Asia Pac Allergy. 2019 Apr;9(2):e15
https://doi.org/10.5415/apallergy.2019.9.e15
pISSN 2233-8276·eISSN 2233-8268

Asia Pacific allergy

Original Article

Tick killing *in situ* before removal to prevent allergic and anaphylactic reactions in humans: a cross-sectional study

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Received: Feb 2, 2019
Accepted: Apr 17, 2019

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Conflict of Interest
The authors have no financial conflicts of interest.

ABSTRACT

Background: Tick anaphylaxis is a potentially fatal outcome of improper tick removal and management.
Objective: To investigate whether killing ticks in-situ with ether-containing sprays or permethrin cream, before careful removal by the mouthparts could reduce this risk.
Methods: This was a prospective study at Mona Vale Hospital Emergency Department (ED) in Sydney, New South Wales, over a 6-month period during the peak tick season of 2016. Tick removal methods, allergic/anaphylactic reactions were recorded for patients presenting with ticks *in situ* or having already removed the ticks themselves. Primary endpoint was allergic/anaphylactic reaction after tick killing/removal.
Results: One hundred twenty-one patients met study inclusion criteria. Sixty-one patients (28 known tick-hypersensitive) had ticks killed with Wart-Off Freeze or Lyclear Scabies Cream (5% w/w permethrin) before removal with fine-tipped forceps or Tick Twister. Three patients (2 known tick-hypersensitive) had allergic reactions (5%), none anaphylactic. The 2 known hypersensitive patients suffered reactions during the killing process and the third patient had a particularly embedded tick meaning it could not be removed solely by mouthparts. Fifty patients presented to the ED posttick removal by various methods, none using either fine-tipped forceps or Tick Twister, of which 43 (86%) experienced allergic reactions – 2 anaphylactic. Five patients suffered allergic reactions before presentation despite no attempt at kill or removal, but ticks had likely been disturbed by some other method. Five patients had live ticks removed in ED – 3 refused killing and had no reaction despite 1 having known hypersensitivity; 2 had ticks on eyelids contraindicating killing, 1 with known hypersensitivity but both had allergic reactions post removal.
Conclusion: Results support killing ticks in-situ before careful removal by mouthparts to reduce allergic/anaphylactic reactions although further research is still required.

Keywords: Tick bites; Ticks; Anaphylaxis; Humans; Tick toxicoses

Author Contributions

Conceptualization: Benjamin William Phillips Taylor, Andrew Ratchford, Sheryl van Nunen. Data curation: Benjamin William Phillips Taylor, Andrew Ratchford. Formal analysis: Benjamin William Phillips Taylor. Investigation: Benjamin William Phillips Taylor, Andrew Ratchford, Sheryl van Nunen, Brian Burns. Project administration: Andrew Ratchford, Brian Burns. Resources: Andrew Ratchford, Brian Burns. Supervision: Andrew Ratchford. Validation: Benjamin William Phillips Taylor, Andrew Ratchford. Writing - original draft: Benjamin William Phillips Taylor, Andrew Ratchford, Sheryl van Nunen, Brian Burns. Writing - review & editing: Benjamin William Phillips Taylor, Andrew Ratchford, Sheryl van Nunen, Brian Burns.

INTRODUCTION

Ticks are ectoparasite members of the arachnid family, feeding solely on the blood of their hosts [1]. Ticks 'quest' opportunistically for passing hosts by waiting on low-level branches or blades of grass with limbs oustretched [1]. A suitable, well-vascularised area is then sought out, where they use sharp chelicerae to create a small defect in the skin through which to insert their hypostome - a barbed feeding tube [1]. Some ticks then secrete a cement to anchor themselves in place whilst others rely on a deeper barbed hypostome for secure attachment [2]. The feeding process for hardback ticks, alternating between salivating and ingesting, can take days to weeks, varying with species and lifecycle stage [1, 3]. Their bites may have various acute and delayed effects on humans (**Table 1**).

Tick saliva is a venom—a toxic secretion injected through a bite or sting—containing hundreds of functionally versatile proteins, secreted in varying amounts throughout the feeding process [4]. As in vampire bats, saliva proteins have anaesthetic, anticoagulant, vasodilatory, anti-inflammatory and immunosuppressant properties designed to avoid host detection and optimise blood pool-feeding [4]. Ticks are second only to mosquitoes for vector-borne disease worldwide [5] and like bees, wasps and scorpions their venom can cause local or systemic allergic reactions and/or paralysis [4].

To cause host paralysis, a tick must be attached for 4 or 5 days [2] whilst transmission time for tick-borne disease varies by pathogen but is generally at least 24 hours post attachment [6]. Consequently, both may be avoided by removing ticks within a critical time-period. For this reason, health authorities worldwide, including the World Health Organisation [7], the USA Centers for Disease Control and Prevention [8] and the Australian DoH (Department of Health) [9], advise that ticks should be removed as soon as possible, because of the concerns regarding infectious disease transmission.

Table 1. Acute and delayed tick bite effects in Australia

Acute effects		
Localised reactions	Small local reaction	Papules (small bumps) may form at the site of attachment within 1 to 3 days, not thought to be allergic response [11].
	Large local reaction	Localised erythema and oedema greater than 5-cm diameter, commencing 4 hours postbite and lasting up to 10 days [12]. Typically self-limiting but IgE-mediated so can indicate hypersensitivity and therefore increased risk of tick anaphylaxis [13].
Systemic allergic reactions	Allergic reaction (mucocutaneous)	Urticaria, erythema/flushing and/or angioedema distant from bite site, typically shortly after disturbing or attempting to remove a tick [13, 14].
	Anaphylaxis	Typical skin features plus involvement of respiratory, cardiovascular and/or gastrointestinal symptoms, typically shortly after disturbing or attempting to remove a tick [13, 14].
Delayed effects		
Paralysis	Ascending flaccid paralysis	Holocyclotoxins cause inhibition of acetylcholine release at the neuromuscular junction [15]. Symptoms become apparent from day 3 but peak on day 4 or 5, may be acutely worsened by removal and progress for up to 48 hours after removal [16].
Systemic allergic reaction	Mammalian meat allergy	First described by van Nunen et al. (2007) [23], cross-reactive hypersensitivity to the carbohydrate moiety alpha-gal, likely picked up from a previous feed on a bandicoot or other mammal, causes anaphylactic reaction 3–6 hours after consuming mammalian meat [18].
Infective	Tick-borne disease	Queensland Tick Typhus (*Rickettsia australis*) [19]
		Q fever (*Coxiella burnetti*) [19]
		Australian Spotted Fever (*Rickettsia honei* subsp. *Marmionii*) [19]
		Flinders Island Spotted Fever (*Rickettsia honei*) [19]
		Lyme disease (*Borrelia burgdorferi*) [19] – remains controversial in Australia with no proven vector
	Cellulitis	Opportunistic infection through skin break [20], e.g., staphylococcal
Retained mouthparts	Granuloma	Granulation tissue which forms around foreign body [21]
	Abscess	Foreign body reaction combined with opportunistic pathogen [21]
Autoimmune disease	Graves' disease	Only one documented case published in the literature to date [22]

https://doi.org/10.5415/apallergy.2019.9.e15

Worldwide consensus also exists for the method of removal – fine-tipped forceps should be used to grip ticks by the mouthparts, lifting them away from the skin using firm and even pressure [7-9]. The main aims are to avoid squeezing the tick's abdomen and to avoid snapping off mouthparts anchored in the skin. Again, this advice is aimed at prevention of infectious disease transmission. Squeezing ticks by the abdomen may cause stomach contents and saliva, including toxins, allergens and pathogens, to be ejected into the bite site although this has never been proven. One study on gerbils showed that the method of removal had no effect on pathogen transmission, even when ticks were intensively squeezed for 3 minutes before removal. Only attachment time had a significant effect on pathogen transmission [10].

Similarly unproven is the often-cited potential for retained or snapped-off mouthparts to increase pathogen transmission. Retained mouthparts generally slough off within a few days as the skin naturally sheds or can lead to harmless granuloma formation [11, 12]. Nevertheless, most tick removal studies have focussed on avoiding retained mouthparts as a hypothetical proxy of reduced pathogen transmission [13-18].

Health authorities worldwide generally advise against various folklore methods, such as burning ticks with a hot match, covering ticks with petroleum jelly, nail polish or other suffocating agents, dousing ticks with chemical irritants such as isopropyl alcohol or gasoline to encourage them to self-remove and even blasting ticks with sound waves or electric shocks. The reasons for avoiding these methods are that they do not cause ticks to self-remove, they may lead to retained mouthparts and in one study were associated with increased pathogen transmission – a retrospective study in New Jersey found an association between gasoline and Lyme disease in 39 seropositive patients, 6 of whom did not remember being bitten by a tick. The study did not mention how long ticks were in-situ before or after gasoline use or if any other method was used after the gasoline [19].

Contrary to worldwide consensus on tick management to prevent tick-transmitted infectious diseases, the Australasian Society of Clinical Immunology and Allergy (ASCIA), the main professional body of clinical immunologists and allergy specialists in Australia and New Zealand, recommend killing ticks in-situ with ether-containing spray and allowing them to drop off [20]. The reason for this advice can be traced back 30 years to the work of entomologist Bernard Stone, Australia's leading expert on tick paralysis for many years. Stone's main aim was to create a vaccine for tick paralysis as he estimated that up to 10,000 domestic and farmyard animals were affected every year, with consequent losses for farmers [21]. Whilst a vaccine was never discovered, he made some important discoveries concerning *Ixodes holocyclus* (*IH*).

Up to 21 of the 70 species of ticks in Australia are thought to bite humans [22], with 97% of bites in humans from *IH*, the Australian paralysis tick, which is the most medically significant for a number of reasons:

(1) *IH* has a geographical distribution along the eastern starboard of Australia from as far north as Cape Tribulation to as far south as ACT and Victoria, matching the distribution of a large proportion of Australia's human population [1].
(2) *IH* commonly bites humans as well as other mammals although its main host has been thought to be the bandicoot [1].
(3) *IH* is capable of the most severe effects on humans – anaphylaxis and paralysis
(4) *IH* has also been implicated in causing mammalian meat allergy as well as transmitting the tick-borne diseases Q fever and Australian Tick Typhus [23-25].

During his research, Stone noted that shortly after forceful tick removal, paralysis tended to worsen in cats and dogs. In humans, however, anaphylactic-like symptoms were more common immediately post removal. Since *IH* is an unusual tick in that it does not use cement, instead anchoring itself by inserting its barbed hypostome much deeper than other ticks, Stone et al. [26, 27] hypothesised that it might have a complex bite-site with accumulation of proteins that are somehow dispersed during forced removal. To mitigate this, he suggested killing ticks *in situ* and leaving them to fall off. The ideal tickicidal agent would need to be rapidly penetrating, rapidly acting and suitable for use on human or animal skin. Stone was hypersensitive to tick bites and had already tested the method on himself using household insect repellent containing pyrethrins. He noted that the ticks were killed instantly, that their mouthparts subsequently lost turgidity and the ticks would fall off within 24 hours, without causing an allergic reaction [26].

The Australian Department of Health states that they will review their advice when further evidence-based research becomes available. The Australian Department of Health advice does, however, include a link to the ASCIA website [9].

To date, only one study has examined the technique of tick removal in preventing allergic reactions. Seventy-eight patients who had experienced an anaphylactic reaction to tick bites were counselled on how to kill ticks *in situ* by freezing with ether-containing spray. At follow-up, 6 of these patients had experienced another tick bite. Not one of the 6 patients had experienced another allergic reaction when they killed their ticks *in situ* and left them to fall out [28].

The ED of Mona Vale Hospital (MVH) in Sydney, sees an average of 20 tick bite presentations per month and more than 50 per month during peak tick season. For many years, it has been common practice at MVH ED to kill nymph ticks with Lyclear Scabies Cream (5% w/w permethrin, Made in Belgium for Johnson & Johnson Pacific, Sydney, Australia) and adult ticks with Wart-Off Freeze (dimethylether, Koninklijke Utermohlen NV, Wolvega, The Netherlands, Distributed in Australia by Pharmacare Laboratories, Sydney, Australia). Both agents are well tolerated and approved by the Australian Therapeutic Goods Agency (TGA) for use on human skin. It is believed that killing ticks quickly with these agents immediately prevents further salivation and transmission of allergens.

Once the ticks have been killed, fine-tipped forceps are used to remove them by the mouthparts, avoiding compressing the abdomen. Thus, tick removal methods at MVH ED combine ASCIA recommendations (killing *in situ*) with the worldwide consensus on early removal with fine-tipped forceps.

The aim of this study was to investigate the incidence of allergic/anaphylactic reactions when ticks were killed and removed from patients presenting to MVH ED over a 6-month period.

We hypothesised a low incidence of allergy/anaphylaxis compared with patients using other methods.

MATERIALS AND METHODS

A cross-sectional study of tick management and allergic response was undertaken at Mona Vale Hospital ED in Sydney, NSW, during the 6-month period between July 2016

https://doi.org/10.5415/apallergy.2019.9.e15

and December 2016. The study was approved by local Human Research Ethics Committee (LNR/16/HAWKE/89) and received no funding.

Written informed consent was obtained from all participants using an opt-out signed consent form explaining the study design, rationale and ensuring their care would not be affected either way. Patients were excluded if they were unable to consent to participation.

Unless contraindicated for medical reasons or patient refusal, ticks were killed with the following methods:

(1) Nymphs/Larvae: careful dab of Lyclear Scabies Cream, covering the whole tick
(2) Adult ticks: five sprays of Wart-Off Freeze, held 1 cm above the tick

No change in practice was made other than to inform staff of the study, with education on the data collection sheets and consent forms.

Criteria used for anaphylaxis were as per current ASCIA guidelines [29]:

(1) Any acute onset illness with typical skin features (urticaria, erythema/flushing, and/or angioedema) PLUS involvement of respiratory, cardiovascular and/or gastrointestinal systems
(2) Any acute onset of hypotension or bronchospasm or upper airway obstruction where anaphylaxis is considered possible, even if typical skin features are not present

Allergic reaction for study purposes was defined as typical skin features as listed in ASCIA criteria above (urticaria, erythema/flushing, and/or angioedema), occurring distant from the bite site, therefore excluding small and large local reactions.

Patients were observed for half an hour after tick removal in ED. Patients with allergic reactions were treated with antihistamines and monitored until symptoms had begun to improve. Patients with anaphylactic reactions were treated with adrenaline and monitored for four hours post-adrenaline. An EpiPen (300-μg adrenaline autoinjector, Mylan) and immunology referral was given to patients who had allergic or anaphylactic reactions.

Datasheets were collated in Excel (Microsoft, Redmond, WA, USA) using re-identifiable coding, stored on a secure hospital computer and the datasheets destroyed by hospital confidentiality services.

The primary end-point was allergic/anaphylactic reaction after tick killing/removal. The prevalence of tick allergy in the population and the incidence of allergic reaction in patients with known tick hypersensitivity are both unknown. Therefore, it was not possible to predict an effect size or perform a power calculation for the study.

The sample size was limited by the number of presentations during the 6-month study period and willingness to participate. One hundred tick-bite presentations were predicted based on previous presentation data. Descriptive statistics were used to comment on the incidence of allergic and anaphylactic reactions amongst study participants. Data were also collected on patients who attended having already killed and/or removed ticks themselves.

RESULTS

Fig. 1 illustrates the study inclusion/exclusion criteria showing an 83% participation rate based on electronic medical record data. **Fig. 2** demonstrates the seasonal variability, with peaks in October and November for both tick bite presentations as well as allergic reactions, corresponding to the adult feeding stage of *IH*'s lifecycle.

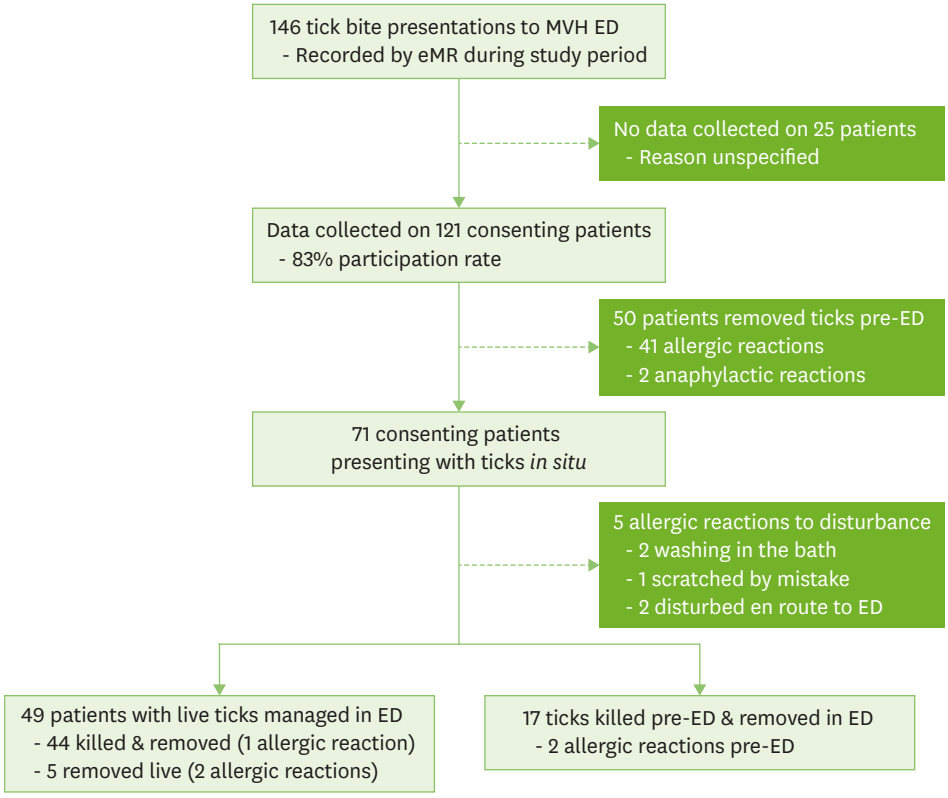

Fig. 1. Inclusion and exclusion criteria flowchart. MVH, Mona Vale Hospital; ED, Emergency Department; eMR, electronic medical record.

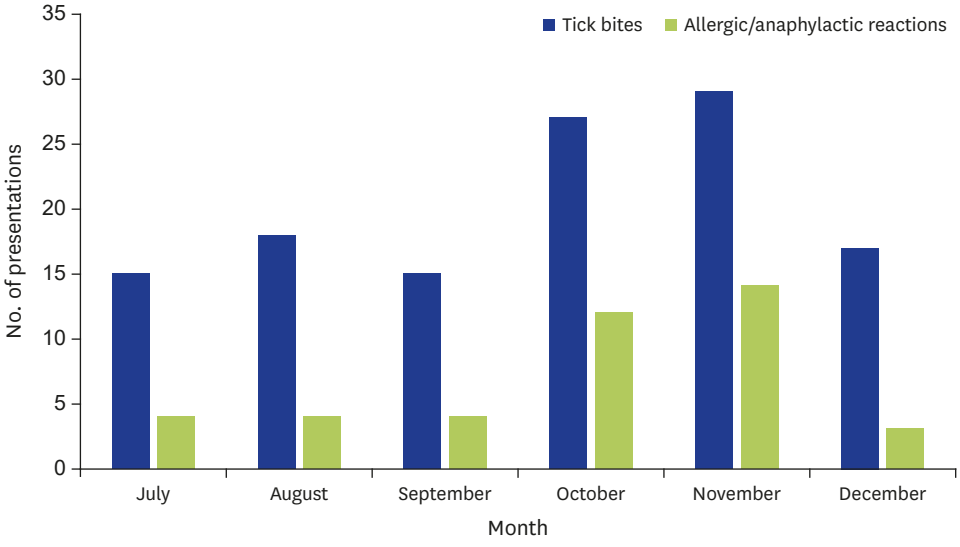

Fig. 2. Incidence of tick presentations and allergic reactions by month.

https://doi.org/10.5415/apallergy.2019.9.e15

Table 2. Removal methods of 50 patients presenting after tick removal (allergic reaction/total)

Tick allergy	Accidental	Tweezers	Fingers	Left to fall off	Needle	Total
Known tick allergy						
Live removal	-	1/1	2/3	-	-	3/4
Wart-Off	-	1/3	1/1	-	-	2/4
Unknown tick allergy						
Live removal	2/2	16*/17	12*/13	-	1/1	31/33
Wart-Off	-	3/4	1/1	-	-	4/5
Lyclear	-	-	-	1/1	-	1/1
Oil	-	1/2	-	-	-	1/2
Betadine	-	1/1	-	-	-	1/1
Total	2/2	23/28	16/18	1/1	1/1	43/50

*One patient in this group had anaphylactic reaction.

Sample demographics matched local population census data. 47.4% were male and the median age was 38.5 (interquartile range, 53).

Two anaphylactic reactions were recorded, both in patients who self-removed live ticks - one with fingers and the other with tweezers. Both occurred shortly after removal and before presentation to ED but were successfully treated with adrenaline. Neither patient had previously had an allergic reaction to tick bite.

A further 41 allergic reactions occurred in the 50 patients who presented to ED having already removed ticks themselves, bringing the total to 43. The methods used by these patients are summarised in **Table 2**.

Ten allergic reactions occurred in the 71 patients presenting to ED with ticks *in situ*, each with a specific reason why optimal tick management had not been performed (**Tables 3** and **4**).

Table 3. Removal methods of 71 patients presenting with ticks *in situ* (allergic reaction/total)

Tick allergy	Fine-tipped forceps	Tick twister	Total
Known tick allergy			
Accidentally disturbed pre-ED	1/1	-	1/1
Live removal (anatomical contraindication)	1/1	-	1/1
Wart-Off pre-ED	2/8	-	2/8
Lyclear pre-ED	0/2	-	0/2
Wart-Off in ED	0/14	-	0/14
Lyclear in ED	0/4	-	0/4
Unknown tick allergy			
Accidentally disturbed pre-ED	4/4	-	4/4
Live removal (anatomical contraindication)	1/1	-	1/1
Live removal (patient refused killing)	0/2	-	0/2
Live removal (reason undocumented)	0/1	-	0/1
Wart-Off pre-ED	0/5	-	0/5
Lyclear pre-ED	0/2	-	0/2
Wart-Off in ED	1/23	0/1	1/24
Lyclear in ED	0/1	0/1	0/2
Total	10/69	0/2	10/71

ED, Emergency Department.

Table 4. Allergic reactions in 71 patients presenting with ticks *in situ*

No.	Reason	Explanation
5	Accidental	No attempt at killing or removing ticks before allergic reaction. Ticks disturbed accidentally by scratching or whilst bathing.
2	Contraindications	Tick on eyelids, ether-containing spray and permethrin cream contraindicated due to potential for damage to eye.
2	Tick disturbance	Allergic reactions when patients attempting to kill with Wart-Off Freeze before presentation.
1	"Embedded" tick	Tick killed in Emergency Department but note written on datasheet stating very embedded tick, impossible to remove by mouthparts only.

https://doi.org/10.5415/apallergy.2019.9.e15

Forty-four patients had ticks killed and removed in ED and only one of these patients had an allergic reaction. As mentioned in **Table 4**, the data collection sheet for this patient stated that the tick was "particularly embedded which precluded gripping by the mouthparts".

Seventeen patients presented to ED with ticks *in situ* which they had already killed at home with either Lyclear or Wart-Off. 15 of these patients had the ticks then removed with fine-tipped forceps without allergic reaction. Two of the 17 patients had allergic reactions, but these had occurred before presentation to ED during attempted killing with Wart-Off Freeze.

DISCUSSION

The paralysis caused by holocyclotoxin, a neurotoxin in the saliva of *IH*, has killed more people in Australia than either the red-back or funnel-web spiders [30, 31]. However, there has not been a fatality from tick paralysis in Australia for over 70 years, since 1945 [1].

Tick anaphylaxis was first described in Australia in 1940 [32]. The severity of reaction can range from Mueller grade I to IV, with one study finding 74% of reactions to be grade IV [28]. There have been four recorded fatalities from tick anaphylaxis between 1979 and 2013, all shortly after removal of a live adult tick and despite resuscitation with adrenaline [33]. Three had known tick allergies but one had not previously reacted to tick bite. This is in keeping with findings in the USA where 50% of fatal reactions to insect sting occurred in individuals with no history of reaction to insect sting [34]. Given the potential for severe reaction and the inability to predict severity based on previous reactions, every tick bite should be managed with care.

Killing ticks *in situ* to prevent anaphylaxis was first suggested 30 years ago [12] and has been previously shown to be effective in one small study [28]. This study was unique in being the first and only tick removal study in humans to include allergic reaction as an outcome. Previous studies worldwide have focussed on removing ticks whole as a hypothetical proxy to reducing pathogen transmission [13-18].

Although tick allergy has been documented in Europe and the USA, it is much more prominent in Australia [24]. Conversely, tick-borne disease is far less of a concern in Australia. Although controversy persists, Lyme disease has never been proven to exist in Australia and neither has a tick capable of carrying the causative pathogen, *Borrelia burgdorferi* [35]. The tick-borne diseases that do exist in Australia – Q fever (caused by *Coxiella burnetii*) and the spotted fever rickettsial diseases (caused by *Rickettsia australis* and *Rickettsia honei*) are associated with less morbidity and mortality, usually responding quickly to oral antibiotics (doxycycline or azithromycin) [25].

In this study, 44 patients had ticks killed with either ether-containing spray or permethrin cream in ED, before being removed with either fine-tipped forceps or Tick Twister. Only one patient suffered an allergic reaction after removal and the datasheet in this case stated that the tick was particularly "embedded" making removal by mouthparts difficult. The term "embedded" suggests that the tick had burrowed further into the skin, but it is more likely that a small local reaction causing oedema and raised papule formation had engulfed the mouthparts of the tick, giving the impression of being "particularly embedded." The fact that

this patient had an allergic reaction despite the tick having been killed beforehand highlights the importance of still removing ticks by the mouthparts even after killing.

Similarly, killing with ether-containing spray did not prevent allergic reaction in 6 of the 9 patients who did so in the community before self-removing ticks with either fingers or household tweezers, likely squeezing ticks by the abdomen. One patient that used permethrin cream in the community also had an allergic reaction to a dead tick. The patient went to bed shortly after application, tick still *in situ*, and awoke some time later with a widespread allergic reaction. Whilst it is possible that this was a reaction to the cream, it seems more likely that the patient lay on the dead tick which then caused the reaction.

Seventeen patients presented to the ED having already killed ticks themselves with ether-containing spray or permethrin cream. They all had ticks then removed by the mouthparts and only 2 of the 17 patients suffered allergic reactions. These unfortunate patients had suffered reactions whilst attempting to use the ether-containing spray, highlighting the importance of taking care when using this method. At MVH ED, the nozzle was held about 1 cm above the tick when the cold sprays are administered. Those attempting to replicate this method in the community need to be careful not to disturb ticks with the device. Since the device has a rounded aperture slightly larger than the tick and instructions for use on warts state to hold this flush with the skin, some may be tempted to try to fit the tick inside the device before spraying. This increases the chances of disturbing the tick. A new ether-containing spray – Tick Off! (dimethylether, Pharmacare Laboratories Pty Ltd.) – sold by the same company has both a wider aperture as well as instructions for use on ticks that advise holding above the skin for exactly this reason.

Five patients in this study made no attempt at killing or removing their ticks but had allergic reactions anyway. This highlights the importance of being careful not to disturb ticks once found. Unfortunately, an allergic reaction can be the first indication of a tick bite since these five patients had accidentally disturbed their ticks by scratching or during bathing.

Five patients presented to ED with a live tick *in situ*, which was not killed before being removed with fine-tipped forceps. Two had refused to have the ticks killed first and no reason was documented in another, but none of these three had allergic reactions. None of the three had a known tick allergy but it is possible that this acted as a sensitising event and they may well prove allergic to future bites. The other 2 patients had ticks in locations that contraindicated killing, on the delicate skin of their eyelids. Only one had known tick allergy but both suffered allergic reactions shortly after removal. Location has previously been shown to be important, for example in the unusual case of a young Indian boy who developed unilateral facial paralysis secondary to a tick in the external ear canal [36]. It may be that the thin, well-vascularised skin of the eyelid increases the risk of allergic reaction post removal and an agent suitable for use in these locations is a potential target for future research.

None of the 50 patients presenting posttick removal had used fine-tipped forceps regardless of whether they killed ticks beforehand or not. The vast majority had allergic reactions, two of them anaphylactic. Most were not previously known to be hypersensitive and may therefore not have been educated about tick bites.

Interestingly, compared with a previous study at MVH ED [37], the number of tick bite presentations remained stable (~290/yr) as did the percentage of these that had

allergic reactions (~36%) but anaphylactic reactions were far fewer – 34 between 2007 and 2009 but only 2 in this 6-month study. Hypersensitivity requires previous exposure and although severity varies slightly unpredictably, it is thought to increase with each bite so one possible explanation is improved public awareness at an earlier stage of hypersensitivity. Local campaigns by the Tick-Induced Allergies Research and Awareness group as well as publications in local [38] and national media [39] are likely responsible. Eighty-nine percent of known hypersensitive patients in this study either presented to ED for management or used Wart-Off Freeze or Lyclear at home and only 7.1% had allergic reactions after approved methods.

Limitations

The main limitations of this study were the sample size and the study design. The sample size was limited by the timeframe (6 months). However, despite the small sample size there was a high participation rate (83%) indicative of the public's awareness and concern over tick allergy. As the first prospective research paper in the field of tick allergy prevention, this is essentially a pilot study on which future research can be based.

No control group was used in this study and since the prevalence of tick allergy and the incidence of reaction in hypersensitive patients are both unknown, extrapolation is guarded. The results support the hypothesis that killing ticks with ether-containing sprays or permethrin cream before removal by the mouthparts reduces the incidence of allergic and/or anaphylactic reaction, but they do not disprove the null hypothesis of no effect since it is unknown how many reactions were truly prevented.

The 50 patients who presented after tick removal do not replace a control group since they were a self-selecting cohort of patients. It is not surprising that most of this group had suffered allergic reactions since they would otherwise not have a reason for presentation. It is more surprising that seven of them presented without a reaction. It is impossible to know how many patients removed ticks in the community by any method, had no allergic reaction and therefore did not present to ED.

Importantly, none of the patients presenting with allergic reactions after removal had used fine-tipped forceps or Tick Twister and even the use of Wart-Off Freeze was not protective for patients that went on to use fingers or tweezers for removal (**Table 2**). This once again highlights that whilst killing ticks *in situ* with ether-containing spray may reduce the risk of allergic reaction, they should still be removed carefully only by the mouthparts with a suitable implement or left to drop off after being killed. However, since this study could not sample patients who had no allergic reaction after removal in the community, it must be noted that they may not be truly representative.

The study was also potentially vulnerable to observer bias since staff were aware of the rationale. A double-blind randomised control trial, the gold standard, would have had clear challenges in blinding either participants or investigators. Control groups could be considered in future studies but might expose control group participants to a higher risk of anaphylaxis.

Another limitation of this study was the lack of follow-up to investigate the incidence of tick-borne disease postremoval. Since it has been shown that attachment time rather than removal method is the significant variable affecting pathogen transmission, however, and patients do not tend to know how long a tick has been *in situ* when they present to ED, it is

https://doi.org/10.5415/apallergy.2019.9.e15

possible that inclusion would have only confounded the results [10]. Future studies could factor this into their design.

Future studies could also investigate the incidence of allergic reaction according to different anatomical location of bite sites and lifecycle stages. Particularly, safe removal methods for ticks in locations precluding the use of freeze sprays and permethrin are needed as both patients in this study with anatomical contraindications had allergic reactions.

In conclusion, *IH* is commonly known as the paralysis tick, but there has not been a death from tick paralysis for 73 years. The anaphylaxis tick might be more appropriate colloquial nomenclature since there have been four fatalities from tick anaphylaxis in Australia in more recent years.

Killing ticks *in situ* to prevent anaphylaxis was first suggested almost 30 years ago, has been routine in MVH ED for many years and is currently advised by ASCIA. Most previous studies have focused primarily on whole tick removal as a proxy for reducing pathogen transmission, but it has been shown that only attachment time has a significant effect on pathogen transmission. Whilst removal method may not have an effect on pathogen transmission, this study supports the hypothesis that accidental tick disturbance, live tick removal with fingers or household tweezers and even dead tick removal with fingers or household tweezers all increase the risk of allergic reaction.

Ether-containing spray and permethrin cream are approved by the TGA for use on human skin in Australia. Within the limitations of this study, results support their use to kill ticks *in situ*, before careful removal by the mouthparts in order to reduce allergic and anaphylactic reactions.

ACKNOWLEDGEMENTS

Many thanks to all the staff of Mona Vale Hospital Emergency Department who helped in the collection of data for this study and the tick-bitten patients who took part. Special thanks to Stephen Doggett, Kevin Broady and Stephen Graves for their expertise and input.

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