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Review

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Arboterrorism: Doubtful Delusion or Deadly Danger

Mackenzie L Kwak*

Department of Economic Development, Jobs, Transport and Resources, Australia

***Corresponding author:** Mackenzie L Kwak, Department of Economic Development, Jobs, Transport and Resources, 5 Ring Road, Bundoora, Victoria 3186, Australia, Tel: +61 408 101 522; E-mail: mackenziekwak@gmail.com

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Abstract

Arboterrorism, the weaponisation and use of arthropod vectors carrying pathogenic microbes, is a worrying possibility in an age of rapidly accelerating biology. Historically, arboterrorism has attracted minimal research and the probability of such attacks occurring has been unclear. For the first time the logistics of such attacks are discussed along with potential vectors and pathogens. A novel biodefence strategy against arboterrorism is also proposed.

Keywords: Arboweapon; Biodefence; Insects; Terrorism; Mosquitoes; Fleas; Ticks; Bioweapon

Arboweapons: A Historical View

Pathogen carrying arthropods employed as a weapons, or arboweapons as they will be referred to herein, have been employed for centuries inadvertently and intentionally. It has been suggested that the first such attack may have been in the 14th century when Mongolians used fleas infected with *Yersinia pestis*, on recently deceased plague victims, to spread bubonic plague in a besieged city [1]. More recently arthropod based weapons have been developed and employed multiple times. Perhaps the most notable example is that of unit 731 of the Imperial Japanese army, active from 1936 to 1945. Unit 731 is infamous for the development and deployment of fleas as biological vectors of plague and house flies (*Musca domestica*) as mechanical vectors of cholera [1,2]. Evidence has also emerged of an offensive biological warfare research programme led by the Waffen-SS of Nazi Germany to weaponise mosquitoes infected with malarial protozoa (*Plasmodia* sp.) [3]. During the Second World War the soviets were also recorded deploying human lice (*Pediculus humanus*) infected with the bacterium *Rickettsia prowazekii*, the etiological agent of epidemic louse-borne typhus, amongst German troops [4]. There is some support for the notion that the soviets may have also used horse flies (Tabanidae) or ticks (Ixodoidea) to spread tularaemia amongst German soldiers in Stalingrad during the summer of 1942 [1,4]. During the cold war the USA entomological warfare program developed a wide array of arboweapons including fleas, mosquitoes, ticks and flies, with associated human pathogens for use on unfriendly powers [1,5]. However, today many countries have signed and ratified the 1972 Biological Weapons Convention and few governments are believed to be engaged in the research and development of biological weapons [6].

Arboterrorism: An Outline

In recent years there has been increased interest in arboterrorism from analysts [1,7,8]. However, insights into development, efficacy, and biodefence strategies for arboweapons are limited. Generally, arboweapons can be thought of as comprising two components, a vector and a disease causing agent which is likely a pathogenic organism but which may also be a toxin. Unlike many biological agents which often require complex techniques to weaponise, arboweapons are conceptually very simple. In theory a vector competence study is sufficient technical information to facilitate the weaponisation of a vector and pathogen into an arboweapon. Such studies describe the techniques required to culture the vector, infect it and then transmit this infection to a host. Studies into the bionimics of vectors and their associated pathogens also provide additional information which may enhance the deadliness of attacks. Perhaps the most major obstacle to potential arboterrorists is the accessibility of agents. The composite nature of the weapons potentially creates the greatest difficulties developing arboweapons, as both a vector and disease causing agent must be collected and combined in most cases. Despite this, once vector and pathogen are collected, the development of arboweapons is theoretically simple to achieve as the technology and equipment requires is commonly used in the education, scientific and agricultural industries and can be sourced easily and inexpensively. However, technical expertise in microbiology and/or entomology may be required to develop such weapons.

Vector-Pathogen Systems and Arboterrorism

A recent assessment of potential agents of bioterrorism analysed 18 different pathogens or pathogen groups for their utility as bioweapons [9]. Of the group assessed, half are known to be transmitted by an arthropod vector [10]. These pathogens and their associated vectors as well as their categorization are presented in table 1 based on published vector pathogen associations and hypothesised threat as bioweapons [9, 10]. Mosquitoes are known to vector several viruses within the viral haemorrhagic fever group, including Rift Valley fever virus, yellow fever virus and dengue fever virus [10]. Ticks are also known to vector several viral haemorrhagic fever group viruses, including the Crimean–Congo hemorrhagic fever and the Kyasanur Forest disease virus [10]. Fleas are the primary vector of *Yersinia pestis*, the cause of bubonic plague [10]. Flies are known to be mechanical vectors of *Bacillus anthracis*, the etiological agent of anthrax [10]. Q fever is known to be vectored mainly by ticks, but also sometimes by horse flies (Tabanidae) [10]. Alphaviruses are primarily vectored by mosquitoes; as is the case for the three assessed category B alphaviruses [10]. Epidemic louse-born typhus is spread by the human lice (*Pediculus humanus*) [10]. This diverse group demonstrates the great number of vectors and pathogens which have been extensively studied and are obvious candidates for arboterrorists.

Category	Disease	Pathogen	Main Arthropod Vector
A	Plague	*Yersinia pestis*	Fleas (Siphonaptera)
A	Anthrax	*Bacillus anthracis*	Flies (Diptera)
A	Crimean–Congo hemorrhagic fever (CCHF)	CCHF Virus	Ticks (Ixodidae)
A	Kyasanur Forest disease (KFD)	KFD Virus	Ticks (Ixodidae)
A	Rift Valley fever (RVF)	RVF Virus	Mosquito (Culicidae)
A	Dengue fever (DF)	DF Virus	Mosquito (Culicidae)
A	Yellow Fever (YF)	YF Virus	Mosquito (Culicidae)
B	Venezuelan equine encephalitis (VEE)	VEE Virus	Mosquito (Culicidae)
B	Eastern equine encephalitis (EEE)	EEE Virus	Mosquito (Culicidae)
B	Western equine encephalitis (WEE)	WEE Virus	Mosquito (Culicidae)
B	Q fever	*Coxiella burnetii*	Ticks (Ixodidae)
B	Epidemic louse-borne typhus	*Rickettsia prowazekii*	Louse (Psocodea)
B	Cholera	*Vibrio cholerae*	Flies (Diptera)

Table 1: Recognised arthropod-borne pathogens and their primary vectors.

Increased globalisation has led to the emergence and re-emergence of many novel and known vector-borne diseases [11]. The re-emergence of a number of important mosquito-borne pathogens in recent years such as Zika virus and Chikungunya fever virus also highlights the potential for new and poorly known pathogens to become available to arboterrorists [12,13].

Flies as Arboweapons

Flies (Diptera) are perhaps the most likely arthropods to be developed as arboweapons due to their great impacts on human and animal health as vectors of disease [14]. Mosquitoes (Culicidae) are known to transmit a diverse assemblage of pathogens including viruses, bacteria, helminths and protozoa, many of which cause severe morbidity and mortality in humans [10]. Tsetse flies (Glossinidae) are also important vectors of disease, being the primary vectors of African sleeping sickness [15]. Sand flies (Phlebotominae) are recognised globally as serious vectors of the protozoa which cause leishmaniasis [10]. House flies (Muscidae) have been incriminated in the transmission of many protozoan pathogens including *Cryptosporidium*, *Giardia* and *Entamoeba* as well as many bacteria and viruses [10]. Notably, mosquitoes, house flies, biting midged (Ceratopogonidae), horse flies (Tabanidae) and black flies (Simuliidae) are known to be vectors of a number of parasitic helminths of medical significance including those which cause Loa loa, human filariasis and thelaziasis [10]. It has previously been noted that helminths pose a significant risk as food-borne bioweapons [16]. However, the potential for transmission by arthropod vectors has not been previously addressed. Arthropod-borne helminths pose a significant risk, especially as many cause stigmatising symptoms and signs in humans and may cause widespread panic. Botflies (Oestridae) are endoparasititc as maggots and have the potential to be weaponised not as vectors but as pathogens. The most likely candidate would be the human botfly *Dermatobia hominis*, which deposits eggs onto anthropophagic flies such as mosquitoes which then feed on humans during which the larvae hatch and burrow into the skin of the human host [17]. Infestations of *D. hominis* can be extremely painful, stigmatising and result in secondary infections around the site of infestation.

Arboterrorist attacks utilizing flies could take a number of different forms but can be loosely divided into direct and indirect attacks. In a direct attack, infected flies would be released with the intention that only those released flies would directly spread disease to a targeted group. In an indirect attack infected flies would be released with the intention of breeding and spreading the disease(s) they carry to native reservoir hosts or vectors which may then go on to cause a disease outbreak. Attacks utilizing flies would likely be enhanced by warm humid conditions with limited wind which provides a favourable environment for most anthropophagic flies. The diversity of fly species as well as their extremely varied life cycles and activity patterns means that an in-depth outline of the potential use of flies as arboweapons is impossible to cover within the scope of this work. However, a direct attack would be most effective in an area with a high number of people confined in a finite space such a train, bus or stadium. An indirect attack would be most effective if the location of release had conditions which favoured the breeding of the type of fly released, as well as suitable host animals to help amplify the pathogen and other indigenous fly species which could also vector the pathogen.

Ticks as Arboweapons

After mosquitoes, ticks are the most significant vectors of arthropod borne diseases on earth [18]. They are known to vector an extremely wide array of pathogens and are found on every continent [19]. Globally, the most important genera of pathogenic tick-borne bacteria with arboterrorism potential are *Borrelia*, *Rickettsia*, *Ehrlichia* and *Francisella*. Amongst the most important tick-borne viruses are the Crimean-Congo hemorrhagic fever virus, Colorado tick fever virus and the SFTS virus [19,20]. The protozoan genera *Babesia* and *Theileria* are also spread by ticks and are of great concern [19]. A number of tick species are also known to cause toxicoses and paralysis in humans during feeding [19]. Such species may be used directly as arboweapons without the need for an accompanying pathogen.

An attack utilizing ticks would most likely follow a similar pattern to a direct attack discussed previously in which infectious ticks would be released into a restricted area such as a train, bus or stadium in which many people were confined. An indirect attack is also possible, although the slow life cycle of many tick species means that such an attack may take many years before any effects are noticed and is therefore unlikely. As in the case of flies, conditions favouring an arboterrorism attack using ticks would be most likely to occur during humid weather during which ticks could survive longer periods off a host without desiccating.

Fleas as Arboweapons

While fleas and flea-borne diseases are of less public health importance today than they have been historically, they still have considerable potential as arboweapons. Fleas are most infamous for the spread of plague, caused by the bacterium *Yersinia pestis* [21]. However, the bacteria *Rickettsia and Bartonella* are also of medical importance [21]. An attack using the fleas *Tunga penetrans* as a direct weapons is also possible as this species burrows into the skin of humans and causes considerable morbidity and would be particularly stigmatising [21].

Much like a tick based arboterrorist attack; an attack using fleas would also likely follow the general pattern of the direct attack. This is due to the fact that fleas cannot survive long periods off of a host as they are chiefly nidicolous and are not well adapted for extensive host seeking [10]. Fleas are more active, and can survive longer periods off the host in humid conditions, and it would be expected that a successful arboterrorist attack would utilise this factor.

Biodefence: The Repel and Kill Method (RAK Method)

Previously, the need for the development of response protocols for arboterrorist attacks has been noted [7]. However, no specific biodefence method has been proposed until now. The RAK method comprises two main objectives, pesticide control of vectors and the use of repellents by civilians and first responders.

Pesticides can be used in two ways, in a pre-emptive deployment and/or a responsive deployment. A pre-emptive deployment would be in small areas deemed to be high risk targets for an arboterrorist attack. Pesticides would be deployed in an effort to kill any arthropod vectors released by terrorists. A responsive deployment would occur if an attack is suspected to have occurred. First responders would disperse pesticides in an effort to kill any arthropod vectors.

The use of repellents is crucial to the RAK method. While pesticides can be extremely effective at killing arthropod vectors, the use of repellents is a secondary barrier of defence against any vectors which may not have been killed initially by pesticides. Much like pesticidal applications, repellents can be applied pre-emptively or responsively depending on when an attack is predicted or believed to have occurred. Repellents should be used by both civilians and first responders to lower the risk of exposure to arthropod-borne pathogens.

The chemicals employed in the two parts of the RAK method may vary depending on the legislations of the country employing the method. However, pesticides used should have a low toxicity to mammals and rapid action. A suitable class of insecticides for use in many places are the neonicotinoids although many others may also be suitable [14]. Various classes of chemical pesticides exist for the control of arthropod vectors including the nicotinoids, oganochlorines, organophosphates and pyrethroids. However, the modes of action, efficacy, and toxicity all vary greatly amongst different compounds in the myriad of different arthropod vectors and discussion of these is outside the scope of this work.

There are a wide range of suitable repellents available and likely more will be developed in coming years. The most commonly available is N,N-diethyl-3-methylbenzamide, more commonly known as DEET [22]. While there has been increased interest in natural repellents composed of botanical extracts, few are widely available and of these only a small number are used in the industrialized world [23,24]. In developing nations, botanical extract based repellents may be essential measures in counterterrorism activities concerned with arboterrorist threats. It should be noted though that DEET has been shown to be more effective than a number of common botanical repellents [25].

Although selection of a pesticide may initially appear simple, care must be taken as common errors can easily be made. Effective insecticides may have little effect if the vectors employed in a biological attack are arachnids, such as ticks. In such a case acaricides must be used instead, as insecticides may have little or no effect [26]. Although highly effective when appropriately applies, other insecticides may also be of no use due to their method of action. Insect growth regulators (IGR) are a class of compound which target the ability of insects to mature to adulthood, effectively destabilising an insect populations by depriving it of fecund adults [27]. This group of compounds is effective in controlling arthropod vectors in agricultural and domestic settings, but due to their slow action, they can often take weeks or months for effects to be seen and would not be suitable for the RAK method.

It should be noted that the RAK method is specifically intended as a defensive measure against a direct arboterrorist attack using technology commonly available today. This method may be modified in future to incorporate emerging technologies such as CRISPR-CAS9 which may one day provide an effective means to inhibit or kill arthropod vectors. However, CRISPR-CAS9 technology is in its infancy and cannot be used in biodefence programs at the present time.

Conclusion

The threat of arboterrorism is of clear importance and requires the attention of global and national security organisations. Arthropod vectors are an extremely specious group with a diverse range of associated pathogens which have not been extensively examined by analysts in the context of bioterrorism. Historically, these weapons have been developed and have caused significant devastation when they have been employed. Today, increasing access to information and technology which could be used for the development of arboweapons has increased the likelihood of such attacks occurring. For this reason attention must also be focused on arboterrorism in biodefence programs. As well as the RAK method, examination of published studies on vector competency, bionomics and insecticidal activity should be used to develop effective regional biodefence protocols against arboterrorism.

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