

REVIEWS

Adv Clin Exp Med 2014, 23, 2, 295–298
ISSN 1899–5276

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Demodex – An Old Pathogen or a New One?

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article; G – other

Abstract

Demodex was first identified over 150 years ago, but only recently has it attracted wider interest as a contributor to chronic diseases such as acne rosacea or marginal blepharitis. *Demodex* is commonly found in the human population, in skin sebaceous glands or follicles. The frequency of *Demodex* infection increases with age, as it is mainly diagnosed after the age of seventy; however, it can sometimes be found in children and teenagers. *Demodex* is supposed to contribute to the development of marginal blepharitis or acne rosacea, but the pathogenic mechanisms have not yet been explained in detail. These diseases are chronic and the long-term treatment effects are not satisfactory. This paper presents the characteristics of *Demodex* as well as its prevalence in the pathogenesis of eye and skin diseases, and describes the diagnostics and treatment of these disorders (*Adv Clin Exp Med* 2014, 23, 2, 295–298).

Key words: *Demodex*, pathogenicity, diagnostics, treatment.

In recent years, an increase in *Demodex* infections has been observed. These microscopic mites, which are commonplace all over the world, were identified in the 19th century, but for years they attracted little scientific interest and were not generally associated with symptoms found in humans. Only a few researchers tried to establish the role *Demodex* plays in the pathogenesis of human and animal diseases. The first reports discussing *Demodex* type mites appeared in 1841, authored by Jakub Henle, the professor of anatomy from Zurich. A year later, a German dermatologist named G. Simon found this pathogen in hair follicles. Six years later, Simon published a book with detailed illustrations presenting *Demodex folliculorum* [1]. In 1875, Becler described *Demodex* found in eyelid margins and eyelash follicles, and Majocchi and Burchard detected the organism in tarsal cyst material [2]. The term *demodecosis* was used for the first time by Ayres in 1961, when human *Demodex* was found in the pathogenesis of acne rosacea. Two years later, Abkulatowa distinguished another variety of the mites: *Demodex brevis*. In 1972, Desh and Nutting showed that *Demodex folliculorum* exists in

hair follicles, whereas *Demodex brevis* was found in the meibomian glands [3, 4].

Demodex belongs to the class of arachnids (*Arachnida*), the scab mites subdivision (*Acarida*) and the hair follicle mites family (*Demodiacidae*). The name *Demodex* comes from the combination of two Greek words: *demos* (skin) and *dex* (worm). These mites prevail all over the world and are characterized by a parasitic existence. They occur in mammal hair follicles, sebaceous glands (Zeiss' glands) and eyelid glands (Meibom's glands). They may evoke demodecosis in both humans and animals, the course of which is chronic [5].

The 2 kinds of *Demodex* mites that have been identified in humans (*Demodex folliculorum* and *Demodex brevis*) commonly appear in seborrheic areas of the facial skin (the forehead, chin, and around the eyes and mouth). They are also observed on the pileous skin of the head, on hairy chests or in the genital area [4, 6–8].

Demodex appears in dogs too, in the form of *Demodex canis*, and may cause severe inflammation of sebaceous glands or hair follicles. The parasites may also penetrate the lymph nodes, liver, spleen and other organs, causing general symptoms and

death. In such cases they can be found in blood, urine and feces [2].

Demodex occurs in other animals as well, including cats (*Demodex cati*), cattle (*Demodex bovis*), goats (*Demodex caprae*), sheep (*Demodex ovis*) and rats (*Demodex rattii*). These kinds are pathogenic for animals only and are not found in humans [5].

Demodex mites are white or yellow in color, and have an elongated oval shape that narrows towards the rear. *Demodex* individuals have 4 pairs of prolegs on their front section (Fig. 1).



Fig. 1. *Demodex* mature form – authors' own observations

The mites' developmental cycle lasts 3–4 weeks and takes place in one host. Larvae with 3 pairs of prolegs hatch out of eggs; after molting, nymphs with four pairs of prolegs are formed, eventually changing into adult males and females after 2 molts. *Demodex folliculorum* is 300–400 μm long, while *Demodex brevis* is 250–280 μm long; their width is similar: 40–45 μm [5, 9]. *Demodex* mites feed on sebum, lymph, plasma and epithelial cells. In humid environments, adult mites can survive for 3 weeks whereas dry conditions cause them to die in 36 h [9].

D. folliculorum mites live in hair follicles or sebaceous glands. They occur in concentrations and the disease progresses as the patient's age increases. In turn, *D. brevis* is usually located in the meibomian glands; it is found to live individually and morbidity is not age dependent [4].

Epidemiology

Demodex occurs all over the world in almost all human races, including various ethnic groups such as Aborigines and Eskimos. About 80–90% of the human population is infected with *Demodex*; however, *D. folliculorum* is more often found in females than in males [6]. According to some studies, it more frequently causes face lesions in middle-aged women who often use makeup remover liquids instead of soap [6].

Demodex infections frequency increase with age; the mites are commonly detected in people over 70 years of age and rarely detected in children and teenagers, which may be caused by the fact that the activity of the glands of Zeiss and the meibomian glands diminishes with age [5]. Some researchers claim that immunological disturbances may favor *Demodex* infections in children [5, 10]; the mites have been observed especially in children with leukemia and with chronic blepharitis [5, 11].

Demodex infection may be the result of direct contact with an infected person's skin, or indirectly through contact with contaminated objects such as towels, combs, blankets, sponges or bed clothing.

Eye Diseases

Demodex is considered to play a role in the pathogenesis of eye diseases by causing chronic blepharitis. The mites' presence in hair follicles causes inflammatory processes in the tissues and damages hair bulbs, which may cause a loss of eyelashes surrounded by cylindrical dandruff. Enlarged blood vessels are visible on the eyelid rims. *Demodex* is supposed to be the vector for a number of antigens also bacterial and mycotic additionally favoured by lacrimal film pH changes. Antigens penetration to conjunctivitis epithelium superficial layers provokes an immunological response in the form of antigen presenting cells, lymphocytes and Langerhans' cells, as well as the secretion of pro-inflammatory cytokines. In ophthalmic demodocosis, examinations of the eye conjunctiva reveal elevated levels of macrophages and CD4 lymphocytes, and the interleukin-1 level was increased in the lacrimal film [12].

Demodex folliculorum is considered to induce the humoral response from IgM and IgG production, whereas *Demodex brevis* is responsible for the cellular response [13].

Demodex is rarely considered an etiological agent in inflammation of the palpebral margins. Due to the number of possible reasons for this disorder, bacterial or mycotic infections, allergy or refractive error are taken into account more often [5]. In the majority of cases, the course of the disease is completely asymptomatic and only sometimes slight itching is observed. *Demodex* may also cause severe inflammation of the palpebral margins. Patients complain of a burning sensation in the eyes, lacrimation and hypersensitivity to light, dust and smoke. The eyelid margins become reddened and there is a deficiency of the lipid layer of the lacrimal film. A chronic condition may result in eyebrow and eyelash loss, inflammatory edema

of the eyelids and conjunctiva, as well as secondary bacterial infections [14, 15]. In cases of severe inflammation of the palpebral margins, microscopic examinations revealed as many as 12 full-grown *Demodex* individuals on one eyelash. [11].

Skin Diseases

The role of *Demodex* in the pathogenesis of skin disorders in adult patients has been widely discussed. Only increased numbers of the mites – more than 5 individuals on 1 cm² of skin – are closely associated with pathogenic activity [7, 16]. *Demodex* may cause a number of lesions in human skin. The mites have been found in patients suffering from papular and papulopustular rosacea, perioral dermatitis and hair folliculitis [4].

Acne rosacea is a chronic disease, located mainly on the face, in which vascular and seboreic lesions constitute the basis for the development of the illness. It is more often diagnosed in women with fair complexions. A number of factors are responsible for acne rosacea: genetics, hormones, environmental influences, diet or *Demodex folliculorum* infections [17].

The symptoms of acne rosacea appear in the central part of the face (the forehead, cheeks, nose and chin), and they are recurrent. The primary symptoms have been defined as paroxysmal erythema, pimples, papules and *telangiectasias*. Secondary symptoms have also been observed: edema, skin dryness, ophthalmic lesions and hypertrophic changes. The role of *Demodex* in the development of acne rosacea can be the blockage of hair follicles, the stimulation of inflammatory reactions or superficial transmission of *Flavobacterium* spp. and *Bacteroides* spp. [3, 18, 19]. Along with the presence of *Demodex*, immunohistological tests show proliferations of accessory T lymphocytes, plasmocytes, histocytes and giant cells. This may indicate the development of a cellular type response [3, 4, 20].

Diagnosing Demodocosis

Diagnosing demodocosis can pose some problems, since *Demodex* is an obligate parasite. Both clinical symptoms and the presence of increased numbers of *Demodex* organisms in lesions are taken into account. The following methods are used in demodocosis diagnostics:

1. Direct eyelash section: after epilation of the upper and lower eyelids, prepared specimens are placed on microscopic slides in dimethylsulphoxide (DMSO) solution or 10% potassium hydroxide.

The specimens are studied at 200 × magnification. The presence of mature *Demodex folliculorum* individuals in the specimens and the form of larvae or chitin exuviae is the evidence of *Demodex* infestation.

2. Direct epidermis preparation: scrapings from diseased epidermis, papules and pimple secretions are placed in a 20% solution of potassium oxide (KOH) and inspected under light microscope.

3. Standardized skin surface biopsy: this method allows the number of mites to be estimated. A slide covered with glue with cyanoacrylate and a marked square 1.03 cm² in size is pressed against the skin surface. After 30 s, the slide is removed and the material stratum with hair follicles – is elicited. The preparation is inspected with the use of a light microscope at 40× and 100× magnification and the number of live mites per 1 cm² can be assessed. The time interval between harvesting the material and evaluating the specimen cannot exceed 4 h [4, 16].

4. Skin biopsy: histologic examination of a skin sample stained with hematoxylin and eosin. This method provides a small amount of material and hair follicles cannot be assessed [4, 7].

The presence of *Demodex* mites in a specimen is not equivalent to a diagnosis of demodocosis. As noted above, the results are considered positive when the number of mites exceeds 5 individuals in 1 cm² of skin surface. Interpreting the examination results may be difficult, as *Demodex* mites often occur in skin lesions with other etiological agents that can impede a correct diagnosis. Differential diagnostics should be carried out, taking both the test results and the clinical symptoms into account.

Treatment

The treatment of diseases caused by *Demodex* mites is difficult and may last for several months. In the case of inflammations of the palpebral margins, local application of sulphuric ointment, yellow mercuric ointment, anticholinesterase, antifungal drugs or antibiotics have been noted to cause clinical improvement; the best results were elicited after the application of metronidazole, mercuric and erythromycin ointments [2, 21, 22]. At the same time, eyelid margin hygiene should be maintained with diluted tea tree extract shampoo, as well as rinsing the face with delicate soap to decrease the danger of mite infestation. The use of 4% pilocarpine gel brought about complete healing in 37.5% of cases, and partial cure in 40.6% of cases [23]. Alternatively, minocycline can be administered for 6 months [2]. Good results have been achieved with medication consisting of onion and chamomile extracts, heparin and allantoin. After

the treatment, improvement in the clinical condition of the eyelid margins was observed, as well as a reduction in the number of mites [24].

The treatment of acne rosacea in which *Demodex* spp. play a pathogenic role is based on oral use of metronidazole and ivermectin as well as local use of lindane cream, crotamiton and permethrin [11].

Demodex was discovered over 150 years ago. However, for years was not the subject of

investigations, due to insufficient knowledge concerning this parasite's part in chronic and severe diseases such as inflammation of the eyelid margins or acne rosacea, and its influence on the exacerbation of other diseases. It is only recently that studies of *Demodex* have contributed to the development of methods that enable proper diagnosis and treatment of the dermatological and ophthalmological disorders.

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Conflict of interest: None declared

Received: 30.06.2012

Revised: 20.07.2012

Accepted: 7.04.2014