tiara Tick Induced Allergies Research & Awareness

SUBMISSION TO THE INQUIRY INTO ALLERGIES AND ANAPHYLAXIS

1. The potential and known causes, prevalence, impacts and costs of anaphylaxis in Australia

Potential and known causes, prevalence:

Tick-induced allergies are the most common medical conditions provoked by tick bites.

Tick-induced allergies comprise: mammalian meat allergy after tick bite (MMA),
tick anaphylaxis (TA),
food carbohydrate induced enterocolitis syndrome (FCIES) and
large local reactions to ticks (LLR).

MMA, first reported in 2007 in Australia (van Nunen et al.), now occurs in 17 countries, on every continent where humans are bitten by ticks.

The allergen in the mammalian meat has been found to be a carbohydrate molecule, galactose-alpha 1,3-galactose ("alpha gal").

Tick anaphylaxis, on the other hand, is due to the development of allergy antibody to tick salivary protein.

World-wide, Australia has the highest prevalence of mammalian meat allergy (MMA) [113/100,000] and tick anaphylaxis (TA).

MMA is the only allergy on the planet where the trigger is known (a tick bite) and therefore it offers unparalleled opportunities for prevention when the following is considered:

- MMA does not occur without having had a tick bite,
- not everyone bitten by a tick develops MMA,
- not uncommonly, more than one person in a family will develop MMA,
- if you are bitten by a tick and develop MMA, then you can more than double your allergy levels if you have a subsequent tick bite,
- if you develop MMA and do not have another tick bite you can significantly reduce your allergy levels over 18 months to two years, with some individuals being able to tolerate mammalian meats again after 3 -4 years, and
- if you lose your MMA and have another tick bite then your MMA can return.

More than 50% of Australians live in regions where *Ixodes holocyclus* (Australian paralysis tick) is endemic and a second tick species has been described recently in Australia as a cause of MMA, *Ixodes (Endopalpiger) australiensis* in WA (Kwak et al.), increasing the exposure of the Australian population to around 60%.

Modelling the effects of global warming indicates higher tick exposure will occur in the future.

In tick endemic regions in the USA and in Germany, sensitisation rates have been established as being as high as 35% with MMA symptoms occurring in only 8-9%.

The majority of TA sufferers develop alpha gal specific IgE and at least 30% develop MMA symptoms as well (van Nunen et al.).

Impacts and Costs:

The impact upon individual tick-induced allergy sufferers and their families is best recounted by those who have these complaints themselves, however, the extraordinary experience at our function for the inception of TiARA at Royal North Shore Hospital in 2013, presided over by The Honourable Anthony Roberts, Member for

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Lane Cove, NSW, brought home the enormity of the everyday problems they and so many others with anaphylaxis face on a daily basis. Nevertheless, they joined us - as our TiARA Ambassador (Joy Cowdery) and as a TiARA Committee member (Janelle Williams), and chose to support others and share their expertise in avoiding the myriad sources of mammalian products with fellow sufferers with MMA and work to prevent other people ending up in the same precarious situation.

Fatalities:

Tick anaphylaxis has been fatal in 4 cases between 1997 and 2013 (Mullins et al.).

Deaths from cetuximab anaphylaxis (2 documented in Australia in DAEN [Database of Adverse Event Notification], 7 other fatalities internationally) are likely due to sensitisation to alpha gal, the allergen within the mammalian meat to which the patients are allergic and so, whilst deaths from MMA per se are not recorded to our knowledge in Australia, these cetuximab deaths should be considered as MMA fatalities.

Impact upon Emergency Medicine Departments in tick hyper-endemic regions:

An inordinate number of presentations to Emergency Medicine Departments in tick hyper-endemic areas are due to tick related allergies. Rappo et al, reported over 500 cases of tick bites presenting to a single New South Wales hospital over a 2 year period, of which 34 resulted in anaphylaxis. Cutaneous symptoms were the most common feature associated with anaphylaxis (32/34, 94%). Forty per cent (13/34) of patients with tick bite anaphylaxis had a history of allergy or previous anaphylaxis. Seventy-six per cent (26/34) of patients were administered adrenaline either prior to presenting or in the ED, while 97% (33/34) were treated with steroids. Fifty-three per cent were referred to an immunologist and one-quarter were discharged with an adrenaline auto-injector.

Clinically apparent allergies are “the tip of the iceberg”:

In tick endemic regions in the USA and in Germany, sensitisation rates (= allergy antibody production rates) have been established as being as high as 35%, with MMA symptoms occurring in only 8-9% (ref).

The above statistics indicate that in tick endemic regions of Australia, up to 25% of the community will have alpha gal specific IgE and be unaware of their sensitisation.

Moreover, individuals may be unaware of having been bitten by a tick, especially if the bite has been from a nymph tick (2mm and resembling a tiny splinter), as they may not recognise this tick stage as being a tick or ticks may be removed without being recognised as being ticks when the individual is not tick aware i.e. is visiting from non-tick endemic regions.

Many individuals with MMA over time become able to consume mammalian meats again but they can have persistent low levels of sensitisation which are sufficient for them to be at risk of many of the therapeutic complications listed below, especially if the medicine is injected rather than taken orally.

The therapeutic consequences of making allergy antibody to alpha gal are myriad and exist

- in those with MMA,
- in those with TA where they have also produced alpha gal specific IgE antibodies,
- in people where sensitisation to alpha gal has occurred without the victim being aware of having had a tick bite and where that person has no clinical reactivity to mammalian meats,
- in those MMA and TA sufferers who have a residual low level of alpha gal allergy antibody but who no longer have any symptoms of MMA.

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In the last three of the above groups of people the risks of allergic reactions/anaphylaxis to the therapeutic agents below would not be appreciated by patients or their attending physicians, *unless* testing for the presence of alpha gal specific IgE is performed before commencing treatment with:

- Cetuximab (a colon cancer drug made in a mouse, therefore alpha gal containing)- anaphylaxis [8.3% in Northern Sydney] or death [2 in DAEN]
- Vaccines containing gelatine e.g. Zostavax (anaphylaxis)
  MMR II (anaphylaxis)
- Heparin (porcine-derived)
- Cell savers containing gelatine
- Medicines in gelatine capsules
- Porcine heart valve prostheses
- Vaccines containing mammalian derived substances used in manufacture usually bovine
- Colloid solutions (used less so nowadays, fortunately)
- Mammalian meat derived substances in tablets (e.g. stearate for the exquisitely hypersensitive MMA sufferers)
- Reduced life of porcine heart valve prostheses
- Snake antivenoms are made in mammals

as examples.

Costs:

Tick-induced allergies are avoidable allergies if the community is thoroughly educated as to the risks to which a tick bite exposes them and, more importantly, thoroughly educated regarding tick bite prevention and management.

Thus, all of the burden to the health sector of the medical costs of Emergency Department attendances, consultations with clinical immunologists/allergists, general practitioners, discussion between treating practitioners to plan treatment to avoid mammalian products during what should be simple, straightforward procedures, cost of adrenaline auto-injectors and their ongoing replacement, cost of antihistamine therapy prophylactically and for acute reactions, the cost of oral corticosteroid courses to settle reactions not requiring adrenaline, cost of alternate therapies (both the opportunity cost of not being able to use the readily available medications and the cost of morbidity resulting from reactions to therapeutic substances) should be largely avoidable.

The overall prevalence of sensitisation to alpha gal (= alpha gal allergy antibody production) in our population is not known precisely (TiARA has had a preliminary discussion with the Australian Red Cross Blood Bank with a view to establishing this statistic, however, funding will be an obstacle [i.e. non-existent at this time], as $50 per sample tested for alpha gal specific IgE, would be a give-away price when the test antigen is supplied to the pathologist at $40 per test unit), however, given the statistics from the USA, Germany and Sweden an assumption of 35% in tick hyper-endemic regions in Australia would be reasonable.

The burden of achieving safe passage for MMA and alpha gal sensitised people through surgery is the enormous amount of time spent by the consultant immunologist. For example, an exquisitely hypersensitive MMA sufferer falls out walking her dog and fractures her ankle and this clinical scenario engenders half an hour on the car phone working with the ED Deputy Director to plan analgesia in the ED, 6 hours of investigation to determine whether the surgery would be free of risk from each analgesic and anaesthetic agent to be used and surgical materials, 2 hours of determining the appropriate anticoagulant, multiple calls for information checking and clarification of meaning of statements which are otherwise comprehensive in drug information inserts and sourcing and giving the original AusPAR (Australian Public Assessment Report) a detailed perusal for each of the drugs to be used. As another example, an MMA patient required an aortic valve replacement and the planning for this involves several hours of checking and cross-checking with surgeon, anaesthetists, perfusionist and the clinical immunologist at the treating hospital. Advice regarding the advisability of simple vaccinations for travel, for example, require six hours of research, several emails

across the globe and requests for additional information from overseas manufacturers and inquiries to track down the manufacturer via the Australian distributors, to then email the patient to state "you may have the Japanese encephalitis vaccine brand JESPECT® as this is made in the African green monkey (Chlorocebus spp.) which is an Old World monkey (after checking the taxonomy of the monkey) and only this brand is currently suitable for you". These clinical problems are a weekly experience for any consultant physician expert in tick-induced allergies.

The safety of certain preventive therapies (apart from vaccines) cannot be guaranteed e.g. some of the monoclonal antibody therapies.

The Public Health problem which is arising as a result of alpha gal sensitisation (whether the individual is clinically allergic to mammalian meats or not) is the recently described association between alpha gal sensitisation and the occurrence of more extensive coronary artery atherosclerotic plaque and more unstable atherosclerotic plaque in the under 65 age group.

An increased risk of coronary artery disease has been described recently in alpha gal sensitised individuals with more unstable arterial plaque in those aged under 65 with an attendant increased risk of myocardial infarct and stroke (Wilson et al.).

As recognised risk factors have become less common over time in patients suffering myocardial infarction In the Northern Sydney region (Vernon et al.), alpha gal sensitisation as an explanation, considering the work of Wilson et al., requires examination and a larger study in an Australian cohort is currently being analysed.

If this research confirms involvement of alpha gal sensitisation as a risk factor for myocardial infarcts and strokes, this would mean that tick bites are a huge public health problem on this basis alone.

2. The adequacy of food and drug safety process and food and drug allergy management, auditing and compliance (including food allergen labelling by manufacturers and food service providers).

The presence of mammalian products in foods does not currently have to be flagged as it is not one of the eight common foods which cause anaphylaxis. This creates a considerable burden for patients and for those who care for them in determining those foods which are safe for them or their family members.

Representations to remedy this situation have been made to FSANZ by Allergy and Anaphylaxis Australia (A & AA) the peak patient support organisation, and to other authorities without success to date.

TiARA and A & AA have developed a patient information card to identify sources of mammalian products in foods and this can be found on our website www.tiara.org.au.

A solution could be to have a QR code notification which lists all ingredients together with their synonyms (for added safety) which could be read with a mobile telephone app.

The knowledge in the food industry has improved with the efforts of Allergy and Anaphylaxis Australia (A & AA) and ASCIA (Australasian Society of Clinical Immunology and Allergy), however, ongoing and additional support for these endeavours is needed to keep patients safe.

Vaccines: it would be very helpful in risk stratification for MMA and alpha gal sensitised patients if vaccine manufacturers were to be asked to measure the amount, if any, of alpha gal in their vaccines. This is already available in regards to egg content in vaccines and it is tremendously helpful to be able to reassure parents of egg allergic children of the unlikelihood of a vaccine with < 1mcg of egg protein causing a significant allergic reaction in their egg allergic child.

Snake antivenoms: as above. There is at least one MMA sufferer who is also a snake handler. Measurement of alpha gal in the antivenoms as a policy to be recommended would be very helpful coupled with an additional warning on the advice as to being particularly prepared for an anaphylaxis in MMA and alpha gal sensitised patients needing treatment for added safety.

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Drug safety: A policy for prevention of cetuximab anaphylaxis by testing for alpha gal sensitisation before cetuximab is given has been developed by a clinical immunologist and allergist together with the clinical oncologists at Royal North Shore Hospital and is being presented at the Clinical Oncology Society of Australia (COSA) conference in Adelaide next month (November 2019), where it will hopefully be taken up by clinical oncologists throughout Australia. Help with dissemination of this policy to all oncologists in Australia would be welcomed at the Department of Health level. The Australian DAEN (Database of Adverse Event Notifications) records 70 episodes of anaphylaxis/hypersensitivity to cetuximab, with 3 deaths.

3. The adequacy and consistency of professional education, training, management/treatment standards and patient record systems for allergy and anaphylaxis.

Because tick-induced allergies are emergent and have not been present as commonly in our population until after 2003, from which time an exponential increase has been seen in the diagnosis of both MMA and TA (and now the additional novel entity of FCIES, described only this year), ensuring adequate professional education has been challenging. TiARA members have spoken at professional meetings for ED physicians, ED nurses, general practitioners, pharmacy assistant conferences, pharmacists' conferences, environmental health professional conferences, council meetings and at several other meetings. TiARA presentations have been presented by a medical student interstate for GPs, regionally for GPs by other GPs and by GPs for medical students, and for the Education Department of NSW conference by an ASCIA colleague.

ASCIA has developed and lodged comprehensive advice on the website www.allergy.org.au for health professionals and patients since 2013.

Advice has also been posted by ED physicians and ED nurses on the Emergency Care Institute website for all health professionals.

TiARA has posted a great deal of educational material which can be downloaded and a video ("How to remove a tick") for health professionals and patients on www.tiara.org.au.

It is important to note that The Australian Department of Health is to be commended upon its current efforts in developing advice regarding tick bite prevention and management (under the leadership of Dr Carl Gibson, with TiARA Committee and ASCIA advice sought), however, programs for disseminating this advice will then be needed to leverage the development of this comprehensive and evidence based Factsheet. When this evidence-based advice is posted it would be fair to state that Australia would then lead the world in having sound advice available to the population at large in the prevention and management of tick bites.

TiARA disseminates research findings and other information on our website in our NEWS section, for health professionals and the community, posted by our Research and Awareness assistant (6 hours per week funded by TiARA).

TiARA is working in partnership with one council in a tick hyperendemic region on disseminating advice regarding the prevention and appropriate management of tick bites to prevent allergy following publication of the research providing the scientific basis for this advice (study completed at Mona Vale Hospital, by staff now at Northern Beaches Hospital, Sydney) Taylor et al..

TiARA members have also worked with the three major councils in the hyperendemic tick region in Northern Sydney in delivering an award -winning program protecting council workers by educating them regarding tick bite prevention and management, made available to all Statecover indemnified councils.

TiARA has also worked with Ku-ring-gai Council over several years now with educational session for the community at council chambers and at the annual Festival on the Green, Narrabeen Reserve, and we have also taken up the kind offer to attend the annual Seniors Expo (2018) held by Mr Trent Zimmerman MP and have taught a large number of Seniors about tick bite prevention and removal there.

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4. Access to and cost of services, including diagnosis, testing, management, treatment and support.
Access to and cost of services:

Inequity characterises the current situation for tick-induced allergies in access to and cost of services, including diagnosis, testing, management, treatment and support.

TiARA has attempted to correct this inequity with the website information and via the info email address for TiARA.

These endeavours would benefit from further support by funding for a Project Officer.

The cost of an alpha gal test is $65 which does constitute a barrier for some of our people.

It is an essential diagnostic tool and every useful in risk stratification for reactivity to therapeutic substances and for gauging the safety of re-introduction of mammalian meats.

Adequate education of GPs would be helpful and TiARA has just completed an educational program for GPs in the Northern Sydney Health District and hopefully this will be able to roll out to other districts.

5. Developments in research into allergy and anaphylaxis including prevention, causes, treatment and emerging treatments (such as oral immunotherapy).

A TiARA member first described the association between tick bites and the development of mammalian meat allergy (van Nunen et al. 2007). Finding this association has proven to be the lynchpin in the prevention of MMA. The link between tick bite and the development of MMA has been since confirmed around the world.

TiARA members have completed the first study in humans world-wide in prevention of tick-induced allergies, confirming that killing the tick in situ is the safe approach (Taylor et al 2019).

A TiARA member has established the utility of personal repellents in tick bite prevention (Sukkanon et al 2019).

Tick-induced allergies are the allergies you do not have to have, as tick bite prevention and correct management of a tick bite is key to their prevention.

Assistance with dissemination of the knowledge regarding tick bite prevention and management would be welcomed as TiARA's members are all voluntary and our resources are limited.

Tick-induced allergies are the example par excellence where an ounce of prevention will save more than a pound of cure!

It is very unlikely that TA would ever have an immunotherapy extract developed commercially as the numbers world-wide would not at this point support such an endeavour.

Development of a designer covalent heterobivalent nanoparticles (as in development for peanut allergy (Deak et al 2019) offers the best hope for TA sufferers. Such development will rely on determination and confirmation of the individual allergens responsible for TA (work in progress and further development will require funding of course).

BAT (Basophil Activation Testing) will be helpful and needs to be developed for the alpha gal allergen. We shall probably have to rely on overseas commercial interests to provide this for routine use and have it taken up by pathology providers here. This will likely need to benefit from a Medicare rebate for equity. The BAT should allow us to discriminate between those people at risk of an allergic reaction sensitisation and those who are not.

All of the advances in immunotherapy of food allergy in general apply to MMA: probiotic potentiated oral immunotherapy, epicutaneous immunotherapy and possibly oral immunotherapy but less certainly with the last modality.

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7. The impact of unnecessary drug avoidance due to unconfirmed drug allergies and its management.

Measurement by manufacturers of alpha gal presence or otherwise would be most helpful in maximising the therapeutic armamentarium available to people with MMA or who are sensitised to alpha gal without MMA.

This has been done by the manufacturers of one monoclonal antibody with very reassuring results and having such a policy at the level of the TGA (Therapeutic Goods Branch) would be very helpful indeed.

Avoidance of several medications on the basis of uncertainty by some of our MMA sufferers and alpha gal sensitised non-MMA people impacts potentially unfavourably upon prevention of other diseases.

The dissemination of tick bite prevention and management information offers the likelihood of keeping effective drugs e.g. cetuximab available to those who are unfortunate enough to need them.

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Thank you for the opportunity to present information which will help in wider recognition of the extent of the problems inherent in tick bites and the consequences of their inappropriate management, of the value to be had from educational endeavours in tick bite prevention and management, for the chance to highlight the public health concern that tick bites constitute, to acquaint you with the proud history of Australian research in this area, to note the considerable mortality and morbidity which might be prevented if their role in promoting vascular disease which thus increases the chance of myocardial infarcts and strokes in the tick-bitten is confirmed, and to engage you in considering what might be done to eliminate these risks to the health of the people of Australia.

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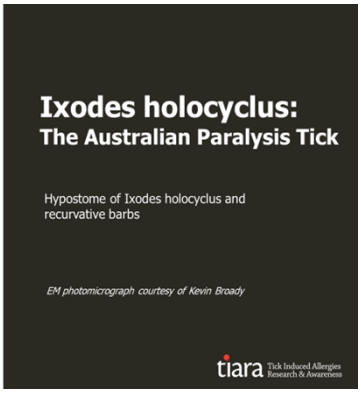
Ixodes holocyclus
Photographs courtesy of Stephen Doggett

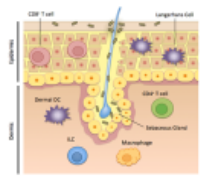


Tick-induced allergies: Mammalian meat allergy & tick anaphylaxis

Are what happens when an accomplished parasite forsakes a cute, furry mammal (or a not so cute furry animal)

For a human with normal skin

Subverts the rich immunological milieu in normal skin



To an allergy promoting environment

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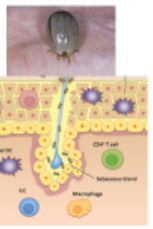
Tick-induced allergies: Mammalian meat allergy & tick anaphylaxis



And then injects the allergen, bypassing the usual tolerance mechanisms we possess, resulting in a switch from IgG to IgE production leading to a cross-reactive allergic reaction to the meat allergen or development of specific IgE directed against a tick salivary protein.

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- ❖To promote awareness of tick-induced allergies by the public, health professionals, those in at-risk occupations, educators and government.
- ❖To provide resources and support for sufferers of tick-induced allergies who live remote from expert medical and dietetic advisors.
- ❖To promote research into the prevention & cure of tick-induced allergies.
- ❖To disseminate established tick management strategies and help develop novel, proven tick management measures.

www.tiara.org.au

Distribution map of the Australian Paralysis Tick (*Ixodes holocyclus*)

Ixodes holocyclus

The Australian paralysis tick may be found 20-30 Km inland along most of the Eastern seaboard of Australia from Cape York (QLD) to Lakes Entrance (VIC).

An estimated 50% of the population of Australia, with the majority of the population of NSW and QLD potentially exposed.

Map adapted from Roberts FHS (1970) Australian Ticks. Yeerongpilly, QLD, Australia by TAGS Inc., Bill Conroy & Norbert Fischer.

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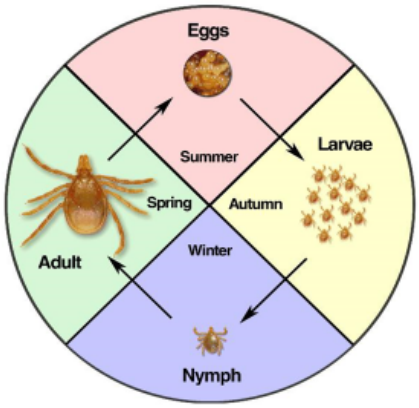

Ixodes holocyclus

Illustrations courtesy of Stephen Doggett,
Dept of Medical Entomology, The University of Sydney, Westmead

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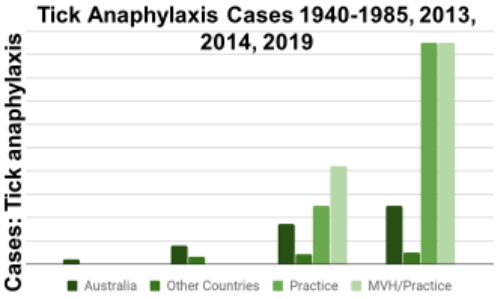

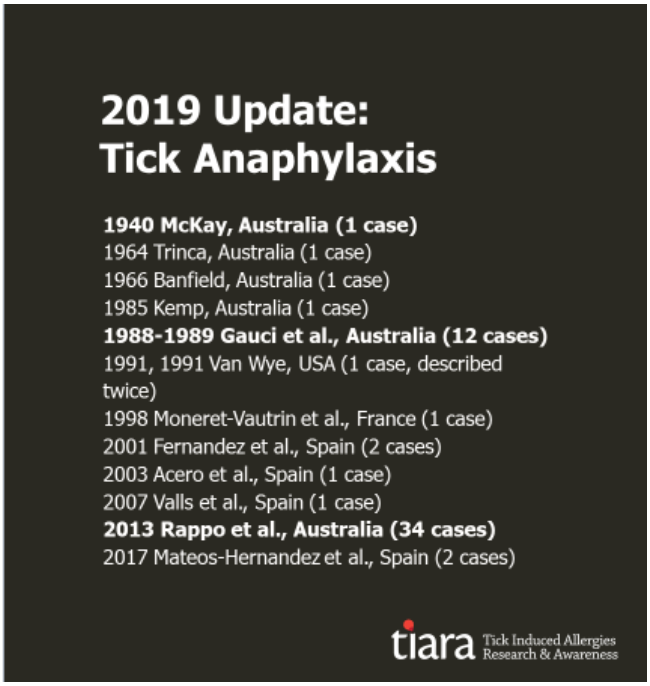

EMA

doi: 10.1111/1742-6723.12083 *Emergency Medicine Australasia* (2013) **25**, 297–301

ORIGINAL RESEARCH

Tick bite anaphylaxis: Incidence and management in an Australian emergency department

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Mona Vale ED over 2 yrs

- 566 tick bites
- 34/566 anaphylaxis
- 32/34 cutaneous symptoms
- 26/34 needed adrenaline

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Anaphylaxis occurred following attempts at tick removal. Not one patient in this series had initially removed their tick as advised by ASCIA (Australasian Society of Clinical Immunology and Allergy), however, with subsequent tick bites (albeit n=8), no patient suffered an anaphylaxis when they killed the tick as ASCIA guidelines advise, suggesting that tick anaphylaxis may be avoidable in up to 98.5% of patients, if people in tick endemic areas were educated in appropriate tick removal practices.

Tick removal methods in tick anaphylaxis sufferers

Tick removal techniques used by 78 tick anaphylaxis sufferers (Mueller grades I-IV), seen by the first author from September 2011-March 2014, were reviewed. In 65/78 (83.3%), details regarding the tick removal technique used were available.

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If you live, work, volunteer or play where ticks live...

DO ***NOT*** SCRATCH ANYTHING YOU CAN'T SEE.

DO ***NOT*** DISTURB A TICK.

KILL THE TICK WHERE IT IS.

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Prevention of Tick Bites

DRESS FOR THE OCCASION
&
TREAT YOUR BACKYARD

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Preventing tick bites: Dress for the Occasion and Treat your Backyard!

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- Wear long-sleeved shirts and long pants when walking or working in areas where ticks occur
- Tuck pants' legs into long socks
- Wear a wide-brimmed hat
- Wear light-coloured clothing, which makes it easier to see ticks
- Brush your clothes to remove ticks before coming inside
- Undress and check for ticks daily, checking carefully on the neck and scalp
- Use insect repellent, particularly ones containing DEET (such as RID®, Tropical RID® or Tropical Aerogard® or Bushmans®) or Picaridin (OFF!®)
- Use permethrin-treated clothing when exposed to ticks (e.g. gardening)

Tick Removal Mantra for the Community

For ticks you can hardly see (larval and nymph stage ticks)

"Dab it, don't grab it!" (Apply the tickicide permethrin cream) Lyclear®

For ticks you can see (adult ticks)

"Freeze it, don't squeeze it!" (Use an ether-containing spray) e.g. Tick Off®

***and remember*: "Household tweezers are tick squeezers"**

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2019 Update: Tick bites & Mammalian Meat Allergy

Mammalian Meat Allergy after Tick Bite

Wider Distribution of Mammalian Meat Allergy after Tick Bite in 2019 vs 2007

- **Mammalian meat allergy 2007: 1 continent**

  Australia

- **Mammalian meat allergy 2019: 6 continents** (all continents where humans are bitten by ticks)

  Australia, USA, France, Spain, Germany, Korea, Japan, Sweden, Switzerland, Panama, UK, Italy, Republic of South Africa, Brazil, Belgium, Ivory Coast, Norway, (New Zealand report in press)

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2019 Update: Tick bites & Mammalian Meat Allergy

Current prevalence rates:

113/100,000 Australia (Sydney Basin)

13/100,000 in Virginia, USA

4/100,000 in Baden-Wurtemberg, Germany

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Yours sincerely

[redacted]

Sheryl van Nunen, Clinical Associate Professor, Northern Clinical School, Sydney Medical School, Faculty of Medicine and Health, The University of Sydney and on behalf of the following TiARA Committee members:

Professor Tony Basten AO and Professor Nicholas Cowdery AO, Co-Chairs
Professor Emeritus Derek Anderson AM, Professor Emeritus Paul Canfield AM,
Dr Andrew Ratchford, Maria Said, Janelle Williams, Stephen Doggett, Kevin Broady and Dr Stephen Ginsborg

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Vaccine	Bovine Material	Gelatine/type	BSA	Other	
Priorix (MMRV)	Y	N	N	N	
Priorix Tetra (MMRV)	Y	N	N	N	
MMR II (MMR)	Y	Y: Hydrolysed gelatine 14.5mg	Y see next column	Y: Foetal bovine serum <1ppm	
Rotarix	Y	N	Y: probable	Dulbeccos medium (BSA)	
Nimenrix	N	N	N	N	
ALT-HIB	N	N	N	N	
PROQUAD	Y	Y: Hydrolysed porcine 11mg	Y	N	
Tripacel	Y	N	N	N	
Pneumovax23	Y	N	N	N	
Gardasil9	N	N	N	N	
VAQTA (Hepatitis A)	Y	N	N	N	
FLU Quadri	N	N	N	N	
Fluarix Tetra	Y	N	N	N	
FLU Quadri Jnr	N	N	N	N	
Alfluria	N	N	N	N	
Fluzone	N	N	N	N	
Fluad	N	N	N	N	
ADT Booster	Y	N	N	N	
Stamaril	Y	N	N	N	
Havrix	Y	N	N	N	
Avaxim	Y	N	Y trace	N	
Varilrix	Y	N	N	N	
IPOL	Y	N	Y trace	N	
Rabipur	N	Y:denatured (polygeline)	N	N	
Vivotif	Y	Y:bovine	N	N	
Engerix B	Y	N	N	N	
Typhim VI	Y	N	N	N	
Zostavax	Y	Y: porcine gelatine 15.58mg	Y Bovine calf serum	N	
Vivaxim	Y	N	Y: BSA trace < 10ng	N	
Adacel Pertussis vaccine, Diphtheria toxoid, Tetanus toxoid, Poliomyelitis vaccine	Y	N	N	N	
Typherix	Y	N	N	N	
Prevenar13	Y	N	N	N	
Twinrix	Y	N	N	N	
Jespect	N	N	N	N	

Infanrix Hexa	Y	N	N	N	
MIRV	Y	N	N	N	
Boostrix	Y	N	N	N	
Q Vax	N	N	N	N	
Dukoral	N	N	N	N	
Hexaxim	Y	N	N	N	
Infanrix	Y	N	N	N	
Infanrix IPV	Y	N	Foetal bovine serum	N	
Quadracel	Y	N	BSA	N	
Adacel Polio	Y	N	N	N	
Boostrix IPV	Y	N	Foetal bovine serum	N	
Synflorix	N	N	N	N	
Meningitec	Y	N	N	N	
NeisVac-C	N	N	N	N	
Menitorix	N	N	N	N	
Menactra	N	N	N	N	
Menveo	N	N	N	N	
Mencevax	N	N	N	N	
Bexsero	N	N	N	N	
Menomune	Y	N	N	N	

The statement “contains bovine material” fully expanded is:

“The manufacture of this product includes exposure to bovine materials. No evidence exists that any case of vCJD considered to be the human form of BSE (bovine spongiform encephalitis) has resulted from the administration of any vaccine product.”

Shingrix (not yet available in Australia, approved by FDA 10/2018) does not contain gelatine.

A/Prof Sheryl van Nunen 2019