Systemic and erythrodermic reactions following repeated exposure to bites from the Common bed bug *Cimex lectularius* (Hemiptera: Cimicidae)

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Abstract Bed bugs (*Cimex* spp.) have undergone a global resurgence over the last 15–20 years. They readily bite humans, producing a range of cutaneous reactions. This article documents systemic reactions in two patients following repeated bites from the common bed bug, *Cimex lectularius*. Both patients had previously fed bed bugs on themselves without any serious complication, however upon feeding a new batch of the insects subsequently developed systemic urticarial reactions. Patient 1 fed 40–50 bed bugs on himself and after 8 min, he developed itch, swelling of the face, lethargy, profuse sweating and widespread wheals on the torso and limbs. The reaction disappeared in 5 h after treatment with systemic prednisone and antihistamines. Patient 2 developed a similar reaction after feeding five to six bed bugs on himself. In this case, the patient also developed chest tightness and breathing difficulties. Following a similar treatment, symptoms disappeared in 4 h. In light of the increasing exposure of this insect to the general public, systemic reactions in patients may present more commonly to the medical practitioner.

Key words clinical, dermatology, medical entomology.

INTRODUCTION

Bed bugs (both the Common species, *Cimex lectularius* and the Tropical species, *Cimex hemipterus*) are haematophagus parasites that readily bite humans (Doggett *et al.* 2012). In recent years, there has been an unprecedented worldwide resurgence of bed bug infestations with the development of insecticide resistance in the insect appearing to be the key factor (Dang *et al.* 2015; Lilly *et al.* 2015). In the United States, bed bugs have been particularly problematic; for example, complaints about bed bugs to New York City council increased 20 fold between the years 2004 and 2009 (Doggett *et al.* 2012), while a recent survey of pest managers in 2015 revealed that bed bug infestations appear to be on the increase (Potter *et al.* 2015). While in Australia, bed bug infestations rose an extraordinary 4500% during the start of the new millennia (Doggett *et al.* 2008; Doggett *et al.* 2011).

Previously, diffuse cutaneous and systemic manifestations have not been widely reported (Goddard & De Shazo 2009b) or have been presented as an ill-defined syndrome (Doggett *et al.* 2012). A recently described case of a systemic reaction in a patient was attributed to a 'common bed bug', although this was based on circumstantial evidence via the presence of one insect, rather than definitive proof following actual exposure to the insect bite (Phan *et al.* 2016). Two cases are presented of researchers working in the field of bed bugs and previously exposed to bites from the insect, who developed acute, erythrodermic and systemic reactions after voluntary exposure.

RESULTS

Patient 1: a 42-year-old male commenced to be bitten by *C. lectularius* in 2007 because of accidental exposure while working in the field. He had regular deliberate exposure while maintaining bed bug colonies for research purposes from 2008 to 2010. In this case, a jar containing dozens of bed bugs was placed on the arm or leg until the bed bugs were fully engorged with blood. Typically, he would notice soon after feeding on the bitten areas mild pain and itch with the development of erythematous wheals that disappeared in a few days.

On 5 February 2011, a jar of bed bugs (between 40 and 50 individuals) was placed onto one leg. Within 1 min, he noticed the pain related to the bugs biting the skin. At 8 min, most bed bugs were fully engorged and the jar removed. He noticed itch on the feeding site but also on both palms. In a few minutes, he noticed oedema on the face with watery eyes, profuse sweating, abdominal pain and felt lethargic. The patient was admitted to emergency and was prescribed a five day supply of: famotidine (20 mg), prednisone (20 mg) and diphenhydramine (50 mg). One hour after the exposure, multiple wheals appeared on the torso and limbs (Fig. 1). At 5 h (2-3 h after taking the three prescribed drugs), the urticarial exanthema disappeared, and only mild itch remained at the feeding site. Since this incident, he has been accidentally exposed to individual bed bug bites more than 10 times up until May 2013. Each time, he has noticed localised pain, itch and the temporary appearance of erythematous wheals on the bitten area. No systematic reactions subsequently occurred.

Patient 2: a 28-year-old male student, who maintained colonies of bed bugs (both *C. hemipterus* and *C. lectularius*) for

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2 R Minocha et al.



Fig. 1. Patient 1, after 5 min of bed bug (*Cimex lectularius*) feeding, the region was intensely oedematous with surrounding erythema, associated with the development of an acute urticarial reaction.

research, fed five to six *C. lectularius* on himself on 24 December 2013. He previously had several exposures to *C. lectularius* bites in the past, with the most recent being in Oct/2013 with no associated systemic or diffuse cutaneous reaction.

The bed bugs were placed on the proximal, right anterior forearm for approximately 15 min. Within 1 min of the start of the bed bugs feeding, the student experienced a gradually increasing amount of pruritis over the bite area. Within 5 min of feeding, the bite region was inflamed and erythematous with wheals. Within 10 min, the patient developed intense pruritis over his scalp, ears and buttocks, with progression to his nose, face and groin (Figs 2, 3). Approximately 20 min after the bites, he became intensely erythrodermic, and he developed systemic symptoms of lethargy, dysphagia, chest tightness and had difficulty breathing. Forty-five minutes after the bite, the student was given an antihistamine (10 mg Cetirizine); however, his urticaria and erythroderma remained intense, and he was assessed in emergency approximately 25 min later.

On examination, the student was normotensive, had a normal heart rate of 65 bpm and an oxygen saturation of 97% in room air; however, he was mildly dyspneic (respiratory rate of 20 breaths/min). He displayed no obvious respiratory distress,



Fig. 2. Patient 2, a 28-year-old Chinese student developed an erythrodermic reaction 20 min after initiation of bed bug feeding over his head and neck.



Fig. 3. Same patient in Figure 2 with dispersed, hypopigmented macules over the neck region.

drooling or stridor and had a normal cardiac and respiratory examination. One and a half hours after the bites, there was a noticeable improvement in his pruritis and the intensity of his rash, and he was treated with 200 mg of IV hydrocortisone and 12.5 mg of IV Phenergan. Blood samples taken during this time were unremarkable (inflammatory markers, IgE and complement C3 and C4 were within normal limits). Two and a half hours after the bites, the student's cutaneous and systemic symptoms had noticeably reduced, and 4 h after the onset of the bites, they had almost resolved. He was discharged from emergency shortly afterwards with a weaning dose of oral prednisone and a course of oral antihistamines with complete resolution of his cutaneous reaction after two and a half weeks. There are a limited number of published cases of systemic reactions to bed bugs and symptomology has been ill defined. Consequently, these reactions can create a diagnostic dilemma for health care professionals. A diverse number of dermatological differential diagnoses exist including erythema multiforme, Sweet's syndrome and vasculitis (Bernardeschi *et al.* 2013). DeShazo *et al.* demonstrated that histopathology of the bullous reactions produced by bed bugs after 24 h resemble the distinctive changes in Churg–Strauss vasculitis (Deshazo *et al.* 2012).

Multiple bed bug bites are typically characterised by a cluster or linear distribution of erythematous macular lesions and can progress to wheals and widespread urticarial (Doggett & Russell 2009). Although rare, systemic reactions can involve widespread pruritis, asthma, anaphylaxis and fever (Doggett *et al.* 2012). There is increasing evidence to support sensitisation after initial exposure to bed bugs with the latency period between bed bug bite and cutaneous reaction decreasing substantially between subsequent bites (Reinhardt *et al.* 2009). In the case of the 28-year-old male, he had been exposed to bed bug bites since November 2012 and has developed progressively more severe cutaneous reactions from each subsequent bite.

The pathogenesis of reactions produced by bed bug bites may correlate with an IgE mediated response directed to *C. lectularius* salivary extract, nitrophorin, which has been shown to induce chemokines that recruit inflammatory mediators; eosinophils, macrophages, neutrophils and other granulocytes and maintain their proliferation by stimulating the release of granulocyte colony stimulating factor. Cytokines produced by these mediators are directed against sites of inflammation and result in a cell-mediated immune response (Goddard *et al.* 2013; Leverkus *et al.* 2006). Although attempts have been made to develop assays that measure IgE antibodies to *C. lectularius* nitrophorin protein, there are no commercially available tests at present, making diagnostic confirmation difficult (Price *et al.* 2012).

The treatment of systemic reactions includes intramuscular epinephrine, antihistamines and oral and topical (Stucki & Ludwig 2008) corticosteroids, dependent upon the severity of the allergic reaction. Clinical trials evaluating the treatment of reactions to bed bug bites have not been conducted, and there is controversy regarding the effectiveness of the current treatment strategies (Goddard & De Shazo 2009a).

CONCLUSION

Physical impacts of bed bug bites are of growing concern, and there has been a surge of legal disputes throughout much of the western world in recent times. State and local Governments have been overwhelmed with complaints by local residents in regards to bed bug infestations, which are at times resistant to pest control measures (Aultman 2013). Infestations with bed bugs have become a particular problem amongst the socially disadvantaged, where infestations often go untreated, leading to massive bed bug populations and ongoing bites. Therefore, patients with systemic reactions may increasingly present to medical practitioners, and bed bugs should be considered in the differential diagnosis for those with symptoms described herein.

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