Allergy to Locusts and Acridid Grasshoppers: a Review

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Allergy to locusts and acridid grasshoppers: a review

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Abstract

Concise characterization of allergy is presented and allergy to insects is discussed. Three kinds of allergy to locusts and grasshoppers are reviewed: 1) occupational allergy, *i.e.*, allergy of personnel working with rearing and breeding these insects; 2) allergic reactions to acridid aggregations in the field; and 3) food allergy. Occupational allergy is the major subject, detailing the results of several relevant studies. Some inconsistent issues regarding reports on field allergy are illuminated and anaphylactic reaction to consumption of locusts/grasshoppers is discussed. Prevention and treatments of allergy to locusts and grasshoppers are described. Approximate molecular masses of locust allergens, as found in three studies, are summarized. A major allergen is the peritrophic membrane (today often termed peritrophic matrix or peritrophic envelope) which is secreted by the gut and excreted as a wrapping around the feces. It is concluded that the molecular structure of locust and grasshopper allergens should be revealed for full characterization.

Key words

occupational allergy, *Locusta migratoria*, *Schistocerca gregaria*, *Melanoplus sanguinipes*, *Chortoicetes terminifera*, field allergy, food allergy, Tettigoniidae

Introduction

Following Frankland's (1953) article on allergy to locusts, much attention was paid to allergy to acridids. The subject has three major aspects: occupational allergy of personnel working in laboratories studying acridids, allergic reactions to dense aggregations of acridids in the field and food allergy among people eating acridids. The occupational allergy is emphasized in this review, but the other aspects are also briefly discussed.

Allergy and allergy to insects

Allergy may be defined as a hypersensitive reaction of the immune system to a definite stimulus, termed allergen, at a dose tolerated by normal subjects (Johansson *et al*. 2001). Allergy is classified according to the organ/tissue affected, or according to the stimulus inflicting it. The former classification includes disorders of the skin, termed dermatitis, such as allergic eczema (Katelaris & Peake 2006; Spiewak 2012) and allergic hives (urticaria), wheals, or angioedema (Zuberbier *et al*. 2009). It also includes disorders of the lungs, most commonly asthma (Lemanske & Busse 2010; Löwhagen 2012), conjunctivitis of the eyes (Saban *et al*. 2013) causing lacrimation and rhinitis of the nasal airways resulting in running nose (Izquierdo-Domínguez *et al*. 2013). Some other organs such as sinuses and the gastrointestinal tract may also be subject to allergic reaction. These disorders are not mutually exclusive and frequently multiple organ systems are affected.

Allergens are recognized by the immune system through a complex process, resulting in production of immunoglobulins by the B cells. Immunoglobulins are antibodies. Immunoglobulin E (IgE) is taken up by receptors in specific cells, termed mast cells. IgE molecules are bound to the surface of the mast cells, but their antigen (allergen) binding section remains free. A subsequent exposure to the same allergen results in binding of the allergen to the mast cell-bound IgE, causing 'degranulation' of the mast cell, meaning release of histamines, cytokines and other chemical mediators. These substances inflict inflammation which is the allergic reaction. Details of the process are presented by Schofield & Calhoun (2011) and in relation to allergy of airways and lungs by Curotto de Lafaille *et al*. (2010). The role of the mast cells is reviewed by Amin (2012) and the mechanism of degranulation by Hua (2013). In a recent review, Oppong *et al*. (2013) discuss the molecular mechanisms of glucocorticoid action in mast cells. Glucocorticoids exert anti-inflammatory effects and they are antiallergic compounds

There are also non-IgE-mediated hypersensitive reactions, also termed 'immediate contact reactions' (Gimenez-Arnau *et al*. 2010; Zhai *et al*. 2012 and references therein).

Extreme cases of allergic reaction may lead to anaphylaxis that can develop very rapidly and can be fatal. Most severe cases of anaphylaxis restrict breathing and blood circulation (National Institute of Allergy and Infectious Diseases 2012; Worm *et al*. 2013).

Anything can be an allergen and insects are not exceptions. Allergy to insects was repeatedly reviewed, (Fuchs 1979; Wirtz 1984; Burgess 1993; Day *et al*. 2004; Goddard 2013; and others). Most cases of insect allergy are associated with stings (components of venom) by Hymenoptera, bites by blood sucking insects (components of oral secretions), other ectoparasites, poisonous spines or hairs and defensive secretions. However, simple contact with insects, or with their excreta, or volatile substances emanating from insects, can also inflict allergy. Cockroaches constitute the most frequent indoor insect allergen in urban communities (Gore & Schal 2007; Sohn & Kim 2012; Perzanowski *et al*. 2013).

Allergy and allergens may be diagnosed *in vivo* by the skin tests There are prick or puncture (percutaneous) tests and intradermal (intracutaneous) test; the latter is more sensitive, but less specific than the former (Cox *et al*. 2008) . Standardization of the prick test is proposed by Heinzerling *et al*. (2013). These authors also suggest a common panel of inhalant allergens, including cockroach (*Blattella germanica*) specific allergens. Alternatively, allergy and allergens may be diagnosed *in vitro* by determination of specific IgE antibodies in the patient's serum (Knol & Knulst 2010; Salo *et al*. 2011). Allergen testing is reviewed by de Bruin-Weller *et al*. (2012), including atopy

patch test in patients with atopic dermatitis. Heinzerling *et al*. (2013) also devoted a section of their review to comparison of the skin prick test with other diagnostic methods. Cox *et al*. (2008), overviewing allergy diagnostics, outlined advantages and disadvantages. Recently, Nishino *et al*. (2013) suggested a non-invasive *in vivo* method for detection of the type of intracutaneous allergy.

Determination of a specific allergen by diagnostic methods does not necessarily mean that the symptoms of the patient's allergy are caused by the defined allergen because in many instances cross-allergy may exist. Extensive cross-allergy between different families and orders of arthropods and even with other non-arthropod invertebrates has been detailed by Panzani & Ariano (2001, pp. 12-13) who used the term 'panallergy'. Often cross-allergy among different species can be reduced to a single factor and/or its derivatives or components at the molecular level. For example, Ayuso *et al*. (2002) found cross-reactivity to tropomyosins from shrimp, lobster, house dust mite and cockroach. In contrast, a species can be the source of several allergens. From the cockroach, *Blattella germanica*, the sixth allergen (termed Bla g 6, with three isoallergens) was characterized relatively recently (Hindley *et al*. 2006). A characterized allergen from a species is abbreviated by the first three letters of the genus, the first letter of the name of the species and a number. Thus, for example, the above mentioned Bla g 6 means the sixth characterized allergen of *Blattella germanica*. Arlian (2002) presents a more detailed discussion of the allergen nomenclature.

Occupational allergy to locusts and acridid grasshoppers

Frankland (1953), treating a patient against hay fever, accidentally discovered that this patient has a mild allergic rhinitis when handling locusts at an experimental research station. This discovery led Frankland to carry out a survey for locust sensitivity of the personnel of several institutions maintaining locust stocks for research. He noted overt symptoms of allergy and performed skin tests. He made extracts for skin tests from homogenates of a mixture of two locust species, *Locusta migratoria* and *Schistocerca gregaria*. Out of 34 workers in contact with locusts at two research stations, four exhibited allergic symptoms and 14 others showed sub-clinical sensitivity by reacting positively to skin test, without overt symptoms. Feces of locusts were found to be no less allergenic than locust bodies. Circumstantial evidence indicated that in some instances locust allergy may constitute cross-allergy to cockroach allergy. However, in later publications, such cross-allergy was found to be very infrequent (Burge *et al*. 1980), or it was not detected (Tee *et a*l. 1988). In a more recent study, Lopata *et a*l. (2005) found in insect laboratory workers that raised IgE titers to *Locusta migratoria* and to cockroaches (*Blattella germanica* and *Periplaneta americana*) are associated with limited cross-reactivity.

Many authors published case reports on allergy to acridids and some representative reports are mentioned here. Gronemeyer (1958) reported several cases of occupational allergy, with symptoms of asthma, dermatitis and rhinitis, to *L. migratoria*. A case of occupational asthma of a patient working for long time with grasshoppers (species not stated) was described by van der Bijl (1963). Ky & Vallery-Radot (1974) shortly reported two cases of allergy to an African grasshopper/locust (species not stated). In one case they observed rhino-conjunctivitis and asthma in a technician working in a laboratory engaged in acridid research. The other case was not occupational allergy; a physician using acridids as baits in trout fishing, showed conjunctivitis, asthma, urticaria and edema caused by the bait. Bessot *et al*. (1978) recorded two cases of respiratory allergy, rhinitis and asthma in research staff of a laboratory with about 15,000 locusts of *L. migratoria*. Monk (1988) reported three cases of allergy provoked by locusts (species not stated) in a laboratory maintaining a large breeding colony. One patient showed symptoms of contact urticaria, another exhibited contact urticaria and conjunctivitis, whereas in the third case asthma constituted the allergy. Soparkar *et al*. (1993) published a case report of a person who showed urticaria, lacrimation, rhinitis, wheezing and shortness of breath (indicating asthma) when handling *Melanoplus sanguinipes* grasshoppers.

Allergy to acridids by symptoms and/or by *in vivo* and/or *in vitro* tests was reported by many authors. Joly (1963) tested various parts of the body of *L. migratoria* and concluded that the surface of the locusts, especially the cement layer, the outermost layer of the epicuticle, is the allergenic factor. Detecting IgE antibodies to many species of insects in subjects with occupational inhalant allergies, Baldo & Panzani (1988) reported allergy to adults and feces of the Australian plague locust, *Chortoicetes terminifera*; the study was carried out by preparing extracts and evaluating the results *in vitro* by Radioallergosorbent test (RAST). The findings of Baldo & Panzani (1988) are mentioned again by Panzani & Ariano (2001). The Overseas Development Natural Resources Institute (ODNRI 1989) published a booklet on allergy to locusts, dealing with its occurrence and symptoms, as well as with protective measures. In his booklet on rearing and breeding of locusts in the laboratory, Harvey (1990) discussed allergy to locusts and preventative, as well as protective actions. Recently, Harris-Roberts *et al*. (2011) investigated work-related respiratory disturbances in a commercial company which is distributing locusts and mealworms, as food for pets, such as reptiles and amphibians. Eighteen workers provided serum for IgE determination using RAST. One worker exhibited locust specific IgE and another showed specific IgE to locusts as well as specific IgE to mealworms. The species of locusts is not stated.

Several comprehensive studies were made on occupational allergy to locusts and grasshoppers. Burge *et al*. (1980) investigated allergy in the same locust-breeding research center that had been studied by Frankland (1953). Burge *et al*. (1980) divided the staff to four groups according to exposure to locusts. Among 43 workers actually handling locusts, including cleaners of locust rooms and cages, 26% showed work-related symptoms of wheeze or breathlessness, indicating asthma, and 35% and 33% exhibited work-related rhinitis and urticaria, respectively. Out of 29 scientists who might have been exposed to occasional contact with locusts (biographers, meteorologists, librarians, etc.), only two persons (≈7%) exhibited asthma, two persons (≈7%) showed work-related urticaria and four persons (≈13%) suffered from work-related rhinitis. Out of 28 administrative staff, without any contact with locusts, only two displayed work-related rhinitis and none showed work-related asthma or urticaria. The fourth group included 18 field workers occasionally heavily exposed in the field to locusts, but with intermittent exposure. Only one claimed work-related rhinitis and one showed work-related urticaria.

Burge *et al*. (1980) and Burge & Edge (1980) implied that their studies were based on 118 (43+29+28+18) workers of a research center. However, Edge & Burge (1980) explicitly stated in a meeting proceedings paper that the 43 workers actually handling locusts came from two research centers.

Burge *et al*. (1980) prepared locust antigens by homogenizing whole frozen males and females of *L. migratoria* and *S. gregaria*. The antigens were *in vivo* skin prick tested and *in vitro* antibody tested. Among 42 skin prick tested workers actually handling locusts, 18 (≈43%) showed positive reaction to locust antigens. In contrast with the low rate of work-related allergic symptoms of the 18 field

workers (see above), six (≈33%) exhibited positive skin prick test to locust antigens.

Based on immunofluorescent staining of serial sections through *S. gregaria*, Edge & Burge (1980) reported that no antigen was present in the anterior third of the locusts. Antibodies from affected workers were specific to the surface of the epidermal cells of the midgut and of the ceca, indicating that the source of the antigen may be the peritrophic membrane. Edge & Burge (1980) also reported significantly higher antibodies to locusts in affected than in non-affected workers.

Tee *et al*. (1885, 1988) studied thirty-five workers of a research center maintaining locusts by questionnaire concerning allergic symptoms, as well as by locust specific skin prick test and IgE antibody measurements. Out of 15 workers exposed to locusts, five showed asthma, rhinitis and contact urticaria, three exhibited rhinitis and urticaria and one complained about rhinitis alone. One additional worker exposed to locusts did not complain but exhibited positive skin prick test. Workers at the same institute, but unexposed to locusts, did not complain about allergic symptoms, nevertheless positive skin prick test was found in two out of 20 persons.

Tee *et al*. (1988) prepared six antigens: adult intact *S. gregaria*, adult intact *L. migratoria*, adult *S. gregaria* gut, adult *L. migratoria* gut, peritrophic membrane (today often termed peritrophic matrix or peritrophic envelope) from the midgut of *S. gregaria*, and mixed feces of *S. gregaria* and *L. migratoria*. They also sampled the atmosphere of the locust room for locust allergens using a high volume air-sampler filter. All locust-exposed persons with positive skin prick test to intact locusts also exhibited positive skin prick tests to gut, peritrophic membrane and feces. The symptoms of allergy inflicted by locusts and the results of skin prick tests to locust extracts were associated with specific IgE antibody in the serum of the workers as measured by RAST

Tee *et al*. (1988) found multiple allergens in locust extracts of approximately 68, 66, 54, 43, 37, 29 and 18 kDa of molecular mass (Table 1). They concluded that the major source of locust allergens seems to be the peritrophic membrane which is produced in the gut and excreted as a wrapping around the feces. This conclusion supported the suggestion of Edge & Burge (1980) that the peritrophic membrane is a major causative factor of locust allergy. Chitin is a component of the peritrophic membrane, but Tee *et al*. (1988) found that chitin does not provoke allergy. In spite of some publications claiming possible associations between chitin and allergy (*e.g.*, Reese *et al*. 2007; Brinchmann *et al*. 2011; and others), it seems that chitin and chitosan are not allergenic (cf. Muzzarelli 2010, for discussion and conclusions).

A study by Soparkar *et al*. (1993) well illuminated that non-locust acridids also inflict occupational allergy. This study was based on a detailed case report (see above), including inhalation test, and on 17 workers, from two research laboratories, exposed to the grasshopper, *Melanoplus sanguinipes*. These workers answered a questionnaire and, except one, underwent skin prick test. Twenty-six persons unexposed to grasshoppers constituted the controls.

Three grasshopper antigen extracts were prepared by Soparkar *et al*. (1993): whole homogenized grasshopper (termed antigen A by the authors) and two extracts from feces and other material collected from the bottom of the grasshopper cages; one of the these (antigen B) contained less amount of discarded food (left-over of grass, bran, lettuce, etc.) than the other (antigen C). Out of the 16 workers exposed to grasshoppers and skin prick tested, six and four complained about cutaneous and respiratory symptoms, respectively. However, only seven exhibited positive skin prick test to antigen extracts B and C and only five to antigen A (whole body extract). The four workers complaining about respiratory symptoms, all showed positive skin prick test. From the non-exposed controls, one subject showed positive skin prick test to antigens B and C, but not to antigen A.

Using questionnaires, skin prick test and assessing specific IgE and IgG in the serum, Lopata *et al*. (2005) investigated ten persons exposed to *Locusta migratoria* in a laboratory. Six of these persons reported locust-related symptoms of allergy (asthma, urticaria and/or rhino-conjunctivitis), seven showed sensitivity to locusts by skin prick test and five demonstrated presence of specific IgE. The authors found a positive correlation between locust-specific IgE and specific IgG. This correlation is not surprising; IgG may be associated with IgE, but its association with allergic symptoms is ambiguous and diagnostically IgG is less useful than IgE (Aalberse *et al*. 2009).

In addition of whole body extracts of locusts (and of some other insects), Lopata *et al*. (2005) prepared protein extracts of locust gut, feces and wings as antibodies. They found allergens in these extracts with molecular mass of about 30, 35, 55 and 70 kDa (Table 1). The allergen(s) of approximately 70 kDa was (were) identified in locust wings and the authors claimed a distinct difference from other known allergens of locusts.

Wirtz (1980) conducted an occupational allergy to arthropods survey, mostly to insects, by mailing questionnaires to institutions maintaining arthropod rearing and asking for individual answers. A total of 115 people reported allergies, with one respondent claiming anaphylactic shock caused by exposure to the grasshopper *Melanoplus differentialis*. Unfortunately, there is no corroborative evidence to this claim. Although the questionnaires were aimed to occupational allergy, the possibility that a respondent reported food allergy cannot be excluded. Even stranger is the claim of another respondent reporting anaphylactic shock caused by exposure to the German cockroach, *B. germanica*, though in this instance food allergy is less probable. No case reports or additional investigations were published. Although Wirtz (1984) included these cases in his review on allergy to non-stinging arthropods, the scientific value of these claims is doubtful.

Allergy associated with exposure to locusts or grasshoppers in the field

The BBC (2003a) reported on October 21, 2003, locust outbreaks in Mauritania, Niger and Sudan. In late October 2003 several communications appeared in the media, stating that locust swarms caused asthma epidemic in Sudan, resulting in death of five people and hundreds hospitalized (Sudan Tribune 2003; TerraDaily 2003; Aljazeera 2003; and others). On November 1, 2003, the BBC (2003b) reported 11 cases of death and more than 1,600 hospitalization after swarms of grasshoppers caused asthma epidemic in Sudan. The reports in the media found their way to semi-scientific and scientific literature (Bhattacharya 2003; Lopata *et al*. 2005; Hill & Goddard 2012).

Surprisingly, however, Desert Locust Bulletin No. 301, issued on November 6, 2003 by the Food and Agricultural Organization of the UN stated that: "A locust outbreak developed during October in northeastern **Sudan** where several small swarms were reported. Breeding continued in this area and locusts formed small groups and bands throughout the month…" (FAO, 2003, p. 1). The question arises how and why "small swarms" (adults) and/or "small groups and bands" (hoppers) did inflict an asthma epidemic. No such epidemic was reported in the literature with much more massive plagues of locusts. Also, it may be recalled that in a research center, Burge *et al*. (1980) studied 18 field workers occasionally heavily

exposed in the field to locusts and only one claimed work-related rhinitis and one suffered from work-related urticaria.

It seems, therefore, that asthma epidemic caused by locusts in 2003 in Sudan is an exceptional event. Opinions on the factor responsible for this epidemic were discussed by Bhattacharya (2003). According to one assumption, a pheromone released by the locusts during their mating season may be a causative factor. However, it is difficult to reconcile this assumption with the fact that no other asthma epidemic was reported from other locust plagues. Occupational allergy to locusts (see former section) is developing rather slowly with prolonged contact with locusts. Another opinion holds that swarms of locusts devastating vegetation can leave lots of dust in the air and chemicals may be released from breakdown of the vegetation. Some additional factors may be added to those discussed by Bhattacharya (2003). Locusts attacked by insecticides or other ways may regurgitate the content of their crop and if they just consumed plants with allergenic chemicals, the regurgitated content may be allergenic. The control measures against the locusts (insecticides?) may also be involved in an allergic response. The BBC (2003b) mentioned that, according to residents, the locusts gave off a strong smell which caused breathing difficulties. If this observation is correct, possibly not the locusts, but some factor originating from the vegetation or from the dust caused the asthma epidemic. In any case, no definite conclusion can be drawn.

Prasad *et al*. (2001) exploring various allergens by intradermal method in patients of bronchial asthma in Lucknow (India), found that the most common allergens were insects. Five types of insect antigens were tested: grasshopper, locust, cricket, cockroach female and cockroach male. No species was stated for these antigens. Without the name of the species, the term 'grasshopper' is ambiguous; it may mean acridids (short-horned grasshoppers), or tettigoniids (long-horned grasshoppers), or both (see below section: "Food allergy to locusts and grasshoppers"). Cross-allergy was not eliminated by Prasad *et al*. (2001) and possible food allergy was not considered. Several years later, Prasad *et al*. (2009) repeated the study, but employing skin prick test and six types of insect antigens: grasshopper, locust female, locust male, cricket, cockroach female and cockroach male. They found again that the most common offending allergens were insects and among the insects locust female followed by locust male. As in the former study, no species was stated, no cross-allergy was eliminated and possible food allergy was disregarded.

Patel & Choudhary (2012) tested allergen sensitivity of patients with nasobronchial allergy in Gujarat (India), using skin prick test and employing various antigens, including grasshopper (acridid or tettigoniid?), locust female, locust male, cricket and cockroach female, as well as eight additional insects from three different orders (Hymenoptera, Lepidoptera and Diptera). No species was stated for any of these antigens. In contrast to the results of the studies in Lucknow (see above), grasshopper, locust female and locust male were minor allergens. No cross-reactivity was considered. Gujarat is in central east India, whereas Lucknow is in Utter Pradesh, rather to the north, bordering Nepal. Both localities are in the invasion area of the desert locust, but the migratory locust is also present in India (Steedman 1990).

There are a few case reports on allergy to acridids in the field. As already outlined (see section on "Occupational allergy…."), a physician, using acridids as bait in fishing, showed allergic reaction to the bait (Ky & Valery-Radot 1974). This case may be somewhat similar to occupational allergy because presumably it developed with repeated contact with the bait. Abbas & Shabbir (1965) reported a field worker who showed sensitivity to locusts. However, this person experienced in the past an occupational allergy to locusts. The symptoms of allergy had disappeared after cessation of contact with locusts, but they returned after field contact with invading locusts. Another case of grasshopper allergy was reported by Schnitzker (1974). In this instance hives were related to contact with grasshoppers (acridids or tettigoniids?) and/or praying mantis by a 14-year-old boy during football practice. Scratch skin test to grasshopper extract (species not stated) resulted in a wheal within two minutes and the wheal continued to expand up to 7 cm in its largest diameter. The conclusion of Schnitzker (1974, p. 281) saying that "Testing proved a definite sensitivity to whole grasshopper extract", was claimed to be misleading by Bergner (1974) who stated that testing did not prove a case and effect relationship between the presence of IgE antibodies and the patient's symptoms of hive. Indeed, there are many variables that may affect skin test reactivity (Cox *et al*. 2008) and cross-reactivity may also exist.

Food allergy to locusts and grasshoppers

Many insects are consumed by humans, mainly in developing countries, but there are possible health risks with this practice, one of which is allergic reaction to some insect species (van Huis 2013). Srivastava *et al*. (2009), reviewing traditional aspects of insects as human food and medicine, list grasshoppers among many other insects which constitute food for people in the Far East and other parts of Asia, as well as in Australia, Africa, South America and the Middle East. However, the authors mention that some people are allergic to grasshopper. Gahukar (2011), reviewing entomophagy, devote a whole section to Orthoptera, namely grasshoppers, locusts, crickets and mole crickets as widespread human food; the author also mentions food allergy to grasshoppers. When no species name is provided, the term grasshopper is ambiguous in these articles and in most of the relevant literature. Leung *et al*. (1996) studied cross-reactive allergen, presumably tropomyosin, in muscle extracts of several invertebrate species. The authors included 'grasshopper' in this study, and they named the species, *Mecopoda elongata*, which is a tettigoniid, not an acridid. Citation of Leung *et al*. (1996) in the literature claiming food allergy to grasshoppers (*e.g.*, Reese *et al*. 1999; Belluco *et al*. 2013) actually means food allergy to a tettigoniid. Therefore, care should be paid to the meaning of the term 'grasshopper'. Perhaps distinction between acridids and tettigoniids by patients and physicians is an unrealistic request; both groups of insects belong to the order Orthoptera and for the layman they look quite similar.

The ambiguity of the term 'grasshopper' exists in the literature on insects as food. After using the term 'grasshopper' for several species of Acrididae, van Huis (2013) uses the same term for *Ruspolia* without mentioning that the latter belongs to Tettigoniidae. This may not be surprising because the relevant sources cited by van Huis (2013) do not refer to Tettigoniidae, rather they refer to *Ruspolia nitidula* as the 'cone-headed grasshopper' (Agea *et al.* 2008), or note that *Ruspolia differens* is a 'long-horned grasshopper' (Kinyuru *et al.* 2010).

Food allergy to grasshoppers may be acute and may result in anaphylaxis. Piromrat *et al*. (2008) reported seven cases of anaphylaxis caused by fried grasshoppers and crickets during a two-year-period in an emergency department of a hospital in Thailand. In this paper no distinction was made between grasshoppers (acridids and/or tettigoniids) and crickets (gryllids). Ji *et al*. (2009) summarized 27 cases of anaphylactic shock caused by consumption of grasshoppers and 27 cases caused by consumption of locusts, as reported in the Chinese literature between 1980 and 2007.

Safety issues concerning consumption of insects, including locusts

and grasshoppers, are reviewed recently by Gahukar (2011), van Huis (2013) and Belluco *et al.* (2013). Saeed *et al.* (1993) reported that locusts with residual phosphorous-containing and chlorine-containing insecticides were eaten in Kuwait. There are other chemical hazards in eating acridids; for example, dried grasshoppers (so called 'chapulines') imported from Mexico to California caused lead poisoning (Handley *et al.* 2007). Grasshoppers take up and accumulate metals in metal contaminated grasslands (Hunter *et al.* 1987; Devkota & Schmidt 2000). Also, many acridids have their own chemical defenses (see Table 9 by Whitman & Vincent 2008), often obtained from toxic plants, and eating toxic acridids may even be fatal (Steyn *et al.* 1962). It is important to distinguish the effects of these hazards from those of food allergy. Transfer of pathogenic microbial organisms from insects consumed by humans constitutes another hazard, which, however, has not been demonstrated for acridids. Nevertheless, the possibility of such transfer was outlined by Johny *et al.* (2009).

Allergy to locusts and grasshoppers without defined source

In these studies people were submitted to *in vivo* or *in vitro* tests to allergens of locusts or grasshoppers, or the authors used sera of persons allergic to locusts, without considering the mode of possible former contact with these insects.

Feinberg *et al.* (1956) selected patients complaining about any kind of allergy and submitted them to several insect antigens by *in vivo* skin scratch test in clinical observations. They found 20 out of 80 patients with allergic reaction to grasshopper (species not stated). It may be recalled that in this instance the term 'grasshopper' means either acridids or tettigoniids (see above). The authors noted that patients who showed positive skin test to one kind of insect, usually reacted to several kinds of insects. This finding indicates cross-allergy.

Testing 17 species of allergenic Indian insects, mostly by *in vivo* intradermal skin test, Shivpuri *et al.* (1971) carried out a large scale study. Among other insects, antigens were made from extracts of locusts, *L. migratoria*, males and, separately, females, as well as from extracts of the grasshopper, *Acridium melanocorne* (Acrididae, today considered as a subspecies of *Valanga nigricornis*). Allergic reactions were estimated by a grading method. The results did not differ much for locust males, locust females and grasshoppers, but no statistical analysis was carried out. Patients with previous respiratory allergy of unidentified sources were more susceptible than healthy persons. Recently, Chen *et al.* (2012) isolated proteins from *L. migratoria manilensis* by SDS polyacrylamide gel electrophoresis and identified allergens by Western-blotting, using sera from patients allergic to locusts. The authors do not state the source of the allergy to locusts. However, they discuss in the introduction and in the conclusion sections food allergy to locusts, noting that locusts are considered as a delicacy. Also, they state that some of the sera from patients allergic to locusts were from the Children's Hospital. Children are not supposed to have occupational allergy. It is feasible to assume, therefore, that all, or at least most of the patients had food allergy to locusts. Chen *et al.* (2012) identified the primary allergens with molecular masses of 19, 29, 38, 70, and 130 kDa (Table 1).

Table 1. Locust allergens in approximate kDa molecular mass as found in several studies.

Tee *et al.* 1988	Lopata *et al.* 2005	Chen *et al.* 2012
		130
	70	70
68		
66		
	55	
54		
43		
		38
37		
	35	
	30	
29		29
		19
18		

Management of locust/grasshopper allergy

Reviewing occupational allergy, Peden & Reed (2010, p. S157) state: "The key is avoidance, avoidance, avoidance...", but "this is easier to say than done". The Overseas Development Natural Resources Institute (ODNRI 1989) also advised people who have developed sensitivity to locust allergens to give up contact with these insects. However, sometime it may be difficult for a technician to find a suitable alternative employment and scientists do not like to give up a more or less important component of their research subject.

Protective measures should be taken not only after appearance of overt allergy to locust/grasshopper, but all time, including new staff and people who did not (yet?) developed allergy. The protective measures described below based on the publications by ODNRI (1989) and Harvey (1990). Locust rooms, including preparation rooms (cleaning cages, preparing food, etc.), should constitute a self-contained unit, well separated from offices and other parts of the premises by a changing room (see below). The unit should be kept under negative pressure to avoid escape of allergens outside the unit.

If cages with perforated false floor are used (see Harvey 1990, pp. 15-16), feces, food particles and dust accumulating in the bottom of the cages should be cleaned using a vacuum cleaner. After cleaning the cages, the floor and the shelving in the locust room(s) should also be cleaned by vacuum cleaner, followed by wiping with a wet mop.

For personal protection, gloves and a dust-mask covering mouth and nose, may be sufficient, especially with a small stock of locusts. For sensitized people working in the locust room(s) a complete protective outfit is recommended. The components of such outfit are: a hat covering the hair (dust with allergens sticking to hair may contaminate pillows at night), a whole face mask (dusk-mask does not cover the eyes and does not prevent allergic conjunctivitis), laboratory coat, gloves, trousers and overshoes. All these components may be united into a protective clothing as shown by Harvey (1990, p. 15, Figs 13 and 14). In extreme cases, the locust room should have a tap of incoming clean air. This tap should be connected by light and flexible tubing to the back of the protecting clothing (which should have an outlet close to the floor). This arrangement maintains a positive pressure within the clothing, preventing penetration of dust. Changing into protecting clothes should be made in a changing room with two air-tight doors, one into the locust rooms and the other into the outside.

Incoming clean air causes positive pressure in the locust rooms. However, positive pressure results in escape of allergens outside the locust rooms, which should be prevented. The solution is filters, charcoal or electrostatic, that are capable of removing allergens from the air of the locust rooms. Such filters should be maintained regularly.

Allergy to locusts/grasshoppers may be treated, similarly to treatment of other allergies like hay fever, house dust mite allergy, etc., by pharmacological means as prescribed by a physician. The established medications are antihistamines and corticosteroids. The mode of action of these and some other medications are described by Holgate & Polosa (2008). These medications temporarily reduce or eliminate the symptoms of allergy, but they are not curative. In the case of asthma, temporary relief is obtained by bronchodilatators (*e.g.*, albuterol). Curative methods are also known (for details see Holgate & Polosa 2008), allergen-specific immunotherapy, leading to hyposensitivity to the allergen, is widespread. This method is used to treat mainly allergic rhinoconjunctivitis and asthma (Bousquet *et al*. 1998; Rolland *et al*. 2013). Dermatitis is treated by medications (Zuberbier *et al*. 2009; Sicherer & Leung 2013), or induction of hyposensitivity (Sicherer & Leung 2013).

Allergen-specific immunotherapy, also termed desensitization, inducing tolerance or hyposensitivity, is based on administration of a specific allergen with increasing doses to habituate the body to that allergen. The treatment usually starts with very low doses. There are two major methods for administration of the diluted allergen, subcutaneous injection or sublingual drops. Allergen-specific immunotherapy, often abbreviated as SIT, has been used for almost 100 years. The mechanism of allergen-SIT is reviewed by Fujita *et al*. (2012). Berin & Sampson (2013) discussed some limitations of immunotherapy-induced desensitization in food allergy. Kagen (1990) and Arlian (2002) reviewed some instances of immunotherapy against insect and mite allergens.

Only few reports deal with treatment of specific allergy to locusts and grasshoppers. Available data are old and not always sufficiently accounted. Frankland (1953) presented a detailed case report of a patient with occupational asthma caused by locusts (*S. gregaria* and/or *L. migratoria*). Skin test showed positive responses to locust extracts, the largest response was obtained with locust feces. A desensitizing immunotherapy course of 25 consecutive increasing injections using locust feces as antigen was successful. The patient received maintenance doses once a month, but after the third continuation the asthma returned. By reducing the dose and taking antihistamines the symptoms of asthma decreased, but the sensitivity to locusts again returned. After nine reduced maintenance doses, the dose was further decreased. Eventually, the patient described his state as cured, though face masks was still necessary in high concentrations of locusts. Also, pricking of the skin with locust spines caused local irritating wheal (urticaria).

A case report of occupational allergy to grasshoppers (species not stated), inflicting asthma, was detailed by van der Bijl (1963). The diagnosis was made by intracutaneous test, using extracts of grass, feces of grasshoppers and living grasshoppers. Treatment with antihistamines was unsuccessful. However, a course of desensitizing immunotherapy yielded good results.

Abbas & Shabbir (1965) also reported a case of allergen-specific immunotherapy, by subcutaneous injections of locust extracts with increasing doses, leading to successful desensitization.

Ky & Vallery-Radot (1974) reported shortly, in a conference abstract, two instances of allergy to African grasshoppers (species not stated) and noted that desensitizing treatment was unsuccessful in one case, but successful in the other. Schnitzker (1974) described a case of allergy to grasshopper and/or to praying mantis (Mantodea). Treatment with steroids and antihistamines yielded only minimal benefits. However, treatment with grasshopper vaccine (species not stated), initially 0.05 ml of $1{:}10^6$ dilution, then increasing doses up to 0.2 ml of $1{:}10^2$ dilution, successfully induced hyposensitization. Some aspects of Schnitzker's (1974) conclusions were criticized by Bergner (1974), also in relation to hyposensitization.

Soparkar *et al*. (1993) presented a case report of occupational allergy of a student investigating *Melanoplus sanguinipes* grasshoppers in a research laboratory. During his working period the student observed onset and gradual increase of urticaria, lacrimation, rhinitis, wheezing and shortness of breath while handling grasshoppers. These phenomena increased with time and the student eventually gave up handling grasshoppers. The urticaria and lacrimation have stopped spontaneously. The wheezing, cough and shortness of breath responded well to inhaled bronchodilatator (albuterol). Some diagnostic data were supplied several weeks after the last exposure to grasshoppers. However, the authors stated that "grasshopper antigens for skin testing were not commercially available", though (presumably later) grasshopper antigen extracts were prepared.

Conclusions

The exact molecular structure of locust and grasshopper allergens has not yet been revealed. However, it is known that these allergens, identified by their approximate molecular mass, are macromolecules of proteinous compounds. The molecular masses of the allergens found in three studies are summarized in Table 1. It should be kept in mind that these molecular masses are approximate; they are based on interpolation between standard molecular mass markers. Therefore, a difference of one kDa between the molecular masses in two different studies does not necessarily mean two different allergens. For example, the molecular mass of 37 kDa found by Tee *et al*. (1988) and that of 38 kDa found by Chen *et al*. (2012) may represent the same, or almost the same allergen. Before discovering the molecular structures of the allergens, no full characterization can be achieved.

Frankland (1953) found that feces of locusts (*S. gregaria* and *L. migratoria*) are allergenic. Feces of the Australian plague locust, *Chortoicetes terminifera*, were also allergenic, though not always very strong (Baldo & Panzani 1988). Other studies showed that the peritrophic membrane (today usually termed peritrophic matrix or peritrophic envelope) is the source of the major allergen of locusts and grasshoppers (Edge & Burge 1980; Tee *et al*. 1988). Beside the peritrophic membrane, cuticular proteins also seem to be allergenic. Lopata *et al*. (2005) identified an approximately 70 kDa allergen in the wings of *L. migratoria*.

Altogether the following species of acridids (short-horned grasshoppers) were found to inflict occupational allergy: *S. gregaria* and *L. migratoria* (see Frankland 1953; Burge *et al*. 1980; Tee *et al*. 1988; Lopata *et al*. 2005; Chen *et al*. 2012), *M. sanguinipes* (see Soparkar *et al*. 1993), *Chortoicetes terminifera* (see Baldo & Panzani 1988) and *Acridium melanocorne* (see Shivpuri *et al*. 1971), today considered probably as a subspecies of *Valanga nigricornis*. The tettigoniid (long-horned grasshopper), *Mecopoda elongata*, may be added to this list (Leung *et al*.1996).

Although field allergy to locusts and grasshoppers exists, published data are insufficient for general conclusions to be drawn. Food allergy to locusts and grasshoppers constitutes a serious danger, but reported cases may include tettigoniids and even crickets.

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References

Aalberse R.C., Stapel S.O., Schuurman J., Rispens T. 2009. Immunoglobulin G4: an odd antibody. Clinical and Experimental Allergy 39: 469-477.

Abbas H.M., Shabbir S.G. 1965. Insect sensitivity. Agriculture Pakistan 16: 325-328.

Agea J.G., Biryomumaisho D., Buyinza, M., Nabanoga G.N. 2008. Commercialization of *Ruspolia nitidula* (nsenene grasshoppers) in central Uganda. African Journal of Food, Agriculture, Nutrition and Development 8: 319-332.

Aljazeera 2003. Deadly grasshoppers sweep Sudan. Swarms of grasshoppers are attacking farm-rich central Sudan, triggering an asthma epidemic that has killed five people. http://www.aljazeera.com/archive/2003/10/20084101146487947l1.html

Amin K. 2012. The role of mast cells in allergic inflammation. Respiratory Medicine 106: 9-14.

Arlian L.G. 2002. Arthropod allergens and human health. Annual Review of Entomology 47: 395-433.

Ayuso R., Reese G., Leong-Kee S., Plante M., Lehrer S.B. 2002. Molecular basis of arthropod cross-reactivity: IgE-binding cross-reactivity epitopes of shrimp, house dust mite and cockroach tropomyosins. International Archives of Allergy and Immunology 129: 38-48.

Baldo B.A., Panzani R.C. 1988. Detection of IgE antibodies to a wide range of insect species in subjects with suspected inhalant allergies to insects. International Archives of Allergy and Applied Immunology 85: 278-287.

BBC 2003a. Locust outbreak threatens Africa. Crops in north Africa are under treat from swarms of locusts, says the UN Food and Agriculture Organization. http://news.bbc.co.uk./2/hi/africa/3210464.stm

BBC 2003b. Locusts cause Sudan asthma death. Eleven people have died in the past two weeks in central Sudan after a swarm of grasshoppers caused an asthma epidemic. http://news.bbc.co.uk/2/hi/africa/3234325.stm

Belluco S., Losasso C., Maggioletti M., Alonzi C.C., Paoletti M.G., Ricci A. 2013. Edible insects in a food safety and nutritional perspective: A critical review. Comprehensive Reviews in Food Science and Food Safety 12: 296-313.

Bergner R.K. 1974. Misconceptions regarding grasshopper allergy. Pediatrics 54: 255-256.

Berin M.C., Sampson H.A. 2013. Food allergy: an enigmatic epidemic. Trends in Immunology 34: 390-397.

Bessot J.C., Pauli G., Kerschen C., Moreau G., Hirth C. 1978. Allergie respiratoire au criquet migrateur. Revue Français d'Allergologie et d'Immunologie Clinique 18: 19-24.

Bhattacharya S. 2003. Plague of locusts causes mass allergy attack. http://www.newscientist.com/article/dn4339-plague-of-locusts-causes-mass-allergy-attack.html.

Bousquet J., Lockey R., Malling H.-J. and the WHO panel members. 1998. Allergen immunotherapy: Therapeutic vaccines for allergic diseases. A WHO position paper. Journal of Allergy and Clinical Immunology 102: 558-562.

Brinchmann B.C., Bayat M., Brøgger T., Muttuvelu D.V., Tjønneland A., Sigsgaard T. 2011. A possible role of chitin in the pathogenesis of asthma and allergy. Annals of Agricultural and Environmental Medicine 18: 7-12.

Burge P.S., Edge G. 1980. Occupational asthma and rhinitis in locust workers. Clinical Allergy 10: 346-347.

Burge P.S., Edge G., O'Brien I.M., Harries M.G., Hawkins R., Pepys J. 1980. Occupational asthma in a research centre breeding locusts. Clinical Allergy 10: 355-363.

Burgess I. 1993. Allergic reactions to arthropods. Indoor Environment 2: 64-70.

Chen Y.-K., Wu Y.-L., Liu Z.-G. 2012. Purification and identification of allergens in *Locusta migratoria manilensis*. Chinese Journal of Applied Entomology 49: 244-247. [In Chinese with English abstract].

Cox L., Williams B., Sicherer S., Oppenheimer J., Sher L., Hamilton R., Golden D. 2008. Pearls and pitfalls of allergy diagnostic testing: report from the American College of Allergy, Asthma and Immunology/American Academy of Allergy, Asthma and Immunology Specific IgE Test Task Force. Annals of Allergy, Asthma & Immunology 101: 580-592.

Curotto de Lafaille M.A., Lafaille J.J., Graça L. 2010. Mechanisms of tolerance and allergic sensitization in the airways and the lungs. Current Opinion in Immunology 22: 616-622.

Day J.F., Edman J.D., Kunz S.E., Wikel S.K. 2004. Direct injury: phobias, psychoses, annoyance, allergies, toxins, venoms and myiasis, pp.99-149. In: Eldridge B.F., Edman J.D. (Eds) Medical Entomology. Kluwer Academic Publishers, Dordrecht, The Netherlands.

de Bruin Weller M.S., Rockmann H., Knulst A.C., Bruijnzeel-Koomen C.A.F.M. 2012. Evaluation of the adult patient with atopic dermatitis. Clinical et Experimental Allergy 43: 279-291.

Devkota B., Schmidt G.H. 2000. Accumulation of heavy metals in food plants and grasshoppers from the Taigetos Mountains, Greece. Agriculture, Ecosystems and Environment 78: 85-91.

Edge G., Burge P.S. 1980. Immunological aspects of allergy to locusts and other insects. Clinical Allergy 10: 347.

FAO 2003. Desert Locust Bulletin, No. 301, 6 November, 2003. Food and Agriculture Organization of the UN, Emergency Centre for Locust Operations.

Feinberg A.R., Feinberg S.M., Benaim-Pinto C. 1956. Asthma and rhinitis from insect allergens. Journal of Allergy 27: 437-444.

Frankland A.W. 1953. Locust sensitivity. Annals of Allergy, 11: 445-453.

Fuchs E. 1979. Insects as inhalant allergens. Allergologia et Immunopathologia 7: 227-230.

Fujita H., Soyka M.B., Akdis M., Akdis C.A. 2012. Mechanisms of allergen-specific immunotherapy. Clinical and Translational Allergy 2: article 2.

Gahukar R.T. 2011. Entomophagy and human food security. International Journal of Tropical Insect Science 31: 129-144.

Gimenez-Arnau A., Maurer M., De La Cuadra J., Maibach H. 2010. Immediate contact skin reactions, an update of contact urticaria, contact urticaria syndrome and protein contact dermatitis – "A never ending story". European Journal of Dermatology 20: 552-562.

Goddard, J. 2013. Physician's Guide to Arthropods of Medical Importance, 6th ed. CRC Press, Taylor & Francis Group, Boca Raton, FL.

Gore J.C., Schal C. 2007. Cockroach allergen biology and mitigation in the indoor environment. Annual Review of Entomology 52: 439-463.

Gronemeyer W. 1958. Das gewerbliche Asthma. Deutsche Medizinische Wochenschrift 83: 30-39.

Handley M.A., Hall C., Sanford E., Diaz E., Gonzalez-Mendez E., Drace K., Wilson R., Villalobos M., Croughan M. 2007. Globalization, binational communities, and imported food risk: Results of an outbreak investigation of lead poisoning in Monterey County, California. American Journal of Public Health 97: 900-906.

Harris-Roberts J., Fishwick D., Tate P., Rawbone R., Stagg S., Barber C.M., Adisesh A. 2011. Respiratory symptoms in insect breeders. Occupational Medicine 61: 370-373.

Harvey A. 1990. Rearing and Breeding of Locusts in the Laboratory. Natural Resources Institute, Chatham, UK.

Heinzerling L., Mari A., Bergmann K.-C., Bresciani M., Burbach G., Darsow U., Durham S., Fokkens W., Gjomarkaj M., Haahtela T., Todo Bom A., Wöhrl S., Maibach H., Lockey R. 2013. The skin prick test – European standards. Clinical and Translational Allergy 3: article 3.

Hill J.G., Goddard J. 2012. Medical and veterinary importance of grasshoppers, katydids and crickets (Hexapoda: Orthoptera). Journal of the Mississippi Academy of Sciences 57: 172-177.

Hindley J., Wünschmann S., Satinover S.M., Woodfolk J.A., Chew F.T., Chapman M.D., Pomés A. 2006. Bla g 6: A troponin C allergen from *Blattella germanica* with IgE binding calcium dependence. Journal of Allergy and Clinical Immunology 117: 1389-1395.

Holgate S.T., Polosa R. 2008. Treatment strategies for allergy and asthma. Nature Reviews Immunology 8: 218-230.

Hua S.Z. 2013. Mapped! A machinery of degranulation in mast cells. Focus on "Serum- and glucocorticoid-inducible kinase SGK1 regulates reorganization of actin cytoskeleton in mast cells upon degranulation". American Journal of Physiology–Cell Physiology 304: C36-C37.

Hunter B.A., Hunter L.M., Johnson M.S., Thompson D.J. 1987. Dynamics of metal accumulation in the grasshopper *Chorthippus brunneus* in contaminated grasslands. Archives of Environmental Contamination and Toxicology 16: 711-716.

Izquierdo-Domínguez A., Valero A.L., Mullol J. 2013. Comparative analysis of allergic rhinitis in children and adults. Current Allergy and Asthma Reports 13: 142-151.

Ji K., Chen J., Li M., Liu Z., Wang C., Zhan Z., Wu X., Xia Q. 2009. Anaphylactic shocks and lethal anaphylaxis caused by food consumption in China. Trends in Food Science & Technology 20: 227-231.

Johansson S.G.O., Hourihane J. O'B., Bousquet J., Bruijnzeel-Koomen C., Dreborg S., Haahtela T., Kowalski M.L., Mygind N., Ring J., van Cauwenberge P., van Hage-Hamsten M., Wüthrich B. 2001. A revised nomenclature for allergy – An EAACI position statement from the EAACI nomenclature task force. Allergy 56: 813-824.

Johny S., Larson T.M., Solter L.F., Edwards K.A., Whitman D.W. 2009. Phylogenetic characterization of *Encephalitozoon ramaleae* (Microsporidia) from grasshopper host: Relationship to *Encephalitozoon* spp. infecting humans. Infection, Genetics and Evolution 9: 189-195.

Joly P. 1963. Localisation et signification biologique de la substance provoquant des accidents allergiques chez les personnes exposées à un contact prolongé avec les grands Acridiens (*Locusta migratoria*). Comptes rendus des Séances de la Societé de Biologie et ses Filiales 157 : 2299-2300.

Kagen S.L. 1990. Inhalant allergy to arthropods. Clinical Reviews in Allergy 8: 99-125.

Katelaris C.H., Peake J.E. 2006. Allergy and the skin: eczema and chronic urticaria. Medical Journal of Australia 185: 517-522.

Kinyuru J.N., Kenji G.M., Njoroge S.M., Ayieko M. 2010. Effect of processing methods on the in vitro protein digestibility and vitamin content of edible winged termite (*Macrotermes sunhylanus*) and grasshopper (*Ruspolia differens*). Food and Bioprocess Technology 3: 778-782.

Knol E.F., Knulst A.C. 2010. Application of multiplexed immunoglobulin E determination on a chip in component-resolved diagnostics in allergy. Clinical et Experimental Allergy 40: 190-192.

Ky N.-T., Vallery-Radot C. (1974). Allergie à la sauturelle. Revue Français d'Allergologie et d'Immunologie Clinique 14 : 218.

Lemanske R.F.Jr., Busse W.W. 2010. Asthma: Clinical expression and molecular mechanism. Journal of Allergy and Clinical Immunology 125, Suppl. 2: S95-S102.

Leung P.S.C., Chow W.K., Duffey S., Kwan H.S., Gershwin M.E., Chu K. H. 1996. IgE reactivity against a cross-reactive allergen in crustacea and mollusca: Evidence for tropomyosin as the common allergen. Journal of Allergy and Clinical Immunology 98: 954-961.

Lopata A.L., Fenemore B., Jeebhay M.F., Gäde G., Potter P.C. 2005. Occupational allergy in laboratory workers caused by the African migratory grasshopper *Locusta migratoria*. Allergy 60: 200-205.

Löwhagen O. 2012. Diagnosis of asthma – a new approach. Allergy 67: 713-717.

Monk B.E. 1988. Contact urticaria to locusts. British Journal of Dermatology 118: 707-708.

Muzzarelli R.A.A. 2010. Chitins and chitosans as immunoadjuvants and non-allergenic drug carriers. Marine Drugs 8: 292-312.

National Institute of Allergy and Infectious Diseases. 2012. Allergic diseases – Anaphylaxis. http://www.niaid.nih.gov/topics/allergicDiseases/understanding/Pages/Anaphylaxis.aspx

Nishino K., Fujiyama T., Hashizume H., Nakauchi S. 2013. Detection and visualization of intracutaneous allergic type-specific elements using long-wavelength near-infrared hyperspectral imaging. Skin Research and Technology 19: e157-e166.

Oppong E., Flink N., Cato A.C.B. 2013. Molecular mechanisms of glucocorticoid action in mast cells. Molecular and Cellular Endocrinology 380: 119-126.

ODNRI (Overseas Development Natural Resources Institute) 1989. Note on Allergy to Locusts, 2nd edition. Overseas Development Natural Resources Institute, Chatham, UK.

Panzani R.C., Ariano R. 2001. Arthropods and invertebrates allergy (with the exclusion of mites): the concept of panallergy. Allergy 56, Suppl. 69: 1-22.

Patel A., Choudhary S. 2012. Prevalence of allergen sensitivity in nasobronchial allergy in Gujarat, India. National Journal of Medical Research 2: 431-434.

Peden D., Reed C.E. 2010. Environmental and occupational allergies. Journal of Allergy and Clinical Immunology 125, Suppl. 2: S150-S160.

Perzanowski M.S., Chew G.L., Divjan A., Jung K.H., Ridder R., Tang D., Diaz D., Goldstein I.F., Kinney P.L., Rundle A.G., Camann D.E., Perera F.P., Miller R.L. 2013. Early-life cockroach allergen and polycyclic aromatic hydrocarbon exposures predict cockroach sensitization among inner-city children. Journal of Allergy and Clinical Immunology 131: 886-893e6.

Piromrat K., Chinratanapisit S., Trathong S. 2008. Anaphylaxis in an emergency department: A 2-year study in a tertiary-care hospital. Asian Pacific Journal of Allergy and Immunology 26: 121-128.

Prasad R., Kumar R., Verma S.K., Pandey U.S. 2001. A study of skin sensitivity to various allergens by intradermal test in patients of bronchial asthma. Indian Journal of Allergy, Asthma and Immunology 15: 17-21.

Prasad R., Verma S.K., Dua R., Kant S., Kushwaha R.A.S., Agarwal S.P. 2009. A study of skin sensitivity to various allergens by skin prick test in patients of nasobronchial allergy. Lung India 26: 70-73.

Reese G., Ayuso R., Lehrer S.B. 1999. Tropomyosin: An invertebrate pan-allergen. International Archives of Allergy and Immunology 119: 247-258.

Reese T.A., Liang H.-E., Tager A.M., Luster A.D., Van Rooijen N., Voehringer D., Locksley R.M. 2007. Chitin induces accumulation in tissue of innate immune cells associated with allergy. Nature 447: 92-96.

Rolland J.M., Prickett S., Gardner L.M., O'Hehir R.E. 2013. T cell targeted strategies for improved efficacy and safety of specific immunotherapy for allergic disease. Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry 12: 201-222.

Saban D.R., Calder V., Kuo C.-H., Reyes N.J., Darrt D.A., Ono S.J., Niederkorn J.Y. 2013. New twists to an old story: Novel concepts in the pathogenesis of allergic eye diseases. Current Eye Research 38: 317-330.

Saeed T., Abu Dagga F., Saraf M. 1993. Analysis of residual pesticides present in edible locusts captured in Kuwait. Arab Gulf Journal of Scientific Research 11: 1-5.

Salo P.M., Calatroni A., Gergen P.J., Hoppin J.A., Sever M.L., Jaramillo R., Arbes S.J jr., Zeldin D.C. 2011. Allergy-related outcomes in relation to serum IgE: Results from the National Health and Nutrition Examination Survey 2005-2006. Journal of Allergy and Clinical Immunology 127: 1226-1235e7.

Schnitzker W.F. 1974. Grasshopper allergy. Pediatrics 53: 280-281.

Schofield M., Calhoun K.H. 2011. Immunology of allergy. Otolaryngologic Clinics of North America 44: 591-601.

Shivpuri D.N., Shali P.L., Agarwal M.K., Parkash D., Bhatnager P.L. 1971. Insect allergy in India. Annals of Allergy 29: 588-597.

Sicherer S.H., Leung D.Y.M. 2013. Advances in allergic skin disease, anaphylaxis, and hypersensitivity reactions to foods, drugs, and insects in 2012. Journal of Allergy and Clinical Immunology 131: 55-66.

Sohn M.H., Kim K.-E. 2012. The cockroach and allergic diseases. Allergy, Asthma et Immunology Research 4: 264-269.

Soparkar G.R., Patel P.C., Cockcroft D.W. 1993. Inhalant atopic sensitivity to grasshoppers in research laboratories. Journal of Allergy and Clinical Immunology 92: 61-65.

Spiewak R. 2012. Contact dermatitis in atopic individuals. Current Opinion in Allergy and Clinical Immunology 12: 491-497.

Srivastava S.K., Babu N., Pandey H. 2009. Traditional insect bioprospecting – As human food and medicine. Indian Journal of Traditional Knowledge 8: 485-494.

Steedman A. (Ed.) 1990. Locust Handbook, 3rd edition. Natural Resources Institute, Chatham, UK.

Steyn D.G., Grasshopper (*Phymateus leprosus* Fabr.) poisoning in a bantu child. South African Medical Journal 36: 822-823.

Sudan Tribune 2003. Grasshopper plague threatens Sudanese crops, causes asthma epidemic. October 27 2003. http://www.sudantribune.com/spip.php?article713

Tee R.D., Gordon D.J., Hawkins E.R., Nunn A.J., Lacey J., Venables K.M., Cooter R.J., McCaffery A.R., Newman Taylor A.J. 1988. Occupational allergy to locusts: An investigation of the sources of the allergen. Journal of Allergy and Clinical Immunology 81: 517-525.

Tee R.D., Gordon D.J., Newman Taylor A.J. 1985. Allergy to locusts (Schistocerca gregaria and Locusta migratoria). Journal of Allergy and Clinical Immunology 75: 122.

TerraDaily 2003. Grasshopper plague threatens Sudanese crops, causes asthma epidemic. October 27, 2003. http;//www.teradaily.com/2003/031027103513.2i66xtku.html

van der Bijl W.J.F. 1963. Asthma als Berufskrankheit: Allergie gegen Heuschrecken. Allergie und Asthma 9: 154-155.

van Huis A. 2013. Potential of insects as food and feed in assuring food security. Annual Review of Entomology 58: 563-583.

Whitman D.W., Vincent S. 2008. Large size as an antipredator defense in an insect. Journal of Orthoptera Research 17: 353-371.

Wirtz R.A. 1980. Occupational allergies to arthropods – Documentation and prevention. Bulletin of the Entomological Society of America 26: 356-360.

Wirtz R.A. 1984. Allergic and toxic reactions to non-stinging arthropods. Annual Review of Entomology 29: 47-69.

Worm, M., Babina M., Hompes S. 2013. Causes and risk factors for anaphylaxis. Journal der Deutschen Dermatologischen Gesellschaft 11: 44-50.

Zhai H., Zheng, Y., Fautz R., Fuchs A., Maibach H.I. 2012. Reactions of non-immunologic contact urticaria on scalp, face and back. Skin Research and Technology 18: 436-441.

Zuberbier T., Asero R., Bindslev-Jensen C., Walter Canonica G., Church M.K., Giménez-Arnau A.M., Grattan C.E.H., Kapp A., Maurer M., Merk H.F., Rogala B., Saini S., Sánchez-Borges M., Schmid-Grendelmeier P., Schünemann H., Staubach P., Vena G.A., Wedi B. 2009. EAACI/GA²LEN/EDF/WAO guideline: management of urticaria. Allergy 64: 1427-1443.