

Stinging ants

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Ants belong to the order *Hymenoptera*, along with bees, wasps, yellow jackets, etc., they are the most successful animal genera in this world. It is their selfless social structure which accounts for their huge impact. Their effect on man ranges from the parasol ant, which makes plant cultivation untenable in certain parts of South America, to *Solenopsis Invicta* in the southeastern United States of America, which kill ground dwelling birds and small animals, harass livestock, and renders farmland unusable. With the exception of the Bulldog Ant of Australia (which is the size of a medium cockroach) direct toxic effects are not a lethal threat to man. Human fatalities and morbidity are related to secondary infections of excoriated stings or allergic anaphylaxis. This article reviews history and recent developments regarding stinging ants around the world.

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Abbreviations

IFA imported fire ant
RAST radioallergosorbent test

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Introduction

Solenopsis richteri, the black fire ant, was introduced from Uruguay into Mobile, Alabama, USA, in the early 1900s, and now occupies a small area in northern Mississippi and Alabama [1]. *Solenopsis invicta*, the red fire ant, was introduced from Brazil around the time of World War II, and occupies 12 southern US states, with penetration into Puerto Rico, Arizona, New Mexico and California [2•]. It constitutes 90% of all the ants in heavily infested areas [3], having eaten all of the competing indigenous and other imported species. The unique venom of the imported fire ant (IFA) (see Fig. 1) is a simple alkylloid that results in a characteristic sterile pustule. The antigens responsible for allergic sensitization (Sol i 1–4) are contained in the 5% aqueous phase. In heavily infested areas in the southern United States, sting rates may exceed 50% of the population per season. In these areas, the incidence of, and the rate of desensitization for, systemic anaphylaxis exceeds that for all other *Hymenoptera*. Over 80 deaths caused by IFA anaphylaxis have been reported [2•]. Other ant species have been reported to cause anaphylaxis, with less frequency. Treatment with the whole-body extract of *S. invicta* has generally been effective.

Of an estimated 10^{18} living insects at any given time, one of every thousand is an ant. The Japanese ideograph for ant is a composite of the characters for insect, unselfishness, justice, and courtesy [4]. They will fight when cut in half, walk up a 90° surface, carry several times their own weight, 'see' in the ultraviolet spectrum as well as the plane of polarized light, tell time, sun-compass orient, and learn a maze with only four times the error rate of a rat. They can follow a chemical trail via the bi-directional sensing of chemical gradients in picamolar amounts. Communication is principally by pheromones (volatile short-chain carbon compounds, which include mating, queen tending, trailing, etc.). Fire ants are omnivorous and highly effective predators. There have been reports of fire ants tending aphids ('keeping cows') [4]. Genetic studies of *S. invicta* [5•] indicate that the fire ant genome is much larger and more complex than those of a number of other *Hymenoptera* and other insects. *S. invicta* originates from an open grassland, which floods annually, and they spread as the entire colony clings together, rolling as a ball until they make contact with high ground [3]. They have out-competed the indigenous forest-dwelling species. Arnett sampled ants every 30–50 miles from Florida to New York between May and July. The number of ants per trap (20) was small but the number of species

Figure 1. *Solenopsis invicta* worker

increased from a few in New York to 15 in southern Virginia. As IFA appeared, ants per trap increased up to 500, whereas the number of species dropped to four in Florida [6•]. All members of the colony are female, except for a short time when haploid males are produced for mating flights. Virgin queens mate with several males while flying at 800–1000 ft, and will produce fertilized eggs for her 6–7-year life span from this one mating [7,8]. Queens are determined, as in the case of bees, not by genetics, but by what larvae are fed. In a competitive adaptation, IFA have developed multiple queens per colony and hybridization between *S. invicta* and *S. richteri*, increasing cold tolerance and extending their range farther north. When a mound is threatened, the fire ants swarm onto the intruder and sting simultaneously.

Venom

The venom of the fire ant is unique. It is principally composed of 2-methyl-6-alkylpiperidines. Some of these alkyloids are found nowhere else in the animal or plant world [9]. 'It is the only known non-proteinacious venom delivered by bite or sting', and it is this compound that causes their sting to burn like fire and give them the name 'fire ant'. The venom of the rattlesnake (*Crotalis*), yellow jacket (*Vespula*) are similar in components and intent (that is to immobilize and predigest), with the largest difference being in the dosage [10]. These simple piperidines, with carbon side chains, are tissue destructive, hemolytic, bactericidal, fungistatic, are responsible for the sterile pustule (which is pathognomonic), and are lethal to other insects and small animals [3,10]. The structure of these alkyloids was worked out by Blum and colleagues [11,12], who further demonstrated an evolu-

tion of longer and more saturated side chains, and *cis* to *trans* isomer from *Solenopsis xyloni* to *S. invicta* (with increasing competitive advantage) [13]. Side chain saturation increases with worker age [14••]. Queen venom is of the least evolved type [15]; queens apply venom to their eggs, apparently for its fungistatic properties. Gas chromatography of venom further demonstrated hybridization between *S. richteri* and *S. invicta* in the United States [16]. After milking 10 *S. invicta* workers to fill a 1 μ l capillary tube and centrifugation, a small turbid phase is seen above the crystal clear alkyloid phase (personal experience). This 5% aqueous phase contains the proteins responsible for allergic sensitization. These proteins have been well characterized in a series of papers by Hoffman [17], and were designated Sol i 1–4. Sol i 2 comprises approximately two-thirds of the venom protein. Sol i 1 has phospholipase activity and crossreacts with other *Hymenoptera* [18,19]. This accounts for the clinical observation that some individuals have anaphylaxis to their first known fire ant sting. Seasonal variations in the potency of the venom have been described [20]. The venom of the fire ant is otherwise not toxic to humans. Over 5000 stings have been reported as a complication of alcoholism without untoward effects [21], the exception being an infant with over 5000 stings [22].

Epidemiology

S. invicta has spread to occupy 310 million acres [2••]. This range has continued to expand with extension into Virginia in 1990 [23], to more recent advances into New Mexico, Arizona, and California. It is anticipated that favorable conditions for its spread will carry it up the

west coast of the United States to Oregon [2•]. The fire ant has spread by shipments of sod and nursery stock, mating flights, floods, and has even been found in frozen food shipments. In heavily infested areas, such as Florida, newly mated queens may dig in at five per square yard [24•,25]. Workers are produced within 30 days. By maturity at 3 years or more, colonies will number over 250 000, and there may be over 200 mounds per acre [24•,25]. Fire ants are drawn to electrical fields, infesting electrical wiring, transformers, etc. [2•]. This is said to be one of the reasons for the cancellation of the super collider project in Texas. There are few reports of systemic reactions to other ant species and areas in the world [26–28,29•,30•,31–36]. Triplett, in an unpublished survey of Mississippi, Georgia, and Alabama, reported in 1969 (9422 cases) to 1971 (12 478 cases) on individuals treated for fire ant stings. He reported 154 cases of anaphylactic shock and 17 deaths. It was unclear how many of these were from infectious complications [3]. We surveyed 29 205 physicians in 1989. The 2022 responding reported 20 755 patients per year treated for IFA stings, of whom 413 (2%) had anaphylaxis [37]. Sting attack rates range from 25 to 58% of the population per season [38]. Freeman [38] studied medical students temporarily assigned to San Antonio, Texas. The sting attack rate was 51%; 16% developed positive skin tests and radioallergosorbent tests (RAST) to *S. invicta* [39]. Caldwell *et al.* [40] found 57% of treatment was for children under 15 years of age, of 33.8 IFA treatment encounters/10 000 population. The highest attack rates occur between April and September. The potency and composition of the venom may vary with the season [20]. Ginsburg [41] estimated an annual incidence of two to three new cases of anaphylaxis to the IFA per 100 000 in a pediatric population. We estimated 3.8 new cases per 100 000 population per year [42]. In endemic areas, the incidence of anaphylaxis to IFA exceeds that of all other *Hymenoptera* combined [43].

Clinical

Our analysis of 104 patients showed an equal male:female ratio, with the majority being under the age of 20 years, the average number of stings was 10; anaphylactic reactions can occur with one sting, a 34% atopic history, and a 7% history of other insect sensitivity. Eighteen per cent had a history of previous reactions to ant stings. Pustules were documented in 86% of cases. The onset of symptoms was within 60 min in all cases. Skin testing was positive to *S. invicta* whole-body extract in 86 [43]. Shuman *et al.* [44•] surveyed allergists in SC in 1989 and in 1999. They reported a decrease in the average delay from the first systemic reaction to referral to an allergist from 21.6 to 17.5 months (with the entire improvement being in children). A failure to appreciate the potential severity by primary and emergency room physicians was seen in other surveys. Some articles [45–52] have

appeared to increase awareness among these physicians. Stings occurring inside buildings have increasingly been noted [53]. Skin testing with whole-body extract to *S. invicta* has proved to be reliable [3]. There is almost complete crossreaction between *S. invicta* and *S. richteri*; but most commercial extracts contain both species [3]. Commercial extracts of IFA contain Sol i 1–4 concentrations at approximately one-tenth that of fire ant venom [54]. There was a good degree of concordance between three commercial sources [55]. Studies comparing whole-body extract skin testing with venom skin testing and with venom and whole-body RAST testing for IFA [56,57] found good concordance between venom and whole-body skin testing. There was good agreement with fire ant venom RAST, but significantly poorer correlation with commercial whole-body fire ant RAST [54]. There is a positive skin test rate of approximately 23–30% in allergic patients who are not insect allergic, and in the non-allergic population [58]. Complications have been reported, including mononeuropathy and seizures [59,60].

Deaths

Over 80 deaths have been reported as a result of anaphylaxis to IFA [2•,61]. Our group reported 32 of these deaths; others are known, but not in the literature. Those who died were predominantly male, from infancy to 65 years of age. Most deaths were caused by less than five stings. Approximately the same number of deaths occurred near the patient's home as opposed to field settings. Two patients were resuscitated from near fatal anaphylaxis [62]. There is one report of the death of a fetus after ant anaphylaxis in pregnancy [63]. There are two reported autopsy series of patients dying of fire ant anaphylaxis. The findings are those of anaphylaxis of any etiology [64,65]. Mast cell tryptase and RAST to *S. invicta* can be obtained post mortem and may aid greatly in making the diagnosis of IFA anaphylactic death [64].

Pathology

The venom is injected by the stinger, a modified ovipositor. Almost universally a sterile pustule is formed at 24 h. This lesion is pathognomonic for fire ant envenomation [3]. At 24 h, a superficial pustule is present, with a floor of necrotic connective tissue polymorphonuclear leukocytes and lymphocytes. At 72 h, the pustule contains many eosinophiles and plasma cells in addition to the cells present in the 24 h lesion [66•,67–69]. Between 17 and 56% of patients will develop large local reactions. These lesions have an infiltrate of eosinophils and neutrophils with fibrin deposition and edema. This pattern resembles that of mast cell-dependent late phase reactions of the type seen with the intradermal injection of ragweed extract [70].

Control

The quest for fire ant control has been long and not very successful. A review of the potential control mechanisms both chemical and biological were contained in an article by Lofgren *et al.* in 1975 [71]. During the past 25 years, fire ants have developed multiple queening, which increased colony size, density, and resistance to extermination (any surviving queen will maintain the colony), and hybridization of *S. invicta* and *S. richteri*. We have been unable to take advantage of natural parasites of the *Solenopsis*, nor make any major breakthroughs in pesticide control. In 1968 Richard Nixon, in an attempt to capture southern votes, promised 'effective control' of the IFA [72]. This resulted in the aerial spreading of Heptachlor and Dieldrin, which resulted in the death of beneficial insects, birds, and small animals. In response to this, Rachel Carson published her book *The Silent Spring* and the environmental movement gained momentum. The subsequent use of Mirex, although a more selective insecticide and a more rational delivery system (even though supported by 12 southern state governors and congressmen and senators), was banned by the Environmental Protection Agency. Ultimately, Mirex was flawed in that it accumulated in the fatty tissue of humans in areas of aerial application, and did not result in 100% eradication (personal observation, witness in Environmental Protection Agency hearing).

Abamectin has been the most intellectually satisfying product. It causes the queen to become sterile. She continues to produce queen-tending pheromones, so that workers do not abandon the colony. With the death of the last workers in approximately 60 days, the queen will starve to death. Abamectin has not been a major commercial success. Efforts to use natural parasites, such as *Thelohania* sp. [73], bacteria [74•], and fungi have been unsuccessful. A novel approach is currently being investigated. Researchers in Texas are starting field trials with phorid flies [75]. Phorid flies are natural predators of a number of species of ants. Certain wasps will paralyse honey bees and lay their eggs in the paralysed insect. Phorid flies will dart in, sting the ant and lay eggs in the living ant. These mature, migrate to the head of the ant, and at maturity, the ant decapitates releasing mature phorid flies [4]. A comprehensive review of available chemicals for IFA control is contained in the article by Kemp *et al.* [2••]. There is ongoing basic research on the IFA, which may contribute to control in the future [76•].

Treatment

Experimental treatment of the local reaction was performed in rabbits by Lockey *et al.* [77]. Neither prophylactic nor treatment post-sting, topical or systemic, with antihistamines or steroids had any effect on

the development of the pustule. Topical treatment with aluminum sulphate also had no effect [78].

At the time immunotherapy was first attempted for IFA desensitization, whole-body extract was standard therapy for *Hymenoptera* sensitivity. By good fortune, the relevant antigens are contained in the whole-body extract of *S. invicta*. This has been successful, with rare treatment failures reported [79,80]. Triplett [81] reported successful results in 1973; we reported similar success [10]. Freeman *et al.* [82] found that out of 65 patients on IFA immunotherapy, with 112 subsequent field stings, there was only one episode of anaphylaxis (not life-threatening) compared with six out of 11 patients not on immunotherapy, all of whom had anaphylaxis when resting. Maintenance immunotherapy is usually 0.5cc 1/10–1/100 wt/vol whole-body extract of *S. invicta/richteri* [83].

One case of successful rush immunotherapy has also been reported [84]. A series of over 50 successful rush immunotherapy cases are in press (personal communication). The discontinuation of immunotherapy, with no reaction on resting, has been reported [85].

In a survey of allergists, 96.7% of respondents treated anaphylactic fire ant sensitivity with whole-body immunotherapy [83]. Although it is commercially possible to produce a fire ant venom product, the efficacy of the whole-body extract makes a venom product economically non-viable.

Conclusion

Toxic and allergic reactions to ant envenomation are a worldwide problem. This is particularly true of *S. invicta* in the southern United States, where they are both adapting and expanding. Fatal reactions occur in individuals allergic to IFA. Protection is afforded by whole-body *S. invicta/richteri* immunotherapy.

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