

Demodex, an Eclectic Mite Living in both Hair and Skin: A Review

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ABSTRACT

Demodex is a permanent ectoparasite, living on pilo-sebaceous units and mainly on the faces; two species are specific for humans (*Demodex folliculorum* and *Demodex brevis*).

Demodex infestation produces allergic and inflammatory reactions to the skin, such as redness, hair loss and scarring; it gives rise to a variety of skin conditions collectively termed as demodicosis.

Parasitic infestation of the skin is a common presentation to dermatologists as well as to primary care physicians. The disease burden can cause a debilitating itch or complications from secondary infection. Accurate diagnosis can be facilitated by microscopic examination of skin scrapings, microscopic examination of hair or in some cases biopsy.

The present review summarizes the epidemiological aspects, the eclectic role of the Demodex in skin disorders, and the treatment challenges. It is important to consider Demodex mites in the etiology of unexplained cases of skin diseases.

Keywords: Demodex, Ectoparasite, Demodicosis, Epidemiology, Clinical forms

INTRODUCTION

The mites *Demodex folliculorum* and *Demodex brevis* are ubiquitous and obligatory ectoparasites typically found on man, they asymptotically inhabit the pilo-sebaceous units of most adults (80%-100%) [1].

The two detritivore species mainly involve the face and the head, but *Demodex brevis* has a wider distribution on body [2], these mites are affecting most commonly the perioral, periorbital areas of the face, the lids and lashes [1,3], occurring in 10% of skin biopsies and 12% of follicles [4].

With regard to the terminology of the disease, both "demodicosis" and "demodicidosis" have been used with the latter being more commonly used in the older dermatologic literature. "Demodicidosis" with the suffix "id" is analogous to "tuberculid" or "bacterid" and implies a state of hypersensitivity or allergic reaction to substances of the pathogen. Therefore, "demodicidosis" does not reflect the current view on the pathogenesis of this dermatosis and "demodicosis" would be a preferred term [5,6].

The term demodicosis represents all the cutaneous diseases caused by Demodex mites, the infection usually remains asymptomatic and may have a pathogenic role only with high densities of mites, their extra-follicular location and also because of immune imbalance [1].

Demodex can also exacerbate pre-existing skin conditions [1,3]. Demodex proliferation can result in a number of cutaneous disorders including pustular folliculitis, pityriasis folliculorum, papulopustular and granulomatous rosacea, among others [7,8].

Demodicosis can be classified as primary, in the absence of other inflammatory dermatoses, having a sudden onset, or secondary when associated with other cutaneous or systemic diseases, developing gradually over existing dermatoses [9].

It has been reported that the demodex species which can be infested in human are found common all over the world [10]. According to various sources, the incidence of demodicosis

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is from 2% to 5% and is ranked at the seventh place in terms of frequency among skin diseases. In terms of the structure of acneiform dermatoses, 10.5% are classified as demodicosis [11]. Thus, controlling the mites may help the outcome of inflammatory skin conditions.

CLASSIFICATION

Phylum: Arthropoda

Subphylum: Chelicerata

Class: Arachnida

Order: Trombidiformes

Family: Demodicidae

PATHOGENESIS

Increased mite density has been correlated with increase readiness of lymphocyte to undergo apoptosis and with increased number of NK cells with Fc receptors [12], significant decrease in absolute numbers of lymphocytes and T-cell subsets and significant increase in IgM levels have also been found in patients presenting with Demodex proliferation and facial skin lesions [13], colonization of the skin with Demodex could be a reflection of the immune response of the host to the organism [12].

Penetration of Demodex into the dermis or, more commonly, an increase in the number of mites in the pilo-sebaceous unit of $>5/\text{cm}^2$, is thought to cause infestation, which triggers inflammation [4], demodex mites consume epithelial cells and induce micro-abrasions, which can result in epithelial hyperplasia and reactive hyperkeratinization around the base of the lashes, forming cylindrical dandruff [14].

Several pathogenic mechanisms have been proposed for demodicosis, including:

- (1) Blockage of hair follicles and sebaceous ducts by the mites or the reactive hyperkeratosis;
- (2) Stimulation of the host's humoral and cell-mediated immune reactions by the mites and their waste products;
- (3) A foreign body granulomatous reaction to the mite's chitinous skeleton;
- (4) A vector role for bacteria [15-17].

SEX AND AGE CONSIDERATION OF INFESTATION

Males are more heavily infested than females with both species [2]. Demodex mites can be found in any age groups except the new-borns who are presumably infested soon after birth by direct contact [10]; it is more commonly encountered in young adult when the sebum secretion rate is at its highest [1].

Sengbusch and Hauswirth found a pronounced increase in the prevalence of *Demodex brevis* with increasing age.

Whereas the prevalence of *Demodex folliculorum* tended to remain more constant [18].

PREDISPOSING FACTORS

Though *Demodex folliculorum* isn't an uncommon occurrence, a weakened immune system, dermatitis, skin affection, alopecia, Acne (especially inflammatory types), HIV, malignant neoplasia, chronic use of topical steroids and lymphosarcoma can predispose to demodicosis [1,3,7].

The relationship with the presence of the mite *Demodex folliculorum* and rosacea is one of the most intriguing; It has been suggest that the presence of *Demodex folliculorum* in the affected skin could be related to the development of rosacea [19,20].

MODE OF TRANSMISSION

Demodex infection can be transmitted directly by close contact with the infected people. The mites are transferred between hosts through contact of hair, eyebrows and sebaceous glands [1].

Infection can be transmitted indirectly through household items, as it was shown that the mites can long enough to remain viable outside the host, Demodex can be transferred by contaminated towels, combs, blankets, bath sponge and night clothes.

In addition, practitioners often advise patients to start washing their bed sheets and pillowcases regularly in hopes of preventing re-inoculation.

In severe cases, patients may even need to consider replacing their pillows altogether.

DESCRIPTION OF THE PARASITE

These commensal worm-like mites have semi-transparent body, four short pairs of legs on the anterior third of their bodies, attached to the head-neck and the mouth part, are 0.3 to 0.4 mm in length as shown in **Figure 1**, *Demodex brevis* are slightly shorter of 0.15-0.2 mm and have a 14 day life cycle [1,21,22], they exist solely in depth of sebaceous and meibomian glands [10].



Figure 1. Lupus with presence of Demodex and Rosacea with presence of Demodex (Department of Parasitology-Mycology, "Hassani Abdelkader" Hospital, Algeria).

SITES OF INVOLVEMENT

Mites have been retrieved from almost every area of human skin but have a predilection for face. Demodex is typically found on cheeks, nose, chin, forehead, temples, eyelashes, brows, the balding scalp, ear, neck and less commonly upper and medial region of chest and back are also infested [4,17,21] (Figures 2 and 3).



Figure 2. Demodicosis mimicking tinea versicolor (Department of Parasitology-Mycology, “Hassani Abdelkader” Hospital, Algeria).



Figure 3. Demodex folliculorum microscopy (department of Parasitology-Mycology, “Hassani Abdelkader” Hospital, Algeria).

CLINICAL DESCRIPTION

Demodex infection usually remains asymptomatic and may have a pathogenic role only with high densities of mites and also because of immune imbalance [1].

Human demodicosis is clinically characterized (Table 1) by erythema or slight skin redness (Figure 1) that strongly suggest demodicosis [4,23], followed by scaly skin mostly across the forehead [4], characteristic dry follicular scale unsheathing the base of the lanugo hair or plugging the follicular opening [23], dryness or skin that feels rough like sandpaper [4,23], presence of papules or pustules [4,3], itchy skin [4] and burning sensation [23].

Table 1. Symptoms related to demodicosis.

Type of manifestations	Manifestations	References
Ocular manifestations	Bilateral crusting and redness of the lid margins Lashes with cylindrical dandruff Meibomian gland disease Swollen eyelid/itching Conjunctival inflammation Corneal vascularisation Superficial opacities Nodular scarring	[6,14,25,26]
Facial skin manifestations	Itchy eyebrows, scalp and face Oiler skin than normal Enlarged facial pores Cyst and pustules Rosacea or facial flushing Hair loss (madarosis) Swollen nose	[1,10,14,27]

Ocular demodicosis, is including chronic blepharitis, chalazia or less commonly, kerato-conjunctivitis; and auricular demodicosis is including external otitis or myringitis [3,24]. Cylindrical dandruff, which are lipid and keratin accumulations that form distinct cuffs surrounding lash roots, are characteristic of demodectic blepharitis [25].

Other atypical clinical presentations leading to misdiagnosis, are summarizes in Table 2.

Table 2. Atypical clinical forms of demodicosis.

Species	Clinical description	Clinical suspicion	Authors
<i>D. folliculorum</i>	Red Patch on neck (Figure 2)	Tinea versicolor	Merad et al. [28]
	Redness of the face	Rosacea	Chang and Huang [19]
	Redness on right side of face	Hansens disease	Vashisht et al. [29]
	Hair loss, erythema	Folliculitis of the scalp	Helou et al. [30]
	Crusted lesions on face	None	Guerrero-González et al. [7]
	Itchy rash, red skin	Seborrheic dermatitis	Karinaoglu et al. [31]
	Lesions on scalp and forehead	Favus	Garcia-Vergas and Mayorga-Rodrigues [32]
	Papules on face (Figure 1)	Lupus	Mehta et al. [33]
	Abscess of the face	Abscess	Schaller et al. [34]

Skin lesions associated with abnormal increase of *Demodex* mites in patients with other known skin or systemic diseases can be classified as secondary demodicosis [3].

It is important to consider *Demodex* mites in the etiology of unexplained cases of skin diseases. A study by Emre et al. [35] in turkey in 2009 demonstrated that *Demodex folliculorum* infestation was higher in Behcet disease and mite elimination may be useful, even in patients without any complaint, for the treatment of ocular and eyelid discomforts of these patients.

Karinaoglu et al. [31] in Turkey in 2009 demonstrated that the prevalence of *Demodex folliculorum* was higher in patients with seborrheic dermatitis.

The *Demodex folliculorum* mites are more often detected in patients with acne of III and IV degrees and with papular and pustular rosacea; *Demodex folliculorum* provokes more severe clinical forms of acne [11].

It seems that *Demodex folliculorum* is more often associated with erythema and epithelial desquamation, whereas *Demodex brevis* is linked with papulo-pustular eruption, symmetrical rashes and conditions arising on the background of a pre-existing disease [9].

DIAGNOSIS

Infestation with *Demodex* is common, and mites are present in 23% of healthy adults and may have a pathogenic role only when present in high densities or in immunosuppression [1,4,36].

Therefore, a high index of clinical suspicion about the etiological role of demodex in various dermatoses is necessary.

Identification methods used in assessing the presence of mites include, invasive methods (skin scraping, follicular

scales, epilation) or non-invasive *in vivo* detection and quantification of *Demodex* mites by confocal laser scanning microscopy [1,5,11] (**Table 3**).

Table 3. Identification of *Demodex* mites by various diagnostic methods.

Methods	Sampling	References
Direct examination by light microscopy (Potassium hydroxide 10%)	Follicular scales	[1,4,5,8,14,23, 28]
	Skin scraping	
	Comedone extraction (squeezing method)	
	Scotch tape applied on lesion	
	Hair/lashes epilation	
Confocal laser scanning microscopy	Scan various layers of the skin	[11]
Standardized skin surface biopsy	Skin (cheek), eyelid	[1,5]

The density of *Demodex* mites can be studied by KOH preparations of follicular plugs, skin scrapings and standardized skin surface biopsy specimens [6].

It has been suggested that an increasing density of mites correlates with an increasing perifollicular inflammation and

clinical manifestation. A density of more than 5 mites/follicle or 5 mites/cm² of standardized skin surface biopsy specimen has been considered to be pathogenic [1,36]. Symptoms may develop when the follicles become heavily infested, or when the mites penetrate into the dermal tissue [6].

Confocal laser scanning microscope makes it possible to visualize mites that are both found in the deeper layers of the skin and inaccessible to scarification [11], this method has a high potential to be a diagnostic means for demodicosis, which makes it possible to scan various layers of the skin that allows the determination of the depth of mite detection ($\approx 46.63 \mu$), number of mites and also their size. The lack of epithelium trauma and painful procedures are other additional advantages of this method.

COMPLICATIONS

Demodicosis is often diagnosed in patients with severe clinical forms of acne and rosacea, it may worsen acne outbreaks, rosacea rashes, and dermatitis patches [1,3]. This fact suggests that the mites complicate the course of the diseases, and thus promoting the development of inflammatory elements [11]. Demodicosis should be considered in the differential diagnosis of recurrent or recalcitrant rosacea-like, granulomatous rosacea-like and perioral dermatitis-like eruptions of the face [6].

Demodex may act as a vector of transmission of various infections from area of body to another or between individuals by its potential to ingest and transport various microorganisms (*Microsporum canis*, *Bacillus* sp., *Streptococcus* sp.) [14,37].

TREATMENT

Because Demodex are nocturnal, it is important to limit their ability to reproduce and migrate when they are most active.

Demodicosis remains a diagnostic and therapeutic challenge, anti-parasitic therapies used against lice or scabies may fail in control of *Demodex folliculorum* mites [34].

The symptoms of some skin diseases are clearly reduced when this parasite is correctly treated [23,34,38], on the other hand, some symptoms persist when only anti-bacterial therapeutic agents are used [38].

Various regimens have been used to treat demodicosis (Table 4), including systemic metronidazole and ivermectin as well as topical metronidazole, salicylic acid, gamma benzene hexachloride, sublimed sulfur, permethrin, crotamiton, benzyl benzoate and tea tree oil [6,24,25,39]. In severe cases, such as those with HIV infection, oral ivermectin may be recommended [1].

Table 4. Treatments used in demodicosis.

Treatment	Posology/duration	Clinical presentation	References
Metronidazole (oral)	3 time a day/2 weeks	Abscess, folliculitis	[27,34,41]
Ivermectin (oral)	1 dose (200 µg/kg)/repeated after 7 days	Severe cases/HIV Refractory blepharitis	[1,15,26,39] [42]
Ivermectin 1% (cream)	Once daily/2-12 weeks	Papulo-pustular rosacea	[43]
Permethrin 5%	Once daily/3 nights	Papules of the scalp	[7,27]
Topical tea tree oil	2 time a day/6 weeks	Irritation, itchiness of eyelid	[25]
Pilocarpine 4% (gel)	2 time a day/2 weeks	Ocular itching	[44]
ItCrotamiton 10% (cream)	2 time a day/1 week	Acne rosacea-like	[6]

A study, have reported complete recovery, with the disappearance of facial mites in treatment with combinations of oral and topical metronidazole in a case of fulminant rosacea-like eruption with multiples *Demodex folliculorum* mites [40]. Furthermore, oral anti-parasitic drug such as ivermectin is used alone or in combination with metronidazole [39].

Grossmann et al. [41] used 750 mg/day metronidazole for 3 weeks in conjunction with 100 mg/day prednisolone, topical 2% metronidazole and 0.15% lindane emulsion [41]. Baima

and Sticherling used oral ivermectin for skin lesions caused by Demodex, in combination with 4% pilocarpine gel in blepharitis [15].

CONCLUSION

Demodex are permanent ectoparasite of dermatological importance and it has been shown that these mites are playing an important role in the occurrence of a series of skin diseases, but further clarification of these associations is required.

A high index of clinical suspicion about Demodex in various dermatoses can help in early diagnosis and appropriate, timely, and cost effective management.

We strongly recommend including laboratory examination and an acaricide for the treatment to improve the quality of life of some patients.

We conclude that Demodex mites are common but overlooked.

MAJOR HIGHLIGHTS

- Demodex is a permanent ectoparasite, living mainly on the face.
- It asymptotically inhabits the pilo-sebaceous units of most adults.
- Mites are affecting most commonly the perioral, periorbital areas of the face, the lids and lashes.
- Atypical clinical presentations are possible (acne, tinea versicolor, Folliculitis of the scalp, unilateral rosacea).
- It is important to consider Demodex mites in the etiology of unexplained or severe cases of skin diseases.
- Correct skin identification with routine microscopy or confocal laser scanning microscopy is necessary.
- Oral anti-parasitic drug such as ivermectin alone or in combination with metronidazole is required.
- Washing patient bed sheets and pillowcases regularly is recommended in hopes of preventing re-inoculation.

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