

EDITORIAL

Allergenicity of the cat flea

In numerical terms, insects are the dominant form of animal life with, according to some estimates, up to 30 million, but perhaps more likely 5 million, living species [1]. The detrimental effect of insects on the health of humans is immediately recognizable with malaria which involves one Family of mosquitoes, Culicidae, and typhus, transmitted by infected lice *Pediculus humanus* L. These are ready examples of insects acting as vectors for diseases capable of infecting and killing millions of people worldwide.

Amidst humans' phobia of insects, the status afforded the flea as the esteemed guest of the King in Mephistopheles' song from Goethe's 'Faust', and the atmosphere of merriment associated with Mussorgsky's 'Song of the flea', are rare light-hearted treatments of an insect that has justifiably evoked trepidation and revulsion down the ages. The lowly flea, in particular the Indian rat flea *Xenopsylla cheopis* and the common rat flea of Europe *Nosopsyllus fasciatus*, were responsible for transmitting, from infected rats to humans, the plague or 'black death' organism *Yersinia (Pasteurella) pestis*. The plague pandemic of the fourteenth century, arguably the world's greatest catastrophe, is estimated to have caused the deaths of about 25 million people in Europe and, worldwide, about 60 million, or a quarter of the population [2].

Fleas, or Siphonaptera [3], are wingless ectoparasites of mammals and birds. Unlike lice which are host specific, fleas generally parasitize a range of hosts and may transfer from one host species to another. The relationship between the flea, its host and environmental conditions is complex. Fleas have evolved together with their hosts and may show certain adaptations depending upon the species [3]. Besides *X. cheopis* and *N. fasciatus*, the fleas of most importance to man, and animals close to man, are *Pulex irritans* which breeds in human habitations, the sand flea *Tunga penetrans* which may parasitize man beneath the skin, usually of the feet and ankles, the stick-fast flea of poultry *Echidnophaga gallinacea* and dog and cat fleas *Ctenocephalides canis* and *C. felis*. The latter fleas also act as intermediate hosts of certain cestodes, including the dog and cat tapeworm *Dipylidium caninum*.

Allergens are derived from almost every component of the biosystem and, given the number and widespread distribution of insects, their involvement in some allergies is not surprising. The most obvious, and the best studied allergic reactions induced by insects, are the responses to venoms injected by stinging members of the Hymenoptera (bees, wasps and ants) [4]. Bites from insects and

arachnids such as mosquitoes, horse flies, fleas, spiders, ticks and mites also provoke hypersensitivity responses in some individuals but, apart from mosquitoes and fleas, studies have generally focused on the role of arthropods in the transmission of disease. Almost all of the research on allergic reactions to fleas carried out so far has been directed at the study of flea bites [5] and because much of the work employed guinea pigs, the relevance of the findings to man should only be accepted with caution.

The most numerous, widely encountered and often important problems in clinical allergy result from allergens that gain access to the body by inhalation. Obviously, the locations where sensitization and exposure are most likely to occur are the home and the workplace [6]. For most people, exposure to insects generally takes place in the home where there may be a variety of species including flies, moths, beetles, silverfish and cockroaches, often in large numbers, constantly or periodically adding to the allergenic load.

The ill-defined, highly variable and 'unstandardizable' material we call 'house dust' often offers the only clue to a patient's allergic sensitivity. With this in mind, the allergist may seek to include a sample of house dust from the patient's own home in the panel of extracts employed to identify the sensitizing allergen source. While the widespread presence in house dust of house dust mites, and their allergenicity, have been firmly established [7,8], there is less certainty about other allergen source materials in house dust samples. Since the composition of house dust samples will be influenced by a large number of factors ranging from geographical location to the diligence and thoroughness of resident cleaners, both qualitative and quantitative variations in samples from different houses can be expected.

Although the presence of pets is recognized as a possible contributing factor to the allergenic load in a house, the presence of insects or insect-derived allergenic material in house dust has received little attention. The report in this issue by Trudeau *et al.* [9] on allergenicity of the cat flea is interesting, not only because of the insect species involved, but also because reactions studied were responses to inhaled allergens and not to bites. Following their detection of positive skin tests to cat flea extract in subjects assessed for respiratory allergies in Tampa, Florida, Trudeau *et al.* detected IgE antibodies reactive with flea components and, by RAST inhibition, determined the levels of IgE-reactive flea material in house dust samples. When cats and dogs are present in a house, *C. felis* and *C. canis* can reach pest proportions [3] and this point, together with the conclusion of Trudeau *et al.* that

cat flea allergens may contribute to the allergenicity of house dusts, especially in areas of heavy flea infestation, should be recognized by the practising allergist.

The in-house flea extract used in this study was prepared by removing immature fleas from cats and culturing them in a mixture of sand, rodent pellets and blood meal. The species of blood was not given. Adult fleas were harvested from the bottom of the container, extracted with an aqueous solvent, centrifuged and dialysed. Immunoblotting experiments revealed five IgE-binding components with MWs 34, 35, 39, 54 and 60 kD while IgE-binding bands with MWs corresponding to 30, 45, 52 and 65 kD were identified in spent medium. Like the in-house extract, a commercial cat flea extract contained an IgE-binding component with a MW of approximately 34 kD but other components in the commercial extract failed to resolve in SDS-PAGE gels. Even so, the extract proved positive in skin tests on the flea-allergic skin test-positive subjects suggesting that the 34 kD component identified in both extracts may be an important allergen. An important cat flea allergen with a similar MW (approximately 30 kD) was identified in another recent study of patients with suspected allergy to cats [10]. Each of the IgE-binding flea components identified with sera from allergic subjects apparently sensitized by inhalation of flea allergens appear to be quite distinct from the flea salivary antigens studied by others [5].

Results of RAST inhibition and immunoblotting studies on the cat flea and spent medium extracts also suggested that different antigenic proteins are expressed by the cat flea at different stages of its development [9]. Similar observations were made in a recent study of inhalant allergy to the blowfly *Lucilia cuprina* in which IgE antibody-binding properties of proteins from different developmental stages of the fly were assessed [11]. Presumably, each stage of the flea's life-cycle—egg, larva, pupa and adult—may be represented in dust samples and at least some of the allergens in spent medium may reflect these stages.

RAST, RAST inhibition and immunoblotting examinations of IgE antibodies in the sera of subjects with suspected allergy to cats led Rolfsen *et al.* [10] to conclude that some subjects were positive to both cats and cat flea allergens, some were positive only to cats, others only to flea and a few sera showed crossreactivity with both cat and flea allergens. This and the Trudeau *et al.* [9] study raises the question of the potential significance of the cat flea (and perhaps the dog flea) not only as a contributor to the allergens found in house dust, but also for the large number of 'cat-allergic' (and perhaps 'dog-allergic') subjects, many of whom develop asthma symptoms. Demonstration of the allergenic nature of the cat flea also offers a

possible explanation for the curious claim of some patients that other people's cats, but not their own, provoke their allergic attacks.

In conclusion, it may be prudent to pause and reflect on the nature of the sensitizing source of the flea-reactive IgE antibodies detected in the Tampa Bay study. Some preliminary studies we and others have undertaken seem to show that allergenic (IgE-binding) crossreactivity exists right across the Arthropoda embracing cockroaches, flies, moths, beetles, mosquitoes, locusts, silverfish and mites [12] and may even extend to crustaceans and some Mollusca [13, Baldo and O'Neill, unpublished results]. The finding, for example, of IgE to insects indigenous to Australia such as the Bogong moth and Australian plague locust, in the sera of allergic subjects from the South of France and North Africa, led us to suggest that pan-allergy to insects may occur in subjects who have been sensitized to only one, or a few, insects [12]. An alternative explanation of the wide crossreactivity of arthropods demonstrated by some allergic subjects has been advanced by Benjamini and Feingold [5]. While acknowledging the existence of antigens common to many insect species, these authors believe contaminants 'explain the wide range of crossreactivity to arthropod extracts demonstrated by skin-testing and by other immunological techniques'. Whether crossreactions to insects seen in allergic patients are due to endogenous insect allergens or contaminants, the possibility that IgE antibodies to flea, or any other insect species, may not necessarily be a true reflection of the sensitizing arthropod source must be considered. This important point can be examined by undertaking inhibition studies in which sera from allergic subjects are used together with extracts from mites and a variety of insects and house dust samples from the patients' homes. Such a comprehensive check on the possible crossreactive insect recognition spectra of the allergic subjects' IgE antibodies was not undertaken in the Trudeau *et al.* [9] study.

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