Allergy to Crickets: A Review

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Allergy to crickets: a review

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Abstract

Cricket allergy is less severe and less common than allergy to locusts and grasshoppers. A partial cross-reactivity exists between cricket and grasshopper allergens. Cricket allergens are proteinaceous compounds, but their nature is insufficiently known; arginine kinase and hexamerin 1B may play a role. Occupational allergy, *i.e.* allergy of personnel working with rearing and breeding of cricket colonies, is the subject of the majority of reports on cricket allergy. Frequent handling of crickets (for example as fish baits) may inflict allergy which may be considered as a kind of occupational allergy. Crickets are edible insects and are widely consumed in many parts of the world. Nevertheless, food allergy to crickets seems to be relatively rare.

Key words

occupational allergy, cricket allergens, hypersensitivity pneumonitis, Gryllidae, *Acheta domesticus*, *Gryllus bimaculatus*, *Gryllus campestris*

Introduction

The present review is a continuation of my former review on allergy to locusts and acridid grasshoppers (Pener 2014). This former review deals with allergy in general and allergy to insects and these subjects are not repeated here. Crickets (Ensifera: Gryllidae) and short-horned grasshoppers or locusts (Caelifera: Acrididae) represent two different suborders in the same insect order (Orthoptera). In this review I compile the relevant literature related to the identity of some cricket allergens, modes of infliction of cricket allergies and management of these allergies.

Allergy to crickets (Gryllidae) is less investigated than allergy to acridids. Nevertheless, cricket allergy is mentioned in many relevant reviews, sometimes including the name of the allergen species (Seward 1999, Barre *et al*. 2014, Dutau & Lavaud 2014, van Huis 2016), but mostly as a general example of allergy to orthopterans (Mathews 1989, Mairesse & Ledent 2002, Micek *et al*. 2014, Stanhope *et al*. 2015), or just to insects/arthropods (Chan-Yeung & Lam 1986, Chan-Yeung 1990, Bellas 1990, van Kampen *et al*. 2000, Barletta & Pini 2003, Jeong *et al*. 2007, Bousquet *et al*. 2008, Yong & Jeong 2009, Moscato *et al*. 2011, and others).

Cricket allergens

Sensitivity to crickets is usually less severe and less common than that to grasshoppers or locusts (Prasad *et al*. 2001, 2009, Patel & Choudhary 2012).

Investigating allergic-asthmatic children in Cincinnati, Ohio, and using RAST (radioallergosorbent test) of allergen-specific immunoglobulin E (IgE), Lierl *et al*. (1994) revealed a considerable cross-reactivity between cricket and grasshopper allergens. Unfortunately, the authors do not provide the name of the species used in their study, neither for the cricket, nor for the grasshopper.

The cricket-grasshopper cross allergy is not surprising. Cross allergy among different species of insects/arthropods is well known (see for example, Panzani & Ariano 2001). Cross allergy means that the same allergen is present in different taxa and it causes allergy to these taxa. Recently, cross allergy was demonstrated between *Macrobrachium* prawns and the cricket, *Gryllus bimaculatus*; arginine kinase constituted the common allergen (Srinroch *et al*. 2015). This finding contradicts the previous claim that there is no cross allergy between prawns and crickets (Linares *et al*. 2008). However, the cross-reactivity between grasshopper and cricket allergens does not seem to be complete. Comparison of the molecular mass of grasshopper/locust allergens (see Table 1 by Pener 2014) with those of cricket allergens (Bartra *et al*. 2008) reveals partial divergence. On the other hand, similarity (at 65-70 and 130 kDa) exists between grasshopper/locust allergens and hypersensitivity pneumonitis induced antigens, related to arginine kinase, in *Acheta domesticus* (see Park *et al*. 2014).

Srinroch *et al*. (2015) identified hexamerin 1B as a novel and specific allergen in *G. bimaculatus*.

It may be noted that thermal processing may alter allergens. Based on the Bombay locust, *Patanga succincta* (an acridid), Phiriyangkul *et al*. (2015) found differences in the allergens between raw and fried insects. For example, arginine kinase was identified in the former, but not in the latter. Considering that arginine kinase seems to be a common allergen to acridids and gryllids (and other arthropods), it may be assumed that similar changes occur in crickets with thermal procession.

Occupational allergy to crickets

Cazort & Johnston (1955, cited by Bellas 1981) reported sensitivity to crickets in a man raising crickets for fish bait. This was the first report on occupational allergy to crickets.

Two and a half decades later, Bagenstose *et al*. (1980) published two case reports on occupational allergy to crickets. The patients were exposed to crickets while employed at the University of Michigan Amphibian Facility where massive cricket rearing and breeding took place for feeding frogs. Both patients developed allergic rhinitis and bronchial asthma. Temporary cessation of working with crickets resulted in disappearance of these symptoms which reappeared after resumption of the work. The authors prepared an extract of the cricket, *Acheta domesticus*, and tested sensitivity of the patients by several methods, among them *in vivo* bronchial inhalation challenge and skin prick test, as well as by *in vitro* RAST that revealed specific IgE antibodies in the patients' serum. Interestingly, out of 11 other workers at the same facility, three exhibited positive skin prick test and two out of these three showed positive RAST, without overt symptoms of allergy.

Linares *et al*. (2008) reported a case of a 28-year-old woman with occupational rhinitis and asthma, who was exposed for three years to three species of crickets, *G. campestris (*often connoted as *Acheta campestris)*, *G. bimaculatus* and *A. domesticus*, in a farm raising cricket colonies. The authors prepared extracts of each of these three species of crickets with two types of protein extraction. They also made extracts of the food of the crickets. *In vivo* tests included skin prick test, lung function test and bronchial challenge testing. The results of the prick tests were positive for each of the three cricket species, but negative for their food. Specific IgE for each cricket species was determined by *in vitro* enzyme allergosorbent test (EAST), resulting in the values of 2.9, 2.4 and 5.4 kU/L, for *G. campestris*, *G. bimaculatus* and *A. domesticus*, respectively. EAST inhibition assays found a high degree of cross-reactivity among the three species of crickets, up to 86% for *A. domesticus* and *G. campestris*, some cross-reactivity between crickets and the firebug *Pyrrhocoris apterus*, but no cross-reactivity was detected between crickets and prawn, squid, mite or pollen (but see above positive cross-reactivity between *G. bimaculatus* and *Macrobrachium* spp. prawns found by Srinroch *et al*. 2015). Sodium dodecylsulfate – polyacrylamide gel electrophoresis (SDS-PAGE) and IgE immunoblotting showed similarity in IgE binding bands with the three species of whole body cricket extracts. Bands of molecular mass of 64 and 78 kDa were found in non-reducing conditions and bands of 52, 58, 80, 97 and 107 kDa in reducing conditions.

Another case report was published by Bartra *et al*. (2008). A 28-year-old man who had worked in a reptile shop for seven years, where he fed the reptiles with *Acheta campestris*, showed allergy to these crickets. The symptoms of allergy appeared in the fourth year of his work, that is, after a latent period of three years. These symptoms were asthma and rhino-conjunctivitis caused by inhalation and contact urticaria caused by handling the crickets. Skin prick test with a manufactured cricket extract was positive, whereas it was negative for control individuals, for cornmeal (food of the crickets) extracts and for a set of common inhalant allergens. Respiratory function test showed a drop of more than 20% of peak expiratory flow during work period, but it was normal during the weekend when the patient was free from crickets. A specific nasal test with cricket extract yielded positive results whereas the test with the control was negative. Immunoblot experiments of the protein profile of the cricket extract showed several bands with IgE binding, prominently with molecular masses of 17, 32, 47 and 62 kDa.

Investigating the general situation of allergy among pet shop workers, Ranström *et al.* (2011) distributed a questionnaire and received suitable answers from 59 subjects from 24 pet shops around Stockholm, Sweden. The authors tested in details some of the most common allergens like rat and mouse urinary allergens and among insects the darkling beetles (Tenebrionidae), specifically the mealworm beetle (*Tenebrio molitor*) and *Zophobas* droppings and larvae. No special attention was paid to crickets, but the authors mention in a single sentence that "....crickets were reported by several workers to have caused occasional strong allergic reactions" (Ranström *et al*. 2011, p. 1086).

Harris-Roberts *et al.* (2011) made a somewhat similar study, but instead of pet shop workers, they investigated the workers of a specialist insect breeding facility in the UK. Thirty-two persons answered a questionnaire on work-related respiratory symptoms and underwent lung function test; 18 persons provided serum for specific IgE determination. Sensitivity was found to locusts and mealworm beetles. However, a single asthmatic cricket handling worker was submitted to a more detailed clinical investigation. This person suffered from respiratory problems over the preceding two years with increasing periods of absence from work related to sickness. Expiratory wheeze and reduced lung function were found and the patient's serum revealed IgE to bran, locust and cricket (species not stated). After five months without contact to insects, the work-related respiratory symptoms disappeared.

Mairesse *et al*. (2014) studied allergy by skin prick test in 29 workers in a laboratory of entomology and found two persons showing double sensitivity to the mealworm beetle, *T. molitor*, and the cricket, *A. domesticus*.

Subacute hypersensitivity pneumonitis caused by crickets was recently described by Park *et al*. (2014). This disease is an inflammation of the lungs due to hypersensitivity to inhaled allergens. The patient having the disease was described as a 63-year-old male who previously owned an avian pet shop. Although avian proteins are known allergens, the authors' thorough investigation revealed that in this case the source of the allergen was the house cricket, *A. domesticus*, maintained in colonies by the thousands in boxes. The crickets served for feeding the pets. Cricket proteins were extracted and high titer antibodies were found against the extract with specific antigen-antibody precipitins. Additional investigations identified arginine kinase at 65-70, 130, and 160 kDa mass weights as the major allergen. Other cricket proteins may have acted as minor allergens contributing to the severity of the disease. The patient reduced his exposure to crickets and used a face mask resulting in decline of the disease after six months.

Immediate hypersensitivity to crickets

Immediate type hypersensitivity is characterized by appearance of allergic symptoms within a short while after exposure to the allergen, sometimes just minutes, usually less than one hour, though additional allergic symptoms may appear later.

In some instances these symptoms are inflicted by the classic allergic pathway, that is, IgE mediated. For example, immediate systemic reaction of allergy to bee or wasp stings are mostly (though not necessarily) IgE mediated (Przybilla & Ruëff 2012). In some other instances, the symptoms are of typical allergy, but the underlying mechanisms are not mediated by IgE; Kowalski *et al*. (2011) and Gimenez-Arnau *et al*. (2010) discuss some of such mechanisms.

There is a single case in the literature reporting immediate hypersensitivity to cricket (Harfi 1980). A 16-year-old male on two occasions while fishing and using crickets (species not stated) for baits, developed within 30 minutes lacrimation, angioedema of the eyelids, rhinorrhea and some additional symptoms; cough and wheeze followed in about five hours. Confirmation of the diagnosis was carried out, using cricket whole body extract, by challenge to the right conjunctiva that caused rhinorrhea, by scratch test, and by *in vitro* histamine release (that may, or may not mediated, by the IgE pathway), as well as by other tests.

Allergy associated with crickets in outdoor air

Lierl *et al.* (1994) investigated the effect of outdoor airborne allergens from moth, ant, house fly, grasshopper, cricket (species not stated) and spider. They compared by RAST the effect in "allergic asthmatic" children to that in "nonallergic nonasthmatic" children.

Roughly, the two clusters may be considered as atopic and non-atopic children, respectively. The authors employed several extraction procedures for each group of arthropods and used the most potent extract. Concerning crickets, 8 out of 41 (19%) of allergic-asthmatic children exhibited positive RAST, revealing cricket sensitive IgE in their serum. In contrast, none of the 25 nonallergic-nonasthmatic children showed positive RAST. In this study, cross-reactivity of cricket and grasshopper extracts was revealed, expressed by 59% average RAST inhibition (see also section on cricket allergens, above).

As much as four years before the publication of the article by Lierl *et al.* (1994) an abstract was published by the same authors (Lierl *et al.* 1990) estimating the amount of airborne insect-originating particles in outdoor air. They found 9-300 ng per cubic feet per week for cricket (species not stated).

Food allergy to crickets

A considerable part of the world population, in China, the Far East, and the Middle East, in Africa, Mexico, and South America, as well as indigenous people in Australia, feed on edible insects (Srivastava *et al.* 2009, Ramos-Elorduy 2009, Chen *et al.* 2009, Gahukar 2011, van Huis 2013 and others). Crickets (Gryllidae) and mole crickets (Gryllotalpidae) are important constituents of insect diet (Chen *et al.* 2009, Gahukar 2011, Belluco *et al.* 2013, Barennes *et al.* 2015, Megido *et al.* 2016), having high nutritional value (Belluco *et al.* 2013, Yi *et al.* 2013, van Huis 2013, Barennes *et al.* 2015, Megido *et al.* 2016). Rumpold & Schlüter (2013) published a comprehensive review on nutritional composition and nutritive values of edible insects, often referring to Orthoptera as a single unit (crickets, grasshoppers and locusts together), but presenting some specific details on *A. domesticus* from various sources.

Considering the widespread usage of crickets as human food, cases of food allergy to crickets are relatively rare. Piromrat *et al.* (2008) reported seven cases of anaphylaxis within a two-year period in an emergency department of a hospital in Bangkok, Thailand, caused by consumption of fried grasshoppers and crickets. Unfortunately, the authors did not make distinction between grasshoppers and crickets. Possibly, physicians often do not have the knowledge, or they are not confident, to distinguish among different suborders and families of Orthoptera. Ji *et al.* (2009), summarizing anaphylaxes inflicted by food consumption in China, do not mention crickets, though they report on 27 cases of anaphylaxis caused by eating locusts and another 27 cases due to eating grasshoppers.

Allergy to crickets without defined source

In the studies summarized below, possible former exposure to the allergen was not considered, no species was stated, possible cross allergy was disregarded and no statistical analysis was made. Also, the term grasshopper may mean acridid and/or tettigoniid (see Pener 2014).

Prasad *et al.* (2001) carried out 5,760 intradermal skin tests with 68 different antigens, including of five insects, tested on 108 patients with bronchial asthma who attended a medical college in Lucknow, India. Concerning crickets (species not stated), 31 tests were made and out of these three (9.7%) yielded definitely positive response. For comparison, 31 tests with grasshopper antigen resulted in 11 (35.5%) such response. These findings indicate much higher sensitivity to grasshoppers than to crickets.

Eight years later, Prasad *et al.* (2009) reported a similar study in Lucknow, using skin prick test instead of intradermal injected skin test. Forty-eight patients with nasobronchial allergy were tested. Eight of these (16.6%) exhibited definitely positive sensitivity to cricket antigen, whereas 10 (20.8%) showed the same to grasshopper antigen.

Another study was conducted by Patel & Choudhary (2012), testing by skin prick various antigens on patients with nasobronchial allergy in Gujarat, India. The authors found two cases (8.3%) of definitely positive response to cricket antigen. Again, for comparison, they found six (25%) cases of such response to grasshopper antigen. Also, sensitivity was higher to many insects, namely locust, moth, butterfly, mosquito, house fly, honey bee, hornet, yellow wasp and ant, than to cricket. These findings are somewhat controversial to Hosen's (1970) older results using a provocative nasal test conducted in 174 patients with perennial respiratory allergy to some insects of Southeast Texas. Out of the 174 patients, only 69 (33.2%) showed sensitivity to the powdered insect antigens tested. Without stating the species, sensitivity to crickets was more common than to red ant, mosquito, cockroach, moth, fire ant and house fly. Only sensitivity to spider (not an insect, but an arachnid) was more common than that to cricket. Hosen (1970) did not test grasshopper/locust antigen.

Management of cricket allergy

Very few publications deal with management/treatment of allergy to crickets. The patient reported by Linares *et al.* (2008) stopped her exposure to crickets and was treated with inhaled bronchodilator and corticosteroid. She became asymptotic and only occasionally needed inhaled salbutamol. The patient of Harris-Robert *et al.* (2011) was moved to another area of the facility with no direct exposure to insects. An examination five months later revealed that the cricket specific allergy symptoms had disappeared, without change in his inhaled asthma treatment (the patient was diagnosed with asthma 15 years previously). A patient with subacute hypersensitivity pneumonitis caused by house cricket (*A. domesticus*), as reported by Park *et al.* (2014), preferred reducing exposure to crickets and respiratory precaution by face mask instead of taking medicine. Evaluation of the response showed marked improvement of the patient's clinical symptoms.

These examples clearly indicate that the best treatment to cricket allergy is restraining from exposure to crickets. Avoidance of the allergen is a general rule to all kinds of allergy. Sometimes, however, avoidance may be practically difficult. A scientist may not like to change the subject of his/her research. Nevertheless, many entomologists have had to leave their jobs (Stanhope *et al.* 2015 and references therein). A technician may be afraid to lose a job with a reasonable salary.

For personal protection, gloves and dusk mask covering the nose and mouth may be sufficient. A hat is also advisable because dust sticking to hairs may contaminate pillows. Well-fitting laboratory glasses or a whole face mask (instead of a dusk mask that does not cover the eyes) help to avoid allergic conjunctivitis.

In my former article devoted to allergy to locusts and acridid grasshoppers, I described extreme protective measures; complete outfit laboratory coat, trousers and overshoes, as well as specially designed insect room and a changing room (Pener 2014 and references therein). These measures may overshoot the needs of cricket allergy which is less severe and less common than locust/grasshopper allergy. However, they should be implemented partially or fully in a case of a large scale insect rearing and breeding facility.

Allergy to crickets can be treated, like treatments of other allergies, by antihistamines, corticosteroids and bronchodilators. In life threatening cases, like anaphylaxis, intramuscular epinephrine may be administered (Piromrat *et al*. 2008). It should be stressed that these medicines reduce the symptoms of allergy, but they are not curative. Curative treatments include allergen specific immunotherapy, also termed desensitization, resulting in hyposensitivity to the allergen (see Fujita *et al*. 2012, Berin & Sampson 2013, and in relation to arthropods Schwartz 1990 and Kagen 1990). According to Kagen (1990), Cazort & Johnston (1955) describing a case of inhalant sensitivity to crickets, commented that desensitization was effective.

Additional references regarding control of the environment, prevention, protective measures and therapy are found in several older publications (Bellas 1990, Chan-Yeung 1990, Seward 1999 and reference therein); all these references are not specific to crickets, but related to allergy to insects.

Conclusions

Allergy to crickets is relatively infrequent and it is usually less severe than most common allergies. Nevertheless, crickets are listed as an allergen in many recent reviews on the subject. Cricket allergy is rather mild compared to allergy to locusts and grasshoppers, although there is a partial cross-reactivity between acridid and cricket allergy. Most relevant publications report on occupational allergy to crickets; food allergy seems to be rare despite the fact that crickets are edible insects consumed in many Asian, African and South American countries.

At the species level *Gryllus campestris (=Acheta campestris)*, *G. bimaculatus* and *Acheta domesticus*, were found to inflict cricket allergy. Although a high level of cross-reactivity was found among these three species, this cross-reactivity was not total. These three are the most commonly maintained colonies of cricket species in the world. To the best of my knowledge, no other cricket species have been investigated as allergens.

Very little information is available on the chemical identity of cricket allergens. It seems that arginine kinase is a considerable cricket allergen, but arginine kinase is a known allergen in many arthropods. Recently, hexamerin B1 was found as a cricket specific allergen, however, hexamerin B1 is known as an allergen also from some non-gryllid insects.

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