive these drugs, although the true epidemiology of resistance in animals is unknown, and options to treat infections caused by resistant infections are limited.

Key words: Opportunistic fungi, pathogenic fungi, zoophilic fungi, zoonoses, mycotoxicoses, antifungal resistance, mycoses in animals, veterinary mycology.

Introduction

The ISHAM Veterinary Mycology Working Group (ISHAM-VMWG) has been established in 2010 by a group of experts to support all scientific aspects that deals with mycology and veterinary sciences, including: diagnosis and identification of fungal pathogens of veterinary importance, pathophysiology and immunology of fungal diseases in animals, epidemiology, prevention, control and eradication of animal mycoses, mycotoxins and mycotoxicosis in animals, standardization of animal model, and development of alternatives. The first general meeting of ISHAM-VMWG was held in June 2012 during the 18th congress of ISHAM in Berlin, Germany. There was a great opportunity to share expertise, recent activities, and also discuss future plans among members. Attendees were scientists and veterinarians from all over the world. The membership has been open to any with a scientific interest in fungi affecting animal species, understanding a veterinary disease problem, development of animal models of human fungal disease. Since then, ISHAM VMWG was highly involved in international educational activities. The international veterinary mycology course is a 5 days' educational event under the umbrella of ISHAM. The course is organized every two to three years and the next one will be hold in June 2018 in Amsterdam, The Netherlands. ISHAM-VMWG published several scientific articles in the peer-reviewed journals. Attempts are also under way to complete a textbook on emerging and epidemic fungal infection by the end of 2017 and the Atlas of Veterinary Pathogenic Fungi by 2020.

Fungi are relatively uncommon causes of disease in healthy and immunocompetent humans and nonhuman vertebrates, even though hosts are constantly exposed to infectious propagules.[1,2] However, an increasing number of recalcitrant fungal diseases in animals have occurred over the last two decades, originating from opportunistic and pathogenic fungi.[2]

Opportunistic fungi have a preferred habitat independent from the living host and cause infection after accidentally penetration of intact skin barriers, or when immunologic defects or other debilitating conditions exist in the host.[3] In contrast, pathogens are defined as having advantage of the vertebrate host; in obligatory pathogens the host is indispensable to complete their life-cycle and for nutrient acquisition, growth, niche establishment, and reproduction.[4] Zoonoses are infections that can be naturally transmitted between vertebrate animals and humans.[5] From a global prospective, zoonotic infections have been recognized for many centuries, and account for the majority of emerging and reemerging infectious diseases, worldwide.[6]

The present article only highlights a selected list of infections caused by environmental fungi that can be encountered in animals, as well as zoonotic fungi that can be transmitted from animals to humans. Another area of veterinary significance is the presence of mycotoxins in animal feed, and the eventual risks of mycotoxicoses. In addition, the development and epidemiology of antifungal resistance in animals will also be discussed.

Opportunistic fungal infections with no transmission

Aspergillosis

Aspergillosis in animals covers a wide range of diseases from localized conditions to fatal disseminated infections, as well as allergic reactions caused by fungi belonging to the genus *Aspergillus*.[7,8] The numerous members of this genus are saprobic filamentous fungi commonly found in soil, decaying vegetation, and on seeds and grains, with an occasional potential to infect living animal hosts including insects, birds, and mammals.[9,10]

Although there are more than 300 known species in the genus, animal aspergilloses are mainly caused by *A. fumigatus*, and only rarely by a few other species.[9,10] Modern classification of *Aspergillus* species is by polyphasic taxonomy and has led to the distinction of 22 distinct sections, of which *Aspergillus, Fumigati, Circumdati, Terrei, Nidulantes, Ornati, Warcupi*, *Candidi*, *Restricti, Usti, Flavipedes,* and *Versicolores* contain clinically relevant species.[11]

In animals, aspergillosis is primarily a respiratory infection that may become generalized; however, tissue predilection is variable between species. Similar to infections in humans, animals exhibiting inability to produce a normal immune response are at higher risk of infection. Aspergillosis may also occur in healthy animals under environmental stress and other immune-compromising conditions.[12,13]

In invertebrates, *A. sydowii* causes a recently recognized, large epizootic affecting sea fan corals (*Gorgonia* species),[14] first documented in 1995 near Saba the Bahamas and subsequently spreading throughout the Caribbean basin, including in the Florida Keys.[15,16] *Aspergillus* species are also known to infect honeybee (*Apis mellifera*) brood, causing stonebrood disease over all larval stages.[17,18] *Aspergillus* species with the ability to produce mycotoxins such as *A. flavus, A. fumigatus,* and *A. niger* have been suggested to be the primary cause of this disease.[19] In reptiles, *Aspergillus* species such as *A. fumigatus, A. niger* and *A. terreus* have been isolated from both cutaneous and disseminated infections,[20] mainly promoted by immune-compromising conditions, such as husbandry deficiencies or inappropriate temperatures, humidity, or poor enclosure hygiene.[21] Avian aspergillosis is predominantly a disease of the respiratory tract, but all organs can be involved, leading to a variety of acute or chronic manifestations.[22,23] All avian species should probably be considered as susceptible. *Aspergillus fumigatus* has been involved in significant common-source sapronotic die-offs of domestic and free-ranging wild birds.[24] Economic significance of aspergillosis is most readily apparent in poultry production, where disease occurs late in the growing cycle.[25]

Sinonasal, bronchopulmonary, and disseminated infections are major forms of aspergillosis in dogs and cats.[26–28] In dogs, a breed or gender predisposition can be recognized.[29] Aspergillosis also has been also reported in cats stressed by underlying disease (such as feline Immunodeficiency Virus and Feline Leukemia Virus) or immunosuppression.[30–32] *Aspergillus felis* has been the most frequently reported etiologic agent of sinoorbital aspergillosis in cats, followed by cryptic species of the section *Fumigati*, including *A. udagawae* and *A. viridinutans*.[32,33] In ruminants, *Aspergillus* species, particularly *A. fumigatus,* are known worldwide to cause mycotic pneumonia, gastroenteritis, mastitis, placentitis, and abortions.[34] *Aspergillus* species also cause guttural pouch infections, keratomycosis and pneumonia in horses.[35–39] In marine mammals, aspergillosis can be primary or secondary to any chronic infection, physiologic stress, or immunosuppression.[40] Aspergillosis may also occur in various non-human primate species, particularly in immunocompromised hosts.[41]

Mucormycosis

Mucormycosis is a saprobic opportunistic infection caused by fungi in the order *Mucorales* in the former class Zygomycetes.[42] Within the order, the most often identified species belong to the genera *Rhizopus*, *Mucor*, *Rhizomucor*, *Lichtheimia* (formerly *Absidia*), *Apophysomyces*, *Cunninghamella*, and *Saksenaea*. The natural habitat for the *Mucorales* is soil, and they are typically isolated from decaying organic material. The fungi are often also found in indoor and outdoor air, in food stuffs, and in dust.[42] Mucormycosis in animals (both domesticized and wild, and in mammalian and non-mammalian) and humans are similar with respect to epidemiology, portal of entry, localization, and formation of lesions.[43–54]

The opportunistic pathogenic members of the *Mucorales* are ubiquitous within the domesticated environment of animals and in indoor habitats, but infection almost invariably is established only when the normal balance between animal and the agent is disturbed.[43] In line with other opportunistic fungal infections in animals, for example, candidiasis and aspergillosis, predisposing factors are not related to the animal species but to the infected animal *per se.*[43–54] General predisposing factors favoring mucormycosis in humans also apply for animals, that is, infections are seen in hosts that are immunocompromised or otherwise debilitated due to metabolic disorders. However, overwhelming exposure to mucoralean fungi or disturbance of the bacterial microbiota in the forestomach may cause infection in otherwise healthy animals.[55] Two examples in cattle are of interest, that is, mucormycotic ruminitis and lymphadenitis. The rumen of ruminants is anaerobic, but the ruminal wall represents an aerobic-anaerobic interface, which therefore is colonized by microaerobic bacteria.[43] Antibiotic treatment will destroy this normal micro-aerobic bacterial flora, facilitating infection by *Mucorales*. Mucormycotic ruminitis is therefore a well-known sequel to intensive antibiotic treatment of cattle.[52] Heavy exposure to *Mucorales* fungi through contaminated food stuffs is a cause of infection of intestinal lymph nodes. Notably, lesions of mucormycotic lymphadenitis are macroscopically indistinguishable from bovine tuberculosis.[56]

Ruminant mucormycosis may also be respiratory, occur in other parts of the gastrointestinal tract, or systemically.[51,53] Due to the frequently observed angioinvasion of *Mucorales*, hematogenous spread to multiple organs is often reported. In pregnant cows, the fungus frequently spreads to the placenta, although *Aspergillus fumigatus* is the predominant course of bovine mycotic placentitis and abortion.[57]

In horses, mucormycotic lesions have been reported in different organs, especially in the respiratory system and gastrointestinal tract, and may lead to systemic spread to multiple organs.[48] Moreover, cases of localized skin infection have also been described.[47] Mucormycosis in pigs is uncommon, again especially affecting lungs, gastrointestinal tract and lymph nodes.[58] In dogs and cats some cases of mucormycosis have been described as a cause of, for example, enteritis or systemic spread.[59] Few, scattered reports are available on the occurrence of mucormycosis in different kinds of avian species. Especially the respiratory organs and gastrointestinal tract are often involved.[60–63] Cases in wild living animals have been described, for example, in dolphin, bison, and seal.[64,65]

Candidiasis

The genus *Candida* is currently being reclassified along phylogenetic lines. In its classical sense, it comprises over 200 species of which 15 have been isolated from infections in humans and animals.[66,67] Most prominent as causes of disease are *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. tropicalis,* and *C. krusei*.[68–73] These species are also frequently found as part of the microbiota of healthy humans and animals[74–78] and are thus considered as commensal and facultatively pathogenic. While *C. albicans* and *C. glabrata* appear to occur only in association with warm-blooded hosts, other infectious *Candida* species are also known from the environment. Infections are usually caused by strains that commensally precolonized the host rather than by vertical or longitudinal transfer,[79,80] and the zoonotic potential can thus be considered to be low. Although *C. albicans* is the most virulent *Candida* species, others might be more prominent in specific animals depending on the site of infection (Table 1).

Candidiasis can be superficial, affecting the skin, mucosal membranes of the gastrointestinal and urogenital tract. Dissemination of the fungus can lead to candidemia or localized infection of internal organs. In contrast to humans, epidemiological data and systematic analysis of risk factors are lacking for veterinary candidiasis. Animal candidiasis is mentioned in veterinary textbooks as occasionally affecting domestic animals.[81–83] Given the fact that the general factors contributing to candidiasis are not host-specific, it seems likely that the general risk factors described for human patients are also applicable to veterinary medicine.[84,85] Cutaneous candidiasis is rather frequent in dogs, usually in association with atopy, other immune diseases, immunosuppressive disorders, or medical treatment leading to immunosuppression[86–94] and clinically resembles *Malassezia* infections. It can also occur in birds, especially in chicken, but rarely in other species. Mucosal oral and gastrointestinal candidiasis occurs most commonly in birds, where it is the prevalent form of candidiasis. It is referred to as thrush or sour crop, characterized by white-grayish lesions, often accompanied by hyperkeratosis.[95–97] Similar disorders have been described in horses, cattle, dogs, cats, and pigs, usually associated with young age, antibiotic use, or immunosuppression.[81,98—100] Lesions in mammalian hosts are often invasive and ulcerative. Systemic *Candida* infection is usually rare in dogs and cats. However, surgery and trauma, for example, by foreign bodies, can lead to introduction of *Candida* into deeper tissue or the peritoneal cavity, leading to granuloma formation or peritonitis, which has been described in cats and dogs.[101–105] Candidiasis of the urinary tract likewise occurs in dogs and cats, manifesting as candiduria and cystitis, usually in association with antibiotic treatment due to previous bacterial infections, or other underlying diabetes mellitus.[106–113] Environmental *Candida* species, such as *C. parapsilosis, C. tropicalis,* and *C. guilliermondii*, can cause abortion in horses and cattle,[114–118] and *Candida* mastitis is a well-described sequel of intramammary antibiosis in dairy cattle.[119–135] Disseminated candidiasis has been reported in dogs, cats, sheep, calves, horses, ferrets, and alpacas (Table 1). The symptoms of this disease are often unspecific, and may lead to myocarditis, endocarditis or endophthalmitis. Of note, eye infections in horses have rather frequently been reported in the absence of disseminated disease.

Although candidiasis is a rare infection in animals, it is an important differential diagnosis to bacterial infections, and candidiasis can also occur secondary to bacterial infections. It should be considered as a possible option especially when hosts do not respond to antibiotic treatment.

Table 1. Selected case reports of candidiasis in animals. *Candida* spp.: species not determined or several species.

Host species		*Candida* species	Types of infection	Predisposing factors
Birds		*Candida* spp.	Oral and gastrointestinal candidiasis (pigeons, parrots, Galliformes, Passeriformes, raptors)	None; concomitant infections by other pathogens; immunosuppression
		C. albicans		
		C. krusei		
		C. albicans	Pulmonary candidiasis (sun conure, raptors)	–
		C. albicans	Cutaneous candidiasis (Passeriformes, chicken)	–
		C. albicans	Myocarditis (canary)	–
Dogs		*C. guilliermondii*	Joint infection	Leishmaniasis and intra-articular corticosteroid injections
		C albicans, C glabrata	Peritonitis	Intestinal surgery, corticosteroids
		C albicans, *C. guilliermondii, C. parapsilosis*, *C. tropicalis*	Dermatitis, incl. otitis externa	Atopia and other autoimmune diseases, immunosuppressive disorders and drugs, other infections
		C albicans, *C. parapsilosis, C. tropicalis*	Urinary tract	Diabetes mellitus, lower urinary tract diseases incl. bacterial infections and antibiotic treatment, neoplasia
			(candiduria, cystitis)	
		C. albicans, Candida spp.	Disseminated candidiasis (incl. endophtalmitis, pericarditis, spondylitis)	Intestinal surgery, immunosuppression, neoplasia, catheterization
		C. albicans	keratitis	–
		Candida spp.	pneumonia	Concurrent bacterial pneumonia and aspergillosis
Cats		*C. parapsilosis*	Granulomatous rhinitis	Corticosteroid treatment
		C. albicans	Urinary tract	Diabetes mellitus, lower urinary tract diseases incl. bacterial infections an antibiotic treatment, neoplasia
		Candida spp.	(candiduria, cystitis)	
		C. albicans	Intestinal granuloma	Suspected trauma by foreign body
		Candida spp.	Disseminated candidiasis (incl. ocular involvement)	Diabetes mellitus, immunosuppression
		C. albicans	Pyothorax	–
Ruminants	**Cattle**	*C. albicans, C. catenulata, C. guilliermondii, C. kefyr, C krusei, C. maltosa, C. rugosa* and others	Mastitis	Intramammary antibiotic treatment, environmental contamination, milking hygiene
		C. parapsilosis, C. tropicalis	Abortion	–
		Candida spp.	Otitis externa	–
		C. albicans	Gastrointestinal infection	Antibiotics, concurrent gastrointestinal mucormycosis
		C. glabrata		
		C. albicans	Disseminated candidiasis	Antibiotics, young age
		Candida spp.		
		C. krusei	Bronchopneumonia	
	Alpacas, lamas, guanaco	*C. albicans*	Disseminated candidiasis	Immunosuppression suspected
		Candida spp.		
	Camel	*C. albicans*	Dermatitis	
	Sheep	*Candida* spp.	Disseminated candidiasis	
Horses		*Candida* spp.	Keratitis	
		Candida spp.	Arthritis	
		C. parapsilosis	Endocarditis	
		C. albicans	Systemic candidiasis	Birth hypoxia, sepsis
		Candida spp.	Oral candidiasis	Young age and immunodeficiency
		Candida spp.	Gastroesophageal candidiasis	Young age
		C. guilliermondii	Abortion	
		C. pseudotropicalis		
Pigs		*C. albicans*	Mucocutaneous candidiasis	Possibly immunosuppression due to viral infection (porcine circovirus 2)

Cryptococcosis

The genus *Cryptococcus* (teleomorph *Filobasidiella*) comprises basidiomycetous yeast species, most of which are environmental saprophytes that do not cause infections in human or animal.[136] The pathogenic agents of cryptococcosis are classified into two species, *C. neoformans* and *C. gattii*.[137] The species *C. neoformans* comprises two varieties, *C. neoformans* var. *grubii* and *C. neoformans* var. *neoformans*. The species *C. neoformans* consists of the VNI-VNIV and VNB molecular genotypes, comprising var. *grubii* (serotype A or VNI, VNII, and VNB strains), var. *neoformans* (serotype D or VN IV strains), and serotype AD strains (VNIII), which represents hybrids of the two varieties.[138] The species *C. gattii* is subdivided into two serotypes (B and C), and four molecular types VGI, VGII, VGIII, and VGIV varying in virulence, geographic distribution, and possibly susceptibility to antimycotic drugs.[136,139] Diseases caused by other *Cryptococcus* species, such as *Cryptococcus laurentii* and *Cryptococcus albidus*, have been reported infrequently and generally in immunocompromised hosts.[140]

The two species differ ecologically: *C. neoformans* was isolated primarily from bird droppings,[141] whereas *C. gattii* was associated with trees, primarily *Eucalyptus* species, initially in Australia,[142,143] where the importance of koalas feeding on these trees in perpetuating the yeast's persistence in the environment was suggested.[144] Subsequently, infections with *C. gatti* were reported in other regions as well.[145] In addition, differences are found in the population at risk: while *C. neoformans* infects primarily immune-compromised patients, *C. gattii* may affect people with intact immune systems.[146] A large outbreak of human and animal *C. gattii* infections that started in 2000 in Vancouver island have been seen during the following years. Molecular analysis of the isolates showed, however, that more than one type was involved.[147] Of note, identical genotypes were isolated from humans and animals including marine mammals and in the affected environment.[147]

Cryptococcus neoformans infections have been reported in a large variety of animals from lower invertebrates such as soil dwelling amoebae, nematodes, cockroaches, and mites, to higher mammals.[145] Cats are the most frequently infected animals with the involvement of the upper and or lower respiratory tract, subcutaneous granulomata, and disseminated infections. Dogs may present with similar symptoms but central nervous system (CNS) involvement is more common.[148] Moreover, cryptococcosis has been reported causing mastitis in dairy animals[149] and respiratory infections in horses.[150]

Cryptococcus gattii was isolated from different animal species, including cats, dogs, marine mammals, ferrets, and llamas in the regions affected by the outbreak that started in Vancouver Island and subsequently spread to the Pacific Northwest regions of the United States.[151] The upper respiratory tract infections and subcutaneous masses were the most frequent primary lesions, but in several cases the CNS, lymphatic tissue, lungs, oral cavity, and eyes were affected.[152] Among pets, a higher number of CNS involvement in dogs was found, whereas subcutaneous masses were shown more frequently in cats.[153] CNS involvement was associated with higher mortality rates. In addition, gastrointestinal infections in dogs have been reported.[146] Moreover, a disseminated canine infection with *C. neoformans* var. *grubii* was reported.[153] Surveys have shown that incidence of cryptococcosis does not increase in environment contaminated with bird dropping, including immunocompromised patients.[154,155] Nevertheless, molecular analysis indicated in some cases that human and environmental isolates were identical.[156,157]

About eight decades ago, Sangiorgi described the presence of *Cryptococcus* in the large mononuclear cells of liver and spleen of a rat (*Rattus norvegicus*).[158] Further, during their investigation about histoplasmosis, Emmons et al., in 1947 isolated *Cryptococcus* from mice and rats.[159] After a long gap, naturally acquired cryptococcosis was again reported, but this time in the greater bandicoot rat (*Bandicota indica*).[160] Pathological lesions were observed only in liver and lungs but other organs like kidneys, spleen, and brain were found positive for *Cryptococcus neoformans* var. *grubii*. Singh et al. also isolated *C. n. grubii* from animal's burrow and surrounding bamboo debris,[160] thus suggesting *B. indica* as a sentinel animal, which potentially amplified the pathogen in the environment.

Recently, a case cluster of cryptococcosis has been observed in a synanthropic Southeastern Asian murid (*Mus musculus castaneus*).[161] Unlike bandicoot rats, no lesions were recorded in any organ of the animals, however, *C. n.* var. *grubii* was recovered from cultures of tissue homogenates of brain, lungs, liver, and kidneys. The habitat soil and fresh feces of the animals were also positive for the fungus. It is interesting to note that, despite the presence of *Cryptococcus* in the central vein, neither liver nor any other organ exhibited pathological signs. Since the pathogen passes through the animal host without affecting it and all isolates recovered from *M. musculus* were weakly pathogenic to experimental mice, which define the status of *M. musculus* as passenger host for *C. n.* var. *grubii* in a more appropriate manner. It is noteworthy that in most of the cases, *Cryptococcus* yeasts have been isolated from apparently healthy rodents.

Of note, household rodents are nuisance animals and may serve as a continuous source of infection for humans and their pets. On one hand, rodents especially rats and mice have expanded their geographic range dramatically and also have significantly extended the territory of harbored pathogens,[162] but on the other hand, they may play a role to prevent human cases acting as sentinel for the presence of *Cryptococcus* in the environment.[163] On the basis of degree of interaction between host and harbored pathogens, rodents may be termed as natural reservoirs, alternate hosts, sentinel animals, carriers, and passenger hosts.

Infections due to melanized fungi

Several members of melanized fungi have been reported sporadically as causative agents of severe phaeohyphomycoses, chromoblastomycosis, and mycetoma in human and animals.[164,165] However, the potential pathogenicity of infections in crustaceans, captive and farmed fish, amphibians, aquarium animals, and other cold-blooded vertebrates has increasingly been recognized[166–169] (Table 2). In contrast, reports of infections in warm-blooded animals are relatively scant.[170–172] It has been hypothesized that cold blooded animals are more accessible to these fungi by their naked, wet skin, while other vertebrates are protected by fur of feathers.[173] In line with this suggestion, the only non-human vertebrate infections by *Chaetothyriales* are cases of encephalitis in cats and dogs, where the portal of entry is via inhalation and the texture of the skin is irrelevant.[164]

In vertebrates, two basic types of (sub)cutaneous infection are associated with black fungi: (i) those with yeast cells or hyphal elements in tissue leading to necrosis (phaeohyphomycosis) [164]; and (ii) those with muriform cells in tissue leading to host tissue proliferation (chromoblastomycosis).[174] The main types of systemic infections are disseminated—osteotropic or neurotropic—or single-organ; the main organs affected are lungs and brain. In cold-blooded animals such a classification is less apparent; most infections can be regarded as disseminated, while muriform cells have been reported in amphibians.[175,176]

Systemic phaeohyphomycosis occurs mainly in healthy and in debilitated vertebrates. Infections in crustaceans, captive and farmed fish, amphibians, aquarium animals, and other cold-blooded vertebrates have regularly been reported.[164] Susceptibility to infection may enhance due to transportation to adjacent basins, stress under aquarium conditions, environmental pollution, or environmental changes. Mesophilic and oligotrophic, waterborne *Exophiala* species commonly occur in low-nutrient drinking water, aquaria and fish nurseries[173] and may cause massive death upon stress of the animals. *Exophiala psychrophila* caused high mortality in farmed Atlantic salmon smolt (*Salmo salar*).[177] *Exophiala pisciphila* was associated with epizootics in cold-blooded vertebrates[178] and infections in coastal smooth dogfish (*Mustelus canis*)[179] and marine potbelly seahorses (*Hippocampus abdominalis*). *Exophiala aquamarina* repeatedly caused disseminated infections in several species of fish.[180] *Exophiala equina*, originally isolated from limb infection in a horse[181]; however, it has been reported from disseminated infection in a Galapagos giant tortoise (*Geochelone nigra*).[182] The related species *E. cancerae*[173,177] was isolated from tissue of moribund mangrove crabs (*Ucides cordatus*) with Lethargic crab disease (LCD), causing extensive epizootic mortality along the Brazilian coast.[168] Occasional coinfection by another black yeast-like fungus, *Fonsecaea brasiliensis* has been described.[183]

Chromoblastomycosis has been mainly associated with humans.[174] However, several cases of subcutaneous infections have been reported in toads,[184] although the presence of typical muriform cells in the tissues were lacking[174]. Older reports of muriform cells in cold-blooded animals[175,185] need confirmation of the etiologic agent.

Members of the order *Pleosporales* have rarely been reported from animals. In the *Venturiales*, *Verruconis gallopava* has repeatedly been described from brain infections in birds. In the literature *Capnodiales* are represented by *Cladosporium* as reported agent of animal disease, but because of frequent occurrence of this genus as environmental contaminants such cases need additional molecular tests for credibility; none of the animal cases ascribed to *Cladosporium* has been proven by sequencing.[164]

Endemic infections with indirect transmission from the environment

Coccidioidomycosis

There are two distinct cryptic species within the genus *Coccidioides* (Ascomycota, Pezizomycotina, Eurotiomycetes, Onygenales, Onygenaceae): *Coccidioides immitis* and *C. posadasii*.[186] Both species are dimorphic fungi with an environmental saprotrophic phase and a host-associated parasitic phase. By definition, dimorphic fungi are defined by their temperature-dependent transition from a saprophytic mold to a parasitic yeast form upon transition into a mammalian host. Both *Coccidioides* species cause the disease coccidioidomycosis also referred to as San Joaquin Valley fever, valley fever, desert rheumatism, or "cocci/coccy." Although a broad diversity of animals is susceptible to infection by *Coccidioides* species, severe or disseminated disease is mainly reported in pet dogs.[187]

Histoplasmosis

Histoplasma capsulatum is a dimorphic fungus widely distributed in the tropical or subtropical areas of the world

Table 2. Diseases caused by black-yeasts and their filamentous relatives in animals.

Host species		Fungal species	Type of infection
	Class Eurotiomycetes, Order Chaetothyriales, Family Herpotrichiellaceae		
Invertebrates	**Mussel shells (*Bathymodiolus brevior*)**	*Capronia moravica*	Disseminated infection
	Mangrove land crab (*Ucides cordatus*)	*Exophiala cancerae*	Primary disseminated infection
	Earthworms (*Octolasion tyrtaeus*)	*Exophiala jeanselmei*	Late embryonic stages of the earthworm naturally infected presenting healthy-appearing and necrotic eggs
	Worms (*Eisenia foetida*)	*Exophiala jeanselmei*	cocoon albumen naturally infected with healthy-appearing and necrotic eggs
	Mangrove land crab (*Ucides cordatus*)	*Fonsecaea brasiliensis*	Secondary disseminated infection
Amphibians	**Toads, wild and captive frogs (*Hyla caerule*, *H. septentrionali*, *Pternohylaf odiens*, *Phyllobatest rinitatis*, *Rhacophorus* spp.)**	*Fonsecaea pedrosoi*, *Fonsecaea* spp., *Rhinocladiella* spp., *Phialophora* spp.	Skin lesion and disseminated infection with neurological disorders and multifocal dermatitis; pigmented hyphae invaded multiple organs with mild cell necrosis and minimal inflammatory cell response
	Marine toad (*Bufo marinus*), Spadefoot toad (*Scaphiopus holbrooki*)	*Fonsecaea* spp. *Phialophora* spp.	Phaeohyphomycosis: skin lesion and disseminated infection
	Frog (*Bufo japonicus formosus*) False tomato frogs (*Dyscophus guineti*)	*Veronaea botryosa*	Disseminated infection
Reptiles	**Galapagos tortoise (*Geochelone nigra*)**	*Exophiala equina*	Hematogenous dissemination
	Turtle	*Exophiala jeanselmei*	Disseminated infection
Fishes	**Seadragons (*Phyllopteryx taeniolatus*)**	*Exophiala angulospora*	Disseminated infection
	Fish (*Atlantic salmon*; *Channel catfish*; smooth dogfish), Seahorse	*Exophiala pisciphila*	Disseminated infection
	Fish (*Cutthroat trout Atlantic salmon*)	*Exophiala salmonis*	Disseminated infection
	Fish (Siberian sturgeon: *Acipenser baerii*, *A. transmontanus*)	*Veronaea botryosa*	Disseminated infection
Mammals	**Dog, leopard, alpaca**	*Cladophialophora bantiana*	Skin lesion to disseminated infection
	Cat	*Cladophialophora bantiana, Exophiala attenuata, Exophiala spinifera, Fonsecaea multimorphosa, Phialophora verrucosa*	Skin lesion Skin lesion Phaeohyphomycosis Brain disseminated infection
	Horse	*Cladophialophora bantiana, Exophiala equina*	Phaeohyphomycosis with presence of skin ulcerative lesion
	Class Eurotiomycetes, Order *Venturiales*, family *Sympoventuriaceae*		
Birds	**Turkey, Chicken, gray-winged Trumpete, quail, owl**	*Verruconis gallopava*	Encephalitis
Amphibians	**Toad**	*Ochroconis humicola*	Skin lesion
Reptiles	**Tortoise**	*Ochroconis humicola*	Cutaneous lesions
Fishes	**Coho salmon, Atlantic salmon, rainbow trout, scorpion fish, walking catfish**	*Ochroconis humicola*	Disseminated infection
	Fish (*Chinook salmon*)	*Ochroconis tshawytschae*	Disseminated infection
Mammals	**Cat**	*Ochroconis gallopava*	Disseminated infection
	Class Dothideomycetes, Order Capnodiales, family Davidiellaceae		
Mammals	**Cat, dog, sheep**	*Cladosporium* spp.	Disseminated infection
	Class Dothideomycetes, Order Pleosporales, family Pleosporaceae		
Mammals	**Cat, dog, horse**	*Alternaria alternata*	Skin lesion

and infects numerous mammalian hosts. The population of *H. capsulatum* include three distinct subspecies determined by geographical distribution and clinical signs.[188] *Histoplasma capsulatum* var. *capsulatum* has a global distribution, causing pulmonary and systemic infections in a diversity of mammals, including humans. *Histoplasma capsulatum* var. *duboisii* is endemic/enzootic in western and central Africa, which causes lymphadenopathy, and dissemination to the skin and bones, mainly in humans and other primates. *Histoplasma capsulatum* var. *farciminosum* affects the skin and the subcutaneous lymphatic system in equids (horses, donkeys, and mules) but has also been recovered from humans, dogs, cats, and badgers. Disease outcome is variable and depends on the immune status of the host, inoculum size, and the virulence of the isolate.[189]

Paracoccidioidomycosis

Paracoccidioidomycosis is an endemic/enzootic mycosis acquired by airborne inhalation of infective conidia of *Paracoccidioides* spp. present in the environment.[190,191] The disease is caused by *Paracoccidioides brasiliensis* and *P. lutzii,* which are dimorphic fungi belonging to the Ajellomycetaceae.[192] Paracoccidioidomycosis is the major systemic mycosis in Latin American countries and ranks eighth among causes of human death from infectious and parasitic diseases in Brazil.[193,194] Naturally acquired Paracoccidioidomycosis has been reported in dogs[194–195] and armadillos.[197]

Blastomycosis

Blastomycosis is a serious fungal disease of dogs, humans, and occasionally other mammals such as cats and horses caused by geographically restricted, thermally dimorphic fungus *Blastomyces dermatitidis*.[198,199] Blastomycosis is mainly common in dogs residing in or visiting enzootic areas.[200] The incidence of blastomycosis in dogs is 8–10 times that of humans,[201] presumably related to time spent outdoors, proximity to soil, and activities, such as digging, that may result in soil disturbances and increase conidial exposure. Most affected dogs are immunocompetent.[202]

Infections due to zoophilic pathogens with near-direct transmission

Chytridiomycosis

The amphibian fungal disease chytridiomycosis is a major infectious disease responsible for amphibian decline and one of the greatest fungal threats to frog and salamander (urodeal amphibians) biodiversity.[203] This lethal skin disease is caused by members of the genus *Batrachochytrium,* chytridiomycetes belonging to the order *Rhizophydiales*. The first known etiologic agent of amphibian chytridiomycosis, *B. dendrobatidis* (*Bd*), was identified in 1998 and today causes disease in a wide variety of amphibian species across the three orders, that is, frogs and toads (*Anura*), salamandrines and newts (*Urodela*), and caecilians (*Gymnophiona*).[204,205] *Bd* has caused the rapid decline or extinction of an estimated 200 amphibian species,[206] which is probably even an underestimation due to the cryptic behavior of many amphibians and the lack of monitoring.[207] The worldwide emergence of chytridiomycosis is mostly likely due to the rapid worldwide transmission of the virulent lineage '*Bd* Global Panzootic Lineage' (*Bd*GPL).[208] *Bd*GPL has caused declines in Australia, Mesoamerica, North America, and Southern Europe. Determinants of host susceptibility, *Bd* strain virulence[208] and a conducive environment,[209] underpin pronounced differences in the outcome of exposure to *Bd*, which ranges from mass die-offs and population crashes over erratic or even lack of any observed mortality and host-pathogen coexistence.[210] Some host species are refractory to infection.[211]

A second chytrid species, *B. salamandrivorans* (*Bsal*) has recently emerged and has been causing mass mortality in fire salamandrines (*Salamandra salamandra*) in Belgium, the Netherlands, and Germany. This fungus is pathogenic for most western Palearctic salamandrine and newt taxa and is considered a major threat to the region's biodiversity.[212,213] Salamandrines can be resistant (no infection, no disease), tolerant (infection in absence of disease), moderately susceptible (infection resulting in clinical disease with possibility of subsequent recovery), or highly susceptible (infection resulting in lethal disease). Infection experiments demonstrated that frogs and toads are not susceptible to *Bsal* but can act as infectious carriers.[214] *Bsal* is believed to have originated from Asia where it appears to be endemically present.[212,215]

For both (non-zoonotic) species the global trade in amphibians is considered a potent force in spreading novel virulent lineages into naive host populations. Long distance spread is most likely to have occurred due to movement of infected amphibians, particularly through the pet trade but also via accidental movement in the frog meat industry (although the latter is likely significant for ranaviruses, since most frog products are frozen).[216] The listing of *Bd* as an internationally notifiable disease by the OIE, with the aim to improve trade safety, represents the first disease that is listed solely because of a biodiversity concern. Although rigorous quarantine and surveillance protocols are, for example, in place for most livestock diseases, improved standards are needed for wildlife.[217]

Counteracting the impact of chytridiomycosis on amphibian populations remains a major challenge.[218] *Bsal* mitigation is further complicated by the production of encysted spores that remain infective for a long time and are resistant to predation.[214] Although immunization,[219] disinfection,[220] and the use of biocontrol with, for example, probiotics or predatory microorganisms,[221,222] may offer some perspectives for *in situ* mitigation, captive assurance colonies of threatened amphibians currently offer the sole effective, be it last resort solution to prevent amphibian extinction due to chytrid infections.

Bat white-nose syndrome

Pseudogymnoascus destructans (*Pd*) (formerly known as *Geomyces destructans*[223,224]) is the causative agent of white-nose syndrome of hibernating bats in Northeastern America.[225,226] Since its detection in 2006, it caused the worst mass mortality known in mammals with millions of dead bats. Formerly abundant bat species are now regionally extinct.[227]

The psychrophilic fungus *Pd* finds an ideal substrate in the skin of hibernating bats overwintering in cool and moist cavernous hibernacula, as they lower their body temperature to ambient temperature of 12–15°C. As the fungus ceases to grow at temperatures above 20°C,[224] *Pd* will neither be able to infect bats that are active in summer, nor other mammals or humans. The fungal growth mostly remains restricted to the outer skin, but in contrast to dermatophytes the fungus may invade deep into the dermis,[228] leading to severe erosive to ulcerative lesions, particularly on the wing membranes. Macroscopically, aerial hyphae appear as white powdery patches around muzzle and on wing membranes, but the histological diagnostic hallmark—mandatory for the confirmation of the disease—are cup-like epidermal erosions filled with fungal hyphae or their full thickness invasion of the wing membrane.[228] Microscopic evidence of disease are the distinctly asymmetrically curved conidia. In North America *Pd* infection is associated with aberrant hibernation behavior and a distinct increase in arousals from torpor bouts, a physiologic state lasting up to 15 days during which bats reduce metabolic activity and immune response to a minimum as well as lowering their body temperature to ambient degrees. The premature consumption of the stored energy by frequent activity phases is one of the presumed causes of death. Additionally, it is thought that the skin damages could result in a life-threatening imbalance in homeostasis leading to mortality.[229,230]

Since its discovery, *Pd* is spreading in a radial fashion from the index cave in New York State throughout the North American continent. Last year, *Pd* appeared across the Rocky Mountain barrier as the first hibernacula in Washington State tested positive for the fungus.[231] However, all isolates obtained from various affected American hibernacula show a genetic relationship of a single clonal genotype, highlighting that *Pd* seems a novel pathogen introduced into a naïve host population.[232] Currently, eight bat species are confirmed with *Pd* lesions in North America, and an additional six bat species at least carry the fungus. Meanwhile, hibernating bats of 17 species from various parts of Europe were shown to carry the fungus with similar clinical appearance, but neither changes in hibernation behavior nor associated mortality have ever been found.[233] The reasons for these intercontinental differences are not clear, but European bats seem to resist the impact of the infection to a certain degree. Recent investigations in the phylogenetic relationships of *Pd* strains used microsatellites to reveal not only long time diversification of European fungus strains but also found Eurasia as the likely source of origin for the *Pd* clone occurring in North America.[234] Fungal conidia can easily be harvested from affected bats as well as from hibernacula walls,[233] and the accidental transport of *Pd* from Europe via contaminated gear or clothing is the favored hypothesis for the emergence of *Pd* in North America. However, the main transmission of fungal spores seems to be bat-to-bat contacts and *Pd* infection will remain an ongoing threat for hibernating North American bats. As long as the fungus can spread further to unaffected populations, it will result in sinister consequences for biodiversity and the ecological and economical services provided by bats to mankind.[235]

Zoonotic outbreaks with direct animal to human transmission

According to the official definition from the World Health Organization, zoonoses are diseases and infections that are naturally transmitted between vertebrate animals and humans (and *vice versa*). Among transmissible fungal pathogens, a few species should be considered as zoonotic (Table 3).

Microsporum canis from cats

Cats are becoming increasingly popular as pet and companion animals. Tens of thousands of European crossbred cats are abandoned each year and can be adopted for almost free from animal shelters. It is also fashionable to purchase expensive purebred cats from breeding units. In both cases, animals are acquired from communities and may be affected, visibly or not, by diseases that are transmissible to humans. Dermatophytosis caused by *Microsporum canis* is probably the most prevalent zoonosis that may occur in such situations.[236] In shelters, rapid turnover of cats of unknown status, promiscuity, and economic constraints for healthcare increase risks of contagion. In breeding units, *M. canis* is commonly enzootic, and appropriate antifungal treatments are either absent or incomplete. Asymptomatic carriage is frequent, cats being infected without obvious clinical signs.[237]

Table 3. Main fungal species responsible for zoonoses.

Fungal species	Distribution	Main reservoirs of fungal pathogens	Mode of transmission to humans	Human disease
Zoophilic dermatophytes				
Microsporum canis	Worldwide	**Cats, dogs, rabbits**	Direct contact with arthroconidia (formed on the skin of infected animals)	Dermatophytosis (tinea corporis or capitis)
Trichophyton mentagrophytes	Worldwide	**Rodents, rabbits**		
Trichophyton benhamiae	Worldwide	**Rodents (Guinea-pigs for the *lutea* variety)**		
Trichophyton verrucosum	Worldwide	**Cattle**		
Nannizia (Microsporum) persicolor	Worldwide	**Rodents, soil**		
Trichophyton erinacei	Worldwide	**Hedgehogs**		
Microsporidia				
Encephalitozoon cuniculi	Worldwide	**Rabbits**	Ingestion of fungal spores (shed in the urine of rabbits)	Encephalitozoonosis (neurological signs, systemic disease)
Encephalitozoon hellem	Worldwide	**Birds (Psittacidae)**	Inhalation of fungal spores? Ocular contact	Encephalitozoonosis (respiratory signs, systemic disease)
Encephalitozoon intestinalis	Worldwide	**Cattle, goats, pigs. . .**	Ingestion of fungal spores (shed in the feces of infected animals)	Encephalitozoonosis (digestive signs, systemic disease)
Enterocytozoon bieneusi (many genotypes)	Worldwide	**Many mammals**	Ingestion of fungal spores (shed in the feces of infected animals)	Encephalitozoonosis (digestive or respiratory signs)
Dimorphic fungi				
Histoplasma capsulatum capsulatum	Worldwide	**Soil, bats**	Inhalation of fungal spores	Histoplasmosis
Sporothrix schenckii	Worldwide (but more frequent in tropical countries)	**Soil, different mammals**	Traumatic inoculation of contaminated soil, plants, and organic matter into skin or mucosa	Sporotrichosis
Sporothrix brasiliensis	Brazil	**Cats**	Scratches or bites from infected cats	

Cats may be sold while still receiving antifungal, so that they are still infected and contagious for congeners and humans at the time of purchase. *Microsporum canis* infection in cats may be highly polymorphic. This interferes with diagnosis and treatment of feline dermatophytosis.[238] Efficient vaccines against feline dermatophytosis are currently unavailable, partly due to a lack of knowledge on virulence factors. The keratinolytic secreted proteases were thought to be the most likely factors of dermatophyte's pathogenicity, due to peculiar ability of dermatophytes to use hard keratin *in vivo* as a growth substrate.[239] The enzymes were therefore purified from culture supernatants produced *in vitro* in media enriched by keratin. Subsequent characterization at the gene level and complete sequencing of several dermatophyte genomes revealed several exo- and endoproteases, some of them belonging to large, expanded gene families.[240] These virulence genes are candidates for the development of vaccines. As an example, an *M. canis* 31.5 kDa keratinolytic protease, later called Sub3, was highly expressed by the fungus grown *in vitro* in the presence of feline keratin and *in vivo* in naturally infected cats,[241] and experimentally infected guinea pigs.[242]

Using RNA silencing, [243] and a sophisticated model of *in vitro* reconstructed feline epidermis,[244] and *ex vivo* models of human or animal epidermis, Sub3 was shown to contribute to the adherence of *M. canis* to host tissue. However, Sub3 is not required for the invasion of keratinized structures *in vivo*.[245] Putative virulence factors involved in tissue invasion remain to be identified. This could be achieved by comparing *in vivo* and *in vitro* transcriptomes and secretomes, as used for *Trichophyton rubrum* and *T. benhamiae*.[246,247] The importance of newly discovered putative virulence factors could be tested by manipulation of dermatophyte genomes by gene knock-outs;[248] combined with pertinent animal models of dermatophytosis.[249]

Infection due to *Sporothrix brasiliensis* from cats

Recent improvements in the taxonomy of *Sporothrix* led to the recognition of a clinically relevant clade comprising four dimorphic species *S. brasiliensis*, *S. schenckii*, *S. globosa,* and *S. luriei,* remote from environmental clades that included *S. chilensis*, *S. pallida,* and *S. mexicana* causing occasional infections.[250,251] Species from clinical clade show different virulence profiles, antifungal susceptibilities and geographical distributions.[252]

The classical route of transmission for humans and animals involves trauma with soil and plant materials. However, epidemics driven by *S. brasiliensis* usually occur as a result of animal-animal or animal-human transmission in an alternative route.[253] Remarkably, the largest epizootic due to *S. brasiliensis* among felines that lead to massive zoonotic transmission has been reported in the South and Southeast regions of Brazil since the 1990 s.[254] Initially, in Rio de Janeiro state during 1998–2003, 497 humans and 1056 cats were diagnosed with positive culture. Among these humans, 67.4% related scratch or bite from cats with sporotrichosis; 68% were women with mean age of 39 years old.[255] From 2005 to 2011, the total number of cats assisted at the national institute of infectology, Oswaldo Cruz foundation (IPEC/FIOCRUZ) was 2301. The median age of affected cats was 2 years old, and the median time between the observation of the lesions and to take to veterinary assistance was 8 weeks.[256] The most recent surveys indicate that about 244 dogs and 4703 cats were diagnosed through 2015 at IPEC/FIOCRUZ, characterizing the state of Rio de Janeiro as hyperendemic for feline sporotrichosis.[254]

Feline sporotrichosis has also been reported in São Paulo and Rio Grande do Sul states, with a distribution of 190 and 129 cats, respectively.[257,258] However, the number of affected cats may be underestimated, since sporotrichosis is not a notifiable disease. To understand the epidemic scenario caused by *S. brasiliensis* it is necessary to consider some aspects of the host-pathogen-environment interplay, such as the high susceptibility of cats to the fungal species; the high virulence of *S. brasiliensis* circulating during epidemics associated to a recent introduction of the pathogen in an urban feline population. Some characteristics of cat's behavior may be also taken into account, such as toileting habits in contact with soil, sharpening the nails in environment, behavior during mating, and territorial disputes that frequently leads to scratches or bites spreading the fungus to other hosts.[259,260]

Table 4. The most common fungal species producing mycotoxins.

Mycotoxin	Fungal species
Aflatoxins	*Aspergillus flavus, A. parasiticus, A. nomius, A. argenticus,* etc.
Ochratoxin A	*Penicillium verrucosum, P. nordicum, A. ochraceus, A. carbonarius, A. niger, A. sclerotioniger*
Deoxynivalenol	*Fusarium graminearum, F. culmorum, F. sporotrichioides, F. poae, F. tricinctum*
T-2 toxin	*F. sporotrichioides, F. poae*
Diacetoxyscirpenol	*F. graminearum, F. semitectum, F. tricinctum, F. oxysporum,* etc.
Nivalenol	*Fusarium nivale, F. poae*
Zearalenone	*Fusarium graminearum, F. culmorum*
Fumonisin B1	*Fusarium proliferatum, F. verticillioides* (syn. *F. moniliforme), A. niger, A. carbonarius*

Mycotoxins and mycotoxicoses

Mycotoxins are defined as the chemicals of fungal origin being toxic for (warm-blooded) vertebrates.[261,262] Mycotoxins are secondary metabolites produced during consecutive enzyme reactions via several biochemically simple intermediary products from the primary metabolism of acetates, mevalonates, malonite, and some amino acids.[263]

The contamination of foods and animal feeds with mycotoxins is a worldwide problem, and formation of mycotoxins by many important phytopathogenic and food spoilage fungi is undoubtedly one of the most significant risk factors to mammalian health.[264] Mycotoxins are categorized by fungal species, structure, and (or) mode of action. As shown in Table 4, a single species of fungi may produce one or several mycotoxins and individual mycotoxins may be produced by different fungal species.[265,266] Aflatoxins, ochratoxins, trichothecenes, zearalenone, fumonisins, tremorgenic toxins, and ergot alkaloids are main mycotoxins of public health and agro-economic importance.

Mycotoxins cause intoxications in both animals and humans, resulting in severe diseases called acute or chronic mycotoxicoses,[267] depending on species and susceptibility of the host. It is also believed that with a mycosis, mycotoxins produced by the invading fungi can suppress immunity, therefore increasing the infectivity of the fungus.[268] Acute mycotoxicoses have a rapid onset and an obvious toxic response, while the most frequent type of mycotoxicoses occurs after the long-lasting exposure of an

Table 5. General toxic effects of the most common mycotoxins.

Toxicity	Mycotoxins
Dermatotoxic	Trichothecenes, verrucarins, sporidesmins
Estrogenic	Zearalenone
Genotoxic	Aflatoxins, sterigmatocystin, ochratoxin A, zearalenone, patulin, trichothecenes
Hematotoxic	Aflatoxins, ochratoxin A, zearalenone, trichothecenes
Hepatotoxic	Aflatoxins, ochratoxins, rubratoxins, sterigmatocystin etc.
Immunotoxic	Aflatoxins, ochratoxin A, trichothecenes, patulin
Nephrotoxic	Ochratoxin A
Neurotoxic	Fumonisins, penitrem A, fumitremorgens
Gastrotoxic	Trichothecenes

animal/human to low dosages of the toxin(s).[269] The negative effects of mycotoxins on various animals have been extensively described in the literature (Table 5). In poultry farms, contaminated feeds with aflatoxins to broilers causes negative metabolic responses and enzyme activity resulting reduced body weight gain, and tissue necrosis.[270] In dogs, ingestion of a variety of mouldy foods, including grains, walnuts, almonds, and peanuts, as well as nonspecific garbage, has been associated with tremorgenic mycotoxicosis. Dogs are more commonly affected than other species of domestic animals, probably because of their tendency to scavenge; intoxication of several dogs within the same household has also been reported. The most common sources of tremorgenic mycotoxins are fungi of the genus *Penicillium*.[271] Ruminants such as cattle, sheep, goats, and deer are generally resistant to the direct adverse effects of mycotoxins, which appear to be due to capability of rumen's microbiota to degrade mycotoxins.[272] However, bovine production (milk, beef, or wool), reproduction, and growth can be altered when ruminants consume mycotoxin-contaminated feed for extended periods of time.[273] Negative effects of the mycotoxins have been also documented on the pig's reproductive function.[274]

From the public health prospectives, mycotoxins are considered as endogenous contaminants, that is, formed directly in the matrix by toxic mycobiota. The mycotoxins of most concern from a food safety perspective include the aflatoxins (B1, B2, G1, G2, and M1), ochratoxin A, patulin, and toxins produced by Fusarium moulds, including fumonisins (B1, B2, and B3), trichothecenes (principally nivalenol, deoxynivalenol, T-2 and HT-2 toxin) and zearalenone. If edible animals are fed by mouldy materials containing certain mycotoxins, those are either converted into other toxic substances or are accumulating in their products (milk, eggs) or directly in the viscera, muscles dedicated for human consumption.[9] Given the frequent consumption of milk and dairy products particularly by infants, mycotoxins are an issue of considerable importance to public health.[265] Aflatoxins and ochratoxins are the most toxic products and have been shown to be genotoxic, that is, can damage DNA and cause cancer in animal species. By their structure, aflatoxins are difuranocoumarol lactons, recently known in about 20 derivatives. Aflatoxins B1, B2, G1, and G2 are the most frequent one, with the toxicity decreasing in the row AFB1 > AFG1 > AFB2 > AFG2. AFB1 is the most potential proven human carcinogen (IARC class I) of biological origin, and its metabolite AFM1 proved the same toxicity, with hepatocells being the target structures of the action.[265] Ochratoxins are polyketid derivatives of dihydroisocoumarin including ochratoxin A (OTA, the most toxic), B, C (ethylester OTA), and D. The sources include barley, ray, oat, wheat, rice, maize, beer, coffee, tea, wine/ raisins, spices, and porcine products (meat, viscera) and other meat and meat products of nonruminant animals exposed to feedstuffs contaminated with this type of mycotoxin. Ruminants such as cows and sheep are generally resistant to the effects of ochratoxin A due to hydrolysis to the nontoxic metabolites by protozoa in the reticulorumen sac before absorption into the blood.[275] Importantly, OTA in urine was found to be a better indicator of OTA consumption than OTA in plasma. Low blood serum/plasma concentrations of OTA have been reported for healthy persons in many countries.[276]

The European Food Safety Authority (EFSA) has carried out risk assessments on certain mycotoxins in animal feed that are considered to pose a potential risk to human or animal health including aflatoxin B1, deoxynivalenol, zearalenone, ochratoxin A, fumonisins, and T-2 and HT-2. Each of the recommendations has been used as a basis for the current legislative controls on these mycotoxins. The maximum permitted levels (MPLs) for substances that are present in, or on, animal feed that pose a potential danger to animal or human health or to the environment, or could adversely affect livestock production are summarized in Table 6.

Antifungal resistance in animals with fungal infections

Many of the antifungal agents that are used in humans are also used in animals for the treatment of invasive fungal infections. These can include the polyenes (e.g., amphotericin B and nystatin), the azoles, including both the imidazoles and triazoles, the allylamines (e.g., terbinafine), and the echinocandins. Table 7 summarizes the uses of various antifungals that have proved successfully in various animal species.

Table 6. The European Food Safety Authority (EFSA) maximum permitted levels for six mycotoxins in animal feed that are considered to pose a potential risk to human or animal health (Directive 2003/100/EC, amending Directive 2002/3 and Recommendation 2006/576/EC).

	Products intended for animal feed	Maximum content in mg/kg (ppm) relative to a feedingstuff with a moisture content of 12%
Aflatoxin B1	All feed materials	0.02
	Complete feedingstuffs for cattle, sheep and goats with the exception of:	0.02
	- complete feedingstuffs for dairy animals	0.005
	- complete feedingstuffs for calves and lambs	0.01
	Complete feedingstuffs for pigs and poultry (except young animals)	0.02
	Other complete feedingstuffs	0.01
	Complementary feedingstuffs for cattle, sheep and goats (except complementary feedingstuffs for dairy animals, calves and lambs)	0.02
	Complementary feedingstuffs for pigs and poultry (except young animals)	0.02
	Other complementary feedingstuffs	0.005
Deoxynivalenol	Feed materials	
	- cereals and cereal products with the exception of maize by-products	8
	- maize by-products	12
	Complementary and complete feedingstuffs with the exception of:	5
	- complementary and complete feedingstuffs for pigs	0.9
	- complementary and complete feedingstuffs for calves (< 4 months), lambs and kids	2
Zearalenone	Feed materials	
	- cereals and cereal products with the exception of maize by-products	2
	- maize by-products	3
	Complementary and complete feedingstuffs	
	- complementary and complete feedingstuffs for piglets and gilts (young sows)	0.1
	- complementary and complete feedingstuffs for sows and fattening pigs	0.25
	- complementary and complete feedingstuffs for calves, dairy cattle, sheep (including lambs) and goats (including kids)	0.5
Ochratoxin A	Feed materials	
	- cereals and cereal products	0.25
	Complementary and complete feedingstuffs	
	- complementary and complete feedingstuffs for pigs	0.05
	- complementary and complete feedingstuffs for poultry	0.1
Fumonisin B1and B2	Feed materials	
	- maize and maize products	60
	Complementary and complete feedingstuffs for:	
	- pigs, horses (Equidae), rabbits and pet animals	5
	- fish	10
	- poultry, calves (<4 months), lambs and kids	20
T-2 and HT-2	Compound feed for cats	0.05

Mechanisms of antifungal resistance

Resistance to antifungal drugs can occur through various mechanisms. These can include: (1) nonsynonymous point mutations within the gene encoding the target enzyme leading to alterations in the amino acid sequence, (2) increased expression of the target enzyme through increased transcription of the gene encoding it, (3) decreased concentrations of the drug within the fungal cells due to drug efflux, (4) changes in the biosynthetic pathway resulting in reduced production of the target of the antifungal drugs. For the azoles, each of these mechanisms have been associated with reduced susceptibility in *Candida albicans*, and several are

Table 7. Recommended indications of antifungals in veterinary practice. Adapted from reference no. 309 with the permission of authors.

	Antifungal agent	Animal species	Indications
Systemic	**Amphotericin B**	**Birds**	Aspergillosis, Candidiasis
		Dogs	Aspergillosis, Cryptococcosis, Blastomycosis, Histoplasmosis, Coccidioidomycosis, Mucormycosis
		Cats	Aspergillosis, Cryptococcosis, Blastomycosis, Histoplasmosis, Coccidioidomycosis, Mucormycosis
		Horses	Aspergillosis, Candidiasis, Histoplasmosis, Coccidioidomycosis, Sporotrichosis, Mucormycosis
	Nystatin	**Birds**	Candidiasis of the gastrointestinal tract
	Terbinafine	**Dogs**	Cryptococcosis, Sporotrichosis, Dermatophytosis and *Malassezia* dermatitis
		Cats	Cryptococcosis, Sporotrichosis, Dermatophytosis
	Ketoconazole	**Birds**	Aspergillosis, Candidiasis
		Dogs	Blastomycosis, Histoplasmosis, Cryptococcosis, Coccidioidomycosis, Sporotrichosis, *Malassezia* dermatitis and Dermatophytosis
		Cats	Blastomycosis, Histoplasmosis, Cryptococcosis, Coccidioidomycosis, Sporotrichosis, Dermatophytosis
	Parconazole	**Birds (guinea fowl)**	Candidiasis (trush)
	Fluconazole	**Birds**	Candidiasis
		Dogs	Cryptococcosis, Blastomycosis, Aspergillosis (nasal)
		Cats	Aspergillosis (CNS infection), Cryptococcosis, Blastomycosis, Coccidioidomycosis
	Itraconazole	**Birds**	Aspergillosis, Candidiasis
		Dogs	Aspergillosis, Blastomycosis, Histoplasmosis, Cryptococcosis, Coccidioidomycosis, Sporotrichosis, Dermatophytosis and *Malassezia* dermatitis
		Cats	Dermatophytosis Aspergillosis, Sporotrichosis, Cryptococosis, Blastomycosis, Histoplasmosis, Phaeohyphomycosis
		Horses	Aspergillosis, Coccidioidomycosis, Mycotic keratitis, Dermatophytosis
		Rodents, rabbits and fur animals	Dermatophytosis
	Voriconazole	**Birds**	Aspergillosis
		Dogs	Aspergillosis, Scedosporiosis
		Cats	Aspergillosis
		Horses	Aspergillosis (systemic), *Aspergillus* keratitis
	Posaconazole	**Dogs**	Aspergillosis, Mucormycosis
		Cats	Aspergillosis, Mucormycosis
	Flucytosine	**Cats**	Cryptococcosis
	Griseofulvin	**Dogs**	Dermatophytosis
		Cats	Dermatophytosis
		Horses	Dermatophytosis, Sporotrichosis
		Ruminants	Dermatophytosis
		Rodents, rabbits and fur animals	Dermatophytosis
Topical	**Clotrimazole**	**Birds (Raptors)**	Aspergillosis
		Dogs	Aspergillosis, Dermatophytosis and *Malassezia* dermatitis
		Cats	Aspergillosis, Dermatophytosis
		Rodents, rabbits and fur animals	Dermatophytosis
	Miconazole	**Birds**	Aspergillosis
		Dogs	*Malassezia* dermatitis
		Cats	Dermatophytosis, *Malassezia* dermatitis
		Rodents, rabbits and fur animals	Dermatophytosis
	Enilconazole	**Birds**	Aspergillosis Disinfection (*Aspergillus* and other pathogenic fungi)
		Dogs	Dermatophytosis, *Malassezia* dermatitis Aspergillosis
		Cats	Dermatophytosis, *Malassezia* dermatitis Aspergillosis
		Horses	Dermatophytosis Disinfection (dermatophytes and other pathogenic fungi)
		Ruminants	Dermatophytosis Disinfection (dermatophytes and other pathogenic fungi)
		Rodents, rabbits and fur animals	Dermatophytosis Disinfection (dermatophytes and other pathogenic fungi)
	Natamycin	**Horses**	Dermatophytosis
		Ruminants	Dermatophytosis
	Thiabendazole	**Birds**	Disinfection
		Horses	Dermatophytosis
		Ruminants	Dermatophytosis
		Rodents, rabbits and fur animals	Dermatophytosis

associated with resistance in other *Candida* species. Alterations in the target enzyme (lanosterol 14-α-demethylase) due to point mutations in the encoding gene *ERG11* leads to decreased susceptibilities to the azoles.[277–289] Overexpression of the *CDR1*, *CDR2*, and *MDR1* genes that encode for efflux pumps leads to azole resistance.[290,291] Azole resistance has also been documented in *A. fumigatus* and is due to point mutations within the *CYP51A* gene that encodes the enzyme responsible for converting lanosterol to ergosterol.[292–294] In isolates with environmental exposure to the azoles tandem repeats in the promoter region along with along with point mutations in the gene (e.g., TR_{34}/L98H and TR_{46}/Y121F/T289A) have been found and cause increased expression of *CYP51A*.[295]

Reports of antifungal resistance in different animal species

Several studies have analyzed fungal isolates from different animals for resistance to antimycotic agents, and many of them reported surprisingly high levels of azole resistance in yeasts. In a retrospective study, Beltaire et al. analyzed fungal strains isolated from equine uteri collected between 1999 and 2011 and showed resistance rates of 19% and 2% for itraconazole and fluconazole, respectively.[296] Cordeiro et al. investigated 59 *C. tropicalis* isolates predominantly derived from healthy animals and found resistance to fluconazole and/or itraconazole in 50%, whereas all isolates were susceptible to caspofungin and amphotericin B.[297] Using the same microbroth dilution assay, Brilhante et al. analyzed *Candida* isolates from the nasolacrimal duct of healthy horses and found that 40% of the *C. tropicalis* isolates were resistant to fluconazole and itraconazole.[298] The same group found high rates of fluconazole and itraconazole resistance also for *Candida* isolates from rheas and cockatiels,[299,300] and efflux pumps were a major resistance mechanism.[301] Using a commercial kit covering eleven commonly used agents, Lord et al. tested 144 *Candida, Cryptococcus, Rhodotorula,* and *Trichosporon* isolates from bird feces for antifungal resistance.[302] They reported that 45.8% of the strains were resistant to at least four of the 11 drugs, and 18.1% were resistant to all antifungals tested. A recent study found similar resistant levels for 111 *C. glabrata* isolates from the feces of sea gulls and 79 *C. glabrata* isolates from human patients, while other have reported only moderate azole resistance in *Candida* strains isolated from raptors.[303,304] These studies indicate that resistance to certain azoles is a common phenomenon in pathogenic yeasts isolated from some animals. Strikingly, the azole resistance rates of *C. albicans* and *C. tropicalis* isolated from healthy animals are higher than those reported in some studies in humans.[305,306] This indicates that the elevated resistance levels found in animals may not simply reflect a natural resistance of the respective species. However, differences in the methodology and breakpoints used, as well as the limited number of isolates included in several animal studies make a direct comparison of data obtained for animal and human isolates difficult.

Azole resistance has also been described for *Aspergillus,*[292] but up to now reports of resistant strains derived from animals are sparse. Acquisition of azole resistance can occur under prolonged therapy. Clinically, invasive infections caused by azole-resistant *A. fumigatus* are challenging to treat due to the lack of therapeutic options. In humans, lipid formulations of amphotericin B can be used, and 5-flucytosine has also been recommended to be added to other therapies in patients with central nervous system infections caused by resistant isolates.[307] However, both antifungals have limitations, including toxicities, which may prohibit their long-term use in both humans and animals. Depending on the mechanism of resistance, higher doses of certain triazoles may be attempted, and there is a recent report of the successful treatment of invasive aspergillosis caused by an *A. fumigatus* isolate harboring a TR_{46}/Y121F/T289A mutation in a bottlenose dolphin with high dose posaconazole.[308] Here, the oral solution of posaconazole was incorporated into gelatin capsules and administered with a goal of achieving trough concentrations of >3 mg/l, which was achieved after prolonged administration and resulted in clinical improvement.

Fungi that cause disease in humans can also cause serious infections in different animal species, associated with significant morbidity and mortality. Examples of invasive mycoses in animals include infections caused by non-transmissible opportunistic fungi (aspergillosis, mucormycosis, candidiasis, cryptococcosis, and infections caused by melanized fungi, endemic environmental pathogens (coccidioidomycosis, histoplasmosis, paracoccidioidomycosis, and blastomycosis), zoophilic fungal pathogens (chytridiomycosis and Bat White-nose syndrome). The list of zoonotic fungal agents (transmissible mycoses) is limited, however some of species (like *Microsporum canis* and *Sporothrix brasiliensis* from cats) have a strong public health impact. The fungal secondary metabolites ‘mycotoxins’ have been associated with severe toxic effects to vertebrates. Mycotoxins are also a major concern for public health. Majority of antifungal agents including the polyenes, the azoles, and the echinocandins that are used in humans are also used in animals for the treatment of fungal infections. Similarly, many limitations also occur in some animal species, including variable pharmacokinetics, adverse effects, drug interactions, and antifungal resistance.

Declaration of interest

The work of Seyedmojtaba Seyedmousavi was supported by the Intramural Research Program of the NIH, NIAID. All other authors report no conflicts of interest. The authors alone are responsible for the content and the writing of the paper.

References

1. Kohler JR, Casadevall A, Perfect J. The spectrum of fungi that infects humans. *Cold Spring Harb Perspect Med*. 2015; 5: a019273.
2. Fisher MC, Henk DA, Briggs CJ et al. Emerging fungal threats to animal, plant and ecosystem health. *Nature*. 2012; 484: 186–194.
3. Casadevall A, Pirofski LA. Host-pathogen interactions: basic concepts of microbial commensalism, colonization, infection, and disease. *Infect Immun*. 2000; 68: 6511–6518.
4. Guarro J, GeneJ Stchigel AM. Developments in fungal taxonomy. *Clin Microbiol Rev*. 1999; 12: 454–500.
5. Seyedmousavi S, Guillot J, Tolooe A et al. Neglected fungal zoonoses: hidden threats to man and animals. *Clin Microbiol Infect*. 2015; 21: 416–425.
6. Jones KE, Patel NG, Levy MA et al. Global trends in emerging infectious diseases. *Nature*. 2008; 451: 990–993.
7. Seyedmousavi S, Guillot J, Arne P et al. Aspergillus and aspergilloses in wild and domestic animals: a global health concern with parallels to human disease. *Med Mycol*. 2015; 53: 765–797.
8. Tell LA. Aspergillosis in mammals and birds: impact on veterinary medicine. *Med Mycol*. 2005; 43: S71–73.
9. Pitt JI. The current role of *Aspergillus* and *Penicillium* in human and animal health. *J Med Vet Mycol*. 1994; 32: 17–32.
10. Heitman J. Microbial pathogens in the fungal kingdom. *Fungal Biol Rev*. 2011; 25: 48–60.
11. Peterson SW, Varga J, Frisvad JC et al. *Phylogeny and Subgeneric Taxonomy of Aspergillus. Wageningen:* Wageningen Academic Publishers, 2008.
12. Zmeili OS, Soubani AO. Pulmonary aspergillosis: a clinical update. *QJM*. 2007; 100: 317–334.
13. Yamauchi H, Takai Y, Yamasaki H et al. Thoracic mass in a cynomolgus macaque (Macaca fascicularis). *Vet Pathol*. 2011; 48: E1–5.
14. Kim K, Harvell CD. The rise and fall of a six-year coral-fungal epizootic. *Am Nat*. 2004; 164: S52–63.
15. Paddack MJ, Reynolds JD, Aguilar C et al. Recent region-wide declines in Caribbean reef fish abundance. *Curr Biol*. 2009; 19: 590–595.
16. Nagelkerken I, Grol MG, Mumby PJ. Effects of marine reserves versus nursery habitat availability on structure of reef fish communities. *PLoS One*. 2012; 7: e36906.
17. Bailey L. *Infectious Diseases in Honeybee*. London: Land Book, 1963.
18. Gilliam M, Vandenberg JD. *Fungi*. Medina, OH: A.I. Root Company, 1997.
19. Burnside CE. Fungous diseases of the honey bee. *US Department of Agriculture Technical Bulletin* 1930: 149.
20. Girling SJ, Fraser MA. Treatment of *Aspergillus* species infection in reptiles with itraconazole at metabolically scaled doses. *Vet Rec*. 2009; 165: 52–54.
21. Jacobson ER, Cheatwood JL, Maxwell LK. Mycotic diseases of reptiles. *J Exotic Pet Med*. 2000; 9: 94–101.
22. Arne P, Thierry S, Wang D et al. *Aspergillus fumigatus* in poultry. *Int J Microbiol*. 2011; 2011: 746356.
23. Beernaert LA, Pasmans F, Van Waeyenberghe L et al. *Aspergillus* infections in birds: a review. *Avian Pathol*. 2010; 39: 325–331.
24. Mc Dougle HC, Vaught RW. An epizootic of aspergillosis in Canada geese. *J Wildlife Management* 1968; 32: 577–578.
25. Kunkle RA, Sacco RE. Susceptibility of convalescent turkeys to pulmonary aspergillosis. *Avian Dis*. 1998; 42: 787–790.
26. Sharman MJ, Mansfield CS. Sinonasal aspergillosis in dogs: a review. *J Small Anim Pract*. 2012; 53: 434–444.
27. Barrs VR, Halliday C, Martin P et al. Sinonasal and sino-orbital aspergillosis in 23 cats: aetiology, clinicopathological features and treatment outcomes. *Vet J*. 2012; 191: 58–64.
28. Barrs VR, Talbot JJ. Feline aspergillosis. *Veterinary Clinics of North America*. 2014; 44: 51–73.
29. Sharp NJH HC, Sullivan M. Canine nasal aspergillosis/penicilliosis. *Compend Cont Educ Pract Vet*. 1991; 13: 41–49.
30. Barachetti L, Mortellaro CM, Di Giancamillo M et al. Bilateral orbital and nasal aspergillosis in a cat. *Vet Ophthalmol*. 2009; 12: 176–182.
31. Hamilton HL, Whitley RD, McLaughlin SA. Exophthalmos secondary to aspergillosis in a cat. *J Am Anim Hosp Assoc*. 2000; 36: 343–347.
32. Kano R, Itamoto K, Okuda M et al. Isolation of *Aspergillus udagawae* from a fatal case of feline orbital aspergillosis. *Mycoses*. 2008; 51: 360–361.
33. Barrs VR, van Doorn TM, Houbraken J et al. *Aspergillus felis* sp. nov., an emerging agent of invasive aspergillosis in humans, cats, and dogs. *Plos One*. 2013; 8: e64871.
34. Puntenney SB, Wang Y, Forsberg NE. Mycotic infections in livestock: recent insights and studies on etiology, diagnostics and prevention of hemorrhagic bowel syndrome. *Southwest Nutrition and Management Conference*. Tuscon: University of Arizona Department of Animal Science, 4963.
35. Dobesova O, Schwarz B, Velde K et al. Guttural pouch mycosis in horses: a retrospective study of 28 cases. *Veterinary Rec*. 2012; 171: 561.
36. Blomme E, Del Piero F, La Perle KMD et al. Aspergillosis in horses: a review. *Equine Vet Educ*. 1998; 10: 86–93.
37. Sansom J, Featherstone H, Barnett KC. Keratomycosis in six horses in the United Kingdom. *Veterinary Rec*. 2005; 156: 13–17.
38. Wada S, Hobo S, Ode H et al. Equine keratomycosis in Japan. *Vet Ophthalmol*. 2013; 16: 1–9.
39. Scotty N. Equine keratomycosis. *Clin Tech Equine Pract*. 2005; 4: 29–46.
40. Abdo W, Kawachi T, Sakai H et al. Disseminated mycosis in a killer whale (*Orcinus orca*). *J Vet Diagn Invest*. 2012; 24: 211–218.
41. Haustein SV, Kolterman AJ, Sundblad JJ et al. Nonhuman primate infections after organ transplantation. *ILAR J*. 2008; 49: 209–219.
42. Hoffmann K, Pawlowska J, Walther G et al. The family structure of the Mucorales: a synoptic revision based on comprehensive multigene-genealogies. *Persoonia*. 2013; 30: 57–76.
43. Jensen HE. Systemic bovine aspergillosis and zygomycosis in Denmark with reference to pathogenesis, pathology, and diagnosis. *APMIS Suppl*. 1994; 42: 1–48.
44. Cunha SC, Aguero C, Damico CB et al. Duodenal perforation caused by *Rhizomucor* species in a cat. *J Feline Med Surg*. 2011; 13: 205–207.
45. Muir M, Raidal SR. Necrotising ventriculitis due to combined infection with *Rhizopus microsporus* var. chinensis and *Candida krusei* in an eclectus parrot (*Eclectus roratus*). *Aust Vet J*. 2012; 90: 277–280.
46. Reynaldi FJ, Giacoboni G, Cordoba SB et al. Mucormicosys due to *Saksenaea vasiformis* in a dog. *Med Mycol Case Rep*. 2017; 16: 4–7.
47. Guillot J, Collobert C, Jensen HE et al. Two cases of equine mucormycosis caused by Absidia corymbifera. *Equine Vet J*. 2000; 32: 453–456.
48. Thirion-Delalande C, Guillot J, Jensen HE et al. Disseminated acute concomitant aspergillosis and mucormycosis in a pony. *J Vet Med A*. 2005; 52: 121–124.
49. Isidoro-Ayza M, Perez L, Cabanes FJ et al. Central nervous system mucormycosis caused by *Cunninghamella bertholletiae* in a bottlenose dolphin (*Tursiops truncatus*). *J Wildl Dis*. 2014; 50: 634–638.
50. Jensen HE, Schonheyder H, Jorgensen JB. Intestinal and pulmonary mycotic lymphadenitis in cattle. *J Comp Pathol*. 1990; 102: 345–355.
51. Jensen HE, Olsen SN, Aalbaek B. Gastrointestinal aspergillosis and zygomycosis of cattle. *Vet Pathol*. 1994; 31: 28–36.
52. Jensen HE, Basse A, Aalbaek B. Mycosis in the stomach compartments of cattle. *Acta Vet Scand*. 1989; 30: 409–423.

53. Carrasco L, Sierra MA, Schonheyder H et al. Ovine ruminal and abomasal zygomycosis. *Small Ruminant Res.* 1993; 10: 357–362.
54. Jensen HE, Monteros AEDL, Carrasco L. Caprine mastitis due to aspergillosis and zygomycosis: a pathological and immunohistochemical study. *J Comp Pathol.* 1996; 114: 183–191.
55. Jensen HE, Aalbaek B, Basse A et al. The occurrence of fungi in bovine tissues in relation to portals of entry and environmental factors. *J Comp Pathol.* 1992; 107: 127–140.
56. Ortega J, Uzal FA, Walker R et al. Zygomycotic lymphadenitis in slaughtered feedlot cattle. *Vet Pathol.* 2010; 47: 108–115.
57. Jensen HE, Krogh HV, Schonheyder H. Bovine mycotic abortion–a comparative study of diagnostic methods. *Zentralbl Veterinarmed B.* 1991; 38: 33–40.
58. Szeredi L, Szentirmai C. Gastric zygomycosis in a pig affected with postweaning multisystemic wasting syndrome—case report. *Acta Vet Hung.* 2008; 56: 207–213.
59. Awadin W, Mosbah E, Youssef ES et al. A case of subcutaneous destructive facial swelling in a dog caused by *Mucor* species. *J Vet Sci Med Diag.* 2015; 4; doi:10.4172/2325-9590.1000163.
60. Suzuta F, Kimura K, Urakawa R et al. Variations in the morphology of Rhizomucor pusillus in granulomatous lesions of a Magellanic penguin (*Spheniscus magellanicus*). *J Vet Med Sci.* 2015; 77: 1029–1031.
61. Jeffrey JS, Chin RP, Shivaprasad HL et al. Proventriculitis and ventriculitis associated with zygomycosis in ostrich chicks. *Avian Dis.* 1994; 38: 630–634.
62. Gulbahar MY, Agaoglu Z, Biyik H et al. Zygomycotic proventriculitis and ventriculitis in ostriches (*Struthio camelus*) with impaction. *Aust Vet J.* 2000; 78: 247–249.
63. Carrasco L, Gomez-Villamandos JC, Jensen HE. Systemic candidosis and concomitant aspergillosis and zygomycosis in two Amazon parakeets (*Amazona aestiva*). *Mycoses.* 1998; 41: 297–301.
64. de los Monteros AE, Carrasco L, King JM et al. Nasal zygomycosis and pulmonary aspergillosis in an American bison. *J Wildl Dis.* 1999; 35: 790–795.
65. Barnett JE, Davison NJ, Thornton SM et al. Systemic mucormycosis in a hooded seal (*Cystophora cristata*). *J Zoo Wildl Med.* 2011; 42: 338–341.
66. Moran G, Coleman D, Sullivan D. An introduction to the medically important *Candida* species. In: Calderone RA, Clancy CJ, eds., *Candida and Candidiasis*, Washington, DC: ASM Press, 2012.
67. Yapar N. Epidemiology and risk factors for invasive candidiasis. *Ther Clin Risk Manag.* 2014; 10: 95–105.
68. Bassetti M, Merelli M, Righi E et al. Epidemiology, species distribution, antifungal susceptibility, and outcome of candidemia across five sites in Italy and Spain. *J Clin Microbiol.* 2013; 51: 4167–4172.
69. Diekema D, Arbefeville S, Boyken L et al. The changing epidemiology of healthcare-associated candidemia over three decades. *Diagn Microbiol Infect Dis.* 2012; 73: 45–48.
70. Lewis RE. Overview of the changing epidemiology of candidemia. *Curr Med Res Opin.* 2009; 25: 1732–1740.
71. Maubon D, Garnaud C, Calandra T et al. Resistance of *Candida* spp. to antifungal drugs in the ICU: where are we now? *Intensive Care Med.* 2014; 40: 1241–1255.
72. Pappas PG. Invasive candidiasis. *Infect Dis Clin North Am.* 2006; 20: 485–506.
73. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. *Clin Microbiol Rev* 2007; 20: 133–163.
74. Odds FC. Ecology of *Candida* and Epidemiology of Candidosis. In: *Candida and Candidosis*. London: Bailliere Tindall, 1988: 68–93.
75. Al-Yasiri MH, Normand AC, Piarroux R et al. Gut yeast communities in *Larus michahellis* from various breeding colonies. *Med Mycol.* 2016; 55: 436–444.
76. Pacynska JA. Yeast-like fungi and yeasts isolated from healthy breeding horses. *Polish J Vet Sci.* 2013; 16: 69–76.
77. Rozanski P, Slaska B, Rozanska D. Prevalence of yeasts in English full blood mares. *Mycopathologia.* 2013; 175: 339–344.
78. Brito EH, Fontenelle RO, Brilhante RS et al. The anatomical distribution and antimicrobial susceptibility of yeast species isolated from healthy dogs. *Vet J.* 2009; 182: 320–326.
79. Odds FC, Davidson AD, Jacobsen MD et al. *Candida albicans* strain maintenance, replacement, and microvariation demonstrated by multilocus sequence typing. *J Clin Microbiol.* 2006; 44: 3647–3658.
80. Nucci M, Anaissie E. Revisiting the source of candidemia: skin or gut? 2001; 33: 1959–1967.
81. Van Cutsem J, Rochette F. *Mycoses in Domestic Animals*. Beerse, Belgium: Janssen Research Foundation, 1991.
82. Quinn BKM PJ, Carter ME, Doennelly WJ, Leonard FC. *Veterinary Microbiology and Microbial Disease*. Oxford, UK: Blackwell Science, 2002.
83. Pohlman LM, Chengappa MM. *Veterinary Microbiology; Yeasts—Cryptococcus, Malassezia, and Candida*: Wiley-Blackwell, 2013.
84. Eggimann P, Pittet D. *Candida* colonization index and subsequent infection in critically ill surgical patients: 20 years later. *Intensive Care Med.* 2014; 40: 1429–1448.
85. Kullberg BJ, Arendrup MC. Invasive Candidiasis. *N Engl J Med.* 2015; 373: 1445–1456.
86. Yurayart C, Chindamporn A, Suradhat S et al. Comparative analysis of the frequency, distribution and population sizes of yeasts associated with canine seborrheic dermatitis and healthy skin. *Vet Microbiol.* 2011; 148: 356–362.
87. Lee HA, Hong S, Choe O et al. Mural folliculitis and alopecia with cutaneous candidiasis in a beagle dog. *Lab Animal Res.* 2011; 27: 63–65.
88. Moretti A, Posteraro B, Boncio L et al. Diffuse cutaneous candidiasis in a dog: diagnosis by PCR-REA. *Rev Iberoam Micolog.* 2004; 21: 139–142.
89. Mueller RS, Bettenay SV, Shipstone M. Cutaneous candidiasis in a dog caused by *Candida guilliermondii. Vet Rec.* 2002; 150: 728–730.
90. McEwan NA. Malassezia and *Candida* infections in bull terriers with lethal acrodermatitis. *J Small Anim Pract.* 2001; 42: 291–297.
91. Blanco JL, Guedeja-Marron J, Hontecillas R et al. Microbiological diagnoses of chronic otitis externa in the dog. *Zentralbl Veterinarmed B.* 1996; 43: 475–482.
92. Dale JE. Canine dermatosis caused by *Candida parapsilosis. Vet Med.* 1972; 67: 548–549.
93. McKellar QA, Rycroft A, Anderson L et al. Otitis externa in a foxhound pack associated with *Candida albicans. Veterinary Rec.* 1990; 127: 15–16.
94. Bernardo FM, Martins HM, Martins ML. A survey of mycotic otitis externa of dogs in Lisbon. *Rev Iberoam Micolog.*1998; 15: 163–165.
95. Redig P. Mycotic infections in birds II: *Candida*, Cryptococcosis and avian gastric bacteria (FKA Megabacteria). North American Veterinary Conference. Orlando, FL, USA.
96. Dhama K, Chakraborty S, Verma AK et al. Fungal/mycotic diseases of poultry-diagnosis, treatment and control: a review. *Pak J Biol Ssci.* 2013; 16: 1626–1640.
97. Harrison GJ, Lightfoot T. *Clinical Avian Medicine. **1***. Palm Beach, FL: Spix Publishing, 2005.
98. McClure JJ, Addison JD, Miller RI. Immunodeficiency manifested by oral candidiasis and bacterial septicemia in foals. *J Am Vet Med Assoc.* 1985; 186: 1195–1197.
99. Gross TL, Mayhew IG. Gastroesophageal ulceration and candidiasis in foals. *J Am Vet Med Assoc.* 1983; 182: 1370–1373.
100. Zlotowski P, Rozza DB, Pescador CA et al. Muco-cutaneous candidiasis in two pigs with postweaning multisystemic wasting syndrome. *Vet J.* 2006; 171: 566–569.
101. Bradford K, Meinkoth J, McKeirnen K et al. *Candida* peritonitis in dogs: report of 5 cases. *Vet Clin Pathol.* 2013; 42: 227–233.
102. Ong RK, Raisis AL, Swindells KL. *Candida albicans* peritonitis in a dog. *J Vet Emerg Cri Care.* 2010; 20: 143–147.
103. Burgess HJ, Gaunt MC. Pathology in practice: Peritonitis caused by C *albicans* infection in a dog. *J Am Vet Med Assoc.* 2014; 245: 1107–1109.

104. Rogers CL, Gibson C, Mitchell SL et al. Disseminated candidiasis secondary to fungal and bacterial peritonitis in a young dog. *J Vet Emerg Crit Care*. 2009; 19: 193–198.
105. Duchaussoy AC, Rose A, Talbot JJ et al. Gastrointestinal granuloma due to *Candida albicans* in an immunocompetent cat. *Med Mycol Case Rep*. 2015; 10: 14–17.
106. Kano R, Hattori Y, Okuzumi K et al. Detection and identification of the *Candida* species by 25S ribosomal DNA analysis in the urine of candidal cystitis. *J Vet Med Sci*. 2002; 64: 115–117.
107. Pressler BM, Vaden SL, Lane IF et al. *Candida* spp. urinary tract infections in 13 dogs and seven cats: predisposing factors, treatment, and outcome. *J Am Anim Hosp Assoc*. 2003; 39: 263–270.
108. Alvarez-Perez S, Garcia ME, Cutuli MT et al. Acquired multi-azole resistance in *Candida tropicalis* during persistent urinary tract infection in a dog. *Med Mycol Case Rep*. 2016; 11: 9–12.
109. Ozawa H, Okabayashi K, Kano R et al. Rapid identification of *Candida tropicalis* from canine cystitis. *Mycopathologia*. 2005; 160: 159–162.
110. Toll J, Ashe CM, Trepanier LA. Intravesicular administration of clotrimazole for treatment of candiduria in a cat with diabetes mellitus. *J Am Vet Med Assoc*. 2003; 223: 1156–1158, 29.
111. Jin Y, Lin D. Fungal urinary tract infections in the dog and cat: a retrospective study (2001-2004). *J Am Anim Hosp Assoc*. 2005; 41: 373–381.
112. Fulton RB, Jr., Walker RD. *Candida albicans* urocystitis in a cat. *J Am Vet Med Assoc*. 1992; 200: 524–526.
113. Enders A, van der Woerdt A, Donovan T. Endogenous mycotic endophthalmitis in a dog with candiduria and Evans syndrome. *Vet Ophthalmol*. 2017; 20: 84–88.
114. Sikdar A, Singh G, Banerjee MC et al. Isolation of *Candida pseudotropicalis* from cases of abortion among mares: a note. *Indian J Animal Sci*. 1972; 42: 737–738.
115. Stefanetti V, Marenzoni ML, Lepri E et al. A case of *Candida guilliermondii* abortion in an Arab mare. *Med Mycol Case Rep*. 2014; 4: 19–22.
116. Sanford SE, Josephson GK. Ontario. *Candida parapsilosis* abortion in a cow. *Can Vet J*. 1988; 29: 458.
117. Foley GL, Schlafer DH. *Candida* abortion in cattle. *Vet Pathol*. 1987; 24: 532–536.
118. Wohlgemuth K, Knudtson W. Bovine abortion associated with *Candida tropicalis*. *J Am Vet Med Assoc*. 1973; 162: 460–461.
119. de Casia dos Santos R, Marin JM. Isolation of *Candida* spp. from mastitic bovine milk in Brazil. *Mycopathologia*. 2005; 159: 251–253.
120. Scaccabarozzi L, Locatelli C, Pisoni G et al. Short communication: Epidemiology and genotyping of *Candida rugosa* strains responsible for persistent intramammary infections in dairy cows. *J Dairy Sci*. 2011; 94: 4574–4577.
121. Krukowski H, Tietze M, Majewski T et al. Survey of yeast mastitis in dairy herds of small-type farms in the Lublin region, Poland. *Mycopathologia*. 2001; 150: 5–7.
122. Costa EO, Gandra CR, Pires MF et al. Survey of bovine mycotic mastitis in dairy herds in the State of Sao Paulo, Brazil. *Mycopathologia*. 1993; 124: 13–17.
123. Kitamura H, Anri A, Fuse K et al. Chronic mastitis caused by *Candida maltosa* in a cow. *Vet Pathol*. 1990; 27: 465–466.
124. Elad D, Shpigel NY, Winkler M et al. Feed contamination with *Candida krusei* as a probable source of mycotic mastitis in dairy cows. *J Am Vet Med Assoc*. 1995; 207: 620–622.
125. Spanamberg A, Wunder EA, Jr., Brayer Pereira DI et al. Diversity of yeasts from bovine mastitis in Southern Brazil. *Rev Iber Micol*. 2008; 25: 154–156.
126. Aalbaek B, Stenderup J, Jensen HE et al. Mycotic and algal bovine mastitis in Denmark. *APMIS*. 1994; 102: 451–456.
127. Farnsworth RJ, Sorensen DK. Prevalence and species distribution of yeast in mammary glands of dairy cows in Minnesota. *Can J Comp Med*. 1972; 36: 329–332.
128. Crawshaw WM, MacDonald NR, Duncan G. Outbreak of *Candida rugosa* mastitis in a dairy herd after intramammary antibiotic treatment. *Vet Rec*. 2005; 156: 812–813.
129. Dworecka-Kaszak B, Krutkiewicz A, Szopa D et al. High prevalence of *Candida* yeast in milk samples from cows suffering from mastitis in poland. *Sci World J*. 2012; 2012: 196347.
130. Farnsworth RJ. Significance of fungal mastitis. *J Am Vet Med Assoc*. 1977; 170: 1173–1174.
131. Gaudie CM, Wragg PN, Barber AM. Outbreak of disease due to *Candida krusei* in a small dairy herd in the UK. *Veterinary Rec*. 2009; 165: 535–537.
132. Hayashi T, Sugita T, Hata E et al. Molecular-based identification of yeasts isolated from bovine clinical mastitis in Japan. *J Vet Med Sci*. 2013; 75: 387–390.
133. Ksouri S, Djebir S, Hadef Y et al. Survey of bovine mycotic mastitis in different mammary gland statuses in two north-eastern regions of Algeria. *Mycopathologia*. 2015; 179: 327–331.
134. Zhou Y, Ren Y, Fan C et al. Survey of mycotic mastitis in dairy cows from Heilongjiang Province, China. *Trop Animal Health Pprod*. 2013; 45: 1709–1714.
135. Richard JL, McDonald JS, Fichtner RE et al. Identification of yeasts from infected bovine mammary glands and their experimental infectivity in cattle. *Am J Vet Res*. 1980; 41: 1991–1994.
136. Kwon-Chung KJ, Bennett JE, Wickes BL et al. The case for adopting the "species complex" nomenclature for the etiologic agents of cryptococcosis. *mSphere*. 2017; 2.
137. Meyer W, Aanensen DM, Boekhout T et al. Consensus multi-locus sequence typing scheme for *Cryptococcus neoformans* and *Cryptococcus gattii*. *Med Mycol*. 2009; 47: 561–570.
138. Kwon-Chung KJ, Varma A. Do major species concepts support one, two or more species within Cryptococcus neoformans? *Fems Yeast Res*. 2006; 6: 574–587.
139. Boekhout T, Theelen B, Diaz M et al. Hybrid genotypes in the pathogenic yeast *Cryptococcus neoformans*. *Microbiology*. 2001; 147: 891–907.
140. Harris J, Lockhart S, Chiller T. *Cryptococcus gattii*: where do we go from here? *Med Mycol*. 2012; 50: 113–129.
141. Weber A, Schafer R. The occurrence of Cryptococcus neoformans in fecal samples from birds kept in human living areas. *Berl Munch Tierarztl Wochenschr*. 1991; 104: 419–421.
142. Lazera MS, Cavalcanti MA, Trilles L et al. *Cryptococcus neoformans* var. *gattii*—evidence for a natural habitat related to decaying wood in a pottery tree hollow. *Med Mycol*. 1998; 36: 119–122.
143. Ellis DH, Pfeiffer TJ. Natural habitat of *Cryptococcus neoforman*s var. *gattii*. *J Clin Microbiol*. 1990; 28: 1642–1644.
144. Gilad A, Bakal-Weiss M, Blum SE et al. Environmental survey for *Cryptococcus gattii* in an Israeli zoo populated with animals originating from Australia. *Isr J Vet Med*. 2015; 70: 47–51.
145. Voelz K, Johnston SA, Smith LM et al. 'Division of labour' in response to host oxidative burst drives a fatal *Cryptococcus gattii* outbreak. *Nat Commun*. 2014; 5: 5194.
146. de Abreu DPB, Machado CH, Makita MT et al. Intestinal lesion in a dog due to *Cryptococcus gattii* Type VGII and review of published cases of canine gastrointestinal cryptococcosis. *Mycopathologia*. 2017; 182: 597–602.
147. Kidd SE, Hagen F, Tscharke RL et al. A rare genotype of *Cryptococcus gattii* caused the cryptococcosis outbreak on Vancouver Island (British Columbia, Canada). *Proc Natl Acad Sci U S A*. 2004; 101: 17258–17263.
148. Castella G, Abarca ML, Cabanes FJ. Cryptococcosis and pets. *Rev Iber Micol*. 2008; 25: S19–24.
149. Pal M, Mehrotra BS. Cryptococcal mastitis in dairy animals. *Mykosen*. 1983; 26: 615–616.
150. Secombe CJ, Lester GD, Krockenberger MB. Equine pulmonary cryptococcosis: a comparative literature review and evaluation of fluconazole monotherapy. *Mycopathologia*. 2017; 182: 413–423.
151. Stephen C, Lester S, Black W et al. Multispecies outbreak of cryptococcosis on southern Vancouver Island, British Columbia. *Can Vet J*. 2002; 43: 792–794.

152. Duncan C, Stephen C, Campbell J. Clinical characteristics and predictors of mortality for Cryptococcus gattii infection in dogs and cats of southwestern British Columbia. *Can Vet J*. 2006; 47: 993–998.
153. Headley SA, Mota FC, Lindsay S et al. *Cryptococcus neoformans* var. *grubii*-induced arthritis with encephalitic dissemination in a dog and review of published literature. *Mycopathologia*. 2016; 181: 595–601.
154. GarciaHermoso D, MathoulinPelissier S, Couprie B et al. DNA typing suggests pigeon droppings as a source of pathogenic *Cryptococcus neoformans* serotype D. *J Clin Microbiol*. 1997; 35: 2683–2685.
155. Hajjeh RA, Conn LA, Stephens DS et al. Cryptococcosis: population-based multistate active surveillance and risk factors in human immunodeficiency virus-infected persons. *Cryptococcal Active Surveillance Group*. *J Infect Dis*. 1999; 179: 449–454.
156. Elad D. Immunocompromised patients and their pets: still best friends? *Vet J*. 2013; 197: 662–669.
157. Yamamoto Y, Kohno S, Koga H et al. Random amplified polymorphic DNA analysis of clinically and environmentally isolated *Cryptococcus neoformans* in Nagasaki. *J Clin Microbiol*. 1995; 33: 3328–3332.
158. Sangiorgi G. Blastomicosi spontanea nei muridi. *Pathology*. 1922; 14: 493–495.
159. Emmons CW, Bell JA, Olson BJ. Naturally occurring histoplasmosis in *Mus musculus* and *Rattus norvegicus*. *Publ Health Rec*. 1947; 62: 1642–1646.
160. Singh SM, Naidu J, Sharma A et al. First case of cryptococcosis in a new species of bandicoot (*Bandicota indica*) caused by *Cryptococcus neoformans* var. *grubii*. *Med Mycol*. 2007; 45: 89–93.
161. Singh K, Rani J, Neelabh Rai GK, Singh M. The Southeastern Asian house mouse (*Mus musculus* castaneus Linn.) as a new passenger host for *Cryptococcus neoformans* var. *grubii* molecular type VNI. *Med Mycol* 2017; doi: 10.1093/mmy/myx001.
162. Aplin KP, Suzuki H, Chinen AA et al. Multiple geographic origins of commensalism and complex dispersal history of black rats. *PLoS One*. 2011; 6: e26357.
163. Morera N, Hagen F, Juan-Salles C et al. Ferrets as sentinels of the presence of pathogenic *Cryptococcus* species in the Mediterranean environment. *Mycopathologia*. 2014; 178: 145–151.
164. Seyedmousavi S, Guillot J, de Hoog GS. Phaeohyphomycoses, emerging opportunistic diseases in animals. *Clin Microbiol Rev*. 2013; 26: 19–35.
165. Revankar SG, Sutton DA. Melanized fungi in human disease. *Clin Microbiol Rev*. 2010; 23: 884–928.
166. Yanong RP. Fungal diseases of fish. *Vet Clin North Am*. 2003; 6: 377–400.
167. Densmore CL, Green DE. Diseases of amphibians. *Ilar J*. 2007; 48: 235–254.
168. Boeger WA, Pie MR, Ostrensky A et al. Lethargic crab disease: multidisciplinary evidence supports a mycotic etiology. *Mem Inst Oswaldo Cruz*. 2005; 100: 161–167.
169. Boeger WA, Pie MR, Vicente V et al. Histopathology of the mangrove land crab *Ucides cordatus* (Ocypodidae) affected by lethargic crab disease. *Dis Aquat Org*. 2007; 78: 73–81.
170. Frank C, Vemulapalli R, Lin T. Cerebral phaeohyphomycosis due to *Cladophialophora bantiana* in a *Huacaya alpaca* (*Vicugna pacos*). *J Comp Pathol*. 2011; 145: 410–413.
171. Haligur M, Ozmen O, Dorrestein GM. Fatal systemic cladosporiosis in a merino sheep flock. *Mycopathologia*. 2010; 170: 411–415.
172. Seyedmousavi S, Netea MG, Mouton JW et al. Black yeasts and their filamentous relatives: principles of pathogenesis and host defense. *Clin Microbiol Rev*. 2014; 27: 527–542.
173. de Hoog GS, Vicente VA, Najafzadeh MJ et al. Waterborne *Exophiala* species causing disease in cold-blooded animals. *Persoonia*. 2011; 27: 46–72.
174. Queiroz-Telles F, de Hoog S, Santos DW et al. Chromoblastomycosis. *Clin Microbiol Rev*. 2017; 30: 233–276.
175. Velasquez LFV, Restrepo AM. Chromomycosis in the toad (*Bufo marinus*) and a comparison of the etiologic agent with fungi causing human chromomycosis. *Sabouraudia*. 1975; 13: 1–9.
176. Bube A, Burkhardt E, Weiss R. Spontaneous chromomycosis in the marine toad (*Bufo marinus*). *J Comp Pathol*. 1992; 106: 73–77.
177. Langvad F, Pedersen O, Engjom K. A fungal disease caused by Exophiala sp. nov in farmed Atlantic salmon in Western Norway. In: *Fish and Shellfish Pathology*. London: Academic, 1985.
178. Carvalho TF, Tinoco HP, Malta MCP et al. Systemic infection by *Spencermartinsiella* sp. in a Nile crocodile (*Crocodylus niloticus*). *Braz J Vet Res Anim Sci*. 2016; 53: 1–7.
179. Gaskins JE, Cheung PJ. *Exophiala pisciphila*: A study of its development. *Mycopathologia*. 1986; 93: 173–184.
180. Nyaoke A, Weber ES, Innis C et al. Disseminated phaeohyphomycosis in weedy seadragons (*Phyllopteryx taeniolatus*) and leafy seadragons (*Phycodurus eques*) caused by species of *Exophiala*, including a novel species. *J Vet Diagn Invest*. 2009; 21: 69–79.
181. Pollacci G. Miceti del corpo umano e degli animali. *Sci Botan Med*. 1923; 18: 1–9.
182. Manharth A, Lemberger K, Mylniczenko N et al. Disseminated phaeohyphomycosis due to Exophiala species in a Galapagos tortoise, *Geochelone nigra*. *J Herpetol Med Surg*. 2005; 15: 20–26.
183. Vicente VA, Orelis-Ribeiro R, Najafzadeh MJ et al. Black yeast-like fungi associated with lethargic crab disease (LCD) in the mangrove-land crab, *Ucides cordatus* (Ocypodidae). *Vet Microbiol*. 2012; 158: 109–122.
184. Miller EA, Montali RJ, Ramsay EC et al. Disseminated chromoblastomycosis in a colony of ornate-horned frogs (*Ceratophrys ornata*). *J Zoo Wildlife Med*. 1992; 23: 433–438.
185. Elkan E, Philpot CM. Mycotic infections in frogs due to a *Phialophora*-like fungus. *Sabouraudia*. 1973; 11: 99–105.
186. Fisher MC, Koenig GL, White TJ et al. Molecular and phenotypic description of *Coccidioides posadasii* sp. nov., previously recognized as the non-California population of *Coccidioides immitis*. *Mycologia*. 2002; 94: 73–84.
187. Barker MB. Coccidioidomycosis in animals. In: Seyedmousavi S, Guillot J, De Hoog S et al., eds. *Emerging and Epidemic Fungal Infections in Animals*. New York.: Springer, 2017.
188. De Hoog S, Guarro J, Gene J. *Atlas of Clinical Fungi: The Ultimate Benchtool for Diagnostics*. Utrecht, Netherlands: *Centraalbureau voor Schimmelcultures*, KNAW Fungal. Biodiversity Centre/Universitat Rovira i Virgili, 2009.
189. Guillot J, Guérin C, Chermette R. Histoplasmosis in animals. In: Seyedmousavi S, Guillot J, De Hoog S et al., eds. *Emerging and Epidemic Fungal Infections in Animals*. New York: Springer, 2017.
190. Brummer E, Castaneda E, Restrepo A. Paracoccidioidomycosis: an update. *Clin Microbiol Rev*. 1993; 6: 89–117.
191. Bocca AL, Amaral AC, Teixeira MM et al. Paracoccidioidomycosis: eco-epidemiology, taxonomy and clinical and therapeutic issues. *Future Microbiol*. 2013; 8: 1177–1191.
192. Teixeira MM, Theodoro RC, Nino-Vega G et al. Paracoccidioides species complex: ecology, phylogeny, sexual reproduction, and virulence. *PLoS Pathog*. 2014; 10: e1004397.
193. Shikanai-Yasuda MA, Telles Filho F de Q, Mendes RP et al. Guidelines in paracoccidioidomycosis. *Rev Soc Bras Med Trop*. 2006; 39: 297–310.
194. Coutinho ZF, Wanke B, Travassos C et al. Hospital morbidity due to paracoccidioidomycosis in Brazil (1998–2006). *Trop Med Int Health*. 2015; 20: 673–680.
195. Ricci G, Mota FT, Wakamatsu A, Serafim RC, Borra RC, Franco M. Canine paracoccidioidomycosis. *Med Mycol*. 2004; 42: 379–383.
196. Farias MR, Condas LAZ, Ribeiro MG et al. Paracoccidioidomycosis in a dog: case report of generalized lymphadenomegaly. *Mycopathologia*. 2011; 172: 147–152.
197. Bagagli E, Franco M, Bosco Sde M et al. High frequency of *Paracoccidioides brasiliensis* infection in armadillos (*Dasypus novemcinctus*): an ecological study. *Med Mycol*. 2003; 41: 217–223.
198. Bradsher RW, Jr. The endemic mimic: blastomycosis an illness often misdiagnosed. *Trans Am Clin Climatol Assoc*. 2014; 125: 188–202; discussion -3.

199. Gilchrist TC, Stokes WR. A case of pseudo-*Lupus vulgaris* caused by a blastomyces. *J Exp Med*. 1898; 3: 53–78.
200. Baumgardner DJ, Paretsky DP, Yopp AC. The epidemiology of blastomycosis in dogs: north central Wisconsin, USA. *J Med Vet Mycol*. 1995; 33: 171–176.
201. Herrmann JA, Kostiuk SL, Dworkin MS et al. Temporal and spatial distribution of blastomycosis cases among humans and dogs in Illinois (2001–2007). *J Am Vet Med A*. 2011; 239: 335–343.
202. Sykes JE, Merkel LK. Blastomycosis. In: Sykes JE, ed. *Canine and Feline Infectious Diseases*. St. Louis, MO: Elsevier, 2014, 574–586.
203. Van Rooij P, Martel A, Haesebrouck F et al. Amphibian chytridiomycosis: a review with focus on fungus-host interactions. *Vet Res*. 2015; 46: 137.
204. Berger L, Speare R, Daszak P et al. Chytridiomycosis causes amphibian mortality associated with population declines in the rain forests of Australia and Central America. *Proc Natl Acad Sci U S A*. 1998; 95: 9031–9036.
205. Lips K, Diffendorfer J, Mendelson IJ et al. Riding the wave: reconciling the roles of disease and climate change in amphibian declines. *PLoS Biology*. 2008; 6: 441–454.
206. Skerratt LF, Berger L, Speare R et al. Spread of chytridiomycosis has caused the rapid global decline and extinction of frogs. *Ecohealth*. 2007; 4: 125–134.
207. Rovito SM, Parra-Olea G, Vasquez-Almazan CR et al. Dramatic declines in neotropical salamander populations are an important part of the global amphibian crisis. *Proc Natl Acad Sci U S A*. 2009; 106: 3231–3236.
208. Farrer RA, Weinert LA, Bielby J et al. Multiple emergences of genetically diverse amphibian-infecting chytrids include a globalized hypervirulent recombinant lineage. *P Natl Acad Sci U S A*. 2011; 108: 18732–18736.
209. Schmeller DS, Blooi M, Martel A et al. Microscopic aquatic predators strongly affect infection dynamics of a globally emerged pathogen. *Curr Biol*. 2014; 24: 176–180.
210. Rosa GM, Sabino-Pinto J, Laurentino TG et al. Impact of asynchronous emergence of two lethal pathogens on amphibian assemblages. *Sci Rep*. 2017; 7: 43260.
211. Pasmans F, Van Rooij P Blooi M et al. Resistance to chytridiomycosis in European plethodontid salamanders of the genus *Speleomantes*. *PloS One*. 2013; 8: e63639.
212. Martel A, Blooi M, Adriaensen C et al. Recent introduction of a chytrid fungus endangers Western Palearctic salamanders. *Science*. 2014; 346: 630–631.
213. Spitzen-van der Sluijs A, Martel A, Asselberghs J et al. Expanding distribution of lethal amphibian fungus *Batrachochytrium salamandrivorans* in Europe. *Emerg Infect Dis*. 2016; 22: 1286–1288.
214. Stegen G, Pasmans F, Schmidt BR et al. Drivers of salamander extirpation mediated by *Batrachochytrium salamandrivorans*. *Nature*. 2017; 544: 353–356.
215. Laking AE, Ngo HN, Pasmans F et al. *Batrachochytrium salamandrivorans* is the predominant chytrid fungus in Vietnamese salamanders. *Sci Rep*. 2017; 7: 44443.
216. Kolby JE, Smith KM, Berger L et al. First evidence of amphibian chytrid fungus (*Batrachochytrium dendrobatidis*) and ranavirus in Hong Kong amphibian trade. *PLoS One*. 2014; 9: e90750.
217. Grogan LF, Berger L, Rose K et al. Surveillance for emerging biodiversity diseases of wildlife. *PLoS Pathog*. 2014; 10: e1004015.
218. Garner TW, Schmidt BR, Martel A et al. Mitigating amphibian chytridiomycoses in nature. *Philos Trans R Soc Lond B Biol Sci*. 2016; 371; doi: 10.1098/rstb.2016.0207.
219. McMahon TA, Sears BF, Venesky MD et al. Amphibians acquire resistance to live and dead fungus overcoming fungal immunosuppression. *Nature*. 2014; 511: 224–227.
220. Bosch J, Sanchez-Tome E, Fernandez-Loras A et al. Successful elimination of a lethal wildlife infectious disease in nature. *Biol Lett*. 2015; 11: 20150874.
221. Bletz MC, Loudon AH, Becker MH et al. Mitigating amphibian chytridiomycosis with bioaugmentation: characteristics of effective probiotics and strategies for their selection and use. *Ecol Lett*. 2013; 16: 807–820.

222. Schmeller DS, Blooi M, Martel A et al. Microscopic aquatic predators strongly affect infection dynamics of a globally emerged pathogen. *Curr Biol*. 2014; 24: 176–180.

223. Blehert DS, Hicks AC, Behr M et al. Bat white-nose syndrome: an emerging fungal pathogen? *Science*. 2009; 323: 227.
224. Gargas A, Trest MT, Christensen M et al. Geomyces destructans sp nov associated with bat white-nose syndrome. *Mycotaxon*. 2009; 108: 147–154.
225. Lorch JM, Meteyer CU, Behr MJ et al. Experimental infection of bats with *Geomyces destructans* causes white-nose syndrome. *Nature*. 2011; 480: 376–378.
226. Minnis AM, Lindner DL. Phylogenetic evaluation of *Geomyces* and allies reveals no close relatives of *Pseudogymnoascus destructans*, comb. nov., in bat hibernacula of eastern North America. *Fungal Biol*. 2013; 117: 638–649.
227. Frick WF, Puechmaille SJ, Hoyt JR et al. Disease alters macroecological patterns of North American bats. *Global Ecol Biogeogr*. 2015; 24: 741–749.
228. Meteyer CU, Buckles EL, Blehert DS et al. Histopathologic criteria to confirm white-nose syndrome in bats. *J Vet Diagn Invest*. 2009; 21: 411–414.
229. Cryan PM, Meteyer CU, Boyles JG et al. Wing pathology of white-nose syndrome in bats suggests life-threatening disruption of physiology. *BMC Biol*. 2010; 8: 135.
230. Warnecke L, Turner JM, Bollinger TK et al. Pathophysiology of white-nose syndrome in bats: a mechanistic model linking wing damage to mortality. *Biol Lett*. 2013; 9: 20130177.
231. Lorch JM, Palmer JM, Lindner DL et al. First Detection of Bat White-Nose Syndrome in Western North America. *mSphere*. 2016; 1; doi: 10.1128/mSphere.00148-16.
232. Rajkumar SS, Li XJ, Rudd RJ et al. Clonal genotype of geomyces destructans among bats with white nose syndrome, New York, USA. *Emerg Infect Dis*. 2011; 17: 1273–1276.
233. Puechmaille SJ, Wibbelt G, Korn V et al. Pan-European distribution of white-nose syndrome fungus (*Geomyces destructans*) not associated with mass mortality. *PloS One*. 2011; 6: e19167.
234. Leopardi S, Blake D, Puechmaille SJ. White-nose syndrome fungus introduced from Europe to North America. *Curr Biol*. 2015; 25: R217–219.
235. Maine JJ, Boyles JG. Bats initiate vital agroecological interactions in corn. *Proc Natl Acad Sci U S A*. 2015; 112: 12438–12443.
236. Chermette R, Ferreiro L, Guillot J. Dermatophytoses in animals. *Mycopathologia*. 2008; 166: 385–405.
237. Mignon BR, Losson BJ. Prevalence and characterization of *Microsporum canis* carriage in cats. *J Med Vet Mycol*. 1997; 35: 249–256.
238. Moriello KA, Coyner K, Paterson S, Mignon B. Diagnosis and treatment of dermatophytosis in dogs and cats.: Clinical Consensus Guidelines of the World Association for Veterinary Dermatology. *Vet Dermatol*. 2017; 28: 266–e68.
239. Vermout S, Tabart J, Baldo A et al. Pathogenesis of dermatophytosis. *Mycopathologia*. 2008; 166: 267–275.
240. Brouta F, Descamps F, Monod M et al. Secreted metalloprotease gene family of *Microsporum canis*. *Infect Immun*. 2002; 70: 5676–5683.
241. Mignon B, Swinnen M, Bouchara JP et al. Purification and characterization of a 315 kDa keratinolytic subtilisin-like serine protease from Microsporum canis and evidence of its secretion in naturally infected cats. *Med Mycol*. 1998; 36: 395–404.
242. Mignon BR, Leclipteux T, Focant C et al. Humoral and cellular immune response to a crude exo-antigen and purified keratinase of *Microsporum canis* in experimentally infected guinea pigs. *Med Mycol*. 1999; 37: 123–129.
243. Vermout S, Tabart J, Baldo A et al. RNA silencing in the dermatophyte Microsporum canis. *FEMS Microbiol Lett*. 2007; 275: 38–45.
244. Tabart J, Baldo A, Vermout S et al. Reconstructed interfollicular feline epidermis as a model for *Microsporum canis* dermatophytosis. *J Med Microbiol*. 2007; 56: 971–975.

245. Baldo A, Mathy A, Tabart J et al. Secreted subtilisin Sub3 from *Microsporum canis* is required for adherence to but not for invasion of the epidermis. *Brit J Dermatol*. 2010; 162: 990–997.
246. Mehul B, Gu Z, Jomard A et al. Sub6 (Tri r 2), an onychomycosis marker revealed by proteomics analysis of *Trichophyton rubrum* secreted proteins in patient nail samples. *J Invest Dermatol*. 2016; 136: 331–333.
247. Tran VD, De Coi N, Feuermann M et al. RNA sequencing-based genome reannotation of the dermatophyte *Arthroderma benhamiae* and characterization of its secretome and whole gene expression profile during infection. *mSystems*. 2016; 1: e00036–16.
248. Alshahni MM, Yamada T. Genetic manipulations in dermatophytes. *Mycopathologia*. 2017; 182: 33–43.
249. Cambier L, Heinen MP, Mignon B. Relevant animal models in dermatophyte research. *Mycopathologia*. 2017; 182: 229–240.
250. Marimon R, Cano J, Gené J et al. *Sporothrix brasiliensis*, *S. globosa*, and *S. mexicana*, three new *Sporothrix* species of clinical interest. *J Clin Microbiol*. 2007; 45: 3198–3206.
251. Rodrigues AM, Cruz Choappa R, Fernandes GF et al. *Sporothrix chilensis* sp. nov. (*Ascomycota*: *Ophiostomatales*), a soil-borne agent of human sporotrichosis with mild-pathogenic potential to mammals. *Fungal Biol*. 2016; 120: 246–264.
252. Zhang Y, Hagen F, Stielow B et al. Phylogeography and evolutionary patterns in *Sporothrix* spanning more than 14,000 human and animal case reports. *Persoonia*. 2015; 35: 1–20.
253. Rodrigues AM, de Hoog GS, Camargo ZP. *Sporothrix* species causing outbreaks in animals and humans driven by animal-animal transmission. *PLoS Pathog*. 2016: doi: 10.1371/journal.ppat.1005638.
254. Gremiao IDF, Miranda LHM, Reis EG et al. Zoonotic epidemic of sporotrichosis: cat to human transmission. *Plos Pathogens*. 2017; doi: 10.1371.jounal.ppat.1006677.
255. Schubach A, Schubach TM, Barros MB et al. Cat-transmitted sporotrichosis, Rio de Janeiro, Brazil. *Emerg Infect Dis*. 2005; 11: 1952–1954.
256. Pereira SA, Gremiao IDF, Kitada AAB et al. The epidemiological scenario of feline sporotrichosis in Rio de Janeiro, State of Rio de Janeiro, Brazil. *Rev Soc Bras Med Tro*. 2014; 47: 392–393.
257. Montenegro H, Rodrigues AM, Galvão Dias MA et al. Feline sporotrichosis due to *Sporothrix brasiliensis*: an emerging animal infection in São Paulo, Brazil. *BMC Vet Res*. 2014; 10: 269.
258. Sanchotene KO, Madrid IM, Klafke GB et al. *Sporothrix brasiliensis* outbreaks and the rapid emergence of feline sporotrichosis. *Mycoses*. 2015; 58: 652–658.
259. Alba-Fierro CA, Pérez-Torres A, Toriello C et al. Immune response induced by an immunodominant 60 kDa glycoprotein of the cell wall of *Sporothrix schenckii* in two mice strains with experimental sporotrichosis. *J Immunol Res*. 2016; 2016: 6525831.
260. Nascimento RC, Almeida SR. Humoral immune response against soluble and fractionate antigens in experimental sporotrichosis. *FEMS Immunol Med Microbiol*. 2005; 43: 241–247.
261. Niyo KA, Richard JL, Niyo Y et al. Effects of T-2 mycotoxin ingestion on phagocytosis of *Aspergillus fumigatus* conidia by rabbit alveolar macrophages and on hematologic, serum biochemical, and pathologic changes in rabbits. *Am J Vet Res*. 1988; 49: 1766–1773.
262. Niyo KA, Richard JL, Niyo Y et al. Pathologic, hematologic, and serologic changes in rabbits given T-2 mycotoxin orally and exposed to aerosols of *Aspergillus fumigatus* conidia. *Am J Vet Res*. 1988; 49: 2151–2160.
263. Aupanun S, Poapolathep S, Giorgi M et al. An overview of the toxicology and toxicokinetics of fusarenon-X, a type B trichothecene mycotoxin. *J Vet Med Sci*. 2017; 79: 6–13.
264. Kabak B, Dobson AD, Var I. Strategies to prevent mycotoxin contamination of food and animal feed: a review. *Crit Rev Food Sci Nutr*. 2006; 46: 593–619.
265. Kensler TW, Roebuck BD, Wogan GN et al. Aflatoxin: a 50-year odyssey of mechanistic and translational toxicology. *Toxicol Sci*. 2011; 120: S28–48.
266. Hussein HS, Brasel JM. Toxicity, metabolism, and impact of mycotoxins on humans and animals. *Toxicology*. 2001; 167: 101–134.
267. Bennett JW, Klich M. Mycotoxins. *Clin Microbiol Rev*. 2003; 16: 497–516.
268. Reeves EP, Messina CG, Doyle S et al. Correlation between gliotoxin production and virulence of *Aspergillus fumigatus* in *Galleria mellonella*. *Mycopathologia*. 2004; 158: 73–79.
269. Strosnider H, Azziz-Baumgartner E, Banziger M et al. Workgroup report: public health strategies for reducing aflatoxin exposure in developing countries. *Environ Health Perspect*. 2006; 114: 1898–1903.
270. Smith EE, Kubena LF, Braithwaite CE et al. Toxicological evaluation of aflatoxin and cyclopiazonic acid in broiler chickens. *Poult Sci*. 1992; 71: 1136–1144.
271. Barker AK, Stahl C, Ensley SM et al. Tremorgenic mycotoxicosis in dogs. *Compend Contin Educ Vet*. 2013; 35: E2.
272. Diekman MA, Green ML. Mycotoxins and reproduction in domestic livestock. *J Anim Sci*. 1992; 70: 1615–1627.
273. Diekman MA, Green ML. Mycotoxins and reproduction in domestic livestock. *J Anim Sci*. 1992; 70: 1615–1627.
274. Riet-Correa F, Rivero R, Odriozola E et al. Mycotoxicoses of ruminants and horses. *J Vet Diagn Invest*. 2013; 25: 692–708.
275. Duarte SC, Pena A, Lino CM. Human ochratoxin a biomarkers—from exposure to effect. *Crit Rev Toxicol*. 2011; 41: 187–212.
276. Scott PM. Biomarkers of human exposure to ochratoxin A. *Food Addit Contam*. 2005; 22: 99–107.
277. Lamb DC, Kelly DE, Schunck WH et al. The mutation T315A in *Candida albicans* sterol 14alpha-demethylase causes reduced enzyme activity and fluconazole resistance through reduced affinity. *J Biol Chem*. 1997; 272: 5682–5688.
278. Lamb DC, Kelly DE, White TC et al. The R467K amino acid substitution in *Candida albicans* sterol 14 alpha-demethylase causes drug resistance through reduced affinity. *Antimicrob Agents Chemother*. 2000; 44: 63–67.
279. Loffler J, Kelly SL, Hebart H et al. Molecular analysis of cyp51 from fluconazole-resistant *Candida albicans* strains. *FEMS Microbiol Lett*. 1997; 151: 263–268.
280. Vanden Bossche H, Marichal P, Gorrens J et al. Mutation in cytochrome *P*-450-dependent 14a-demethylase results in decreased affinity for azole antifungals. *Biochem Soc Trans*. 1990; 18: 56–9.
281. White TC. The presence of an R467K amino acid substitution and loss of allelic variation correlate with an azole-resistant lanosterol 14alpha demethylase in *Candida albicans*. *Antimicrob Agents Chemother*. 1997; 41: 1488–1494.
282. Franz R, Kelly SL, Lamb DC et al. Multiple molecular mechanisms contribute to a stepwise development of fluconazole resistance in clinical *Candida albicans* strains. *Antimicrob Agents Chemother*. 1998; 42: 3065–3072.
283. Lopez-Ribot JL, McAtee RK, Perea S et al. Multiple resistant phenotypes of *Candida albicans* coexist during episodes of oropharyngeal candidiasis in human immunodeficiency virus-infected patients. *Antimicrob Agents Chemother*. 1999; 43: 1621–1630.
284. Parkinson T, Falconer DJ, Hitchcock CA. Fluconazole resistance due to energy-dependent drug efflux in *Candida glabrata*. *Antimicrob Agents Chemother*. 1995; 39: 1696–1699.
285. Miyazaki H, Miyazaki Y, Geber A et al. Fluconazole resistance associated with drug efflux and increased transcription of a drug transporter gene, PDH1, in *Candida glabrata*. *Antimicrob Agents Chemother*. 1998; 42: 1695–1701.
286. Sanglard D, Ischer F, Calabrese D et al. The ATP binding cassette transporter gene CgCDR1 from *Candida glabrata* is involved in the resistance of clinical isolates to azole antifungal agents. *Antimicrob Agents Chemother*. 1999; 43: 2753–2765.
287. Katiyar SK, Edlind TD. Identification and expression of multidrug resistance-related ABC transporter genes in Candida krusei. *Med Mycol*. 2001; 39: 109–116.

288. Sanguinetti M, Posteraro B, Fiori B et al. Mechanisms of azole resistance in clinical isolates of Candida glabrata collected during a hospital survey of antifungal resistance. *Antimicrob Agents Chemother*. 2005; 49: 668–679.
289. Brun S, Berges T, Poupard P et al. Mechanisms of azole resistance in petite mutants of *Candida glabrata*. *Antimicrob Agents Chemother*. 2004; 48: 1788–1796.
290. Marr KA, Lyons CN, Rustad TR et al. Rapid, transient fluconazole resistance in *Candida albicans* is associated with increased mRNA levels of CDR. *Antimicrob Agents Chemother*. 1998; 42: 2584–2589.
291. Fling ME, Kopf J, Tamarkin A et al. Analysis of a *Candida albicans* gene that encodes a novel mechanism for resistance to benomyl and methotrexate. *Mol Gen Genet*. 1991; 227: 318–329.
292. Vermeulen E, Lagrou K, Verweij PE. Azole resistance in *Aspergillus fumigatus*: a growing public health concern. *Curr Opin Infect Dis*. 2013; 26: 493–500.
293. Seyedmousavi S, Mouton JW, Melchers WJ et al. The role of azoles in the management of azole-resistant aspergillosis: from the bench to the bedside. *Drug Resist Updat*. 2014; 17: 37–50.
294. Howard SJ, Cerar D, Anderson MJ et al. Frequency and evolution of azole resistance in *Aspergillus fumigatus* associated with treatment failure. *Emerg Infect Dis*. 2009; 15: 1068–1076.
295. Mellado E, Garcia-Effron G, Alcazar-Fuoli L et al. A new *Aspergillus fumigatus* resistance mechanism conferring in vitro cross-resistance to azole antifungals involves a combination of cyp51A alterations. *Antimicrob Agents Chemother*. 2007; 51: 1897–1904.
296. Beltaire KA, Cheong SH, Coutinho da Silva MA. Retrospective study on equine uterine fungal isolates and antifungal susceptibility patterns (1999–2011). *Equine Vet J Suppl*. 2012; 43: 84–87.
297. Cordeiro Rde A, de Oliveira JS, Castelo-Branco Dde S et al. *Candida tropicalis* isolates obtained from veterinary sources show resistance to azoles and produce virulence factors. *Med Mycol*. 2015; 53: 145–152.
298. Brilhante RS, Bittencourt PV, Castelo-Branco Dde S et al. Trends in antifungal susceptibility and virulence of *Candida* spp. from the nasolacrimal duct of horses. *Med Mycol*. 2016; 54: 147–154.
299. Brilhante RS, de Alencar LP, Cordeiro Rde A et al. Detection of *Candida* species resistant to azoles in the microbiota of rheas (*Rhea americana*): possible implications for human and animal health. *J Med Microbiol*. 2013; 62: 889–895.
300. Sidrim JJ, Maia DC, Brilhante RS et al. *Candida* species isolated from the gastrointestinal tract of cockatiels (*Nymphicus hollandicus*): in vitro antifungal susceptibility profile and phospholipase activity. *Vet Microbiol*. 2010; 145: 324–328.
301. Rocha MF, Bandeira SP, de Alencar LP et al. Azole resistance in *Candida albicans* from animals: highlights on efflux pump activity and gene overexpression. *Mycoses*. 2017; 60: 462–468.
302. Lord AT, Mohandas K, Somanath S et al. Multidrug resistant yeasts in synanthropic wild birds. *Ann Clin Microbiol Antimicrob*. 2010; 9: 11.
303. Al-Yasiri MH, Normand AC, L'Ollivier C et al. Opportunistic fungal pathogen Candida glabrata circulates between humans and yellow-legged gulls. *Sci Rep*. 2016; 6: 36157.
304. Brilhante RS, Castelo Branco DS, Duarte GP et al. Yeast microbiota of raptors: a possible tool for environmental monitoring. *Environ Microbiol Rep*. 2012; 4: 189–193.
305. Goncalves SS, Souza AC, Chowdhary A et al. Epidemiology and molecular mechanisms of antifungal resistance in *Candida* and *Aspergillus*. *Mycoses*. 2016; 59: 198–219.
306. Pfaller MA, Messer SA, Woosley LN et al. Echinocandin and triazole antifungal susceptibility profiles for clinical opportunistic yeast and mold isolates collected from 2010 to 2011: application of new CLSI clinical breakpoints and epidemiological cutoff values for characterization of geographic and temporal trends of antifungal resistance. *J Clin Microbiol*. 2013; 51: 2571–2581.
307. Verweij PE, Ananda-Rajah M, Andes D et al. International expert opinion on the management of infection caused by azole-resistant *Aspergillus fumigatus*. *Drug RResist Uupdat*. 2015; 21: 30–40.
308. Bunskoek PE, Seyedmousavi S, Gans SJ et al. Successful treatment of azole-resistant invasive aspergillosis in a bottlenose dolphin with high-dose posaconazole. *Med Mycol Case Rep*. 2017; 16: 16–19.
309. Seyedmousavi S, Wiederhold NP, Ebel F, Hedayati MT, Verweij PE. Antifungal use in veterinary practice and emergence of resistance. In Seyedmousavi S, Guillot JG, de Hoog GS, Verweij PE, eds. *Emerging and Epidemic Fungal Infections*. Springer; 2017. In press.