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A review on canine *Malassezia pachydermatis*

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Abstract
One of the difficult skin conditions caused by *Malassezia* yeast is *Malassezia pachydermatis*. *Malassezia dermatitis* (MD) is a highly itchy kind of dermatitis that solely produces erythema as its primary skin lesion and Secondary skin lesions include excoriations, seborrheic plaques, lichenification, maceration, and intertrigo. It is diagnosed by cytological investigation, and treatment options include antifungal medications and therapeutic assistance.

Keywords: Excoriations, seborrheic plaques, lichenification

Introduction
Dogs are one the closest companion animals to humans. According to Keat *et al*. (2016) [1], having a dog increases an owner's motivation to exercise and lowers stress levels. In addition, it is said that Balinese people keep dogs in practically every home for different reasons. However, as it has grown, numerous health issues, particularly those related to the skin, have been noted in dogs. Skin lesions are typically caused by primary, secondary, or combined illnesses in dermatitis cases in stray dogs (Widyastuti & Utama, 2012) [2]. *Malassezia* spp. is one of the infectious agents of concern that might harm pets and pet owners. According to Mauldin EA *et al*. (1997) [7], *Malassezia dermatitis* in dogs typically develops as a secondary issue as a result of underlying skin conditions such as allergic illness (including canine atopic dermatitis and flea allergy dermatitis), recurring bacterial pyoderma, and endocrine problems (particularly hypothyroidism).
According to Morris (1999) [6] and Brito *et al*. (2009) [40], the yeast *Malassezia pachydermatis* is commensal to canine skin and takes on a pathogenic function when the cutaneous micro-environment in immune-compromised states becomes favourable for its fast proliferation. According to Carlotti (2001) [43] and Cafarchia and Otranto (2004) [42], a variety of cellulolytic enzymes, including phospholipases and proteases, appear to be involved in heightened cutaneous inflammation. Higher pH levels in the specific cutaneous target locations encourage yeast cell multiplication (Mason *et al*., 1996; Matousek *et al*., 2003) [25, 44, 45].
According to Uday Seetha *et al*. (2018) [5], non-descriptive dogs (55%) had the highest prevalence of *Malassezia dermatitis*, followed by Labrador retriever and Spitz (13%), German Shepherd (11%) Chinese Pug (4%), Dalmatian (2%), Doberman, and Great Dane (1%). According to studies by Plant *et al*. (1992) [26], Bond *et al*. (1996) [28], Maulldin *et al*. (1997) [7] certain breeds, including the American Cocker Spaniel, Springer Spaniel, Basset Hound, Daschund, English Setter, West Highland terrier, Silky terrier, German Shepherd, Poodles, Chihuahua, and Collie, are at higher risk. *Malassezia* was much more common in Labrador breeds (45.5%) and Beagle breeds (18.1%). According to Kumar *et al*. (2003) [50], factors like humidity, breed, age, pendulous ears, season, and concurrent diseases may contribute to the high isolation rates of these organisms.

Etiology
Dogs' superficial mucocutaneous areas and external ear canals typically contain low concentrations of this commensal yeast. *Malassezia* is one of the yeasts that cause otitis externa in dogs most frequently (Crespo *et al*., 2002) [34]. The characteristic peanut-shaped or round-to-oval *Malassezia pachydermatis* has monopolar budding. *Malassezia dermatitis* (also known as malasseziosis) in dogs is most frequently associated with the lipophilic, non-lipid dependent, non-mycelial saprophytic yeast organism. *Malassezia sympodialis*, which is smaller than *M. pachydermatis* and has a more rounded bulbous shape with narrower-based monopolar budding and moreover infrequently observed as a cause of *Malassezia dermatitis* (Miller *et al*., 2013) [3].

Proteolytic enzymes produced by *M. pachydermatis* have the potential to harm the epithelium.

When *M. pachydermatis* multiplies excessively as a result of changes to the host defense mechanism, a clinical manifestation of the disease develops. Microenvironmental changes, such as an excessive production of cerumen following treatment with antibiotics or corticoids, as well as concurrent primary conditions, such as food sensitivity, flea bite sensitivity and/or atopy, pyoderma, demodicosis, and endocrine problems (hyperadrenocorticism, hyperthyroidism, diabetes mellitus), also facilitate the growth of *M. pachydermatis* cells (Ashbee, 2007; Nardoni *et al*., 2005) [38, 39] and furthermore brought on by concurrent main diseases, such as atopy, pyoderma, demodicosis, hypersensitivity to food, hypersensitivity to flea bites, hyperthyroidism, and diabetes mellitus (Bond *et al.*, 2002) [64].

M. pachydermatis can be found on the skin, rectum, anal sacs, and vagina in addition to being a common yeast and an opportunistic infection of the external ear canal of dogs and cats (Bond *et al.*, 1996; Dizotti and Coutinho, 2007) [28, 32]. According to Gentilini *et al.* (1991) [33], Crespo *et al.* (2002) [34], and Nascente *et al.* (2004) [35], this yeast is one of the most common bacteria linked to external otitis in dogs. *M. pachydermatis* has also been cited as the root cause of canine dermatitis in recent investigations (Nardoni *et al*., 2007; Leite *et al*., 2003) [36, 37].

Although a symbiotic association between the two species has been suggested and *Malassezia dermatitis* and staphylococcal pyoderma may coexist, inhibiting staphylococci does not appear to hinder *Malassezia* growth (Mason, 1996) [25, 44] In fact, it has been suggested that using antistaphylococcal drugs may promote *Malassezia* overgrowth, however, this is not a typical side effect (Plant *et al.*, 1992) [26].

Malassezia may act as an allergen in patients with atopic dermatitis as evidenced by the higher levels of *Malassezia*-specific immunoglobulin E identified in atopic dogs compared to healthy dogs (Nuttal and Halliwell, 2001) [11]. According to Kieffer *et al*. (1990) [12], hypersensitivity to *Malassezia* antigens is also regarded to be significant in atopic people.

Clinical signs

Affected areas of *Malassezia dermatitis* in dogs include the peri vulvar skin, perianal skin, axillae, groin, ventral neck, interdigital skin, facial folds, or tail folds (Patterson A.P., Frank L.A. 2002) [8]. A significant symptom is pruritus, which is typically intense and will have an awful scent. *Malassezia dermatitis* (MD), which is caused by an overgrowth of *Malassezia*, is often extremely itchy, with erythema as the only major lesion. Excoriations, seborrheic plaques, lichenification, maceration, and intertrigo are common secondary lesions that, in the majority of instances, cannot be confidently separated from staphylococcal pyoderma without cytological investigation. The irritated skin may be oily (seborrhea oleosa) or dry and flaking.

Intense itching and a potent scent of rotting fat are two significant clinical signs of *Malassezia* infection. Alopecia, localized or generalized erythema, erythematous papules and macules, crusts, and scaly skin on the face, trunk, perianal and interdigital areas, as well as in skin folds, are clinical symptoms of infection in its early stages. Hyperpigmentation and other secondary lesions brought on by repeated licking and scratching have been documented in chronic cases (Dorogi, 2002) [49].

With or without more extensive MD, paronychia (Inflammation of the claw beds) can happen. Claw-biting or paw-licking is one of the primary complaints of patients with *Malassezia* paronychia. Physical examinations typically indicate a waxy exudate in the claw fold or reddish-brown staining of the proximal claw, together with inflammation of the soft tissue around it (Gryphon, 1996) [27]. In the majority of cases, interdigital pododermatitis is also caused by the yeast.

According to Yurayart *et al*. (2010) [19], frequency of isolation was more common in the neck region, followed by the dorsal and ventral trunk, ear pinnae, hind legs, pre scrotal region, fore legs, perineal region, and interdigital area.

Additionally, *M. pachydermatis*, which is frequently quite proinflammatory, seems to have a significant role in cases with ceruminous otitis externa. The lowest number of yeast organisms that might correspond with harmful effects is unknown because studies to quantitatively measure the anticipated (Commensal) populations of *Malassezia* yeast dwelling in the external ear canal have not been reported. Otitis media cases in which *Malassezia* is the only infectious agent found are rare, although they do happen. These instances must be the result of the virus spreading through a ruptured tympanum. Cats' dermatitis and otitis have also been linked to *M. pachydermatis* (Carlotti, 1993) [30].

Zoonotic importance:

Dogs with inflammatory skin illness have yielded lipid-dependent and anthropophilic species like M. furfur (D. 0. Morris, unpublished data, 1998), while feline skin has yielded the species M. sympodialis and M. globosa (Bond *et al*., 1996; Bond *et al.*, 1997) [28, 29]. It is unknown whether these studies show a human-to-animal reverse zoonosis. *M. pachydermatis* has been linked to a zoonotic outbreak in a neonatal intensive care unit where doctors and nurses are suspected of infecting newborn humans with their own family pets (Chang *et al.*, 1998) [31].

Diagnosis

As per Coyner, (2019) [4], skin cytology examination aims to determine the presence of inflammatory cells and bacterial or fungal infections. The tape smear method was used to gather samples. The region of the skin lesion that is thought to be contaminated with fungi is covered with transparent plaster media (tape), which has been applied twice. (Morris *et al*., 2005) [6] The plaster was fastened to a glass object that was sterile. After that, the sample was stained with Methylene Blue and examined under a 400X microscope (Seetha *et al*., 2018) [5]. The fungus that is causing the infection is subsequently identified through microscopic investigation. If *Malassezia* species are present, they include *Malassezia pachydermatis*, which has monopolar budding and a round to oval form. Other *Malassezia* sps, such as M. sympod ialis, which is smaller than *Malassezia pachydermatis*, has a more rounded bulbous shape and narrow er based monopolar budding, may infrequently be observed as a cause of *Malassezia dermatitis* (Miller *et al*., 2013) [3].

Malassezia organisms are not always detected by cutaneous cytology. In the author's experience, trial therapy is of little benefit in the absence of cytological evidence of *Malassezia* organisms, despite some literature suggesting that the clinician should rely on clinical lesion patterns to make a tentative diagnosis of *Malassezia dermatitis* in such a situation (Hnilca KA, 2011) [9]. *Malassezia dermatitis* should

ultimately be diagnosed based on a combination of the clinical presentation and skin cytology. If samples are taken from itchy, inflammatory skin, even small quantities of *Malassezia* organisms may indicate *Malassezia dermatitis*. The results of cutaneous cytology can differ between examinations, thus if the patient develops new lesions or clinical complaints, the results of a previously normal cytological investigation shouldn't be taken as current. Because *M. pachydermatis* are commensal organisms, their isolation in culture has little to no diagnostic value (Miller *et al*., 2013; Mauldin *et al*., 1997) [3, 7]. As a result, fungi cultures are not helpful. *Malassezia pachydermatis* is distinctive among the species in that it frequently thrives on common mycological media without the addition of lipids (Ahearn *et al.,* 1998) [14]. According to Bauer *et al*.'s (1966) [17] standard disc diffusion method, an antifungal susceptibility test should be conducted.

The most prevalent anaemia in dogs with fungal, bacterial, viral, and protozoal infections is mild to severe non-regenerative anemia. It was also claimed that anaemia could develop in the aforementioned settings as a result of decreased erythrocyte synthesis, erythrocyte elimination by immunologic processes, or oxidative damage (Takahira 2009) [13].

A quantitative PCR method based on the amplification of the single copy ß tubulin gene was developed in an effort to incr ase the sensitivity of cytological sampling for *M. pachydermatis* in the canine ear. It was judged that the results were accurate and showed improved sensitivity over cytology; this method may have useful applications in diagnosis, therapeutic monitoring, and studies of pathogenesis and therapeutic product development (Puig *et al.,* 2019) [54].

Clinical management

The creation of clinical consensus recommendations for the diagnosis and treatment of *Malassezia dermatitis* in dogs and cats was recently commissioned by the World Association of Veterinary Dermatology (Bond *et al.,* 2020) [53]. The use of a shampoo containing 2% miconazole and 2% chlorhexidine, applied twice weekly, was found to have "strong" support in a recent evidence-based review on the management of canine *Malassezia dermatitis* (Bond *et al.,* 1995; Maynard *et al*., 2011) [62, 63]. For a shampoo containing 3% chlorhexidine, "moderate" evidence was available (Maynard *et al.,* 2011) [63]. There was "moderate" evidence for the use of ketoconazole at 5-10 mg/kg orally once or twice daily and itraconazole at 5 mg/kg orally once day or two consecutive days per week for canine instances where topical therapy is unsuccessful or impractical (Bond *et al*., 2020) [53].

Although the majority of studies have found little evidence for in vitro antifungal resistance, numerous reports have demonstrated sporadic very high anti-fungal MICs in individual *Malassezia* species and strains (Robson *et al.,* 2010) [21]. Clinical resistance to antifungal drugs by *Malassezia* species has only rarely been reported in veterinary or human medicine. *M. pachydermatis* (Nakamura and al., 2000) [20], M. furfur (Duarte *et al*., 2006) [22], M. globosa, and M. restricta (Rincon *et al.,* 2006) [24] are the species that have been found to be more resistant. M. sympodialis, however, has frequently been found to be more responsive to the antifungals that have been tried (Miranda *et al.,* 2007).

Secondary yeast and bacterial infections frequently coexist in canine dermatitis episodes that are clinically diagnosed. In accordance with an earlier communication (Sickafoose *et al.,* 2010) [46], wide spectrum antibiotic cephalexin was therefore used in combination with anti-fungal medications. According to Chen and Hill (2005) [47], miconazole works by preventing the manufacture of ergosterol, a crucial part of the fungal cell membranes. It also has a pronounced anti-bacterial effect against Gramme positive bacteria such *Staphylococcus* spp. Negre *et al*. (2009) [48] suggested giving dogs with *Malassezia dermatitis* a topical solution of 2% miconazole and 2% chlorhexidine. Twice daily topical application of organic shampoo was very effective in addition to the use of miconazole chlorhexidine shampoo (should be advised once weekly). Prudent application of this combined topical medication is anticipated to prevent repeated tenacious bouts of *Malassezia dermatitis* in companion dogs when used in conjunction with orally administered holistic antibacterial and supportive regimens. In some refractory individual dogs, the recommended course of oral anti-microbial and supportive therapy, along with the appropriate anti-allergic diet and other precautionary measures, may need to be continued past the customary 4-week time frame until recovery is achieved, depending on clinical judgement. The efficacy of shampoos with two active components may be improved (Hnilca KA, 2011) [9]. *M. pachydermatis* can be controlled with medicated antifungal wipes or pads comprising 0.3% chlorhexidine, 0.5% climbazole, and Tris EDTA solution (Cavana *et al*., 2015) [10].

Cleaning the infected dogs' ears of debris and lipid substrates was the first step in treatment. Next, an antifungal medication such clotrimazole should be applied locally, and ketoconazole was given orally once daily for 10 to 15 days. According to e arlier studies (Jacobson, 2002; Peano and Gallo *et al*., 2008) [51, 42], ketoconazole is extremely effective.

Antimicrobial resistance has become a major concern for both human and animal health on a global scale (Fera *et al.,* 2009) [55]. It has been noted previously (Velegraki *et al*., 2004; Cafarchia *et al*., 2012a, b; Weiler *et al*., 2013) [58, 42, 59, 60] that the majority of wild-type *Malassezia* yeasts are still susceptible to the commonly used azole drugs such as itraconazole, ketoconazole, and miconazole. Fluconazole, however, has a more variable efficacy. Caspofungin and itraconazole or fluconazole have been shown to work synergistically in *M. pachydermatis* isolates from canine otitis externa, while Amphotericin B inhibited the activity of itraconazole but not that of fluconazole or posaconazole (Alvarez-Perez *et al.,* 2019) [61].

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