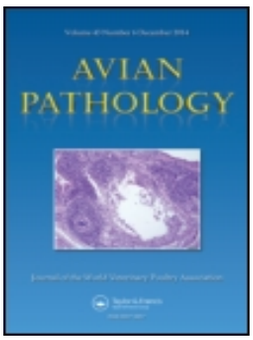

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REVIEW

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Dermanysuss gallinae attacks humans. Mind the gap!

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ABSTRACT

Dermanyssus gallinae is a haematophagous ectoparasite primarily known as a pest of domestic and wild birds. It occasionally feeds on a range of mammals, and, more importantly, is of growing concern in human medicine. This review highlights mite attacks on people working with poultry, and updates the increasing incidence of dermanyssosis in urban environments in Europe. Although several cases of dermanyssosis have been documented, there are a number of reasons why diagnosis of *D. gallinae* infestations in humans is likely to be underestimated. Firstly, medical specialists are not well aware of *D. gallinae* infestations in humans. There is also a lack of collaboration with specialists from other disciplines. The problem is compounded by misdiagnoses and by the lack of diagnostic tools. We review the literature on human dermanyssosis cases in Europe, and also provide information on the epidemiology, clinical, histo-pathological and immunological aspects of dermanyssosis. We stress the need for improved recognition of this challenging infestation in humans, and provide straightforward recommendations for health practitioners, starting with collection of the correct anamnestic information and including appropriate management methods for case recognition and resolution. Finally, we indicate the most urgent areas to be addressed by future research.

RESEARCH HIGHLIGHTS

- *Dermanyssus gallinae* is of growing concern in human medicine.
- Most physicians are not well aware of dermanyssosis in humans.
- Bio-epidemiological and clinical aspects of this ectoparasitosis are highlighted.
- Practical key actions for diagnosis and correct management of infestation in humans are provided.

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Dermanyssus gallinae; humans; Europe; dermatitis; diagnosis; management; future needs

Introduction

Dermanyssus gallinae (Arthropoda: Dermanyssidae) is a cosmopolitan haematophagous ectoparasite of birds. It is primarily a well-known pest of poultry farms worldwide, affecting over 80% of European poultry farms, with peaks above 90% in the Netherlands, Germany and Belgium (Mul *et al.*, 2017). The infestation burden on caged laying hens can be up to 500,000 mites per bird in severe cases (Kilpinen, 2005); this causes extreme stress, associated with feather-pecking, increased self-grooming and cannibalism (Kilpinen, 2005; Mul *et al.*, 2009), in addition to blood loss. As a consequence, the welfare, health and productivity of the birds are severely affected (Wójcik *et al.*, 2000; Cosoroaba, 2001; Kilpinen, 2005). In addition, *D. gallinae* serves as a vector for a number of viral and bacterial avian pathogens (Valiente Moro *et al.*, 2009; Circella *et al.*, 2011; Chu *et al.*, 2015; Sommer *et al.*, 2006).

It also poses a threat to other birds, such as broilers, turkeys and ducks, and also to canaries, budgerigars and synanthropic birds typically found in urban centres (e.g. pigeons, sparrows, starlings, doves).

D. gallinae mites are temporary nocturnal visitors; they remain hidden in close proximity to their hosts during daylight hours, and move onto their hosts at nightfall in order to feed. The life cycle consists of the following stages: egg, larva, two nymphal stages, adult male and female. All legged stages, except larvae, feed on blood. The complete life cycle typically takes two weeks, but under ideal conditions (35 °C and relative humidity over 70%), it may require only one week (Sparagano *et al.*, 2014).

Although *D. gallinae* is largely considered an avian-specific ectoparasite, when the natural host is absent

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hungry mites will occasionally feed on a range of mammals, i.e. cats (Grant, 1989; Di Palma *et al.*, 2018), dogs (Declerq & Nachtegaele, 1993), gerbils (Lucky *et al.*, 2001), other rodents (Kowal *et al.*, 2014), horses (Mignon & Losson, 2008), and humans. They may attack any person working in infested poultry farms or living in an urban environment where there are synanthropic birds.

The most important point related to human infestation is that physicians are usually unfamiliar with the dermatitis caused by several zoonotic ectoparasites, including *D. gallinae* (Haag-Wackernagel, 2005; Cafiero *et al.*, 2008; Collgros *et al.*, 2013). It is actually very difficult to diagnose a *D. gallinae* infestation from the cutaneous reactions it causes in humans; since the reactions are uncharacteristic (Kavallari *et al.*, 2018), infestations are often misdiagnosed. The lack of guidelines and/or recommendations, and the insufficient awareness of physicians/dermatologists with this infestation and with the eco-biology of this ectoparasite, can prevent them from managing affected patients correctly. Furthermore, misdiagnosis of an infestation, and the inevitable relapses, negatively affect patients' quality of life (Dogramaci, Culha, & Ozçelik, 2010). The problem of misdiagnosis is also worrying due to the possible role of *D. gallinae* as a vector/reservoir of several zoonotic pathogens (De Luna *et al.*, 2008; Circella *et al.*, 2011; Boseret *et al.*, 2013).

According to the recent strategic document provided by the tripartite agreement of FAO, OIE and WHO (2017), the impact of *D. gallinae* on human health can be fully considered as a One Health issue.

This article is concerned with improvements in understanding dermanyssosis in humans. It aims to highlight salient aspects and key features of this ectoparasite, starting with its epidemiology by bringing order to the literature and updating, to the best of our knowledge, the case reports in Europe, and considering the clinical and diagnostic aspects involved. It provides physicians/dermatologists with practical information about the key actions needed for correct management of infestations in humans, and informs the scientific community about future research priorities to fill the gaps in the current knowledge of dermanyssosis.

Epidemiology and public health significance of *D. gallinae* in Europe

Given the high percentage of infected poultry farms (on average 83% of the European laying hen farms) (Mul *et al.*, 2013) human dermanyssosis in this specific context can be regarded as "occupational cases" (Cafiero *et al.*, 2011), while those related to synanthropic birds can be regarded as "urban cases" (Figure 1). Table 1 summarizes the cases of dermanyssosis (occupational and urban) documented to date.

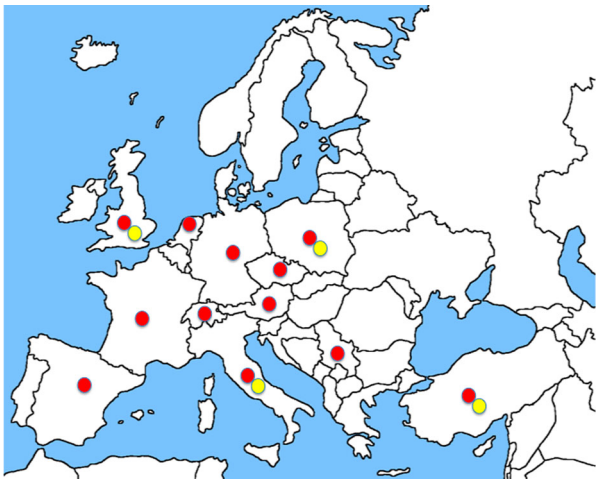

Figure 1. Dermanyssosis cases in Europe (red dots: urban cases; yellow dots: occupational cases). (Colour online)

Occupational cases

Despite the high occurrence of dermanyssosis among poultry industry farmers, technicians and veterinarians working in infested farms (Camarda, personal communication, January 23, 2019), there are very few case-reports linked to poultry in the literature. Attacks on humans in poultry sheds occur when the infestation level in poultry farms is high, and when farmers, employees or visitors do not wear adequate protective clothing. *D. gallinae* bites can be considered a serious health hazard, and a source of discomfort and stress for all personnel working in poultry houses including amateurs. In these conditions, and given that the mite can bite in less than 1 s (Auger *et al.*, 1979), there can be a major risk of attacks on humans handling birds and/or cages and collecting eggs (Rosen *et al.*, 2002), or even visiting an infested farm. In some countries this has become a socio-economic problem for poultry workers, who demand three times the usual rate of pay before they are willing to work with *D. gallinae*-infested birds (Sahibi *et al.*, 2008). Several occupational cases of human dermanyssosis have been registered worldwide (Sparagano *et al.*, 2014).

In Europe, although it is very common in the field, and a well-known pest in veterinary handbooks, there are few published records of poultry workers being attacked by *D. gallinae* (Table 1). However, cases have been recorded since the 1950s in Poland (Litwinski, 1955), and later in the UK (Rossiter, 1997), Italy (Pampiglione *et al.*, 2001; Cafiero *et al.*, 2011) and Turkey (Dogramaci *et al.*, 2010; Şengül *et al.*, 2017).

Case records concern both people living in rural areas, who rear free-range hens as a hobby (Pampiglione *et al.*, 2001; Şengül *et al.*, 2017), and poultry farmers (Rossiter, 1997; Dogramaci *et al.*, 2010). Although there are several case reports, only one study has investigated the prevalence of cases involving

Table 1. Reports of *Dermanyssus gallinae* on humans in Europe

Year of record	City, region, country	Type of infestation	Number of outbreaks	Location and number of people attacked	Source	References
1930	Zurich, Switzerland	Urban	1	Unknown	Synanthropic birds	Schrafl (1930)
1953	Poland	Occupational	1	Poultry house, one farmer	Infested poultry farm	Litwinski (1955)
1961	Rotterdam, the Netherlands	Urban	8	Apartments Twenty-three persons (one adult, three children; three times one child; two adults, four children; two adults, three children,; two children; two adults, one child)	Pigeons, tiger finches, parakeets, canaries	Frenken (1965)
1967	Hamburg, Germany	Urban	1	Hospital, Twelve patients	Ventilation openings infested by mites from birds' nest	Winkler (1967)
1967 and 1968	Cornwall, UK	Urban	2	Private apartments Two children (1967), One girl (1968)	Starlings' nest found in crevice where waste pipe exits the house (1967) Nesting material found in loft close to girl's bedroom (1968)	Reed *et al.* (1969)
1967	Danzig, Poland	Urban	1	Hospital Unknown number of patients and hospital staff	Pigeons' nest	Skierska (1968)
1969	London, UK	Urban	1	Hospital Many patients (number unknown)	Abandoned pigeons' nests	Freeman & Kataria (1969)
1971	Danzig, Poland	Urban	1	Railway shipment Unreported number of office employers	Pigeons' nests	Wegner (1973)
1974	Kielce, Poland	Urban	1	Office One employee	Immediately following removal of pigeons' nest close to office	Kowalska & Kupis (1976)
1981	Vienna, Austria	Urban	1	Optical instruments factory Four employees	Pigeons' nest outside a factory window	Bardach (1981)
1985	UK	Urban	1	Hospital Four elderly patients	Infested pigeons nesting on window ledges of two hospital wards	Neill *et al.* (1985)
1988	Basel, Switzerland	Urban	1	University lab One man	Laboratory infestation by *D. gallinae,* escaped from plastic bag containing pigeon faeces harbouring red mites	Haag-Wackernagel (1988)
1996	Nijmegen region, the Netherlands	Urban	2	Private apartments Two adults and one child	Birds' nests under the roof tiles	Prins *et al.* (1996)
1997	Exeter, UK	Occupational	1	Poultry house Two workers	Chickens	Rossiter (1997)
2001	Emilia Romagna, Italy	Occupational	1	An elderly woman	Small hen house adjacent to patient's house	Pampiglione *et al.* (2001)
2001–2007	Apulia, Basilicata, and Campania regions, Italy	Urban	6	Offices (Law Court/Town Hall) Ten employees (2003) Seven employees (2005) – Private apartments Six adults (2001, 2005, 2007)	Abandoned feral pigeons' nests near infested buildings (hole in the wall/ behind air-conditioning units)	Cafiero *et al.* (2007, 2008)

(*Continued*)

Table 1. Continued.

Year of record	City, region, country	Type of infestation	Number of outbreaks	Location and number of people attacked	Source	References
2003–2008	Amsterdam, the Netherlands	Urban	96	Apartments, several people	Synanthropic birds' nests, mainly pigeons, in outer walls of apartments	Buijs (2009)
2005	Tilburg region, the Netherlands	Urban	1	Private apartment	Pigeons' nest with dead pigeon adjacent to the bedroom window of the patient	Diederen *et al.* (2006)
2005 and 2006	Modena, Italy	Urban	2	Primary school Many pupils, number unknown (2005) – Private apartment One woman (2006)	Feral pigeons roosting and nesting on school roof – Colony of pigeons nesting on chimney-pot of attic	Gelati *et al.* (2007)
2006–2008	Valencia, Bétera-Camp de Turia, Spain	Urban	4	University offices/ army residence/ cottage Unknown number of adults and three children	Abandoned nest close to cottage/pigeons' nest behind air-conditioning units	Fuentes *et al.*, 2009
2007	Modena, Italy	Urban	3	Site unknown Three subjects in total	Removal of pigeons' nests from window ledge	Ferri (2007)
2007	Apulia region, Italy	Urban	1	Two private apartments in the same building Three adults and one child	Abandoned pigeons' nest under gutter between balconies of two apartments	Cafiero *et al.* (2008, 2009)
2007–2009	Apulia region, Italy	Occupational	11	Poultry farms Eleven poultry workers	Caged laying hens	Cafiero *et al.* (2011)
2007	Czech Republic	Urban	1	Apartment Two adults and two children[a]	Mites entered apartment viahole in the roof[b]	Melter *et al.* (2012)
2008	Créteil, France	Urban	1	Hospital An elderly patient	Abandoned pigeons' nest near a window	Bellanger *et al.* (2008)
2008 e 2009	Apulia and Basilicata regions, Italy	Urban	4	Private apartments Seven adults and one child (2008), One adult (2009)	Abandoned pigeons' nests (2008); Sparrow nest (2009)	Cafiero *et al.* (2013)
2009	Kütahya, Turkey	Urban	1	Private apartment A woman and her family members	Mites from pigeons through the air ventilation system	Akdemir *et al.* (2009)
2009	Basel, Switzerland	Urban	1	Renovated old apartment building	Feral pigeons using balcony for roosting /breeding	Haag-Wackernagel & Bircher (2010)
2010	Hatay, Turkey	Occupational	1	Poultry house Elderly worker	Poultry	Dogramaci *et al.* (2010)
2010	Puglia, Italy	Urban	1	Hospital Four ascertained patients and several subjects in previous four months	Feral pigeons using window ledge near the infested rooms for roosting/breeding	Galante *et al.* (2011)
2011	Puglia, Italy	Urban	1	Private apartment Three adults	Following removal of an active pigeons' nest close to the house	Mancini *et al.* (2012)
2013	Barcelona, Spain	Urban	1	Private apartment Three patients (couple and their child)	Pigeons' nests near balcony	Collgros *et al.* (2013)
2008; 2011	Pančevo, Serbia	Urban	1	Private apartment Five patients (couple and their three children)	Mites in nearby dove nest entering apartment through cracks in frame of balcony door	Gavrilović *et al.* (2015)
2015	Apulia, Italy	Urban	1	Office, one employee	Abandoned pigeons nesting in air-conditioner unit surround	Giangaspero *et al.* (2016)

2017	Denizli, Turkey	Occupational	1	Hobby chicken house Old country woman	Chickens raised in patient's garden	Şengül *et al.* (2017)
2013, 2015–2017	Apulia and Molise regions, Italy	Urban	7	Private apartment One child (2013) – Office and apartment Four adults and one child (2015); – Three private apartments Four adults and one child (2016–2017)	Abandoned pigeons' nests (2013, 2015–2017) Caged canaries (2015)	Cafiero *et al.* (2017, 2018)
2015	Ferrara, Italy	Urban	1	Two public conference halls Four people	Colony of feral pigeons located on the roof of the building	Pezzi *et al.* (2017)
2016	Utrecht, Netherlands	Urban	1	Apartment	Pigeons' nest	https://www.hartvannederland.nl/top-nieuws/2016/sabrina-en-zoontje-4-dakloos-door-vogelmijt/

[a]They developed *B. quintana* infection.
[b]Seven mites were found positive for *B. quintana* DNA.

poultry industry workers; a questionnaire among workers in infested poultry farms in Southern Italy revealed that 18% (11 of the 58 people interviewed) had experienced irritating and itchy skin eruptions (Cafiero *et al.*, 2011).

Human infestation mostly occurs in daytime (when mites crawling off their preferential host, or hiding, are disturbed by human activities), and in spring-summer when climatic conditions are favourable to mites. However, given that temperatures in industrial farms are almost constant, infestations can occur in them throughout the year (Sparagano *et al.*, 2014).

The importance of these mites in public health also stems from their role as reservoirs/vectors of zoonotic poultry pathogens, including *Salmonella enterica* (Pugliese *et al.*, 2019), *Erysipelothrix rhusiopathiae* (Chirico *et al.*, 2003; Valiente Moro *et al.*, 2009; Huong *et al.*, 2014), and the avian influenza A virus (Sommer *et al.*, 2006). For these reasons, there has been wholehearted support for official recognition of *D. gallinae* as a zoonotic agent in all occupational safety regulations, and for recognition of this mite dermatitis as an occupational hazard for poultry industry workers (Cafiero *et al.*, 2011).

Urban cases

Reports of dermanyssosis have become more frequent in recent years, particularly in residential contexts in association with common synanthropic birds, such as sparrows, starlings, doves, and mostly with feral pigeons (*Columba livia*). Feral pigeons are among the most successful avian settlers in our cities due to the abundance of available food and the absence of predators (Haag-Wackernagel, 2005). The ever-increasing pigeon populations build their nests close to homes (e.g. crevices and holes on the façades of buildings, behind external air-conditioner units, under eaves and in attics). When bird hosts are not available, mites search for alternative hosts and may migrate into nearby homes, where they bite humans. Most episodes of red mite dermatitis commonly occur in the late spring-early summer (Deoreo, 1958; Bellanger *et al.*, 2008; Cafiero *et al.*, 2013; Giangaspero *et al.*, 2016). The seasonal occurrence of this infestation was extremely evident in an outbreak affecting five members of a family, who suffered recurrent pruritic skin lesions in April and May for four consecutive years before the parasites were observed and identified (Gavrilović *et al.*, 2015). This seasonality reflects the red mite population peak; this is linked to the breeding season of birds, mostly pigeons, which peaks between April and June, when birds leave their nests once the chicks have fledged, and there are greater chances of human contact with mites. In fact, *D. gallinae* and *Argas reflexus* (sometimes in co-infestations) are the principal ectoparasites acquired by humans in urban

environments from feral pigeons (Haag-Wackernagel, 2005; Haag-Wackernagel & Bircher, 2010); the occurrence of feral pigeon ectoparasites increases as the density of their host (i.e. feral pigeons) increases (Haag-Wackernagel, 1991).

In Europe, published/ascertained urban *D. gallinae* infestations have been recorded in 12 countries; these were more frequent in private homes/apartments (with more than 150 outbreaks recorded), but also in hospitals (six records) and offices/public buildings (12 records) (Table 1).

The urban cases of *D. gallinae* infestation have all been caused by mites migrating from synanthropic bird nests of pigeons, starlings or sparrows, except for a few cases: one caused by an accidental laboratory infestation in Switzerland (Haag-Wackernagel, 1988), and other cases caused by caged canaries in Netherlands (Frenken, 1965) and Italy (Cafiero *et al.*, 2017) (Table 1).

The attacks can occur during daytime (mostly in workplaces) or at night (mostly in private homes).

The implications of these infestations in urban environments may well cause concern, since *Chlamydia psittaci* (Circella *et al.*, 2011), and both *Borrelia burgdorferi s.l.* and *Coxiella burnetii* DNA, the agents of Lyme disease and Q Fever, respectively, have recently been detected in *D. gallinae* during three outbreaks of human dermatitis related to sparrow and pigeon nests (Raele *et al.*, 2018). More importantly, *Bartonella quintana* DNA has been detected in *Dermanyssus* mites collected in an apartment during an outbreak of urban trench fever caused by *B. quintana,* which affected a family with high socio-economic status (Melter *et al.*, 2012).

Clinical signs

People attacked by *D. gallinae* mites present erythematous eruptions consisting of 1–3 mm papules (Figure 2) (Bardach, 1981; Collgros *et al.*, 2013), sometimes with a visible central puncture mark or vesicles (Deoreo, 1958; Kowalska & Kupis, 1976; Haag-Wackernagel & Bircher, 2010; Cafiero *et al.*, 2018); urticarioid manifestations have also been described (Rockwell, 1953; Deoreo, 1958; Sexton & Barton, 1975; Auger *et al.*, 1979; Ahmed *et al.*, 2018). Bites can be painful (Berndt, 1952) and skin lesions may occur in any area of the body, except in the interdigital spaces, genitals or skin folds; itching is commonly intense, with reported cutaneous excoriations due to scratching (Gavrilović *et al.*, 2015).

Figure 2. *Dermanyssus gallinae*-dermatitis caused by mites migrating from a sparrows' nest (original, M.A. Cafiero).

In the Italian survey of poultry farm workers, two of the 11 parasitized workers (18.18%) reported skin eruptions on their arms and hands, seven (63.63%) reported symptoms on their chests, and two (18.18%) on their legs. None of these workers usually wore personal protective equipment during their work, including egg collection, so that their skin was exposed, particularly on their hands and arms (Cafiero *et al.*, 2011), as was also reported for poultry farmers in Israel (Rosen *et al.*, 2002).

In addition, there are reports of intriguing cases of persistent infestation in unexpected sites, such as the ears (auditory meatus) in the UK (Rossiter, 1997), and on the scalp, as in the case of an Italian woman living in the country side (Pampiglione *et al.*, 2001) and of two Turkish farmers (Dogramaci *et al.*, 2010; Şengül *et al.*, 2017). Surprisingly, all these cases involved elderly subjects (aged 60+). In all of the above-mentioned cases, symptoms occurred for as long as 9 months.

Urban cases document more severe clinical pictures, involving people attacked at night while sleeping at home, or else bedridden patients attacked in hospitals during the day. In these cases, skin lesions are particularly abundant on body areas covered by pyjamas, e.g. the trunk and limbs (Freeman & Kataria, 1969; Cafiero *et al.*, 2018), or on the patient's entire body; in an outbreak in a Hamburg hospital, one of the 12 parasitized patients suffered over 500 bites (Winkler, 1967). In these cases, cutaneous lesions are often described as grouped and more intense where clothes constrict the body, for example in relation to a belt (Cafiero *et al.*, 2017) or under the breasts (Bellanger *et al.*, 2008). When mites attack sleeping subjects, red spots (crushed mites or mite droppings) can be found on bedclothes and pillows (Regan *et al.*, 1987; Cafiero *et al.*, 2009).

By contrast, attacks in workplaces and public buildings occur during daylight hours. Patients also present intense itching, but their skin reactions are less severe and less numerous, almost always involving exposed body areas, mainly the arms and legs. Victims usually see mites crawling on their clothes or skin and/or on office furniture and usually refer to experiencing a biting/stinging sensation while they work (Fuentes *et al.*, 2009; Giangaspero *et al.*, 2016; Cafiero *et al.*, 2017; Pezzi *et al.*, 2017; Şengül *et al.*, 2017).

Histopathological aspects

There are few studies of histological changes to the skin of animals and humans affected by *D. gallinae*-dermatitis.

In a study of poultry, hyperkeratosis, skin thickness and a focal loss of epidermis were observed in 90% of the birds examined, together with extremely numerous small focal lymphocytic infiltrations in all hens (Sokol & Rotkiewicz, 2010). Another study involving poultry reported severe subcutaneous oedema, congestion of the hypoderma, lymphocytic infiltration, necrosis of feather follicles at 24 h post-infestation (p.i.), and hyperkeratosis, parakeratosis, acanthosis and local epidermal hyperplasia at 72 h p.i. (Hobbenaghi *et al.*, 2012).

A study of infested cats described a perivascular and interstitial inflammatory infiltrate (Di Palma *et al.*, 2018).

In humans, histological examination of skin lesions caused by *D. gallinae* revealed a perivascular inflammatory skin reaction, and sometimes a superficial perivascular eosinophilic infiltration (Hidano & Asanuma, 1976; Kowalska & Kupis, 1976). Moreover, a modest spongiosis and focal parakeratosis were also found in a case of severe *D. gallinae*-related dermatitis (Cafiero, personal communication, February 10, 2019).

Immunological response

Unlike mammalian immunological responses to ectoparasitic arthropods, the humoral and cellular immune response of birds to *D. gallinae* (as for other Gamasida) are still poorly understood, and there is a complete lack of knowledge about human responses.

Figure 3. A pigeons' nest in close proximity to an apartment, identified during an inspection to investigate a *D. gallinae* outbreak (original, M.A. Cafiero).

Arkle *et al.* (2006) found significantly higher ($P < 0.05$) yolk IgY levels in hens' eggs. However, no significant relationship was found between yolk IgY levels and *D. gallinae* population levels, or between serum and yolk IgY levels, although egg and serum samples were not collected from the same bird. Arkle (2007) reported that the level of cytokine expression did not appear to be significantly correlated with *D. gallinae* levels in naturally infested commercial poultry, while numerical and significant associations between IgY and cytokine levels lacked consistency (although there was some suggestion of a relationship between IgY levels and IL-5 and IL-12α expression). These data would suggest that *D. gallinae* blood feeding stimulates a significant IgY immune response by the host; such immune response following natural infestation would allow older birds to better tolerate mite attacks in the presence of high IgY levels and lower side effects from these attacks compared to young chicks. Reports of host inflammation or skin damage following *D. gallinae* infestation of hosts (birds or humans) do not appear in the literature, possibly highlighting counter-immune reactions developed by the mites. Further hypotheses regarding the apparent lack of development of host immunity to *D. gallinae* include the following: (a) *D. gallinae* has a mechanism which modifies host immunity, making it less effective; (b) mite populations adapt to host immunity between the first attack and the later attacks (however it is unclear how mites could communicate within colonies and if the mite population diversity stays the same during the flock life) (Arkle *et al.*, 2006).

Diagnosis

Medical texts and parasitology manuals rarely mention Mesostigmata mites in relation to human infestation. This means that most physicians are unfamiliar with the diagnosis of several less common mite-related forms of dermatitis, including the dermatitis caused by *D. gallinae* (Cafiero *et al.*, 2008; Haag-Wackernagel & Bircher, 2010; Collgros *et al.*, 2013).

This is extremely important, not only because misdiagnosis may lead to failure in the treatment of patients, but also because, as underlined above, *D. gallinae* may be a vector/reservoir of ascertained zoonotic agents (Chirico *et al.*, 2003; Valiente Moro *et al.*, 2009; Brännström *et al.*, 2010; Circella *et al.*, 2011; Melter *et al.*, 2012; Raele *et al.*, 2018).

Clinical recognition of dermatitis due to *D. gallinae* bites (described in the section above) is a challenging task. *D. gallinae* bites may be confused with urticarial atopic dermatitis, or with the dramatically common/widespread delusional ectoparasitosis caused by fragile psychological conditions (Lucky *et al.*, 2001; Bellanger *et al.*, 2008; Akdemir *et al.*, 2009; Cafiero *et al.*, 2013). They may also be confused with lesions caused by

zoonotic mange (Sarcoptidae mite), baker's itch (Acaridae mite), *Cheyletiella*, *Trombicula* and *Cimex lectularius*, if not arranged in linear arrays. Additionally, *D. gallinae* bites may be mistaken for those of avian mites in the *Ornithonyssus* genus (Acari: Macronyssidae); this mite group of zoonotic interest is similar to *D. gallinae,* but less common in Europe, and has a different relationship with the host (Cafiero *et al.*, 2018).

D. gallinae-related dermatitis can be diagnosed by using dermoscopy and reflectance confocal microscopy. However, this tool is helpful only when the mites are present on the patient's skin, although this must be considered a rather rare circumstance (Navarrete-Dechent & Uribe, 2018). Dermoscopy evaluation of *D. gallinae*-induced dermatitis also reveals dilated vessels on an erythematous background in correspondence to the macules and papules, and reflectance confocal microscopy demonstrates the presence of intraepidermal vesicles (Cinotti *et al.*, 2015).

Currently, *D. gallinae*-related attacks on humans can be addressed only via different perspectives/approaches, which require:

- greatly improved awareness of the problem among medical doctors;
- enhanced knowledge of *D. gallinae* taxonomy and eco-biological aspects;
- closer collaboration of doctors with entomologists/acarologists/veterinarians.

Given these starting points, there are some important actions doctors should take when faced with suspected pruritic dermatitis caused by *D. gallinae*.

A series of straightforward recommendations/instructions is listed below, beginning with the collection of the correct anamnestic information and including appropriate/accurate management methods to enable case resolution.

Practical recommendations to physicians

Dermanyssus gallinae should always be suspected when unexplained, recurrent dermatitis occurs in humans.

Detailed personal and environmental anamnesis

In addition to collecting the usual anamnestic data, physicians should ask patients about where they live (i.e. in the countryside, city, etc.), their occupation and their lifestyle. They should also ask patients for details about the onset of pruritus: the place, season and time of day it appeared; the recurrence of the symptoms; whether other family members (including their pets) have/had the same symptoms; whether they live close to a poultry farm; and whether there are pet birds and/or bird nests near their home/workplace.

Figure 4. *Dermanyssus gallinae*, migrated from a pigeons' nest and collected in a home (original, M.A. Cafiero).

Site inspection

For poultry farm workers, it may be relatively simple to predict and identify the cause of their dermatitis, given the prevalence of *D. gallinae* in rearing systems, but in an urban context, it is crucial to have a good knowledge of *D. gallinae* biology/ecology in order to search for the mites. It is strongly recommended that inspections (or requests for inspections) be made for adult stages (which are visible to the naked eye) in the environment where an infestation is suspected. It is important to know that mites are attracted by warm hiding places simulating the body temperature of birds. In apartments, offices and public buildings, the places to inspect are under bed covers, electrical devices. In stand-by mode (e.g. laptop computers, television and radio clocks), and all other sites generating heat. Balconies, attics, eaves, windows and holes near the building must be also inspected for the presence of active or, more probably, abandoned birds' nests (Figure 3).

Environmental sample collection

Having obtained the consent of the house/building owner/s, dust samples must be taken near/under windows, beds, furniture and desks, where people usually rest or work. The dust must be brushed into a

transparent bag, then sealed and labelled with the collection site, date and time. If noticed in a room, arthropod specimens can be collected using scotch tape (Figure 4). Samples have to be examined under a microscope and we strongly recommend that the specimens be correctly identified, since correct identification is the first requirement before applying control methods.

Identification

D. gallinae is relatively small at the adult stage (0.5–1 mm long), with long legs and a greyish-white body that becomes reddish-brown when engorged (Figure 4). However, since cases of dermatitis caused by the avian mites *Ornithonyssus bursa* (Castelli *et al.*, 2015; Mentz *et al.*, 2015; Bassini-Silva *et al.*, 2019) and *Ornithonyssus sylviarum* (Orton *et al.*, 2000; Cafiero *et al.*, 2018), or by the rodent mite *Ornithonyssus bacoti* (Beck & Fölster-Holst, 2009; Cafiero *et al.*, 2016) have been recorded in humans even recently, there may be some confusion over identification of the mite responsible.

Firstly, fresh (or, less efficiently, frozen) specimens must be macerated in lactophenol for one week at 45 °C on a hot plate, and then mounted on slides with Hoyer's medium for light microscopy (LM) observations (Di Palma *et al.*, 2012).

D. gallinae can be identified according to the following principal morphological characters (Di Palma *et al.*, 2012; Giangaspero *et al.*, 2016):

- the dorsal surface has a shield with prominent lateral margins tapering towards the rear, but these do not reach the distal end of the body and are truncated at the end.
- the ventral side has a sternal plate much wider than it is long and bears two pairs of bristles, with a third pair situated posteriorly and apart from the first two pairs.
- the posteriorly rounded genitoventral shield bears one pair of setae.
- the rounded or D-shaped anal plate bears three characteristic setae.
- hair-like chelicerae (when extended).
- chelicerae bases look like wine glasses upside down in the middle of the body when chelicerae are retracted.

Ornithonyssus spp. has different features (see Di Palma *et al.*, 2012 and Giangaspero *et al.*, 2016 for morphological details on this genus).

Molecular identification

It has been demonstrated that *D. gallinae* is a complex of species, which includes *D. gallinae* L1 (a cryptic species related to synanthropic birds) and *D. gallinae sensu stricto* (associated with poultry farms and chickens). Since these are morphologically indistinguishable (Roy & Buronfosse, 2011), it would be helpful to analyze the DNA of specimens from the environment to understand the source of attacks on humans.

Treatment of patients and the environment

Diagnosis of *D. gallinae* dermatitis is challenging, and misdiagnosis can lead to use of antihistamines and steroids to relieve symptoms, sometimes in combination with anti-parasite shampoos, antibiotics and tranquillizers. However, if symptoms are caused by *D. gallinae* infestation, the clinical signs usually return when treatments end.

If physicians suspect and/or confirm dermanyssosis in urban outbreaks, the following measures will achieve complete regression of the symptoms, and no evidence of mites or dermatitis will appear in the follow-up period: (i) patient showering extensively and washing their clothes at 60 °C; (ii) removal of the mite source (abandoned birds' nest); (iii) intensive vacuum cleaning, removal of the vacuum bag which needs to be packed in a sealed plastic bag and thrown away outside in a contained bin; (iv) disinfestation of the infested areas using pyrethroids: (v) steam cleaning or washing of textiles (curtains, carpets, cushions) at 60 °C and then preferably dried with an automated laundry drier. Textiles which cannot be washed at 60 °C should be placed in a plastic bag for a day together with anti-moth balls releasing an acaricide product.

In the case of occupational dermanyssosis, the problem of farm infestation requires intervention using an integrated pest management (Sparagano *et al.*, 2014; Mul, 2017). Moreover, physicians should remind their patients that all poultry workers must be protected by suitable protective clothing, before entering poultry houses.

Conclusions and future research perspectives

Dermatitis due to *Dermanyssus* mites is an increasing but neglected problem. It features as an occupational hazard for poultry workers due to the great prevalence of infested poultry farms, and also appears in urban contexts due to the worrying spread of synanthropic birds to megacities worldwide (George *et al.*, 2015; Kavallari *et al.*, 2018).

Medical specialists should always include *D. gallinae* in their differential diagnosis of patients presenting pruritic dermatitis of unknown aetiology.

The widespread circulation of *D. gallinae* in humans indicates the need for targeted actions at different levels to provide better understanding of this mite, allowing researchers to fill the gaps in current scientific

knowledge and enabling the development of strategies for recognition/diagnosis and control.

Therefore, we suggest that health service practitioners (physicians, medical doctors, dermatologists and occupational doctors) receive the above-mentioned recommendations. This could help to raise their awareness of the role of these ectoparasites in human health, allowing them to suspect and recognize *D. gallinae* infestations in humans, thus increasing the number of case reports.

In addition, there is a need for research with the following aims:

- to carefully describe the symptoms and skin reactions of red mite dermatitis, although they may overlap other diseases;
- to investigate the development of the lesions and haematological parameters (if any) over time;
- to investigate the effects of *D. gallinae* on the human immune and dermal systems;
- to uncover possible immunological host markers for setting up diagnostic tools.

All these efforts are crucial for the future development of a reliable diagnostic protocol that will make it possible to avoid using the wrong treatment products, which can cause side effects and damage patients' health.

Finally, it is of paramount importance for treatment of this disease, as for other zoonotic infestations, that clinicians, parasitologists, microbiologists, veterinarians, epidemiologists and environmental scientists work together according to the "One Health" approach, which is often mentioned but too rarely put into practice.

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