Avian mite dermatitis: Diagnostic challenges and unmet needs

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Human infestation with avian mites is commonly manifested by skin lesions that are difficult to recognize particularly in patients from urban areas [1,2]. The cutaneous condition is a zoonotic acariasis caused by the mites *Dermanyssus gallinae* (poultry red mite, PRM), *Ornithonyssus sylviarum* (northern fowl mite) or *O. bursa* (tropical fowl mite), and referred to as gamasoidosis, avian-mite ectoparasitosis/dermatitis or occasionally as dermanyssosis [1,3]. The PRM is of major economic and veterinary importance for the poultry and egg industry worldwide, whereas the full extent of threats to human health remain elusive [3,4]. The COST Action FA1404 'Improving current understanding and research for sustainable control of the poultry red mite *Dermanyssus gallinae* (COREMI)' is a network of experts from 27 countries supported by the EU Framework Programme Horizon 2020 that aims to foster a multidisciplinary approach for advancing current understanding and disseminating knowledge on PRM biology, control and impact on public health. In addition, this initiative provides a platform for early career investigators to gain up-to-date insights into the field. As part of the cross-sectoral activities of the Action, the working group WG2 organized a problem-based 'One Health' training school in Itea, Greece in August 2017 in order to critically evaluate the available literature on the PRM-associated risks for human health, to raise the awareness of medical professionals on human PRM infestation and to communicate recommendations. The outcomes of the training school are summarised in this report.

D. gallinae as a zoonotic hazard

D. gallinae is a cosmopolitan nocturnal, hematophagous, non-permanent ectoparasite, largely considered as being avian-specific, infesting wild, domestic and synanthropic birds [5]. For over 20 years, numerous reports have focused on the animal health and economic consequences associated with the high PRM prevalence in poultry farms [3]. A recent report states that 83% of the European farms are infested by *D. gallinae*, PRM prevalence reaching 94% in farms in The Netherlands, Germany and Belgium [4]. The typical density of >50,000 mites per bird in the modern poultry housing systems is attributed to the favourable conditions for PRM proliferation, facilitated at 10-35°C and >70% relative humidity [3].

The growing population of laying hens and the wide spread of synanthropic animals, along with the increased travel and trade and the climate change appear to facilitate PRM expansion to non-avian hosts, including humans and companion animals [3]. Although the available evidence remains inconclusive, the PRM vectorial capacity to transmit bacterial and/or viral diseases, such as salmonellosis, is an emerging scientific and public health concern beyond gamasoidosis [3,6]. Moreover, human exposure to the PRM control measures, such as silica-based products, may increase the risk of developing and/or exacerbating respiratory and cardiovascular disease [4]. In addition, the use of a range of licensed, unlicensed and off-label chemical pesticides, including organophosphates, pyrethroids and carbamates poses ecological and environmental threats, as well as serious direct and indirect risks for both animal and human health exemplified by the recent scandal of fipronil-contaminated eggs [4]. In fact, all these 'One Health' aspects have already provided the basis for recommending the inclusion of PRM as a zoonotic and occupational hazard for poultry workers and hobby poultry keepers [7].

Clinical manifestations of PRM infestation in humans

The first report of human PRM infestation dates back to the early 19th century, whereas human blood ingestion by the mite was reported in 1958 [8]. To date, geographically wide-spread sporadic albeit increasing reports (Table 1S) implicate PRM infestation in human

dermatological lesions both in poultry workers, farmers and veterinarians and in urban settings [3]. In the latter case, human PRM infestation is commonly linked to nearby nests of feral birds like pigeons and sparrows, as well as to the presence of pet birds, such as canaries and parrots [3,9].

PRM infestation in humans is characterised by itching affecting various parts of the body, including hands, forearms, back, chest, neck, ears and the scalp that may intensify in the evening. Pruritic, papulosquamous eruptions and erythematous maculopapular rash with or without crusts as a result of excessive scratching are commonly reported [2,3] (Table 1S). Interestingly, although the presence of mite allergens tropomyosin and paramyosin has been demonstrated in *D. gallinae*, the available evidence does not support their natural antigenic properties in humans [10,11]. Moreover, no cases of a PRM-induced typical allergic reaction have been reported (Table 1S). Thus, PRM-associated dermatitis is a local or generalized non-specific skin reaction rather than a systemic response (Fig. 1), bearing the risk of being undiagnosed or misdiagnosed as scabies, pediculosis, general dermatitis or delusional ectoparasitosis and leading to treatment failure [2,3]. The relapse of the symptoms seems to be associated with prior generalized clinical manifestations (Fig. 1), thus pointing to the likely contribution of yet undetermined confounding factors.

Diagnostic challenges in gamasoidosis

The retrospective assessment of the reported cases of avian mite dermatitis is a complicated and occasionally controversial task. The clinical history and the physical examination of the patient are evidently inadequate to provide a firm diagnosis of PRM-associated dermatitis (Box 1), whereas dermoscopic, histologic and/or immunologic diagnostic criteria are virtually lacking [2,3]. The microscopic identification of the mite itself is largely considered as the only currently available confirmatory tool of the causative agent (Fig. 1), also allowing the differentiation of *D. gallinae* versus *O. sylviarum* infestation [1,3]. However, recent studies using ultrastructural morphological observations and DNA sequencing argue for the existence of at least two cryptic species with different host spectra, namely *D. gallinae* s. str. and *D. gallinae* special lineage L1, which have been associated with poultry and pigeons, respectively [2]. Therefore, the regional diversity and the variation of the *D. gallinae* complex appear to be important determinants for the diagnosis of gamasoidosis and for the identification of the mite [2].

Conclusions

The accumulating reports on the opportunistic non-avian feeding of the avian mite *D. gallinae* raise concerns on PRM host expansion and/or switching events and on the consequent threats to human health [2,3,4,7]. Although the putative PRM pathogenicity is widely accepted by the veterinary community, the differential diagnosis of gamasoidosis and the dissection of the underlying pathobiological mechanisms remain challenging unmet needs (Box 1). The increased awareness of *D. gallinae* infestation in humans will foster collaboration and exchange of key information among medical practitioners, veterinarians and academic and industrial researchers under the ‘One Health’ approach, aiming to safeguard both animal and human health.

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Author contributions

All authors were involved in the organization and accomplishment of the training school, and in the writing of the manuscript.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Reported cases of human infestation with the poultry red mite.

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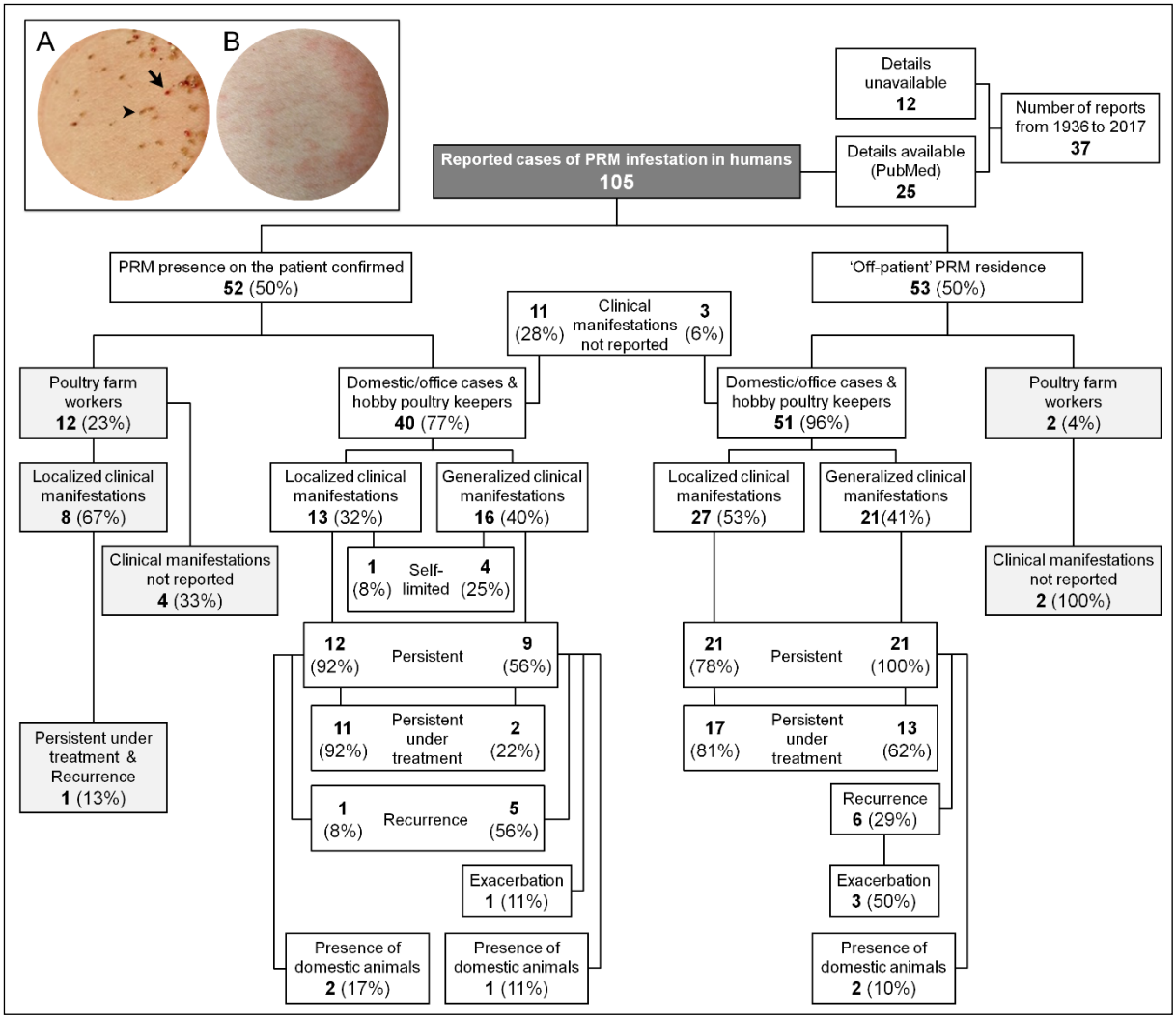

Figure 1 Characteristics of the cases of human infestation with the poultry red mite (PRM; D. gallinae, DeGeer, 1778) reported since 1936. The clinical manifestations are presented following critical evaluation of the available information on 105 cases described in PubMed. The signs and symptoms are retrospectively classified as localized: restricted or limited to a specific part of the body; generalized: spread or affecting the entire body; persistent: lasting more than 5 days. Recurrence refers to the reported relapse of clinical symptoms and signs, ranging between 10 days and 9 months. The reported treatment consisted of combinations of antihistamines and steroids (10 cases between 1962-1987; 30 cases between 1988-2012) or permethrin (4 cases between 2013-2017). No treatment regiment has been reported between 1936-1961. (A) Yellow-brown fasted PRMs (arrow heads) on human skin turn red when they feed on human blood (arrow). (B) Localized, non-itchy cutaneous reaction 18 h after PRM attack on human skin.

Box 1. Key points identified in 105 cases of PRM manifestation in humans.

- The association of PRM virulence to the extent and the severity of the clinical manifestations is currently ill-defined
- The critical analysis of 105 cases described in adequate detail in the literature since the early 20th century revealed that the key drawbacks for the conclusive diagnosis of PRM infestation in humans include:
  - the frequent lack of direct evidence on the presence of PRM on the infested patients, and
  - the scarce and incomplete epidemiological data on avian mite-associated pathologies in poultry workers that, apparently, are most at risk for occupational gamasoidosis and/or vector-borne diseases caused by PRM infestation
- The reported non-occupational cases seem to outrange their occupational counterparts.
- The lack of specific clinical manifestations and the absence of related recommendations to health professionals jeopardize the complete and accurate reporting
- Incidental reporting may be misleading for all relevant stakeholders.
- The relatively high proportion of persistent clinical manifestations questions the effectiveness of drug treatment
- The presence of healthy domestic animals is not associated with the reported PRM -associated clinical manifestations