Immediate Hypersensitivity to Mealworm and Cricket: Beyond Shrimp and House Dust Mite Cross-Reactivity

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Entomophagy, that is, consumption of insects by humans, is a common practice in parts of Asia, Africa, and South America. Less common in Western countries, this diet could become more widespread in the years to come, especially in view of the nutritious properties of insects. Although cross-reactions between insects, shrimps, and mites have been described [1,2], the potential for allergic reactions linked to the consumption of edible insects is still poorly understood.

We report the case of a 47-year-old man who experienced anaphylaxis the first time he ate crickets (Acheta domestica) and mealworm (Tenebrio molitor). His history was remarkable only for anaphylactic reactions at age 20 and 24 years following consumption of crab, mussels, and ground snails. These reactions manifested as hives, digestive disorders, and breathing difficulties, thus leading him to exclude all crustaceans, mollusks, and gastropods from his diet. More recently, the patient consumed a teaspoonful of cricket and mealworm (approximatively 5 g) for the first time. In less than 30 minutes, he developed nausea, erythema on the neck, cough, and difficulty breathing. He was treated with antihistamines, corticosteroids, and epinephrine, followed by hospitalization for 24 hours. No cofactors such as alcohol, nonsteroidal anti-inflammatory drugs, or exercise were reported by the patient.

Skin prick test (SPT) results were positive to native cricket, mealworm, crab, mussel, and snail, thus reinforcing the hypothesis that the reactions were IgE-mediated (Supplementary Data). SPT results were positive for shrimp despite the absence of a clinical reaction and negative for house dust mite (HDM). Serum IgE was positive to shrimp extract, but undetectable for Pen a 1 tropomyosin and HDM. The ISAC allergen microarray revealed no sensitization to the shrimp allergens Pen m 1 (tropomyosin), Pen m 2 (arginine...
Strongly to a protein band of around 60 kDa in the cricket extract. Similar, albeit less intense, binding was also present at 60 kDa in the mealworm, mussel, and snail extracts, but completely absent from the shrimp extract. This profile differed from that of controls, who mainly exhibited IgE reactivity to proteins between 35 kDa and 40 kDa in all extracts. These bands could correspond to tropomyosin or arginine kinases. We hypothesize that an allergen of around 60 kDa might be involved in these reactions between crickets, mealworm, mussels, and snails. However, the presence of this allergen in the shell or hepatopancreas of shrimp cannot be eliminated. Allergens of around 60 kDa have been identified in mealworm. In the present case, the allergen involved in cross-reactivity might be a catalase [2] or an ATP synthase subunit α [3].

Food allergy to insects can be classified as primary allergy and cross-allergy [4]. Cross-allergy is thought to be due to the presence of allergens that are homologous between different invertebrates, thus accounting for the reactions to the first intake of insects. Interestingly, various allergens might be involved, depending on whether the allergy to edible insects is primary or not. Indeed, Broekman et al [4] suggested that the larva cuticle protein could be a major allergen in primary allergy to mealworm. The cockroach allergen-like protein could also be important in this context [5]. However, in patients with cross-allergy to mealworm, tropomyosin and arginine kinase appear to be the most frequently involved allergens [1]. Other allergens, such as actin, troponin T-like protein, or the myosin-like light chain, are also identified as being at risk of cross-reactivity between crustaceans and mealworm [2].

Identifying the risks of cross-reactivity within invertebrates according to the allergens involved remains complex. Broekman et al [6] found that certain allergens seem to be shared only by some insects such as the larva cuticle protein found in only 3 edible insects out of 7 tested. Conversely, cross-reactivity may not occur between all members of a biochemical family, e.g., the arginine kinases of *Acheta domestica* and *Tenebrio molitor* [7]. Finally, some allergens may be present only in certain parts of the invertebrate, such as the hemocyanin identified in the hepatopancreas of *Macrobrachium rosenbergii* (giant freshwater prawn) and absent from the muscle [8]. These elements underscore the complexity of cross-reactivity within invertebrates.

Our findings show that specific cross-reactivities between cricket, mealworm, snail, and mussel can occur without cross-reactivity to shrimp or HDM. This finding paves the way for more precise characterization of the risks of allergy associated with entomophagy. Indeed, the study of patients allergic to invertebrates other than shrimp could lead to the characterization of new cross-reactive allergens. Personalized exclusion advice should therefore be given to patients with allergies to mollusks, gastropods, and arthropods who wish to consume insects.

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**Conflicts of Interest**

Joana Vitte reports personal fees from Thermo Fisher Scientific, Meda Pharma (Mylan), Beckman Coulter, and Sanofi outside the submitted work.
Management of Hypersensitivity to Trimethoprim-Sulfamethoxazole With an Ultrarapid Desensitization Protocol in HIV Infection

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Prophylaxis for opportunistic infections has been a major advance in the treatment of HIV-infected patients, significantly decreasing morbidity and mortality. Nevertheless, these improved treatment options have been accompanied by an increase in reports of hypersensitivity reactions (HSRs) to sulfonamides. The most common cutaneous manifestations of the reactions are as follows: maculopapular rash (36.6%); fixed drug eruption (22%); and type IV HSRs (urticaria) and type I HSRs (angioedema) (12.6%).

Withdrawal of the drug and desensitization are both possible therapeutic approaches following confirmed diagnosis of adverse reactions to cotrimoxazole [1]. Many protocols for desensitization to trimethoprim-sulfamethoxazole in HIV-infected patients are described in the literature. These initially took several days and, more recently, a single day, although few take less than 6 hours [2].

The objective of this study was to report 3 cases of HSR to trimethoprim-sulfamethoxazole in HIV-infected patients and describe their management with a novel ultrarapid 3.25-hour, 13-step oral desensitization protocol. Written informed consent for publication was obtained from the patients.

Three HIV-infected men presented clinical manifestations of drug-induced HSR after receiving treatment with trimethoprim-sulfamethoxazole.

The first patient was a 30-year-old man with a complicated appendectomy and abdominal collections who had recently been diagnosed with HIV infection (CD4+ 140/µL) and syphilis. Trimethoprim-sulfamethoxazole was started owing to fever and intra-abdominal collection. After administration of the third dose, he developed disseminated dermatosis on the head, face, neck, and thorax. He was diagnosed with maculopapular rash secondary to trimethoprim-sulfamethoxazole, and patch testing yielded a positive reaction (+++, vesicles covering 50% of the test site).

Premedication with chlorphenamine was given prior to the protocol (3 solutions [A 1:100, B 1:10, C 1:1]), with no adverse events (Table).

Raphael Piarroux is currently employed by Idbio diagnostics.

The remaining authors declare that they have no conflict of interests.

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