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The past and present threat of vector-borne diseases in deployed troops

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Abstract

From time immemorial, vector-borne diseases have severely reduced the fighting capacity of armies and caused suspension or cancellation of military operations. Since World War I, infectious diseases have no longer been the main causes of morbidity and mortality among soldiers. However, most recent conflicts involving Western armies have occurred overseas, increasing the risk of vector-borne disease for the soldiers and for the displaced populations. The threat of vector-borne disease has changed with the progress in hygiene and disease control within the military: some diseases have lost their military significance (e.g. plague, yellow fever, and epidemic typhus); others remain of concern (e.g. malaria and dengue fever); and new potential threats have appeared (e.g. West Nile encephalitis and chikungunya fever). For this reason, vector control and personal protection strategies are always major requirements in ensuring the operational readiness of armed forces. Scientific progress has allowed a reduction in the impact of arthropod-borne diseases on military forces, but the threat is always present, and a failure in the context of vector control or in the application of personal protection measures could allow these diseases to have the same devastating impact on human health and military readiness as they did in the past.

Keywords: Armed conflict, disease emergence, review, vector control, vector-borne diseases, war

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Introduction

Through the ages, wartime epidemics have severely reduced the fighting strength of armies, caused the suspension and cancellation of military operations, and wrought havoc on the civilian populations of belligerent and non-belligerent states alike. Until World War I (WWI), infectious diseases rather than battle and non-battle injuries were the main causes of morbidity and mortality among soldiers, as well as in the affected civilian populations [1]. Among the 12 'war pestilences' delineated by Prinzing [2], five were vector-borne: plague, yellow fever, malaria, louse-borne typhus, and louse-borne relapsing fever. Since the Russo-Japanese War (1904–1905) and WWI, partly because of developments in weapons and advances in military hygiene and disease-control measures (e.g. vaccination, chemoprophylaxis, antibiotic treatment, personal protection, and control measures against vectors), there has been a continuous decline in the incidence of infectious diseases among soldiers as well as in civilian populations [3]. During World War II (WWII), vector-borne disease presented a permanent threat to the fighting ability of the belligerents [4]. By then, the impacts of many infectious diseases as causes of mortality or morbidity within the military had changed; they had gone from presenting potentially lethal threats to being primarily curable illnesses. However, infectious diseases remain of central importance in developing countries in terms of morbidity or mortality, and the historical impact of war in light of the current emergence or re-emergence of vector-borne diseases worldwide is still relevant today [5]. The military invasion of isolated ecological niches, the disruption of human and zootic habitats, population movement, the destruction of local infrastructures and the promotion of local conditions favourable to the wildlife reservoirs of disease all contribute to the risk of war directly influencing disease emergence or re-emergence [6]. In fact,

FIG. 1. *Aedes albopictus*, courtesy of J Gathany.

FIG. 2. Cutaneous lesihmaniasis in a French soldier, courtesy of JJ Morand.

FIG. 3. Malaria attack in a soldier in Ivory Coast, courtesy of R Migliani.

most conflicts involving Western armies have occurred overseas, often in tropical and subtropical regions, thus increasing the risk of vector-borne disease for the soldiers and for the displaced populations. In 2009, 35 000 French soldiers (Fig. 5) and more than 300 000 US soldiers were engaged or

FIG. 4. Mosquito bites in a French soldier in Gabon, F Pagès.

posted overseas (Fig. 6). Vectors and associated diseases have geographically, qualitatively and quantitatively changed throughout the centuries, and vector-borne diseases pose a growing problem for deployed forces on duty abroad [7,8]. Western armies engaged worldwide are continually forced to develop new vector-control strategies for military deployments. A selection of relevant vector-borne diseases is presented in Table 1, listed according to their past and present impact on the health and military readiness of deployed forces. The diseases that have lost their significance in the context of military operations, owing to progress in science and/or preventive medicine, are detailed in Table 2. The current threats to deployed troops, the corresponding personal protection and control strategies and the impact of war and conflict on public health in general and on the natural course of vector-borne diseases are presented and discussed herein.

Vectors and Vector-Borne Diseases of Military Importance

Mosquito-borne diseases

Malaria. Anopheline mosquitoes are vectors of the five human pathogenic malarial parasites: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and *Plasmodium knowlesi*. In addition to other 'war-stopping' diseases, such as dengue and sandfly fevers, malaria has always been a threat to soldiers on duty, from antiquity to modern conflicts. In 1809, during the Walcheren Expedition, 10 000 of 15 000 British troops became ill, and 4000 may have died from malaria [9]. In Macedonia (during WWI), the malaria-weakened British, French and German armies were unable to proceed for 3 years. Sixty thousand French soldiers were diagnosed as having malaria, and 20 000 of them were withdrawn to France [10]. During WWII, malaria emerged as

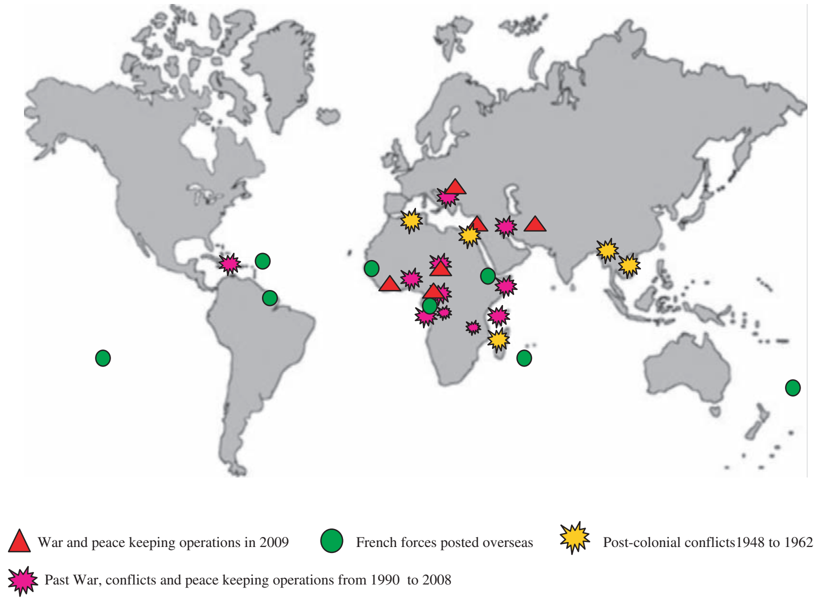

FIG. 5. Current repartition of French forces posted overseas and engagements from World War II to 2009.

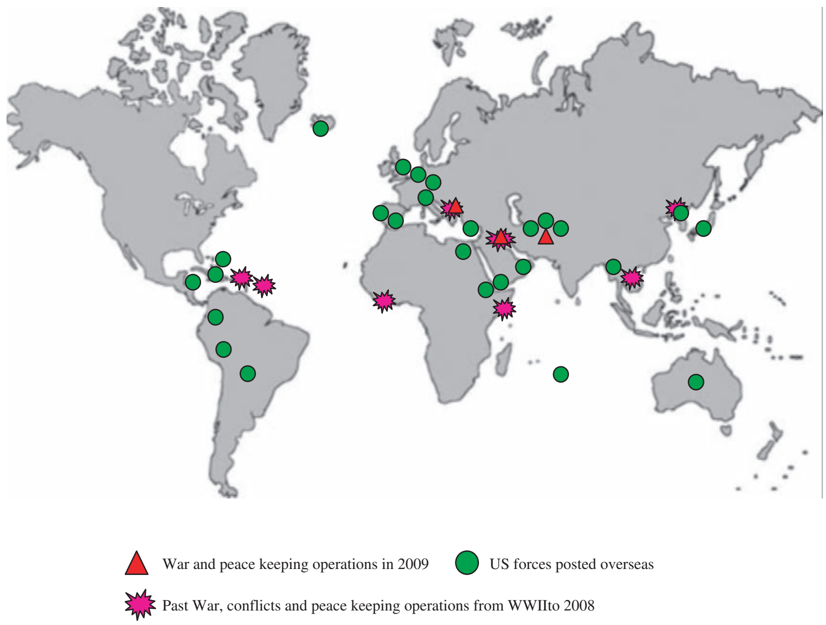

FIG. 6. Current repartition of US forces posted overseas and engagements from World War II to 2009.

one of the main causes of illness among troops in tropical areas. Subsequent to the fall of the Philippines in 1942, in the final stage of battle, the hospitalization rate reached 500–700 personnel per day in US forces, the equivalent of a battalion a day lost to malaria alone [11]. In some Mediterranean zones with a more equable climate, outbreaks of malaria during the transmission season jeopardized several military campaigns [12]. During the Italian campaign in 1944, 8000 British soldiers were struck down by malaria prior to the battle of Monte Cassino. In the Sicilian campaign also, hospital admissions for malaria (21 482) outnumbered battle casualties (17 375) [13].

In May 1943, General MacArthur observed that 'This will be a long war, if for every division I have fighting the enemy, I must count on a second division in the hospital with malaria and a third division convalescing from this debilitating disease' [14].

Victory was possible because, taking into account the experiences in the Spanish–American War in Panama and in WWI, the US Army developed a new Preventive Medicine Service in 1940 that included a Malaria Control Branch as well as an Insect and Rodent Control Branch.

During the post-WWII conflicts (in Indochina, Malaysia, and Korea), malaria's impact on deployed forces was strongly

TABLE 1. Past and present impact of vector-borne diseases of military importance among deployed troops

	Past threats	Present threats	Other diseases of less importance
Sandfly-borne diseases	Sandfly fever Old World cutaneous leishmaniasis New World mucocutaneous leishmaniasis Visceral leishmaniasis	Sandfly fever Old World cutaneous leishmaniasis New World mucocutaneous leishmaniasis Visceral leishmaniasis	Oroya fever
Mosquito-borne diseases	Malaria Lymphatic filariasis Yellow fever Japanese B encephalitis Dengue fever Chikungunya disease	Malaria Dengue fever Chikungunya disease Rift Valley fever virus West Nile virus	O'nyong nyong virus, Semliki Forest virus, Sindbi virus, and other mosquito-borne viruses
Flea-borne diseases	Plague Murine typhus	Plague? Murine typhus?	Flea-borne spotted fever
Louse-borne diseases	Typhus Trench fever Louse-borne relapsing fever		
Tick-borne diseases	Rocky mountain spotted fever Mediterranean spotted fever African tick bite fever Other common tick-borne spotted fevers Ehrlichiosis Q-fever* Tularemia* Crimean–Congo hemorrhagic fever Tick-borne encephalitis	Rocky mountain spotted fever Mediterranean spotted fever African tick bite fever Other common tick-borne spotted fevers Ehrlichiosis Q-fever* Tularemia* Crimean–Congo hemorrhagic fever	New pathogenic rickettsiae (*Rickettsia slovaca*, *Rickettsia helvetica*, and *Rickettsia sibirica mongolitimonae*) 'Rickettsia of unknown pathogenicity' Colorado tick fever Kemerovo tick fever Other tick-borne fevers (Dugbe or Banjha virus) Omsk hemorrhagic fever Kyasianur Forest disease Alkhurma virus hemorrhagic fever Human babesiosis
Mite-borne diseases	Scrub typhus	Scrub typhus	Rickettsial pox
Tsetse fly-borne diseases	Sleeping sickness	Sleeping sickness	
Kissing bug-borne diseases	Chagas disease	Chagas disease	

*: the main risk for forces is not the vector borne transmission.

reduced by the introduction of improved prophylactic drugs and improved vector-control and personal protection measures (PPMs) [14,15]. However, during the Vietnam War, the development of chloroquine resistance resulted in unsustainable losses due to malaria, and threatened the success of military operations [15,16]. Since this period, new antimalarial drugs have been developed for chemoprophylaxis and treatment, and vector-control regimens as well as protective measures have been improved. In the last 30 years, however, training or intervention of Western armies in malaria-endemic areas has led to malaria outbreaks on many occasions [17–23]. Poor compliance with routine prophylaxis (e.g. chemoprophylaxis, repellent use, and proper use of impregnated uniforms) and the impossibility of performing environmental control (e.g. sanitation of potential mosquito breeding places and habitats in combat areas, including the use of impregnated bed-nets) resulted in malaria outbreaks in the US, French, Italian, Australian, British and Dutch Forces [24–32]. During this period, resistance to most of the drugs used in treatment of or chemoprophylaxis for both *P. falciparum* and *P. vivax* increased or emerged [33]. Malaria currently is, and will be, a major threat to the health of soldiers, as well as their readiness for combat.

Mosquito-borne viruses. Many mosquito-borne viruses can have a severe impact on soldiers' health, on their readiness for combat, and on the capability of forces during deployments. Among them, dengue and chikungunya fever viruses, endemic in many parts of the world and still spreading geographically, are the most frequently encountered. With high levels of morbidity, reaching devastating attack rates up to 83% during the 2001 epidemic in Southern America, dengue fever (DF) can be responsible for the incapacitation of a large number of troops. During WWII, nearly 90 000 cases of DF were reported by the US Army [4]. Morbidity was very high in some areas, e.g. Saipan, where nearly one-third of the troops stationed there contracted the disease between June 1944 and September 1944. During the Vietnam War, although a few cases of DF and other mosquito-borne fevers, e.g. chikungunya fever, were reported [34], the results of the studies on fever of unknown origin (FUO) conducted during the evacuation of field hospitals indicated that almost 15% of these fevers were caused by dengue or chikungunya viruses [35,36]. Regarding the high rate of hospitalization for FUO (40–70 admissions/1000 men/year from 1965 to 1970), the impact of these diseases has obviously been underestimated. Since then, DF

TABLE 2. Controlled vector-borne diseases

	Past significance	Control measures
Epidemic typhus	Historically, major epidemic typhus outbreaks occurred in many wars, from the war of Granada (1482–1492) to WWI. During and after WWI, a typhus epidemic raged between 1917 and 1923, in eastern Europe, but owing to the effectiveness of louse-control measures (heating clothing to kill lice and eggs and mandatory bathing for troops), there was no typhus on the western front [126,186]	During WWII, because of advances made in diagnostics, therapeutics, louse-control methods, DDT and vaccine development (Cox's chick embryo vaccine), there were only 104 cases recorded and no deaths in US Army, despite a massive epidemic with up to 10% mortality rates in the civilian population (Egypt, French North Africa, and Naples) [187,188]. Actually, epidemic typhus is no longer a problem for troops [189]. Nevertheless, epidemic typhus can re-emerge as a result of a catastrophic breakdown of social conditions [190–193]
Trench fever	During WWI, trench fever caused one-third of all illness in the British army and one-fifth of all illness of the Allied forces [126]. Trench fever was controlled by the same effective control measures use to control typhus [186]. During WWII, large-scale epidemics occurred on the eastern front in Ukraine and Yugoslavia [126]	Owing to the effectiveness of louse-control measures, trench fever is actually not of concern for troops. Nevertheless, sporadic trench fever cases are regularly described in many parts of the world, and trench fever could re-emerge as a result of war
Louse-borne relapsing fever	From 550 to WWI, louse-borne relapsing fever occurred in massive epidemics in Europe, the Middle East and North Africa [197194]. During WWI, a major outbreak got all Greek army in the oriental front. Soldiers, natives of West Africa returning from Middle East Theatre, introduced the disease into Guinea and started an epidemic which literally decimated the population of the Sudan belt of tropical Africa [197194]	During WWII, owing to scientific advances, only 151 cases occurred in the US Army, despite the fact that an epidemic in North Africa produced an estimated one million cases and some 50 000 deaths. During the Korean War, lice infestations were frequent in South Korean soldiers and North Korean and Chinese prisoners, but only 60 louse-borne relapsing fever cases, with two deaths, were reported by US physicians [198195]. Louse-borne relapsing fever is actually not of concern for troops
Yellow fever	Yellow fever has been a substantial cause of mortality for the forces involved in South America, the West Indies and Africa, and was considered to be the main factor in defeat. During the Haitian–French War (1801–1803), Napoleon's largest expeditionary force (50 000 soldiers) was thoroughly destroyed by yellow fever [9]	Since the introduction of the yellow fever vaccine, this disease has ceased to be a problem. With the systematic immunization of troops before deployment in endemic areas, yellow fever is not a threat for forces
Tick-borne encephalitis	This risk was underscored by serological studies conducted among soldiers or infection studies conducted on ticks collected in the field [80,88,196]	An effective inactivated whole virus vaccine against tick-borne encephalitis is available and is used by most European armies living or deployed in endemic areas. In Bosnia, an accelerated schedule for tick-borne encephalitis vaccination was implemented in deployed US troops [197]
Japanese encephalitis	During the Indochina War and Vietnam War, a few cases of Japanese B encephalitis were recorded; the cases presented a high degree of lethality, but had no effect on French or US forces' fighting strength [14,34]	Currently, with the new highly effective and well-tolerated Japanese encephalitis vaccine, this disease should no longer be a problem for forces deployed in endemic areas
Q-fever	Q-fever is a zoonotic disease distributed worldwide and caused by *Coxiella burnetti*. *C. burnetti*, found in more than 40 tick species, is usually transmitted in humans by inhalation of infectious aerosol [83]. Such outbreaks have already been described in forces on duty [198–202]	Q-fever is of great military concern, but it cannot be considered to be a vector-borne disease threat
Tularemia	Tularemia, a zoonotic disease caused by the highly infective, virulent, non-sporulating Gram-negative coccobacillus *Francisella tularensis*, is found throughout most of the northern hemisphere in a wide range of animal reservoir hosts. It is transmitted to humans by various modes, including direct handling of infectious carcasses, ingestion of contaminated food or water, arthropod bites, including tick bites, or inhalation of infectious dusts or aerosols [203]	The last epidemic manifestations in deployment areas were all waterborne or rodent-borne, and no case has been reported among Western military forces [84]. Tick-borne tularemia is not of military concern, but the use of tularemia as a biological weapon remains a concern [85]

WWI, World War I.

has been considered to be a potential cause of febrile illness in troops deployed in tropical areas; it has been reported among French forces in New Caledonia (1989), French Polynesia, and the West Indies (1997), among US forces in Somalia (1992–1993), and among Australian forces and Italian troops in East Timor (1999–2000) [37–41]. Chikungunya fever has always been of concern for troops engaged in known endemic areas in Asia, and sporadic cases have also been recorded among French troops in Africa. A new variant of the chikungunya virus (CHIKV), formerly vectored mainly by the yellow fever mosquito *Aedes aegypti*, has now been repeatedly associated with a new vector, *Aedes albopictus* (the 'Asian tiger mosquito'), which, coincidentally, has dispersed worldwide after introduction into the USA and subsequent adaption to temperate regions. Consequently, in Gabon and Cameroon, French forces have been affected by CHIKV outbreaks in 2006 and 2007 [42–44]. Recently, *A. albopictus*-vectored new-variant CHIKV outbreaks, characterized by a single adaptive gene mutation providing a selective advantage for transmission by this mosquito, have occurred recently, resulting in massive outbreaks in India, Reunion Island, and Mauritius [45,46]. During the 2005–2006 CHIKV outbreak in Reunion Island, 35% of 770 000 inhabitants were infected during a 6-month period. French forces stationed on the island were also affected [47]. A military cohort of soldiers exposed to CHIKV during this outbreak has been screened for infection. Preliminary results are worrying; the attack rate was as high as that within the general local population, and previously unknown persistent manifestations, e.g. incapacitating chronic peripheral rheumatism or chronic fatigue, are not infrequent [48]. In addition, cardiac forms have been described for the first time [49]. Outside the known range of endemicity, which is limited to Asia and Africa, the first CHIKV epidemic occurred in Italy in 2007, thus proving its potential to become endemic in southern Europe, where the temperate variant of the Asian tiger mosquito was introduced in 1990 [50]. In addition to its public health importance, CHIKV is not only a threat to combat readiness, but also poses a major threat to soldiers' health.

Additionally, many other mosquito-borne viruses are of special concern for the safety of soldiers, and sporadic cases are regularly recorded (e.g. West Nile virus, Rift Valley fever virus, O'nyong nyong virus, Semliki Forest virus, and Sindbi virus) [51–53]. Mosquito-borne viruses, because of their impact on health in general and/or their high morbidity levels, always pose a threat to military forces deployed to disease-endemic areas.

Lymphatic filariasis. Lymphatic filariasis is caused by infection with the filarial nematodes *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*, and—depending on the major local vectors and transmission chains—is transmitted by mosquitoes of different genera (*Anopheles* sp., *Culex* sp., *Aedes* sp., and *Mansonia* sp.). Clinical manifestations vary according to the nematode species, as well as the age, level of infection and immune status of the patient [54]. First acute attacks could occur even after a short exposure [54]. During WWII, numerous outbreaks were reported, with a high rate of morbidity (one-third of the exposed population up to 70%), which had an immediate impact on troop strength [55]. During the Indochina War, one outbreak in returnees was reported [56]. Only serological evidence was found during the Vietnam War and in Australian soldiers deployed for a 6-month duty in Timor-Leste [57,58]. Nevertheless, occidental forces deployed to endemic areas may encounter severe outbreaks, as historically documented during WWII, or sporadic cases; and physicians should not exclude acute manifestations during combat and in returnees.

Sandfly-borne diseases

Phlebotomine sandflies inhabit diverse biotopes, ranging from desert areas of the Middle East to tropical rainforests of South America.

Most adult sandflies are crepuscular and nocturnal in their biting activity. They can transmit several sandfly fever group phleboviruses, *Leishmania* spp., and *Bartonella* spp.

Sandfly fever. The different species responsible for transmission of sandfly fever viruses have a focal, but wide, geographical distribution [59]. Foci are reported from southern Europe, the Middle East and Central Asia, where these species are endemic. In case groups of non-immune soldiers who have been engaged in endemic areas, high infection rates may occur. Owing to the short incubation period and attack rates ranging from 10% to over 50%, the impact of this virus on the fighting ability of military forces can be highly significant [60]. Thus, sandfly fever has long been a disease of considerable medical importance to military forces (e.g. to the British troops in India, Pakistan, and Palestine, and to Austrian soldiers in Yugoslavia in the nineteenth century). During WWII, sandfly fever was a major problem for forces in the Mediterranean basin, and 19 000 cases were reported among Allied forces [61]. Since then, only limited outbreaks have been reported, among Soviet troops in Afghanistan, as well as in Swedish United Nations troops and Greek troops in Cyprus [62–64]. Sandfly fever was considered to be a major threat during the acclimatization process in endemic areas prior to movement into the Gulf War zones. Curiously, with a single small outbreak, sandfly fever has not yet been reported as a problem in Iraq or Afghanistan, even though leishmaniasis, another sandfly-borne disease, is frequent and of great concern [65,66]. Despite the low frequency of occurrence, a recent seroepidemiological study in the native Afghan population, performed in the Kondoz area, revealed a seroprevalence rate of 9.2% against Naples sandfly fever virus, thus indicating that sandfly fever poses a continuous threat (Dobler *et al.*, IMED Congress, 2007, abstract 16.025).

Leishmaniasis. Leishmaniasis, a parasitic disease caused by infection due to protozoa of the genus *Leishmania*, is endemic in many tropical, subtropical and temperate regions of the world, frequently involving the areas of activity of Western armies. Cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis and visceral leishmaniasis (VL) have the potential to cause explosive outbreaks in non-immune communities exposeto the parasite within endemic areas. From 1942 to 1945, among the 1000 cases of CL recorded by the US Army in all theatres, 630 cases occurred within 3 months in a single outbreak in the Karun River Valley of Iraq [60]. Old World CL is endemic in many parts of the Middle East, as well as in Central and Southeast Asia, where it is caused by two species of *Leishmania*: *Leishmania major*, the causative agent of rural zoonotic CL, and *Leishmania tropica*, the causative agent of urban anthroponotic leishmaniasis. In this part of the world, Israeli, Russian and Fijian soldiers have experienced severe episodes of CL [67] (Modi *et al.*, 39th Annual

Meeting of the American Society of Tropical Medicine and Hygiene, 1990, abstract 387).

During the first Gulf War, among the 40 cases of leishmaniasis in US soldiers recorded from Iraq, 12 were VL due to an unexpected high frequency of *L. tropica* visceralization [68].

Viscerotropism had not been previously associated with this species [70]. From 2001 to 2006, the US armed forces experienced only four cases of VL (two from Afghanistan and two from Iraq) but, in the same period, 1283 cases of CL (of which at least 90% occurred after a tour of duty in Iraq) were recorded after an initial outbreak in 2003 near the Iranian border [69]. Estimates of up to 2500 cases of CL among US soldiers have been cited, i.e. an attack rate of 1% among US troops serving in Iraq during the period 2003–2004 [70]. Dutch, German and British forces engaged in the International Security Assistance Force in Afghanistan have also experienced zoonotic CL outbreaks exceeding 200 cases, but have rarely been affected by the outbreaks of anthroponotic leishmaniasis continuously occurring in urban areas of larger towns of the country and in refugee camps [71–73]. Also, 126 cases of VL were reported by US armed forces during WWII, mostly in the Indian, Chinese and Mediterranean theatres [4]. The last cases of VL reported by French forces occurred in Algeria at the end of the colonial period [74]. Unlike the experience of the Gulf Wars, Old World leishmaniasis has been encountered mostly by Western forces, and cases or outbreaks of New World mucocutaneous leishmaniasis have been regularly reported by European and US armed forces in training or in operations in Central and South America [68,75–78] (Grogi *et al.*, Annual Meeting of the American Society of Tropical Medicine and Hygiene, 1993, abstract 169).

Ticks and tick-borne diseases

Hard and soft ticks are ectoparasites that feed on every class of vertebrate blood host and occur almost worldwide [81]. They can transmit bacterial, viral and parasitic diseases. Soldiers on duty overseas or in training camps in their own country frequently enter multiple tick-infested ecological niches, and are therefore highly exposed to soft and hard tick bites. There is always a possibility of outbreaks of tick-borne disease among troops, sometimes threatening the health or the life of soldiers, and simultaneously threatening their mission. Serological studies of armed forces, and tick analyses conducted in training camps or overseas deployments, have underscored these risks. In 1997, 2–15% of the ticks removed from soldiers in US military camps in the USA were infected with *Ehrlichia* sp., and 11–21% were infected with *Borrelia burgdorferi* sensu lato [79]. Among a total of 6071 *Ixodes ricinus* ticks collected on Swiss Army training grounds in five regions of Switzerland, 26.54% harboured *B. burgdorferi* sensu lato, 1.18% harboured members of the *Ehrlichia phagocytophila* genogroup, and 0.32% harboured the European tick-borne encephalitis virus [80]. Antibodies against *B. burgdorferi* were investigated in Finnish Army recruits training during summer in an endemic region, and IgM antibody levels increased in 11.9% of study recruits [81].

In the summer of 2001, Astrakhan fever *Rickettsia* was detected in ticks collected in Kosovo from an asymptomatic French soldier of the United Nations troops [82]. Human babesiosis is not currently of military concern. However, Q-fever and tularemia are of great military concern. Q-fever is mainly transmitted in humans by inhalation of infectious aerosols, and tick-borne transmission is not considered to be important [83]. In the same way, the agents of tularemia in military duty areas such as Kosovo are mainly waterborne or rodent-borne, and are rarely mosquito-borne or hard tick-borne. Another problem is the potential use of *Francisella tularensis* as a biological weapon [84,85].

Lyme disease. Lyme disease, caused by members of the *B. burgdorferi* sensu lato complex, is mainly transmitted by hard ticks of the genus *Ixodes* [86,87]. This disease is recognized in many parts of the world, including large areas of North America, Europe, Asia, Australia, and focally in North Africa. Western armies on duty or in training are regularly confronted with Lyme disease. Serological studies, conducted among soldiers of different armies, have brought attention to the exposure of soldiers to *B. burgdorferi* [88,89]. At present, only sporadic cases have been recorded in armed forces, essentially in US forces in Europe, exceeding the case numbers recorded in training areas in the continental USA [81,90]. Lyme disease is of military concern because of its debilitating and potentially long-term effects on soldiers' health [91]. Doxcycline, employed as a chemoprophylactic regimen, has been proposed in high-endemicity areas to compensate for the shortcomings in PPMs against ticks, but its efficacy is not yet clear.

Tick-borne relapsing fevers. Soft tick-borne *Borrelia* spp. of the relapsing fever group are transmitted by argasid ticks of the genus *Ornithodorus*, and are responsible for tick-borne relapsing fevers in many parts of the world: America, Africa, Asia, and Europe [92]. Tick-borne relapsing fevers are of military concern for two reasons: the possible occurrence of outbreaks and the resulting impact on combat strength; and the potentially lethal pathogenicity associated with some *Borrelia* species, e.g. *Borrelia persica*. Western armies could currently be confronted with tick-borne relapsing fever while on duty in known endemic areas in the Middle East (Lebanon and Cyprus) and Central Asia (Afghanistan), or during training in Africa [92,93].

Tick-borne spotted fevers. More than a dozen types of tick-borne spotted fevers, caused by different species of *Rickettsia*, have been described throughout the world, ranging from benign to potentially fatal disease [94]. Rocky Mountain spotted fever, caused by *Rickettsia rickettsii*, is one of the most severe fevers and is endemic in North, Central and South America.

Rocky Mountain spotted fever, transmitted by *Dermacentor* spp. or *Amblyomma* spp. ticks, is a rickettsial disease with important consequences for the US military, given its prevalence in areas where military training takes place and its lethality (up to 30% in the pre-antibiotic era and 4% nowadays) [94]. During the spring of 1989, members of a military unit originating from a non-endemic area (Maryland, USA) participated in a 2-week-long training manoeuvre in the states of Arkansas and Virginia. A seroepidemiological investigation among unit members revealed that 15% and 2% of the soldiers had been infected by *R. rickettsii* and *Ehrlichia canis*, respectively [95]. Other potentially life-threatening tick-borne rickettsial diseases include Mediterranean spotted fever, transmitted by the brown dog tick, *Rhipicephalus sanguineus*, in southern Europe, northern Africa, and, less frequently, sub-Saharan Africa [96]. Severe forms have been reported in 6% of cases, with mortality rates as high as 2.5%. However, African tick bite fever (ATBF), caused by *Rickettsia africae* and transmitted by *Amblyomma* spp. bites, probably represents the main tick-borne rickettsiosis threatening soldiers in the field in sub-Saharan Africa. *Amblyomma* ticks are usually highly infected and actively attack people or animals that enter their biotope. Thus, cases of ATBF often occur in clusters among subjects entering the bush, e.g. tourists or soldiers [97,98]. US troops have already been involved in such outbreaks; among the 169 US Army soldiers deployed to a remote area of Botswana for 2 weeks in January 1992 for a field training exercise, more than 30% developed a febrile illness within 5 days of their return. This high attack rate, experienced after such a short exposure period, emphasizes the high infection pressure of *R. africae* in endemic areas [99]. Although severe clinical forms have been described, it is usually associated with mild disease only. ATBF infection and clinical manifestations have also been observed in tourists who used daily doses of 100 mg of doxycycline for malaria chemoprophylaxis, but no data concerning compliance with chemoprophylaxis were made available [97]. Many other rickettsiae, including emerging pathogens such as *Rickettsia slovaca* and *Rickettsia helvetica*, have been recently reported in Europe, and may be of concern for military forces [94]. Moreover, rickettsiae of unknown pathogenicity, e.g. *Rickettsia raoultii*, vectored by *Dermacentor reticulatus*, have already been found in ticks removed from soldiers [100]. The aetiology of the most important outbreak (more than 1000 cases recorded at Camp Bullis in Texas during WWII), assumed to have been, probably, tick-borne Bullis fever, is still unknown [101–104]. Tick-borne rickettsial diseases are always considered to be of special concern for armed forces.

Tick-borne ehrlichioses and anaplasmoses. Ehrlichia chaffeensis, *Ehrlichia ewingii* and *Anaplasma phagocytophilum* are emerging tick-borne pathogens [105]. The diseases usually present as flu-like illnesses, but cases range from asymptomatic infection (Europe) to severe illness, sometimes with fatal outcomes (North America). Ehrlichial diseases have been described in North America and in Europe, but cases have also been recorded in Asia, and infected ticks have been identified in Africa. Outbreaks have already occurred in military forces, and serological studies have demonstrated that they have been exposed to these pathogens. An outbreak of ehrlichiosis that occurred in members of an army reserve unit after field training in an area of New Jersey has been described by Petersen *et al.* [106]. A prospective, seroepidemiological study of spotted fever group rickettsiae and *Ehrlichia* infections was performed among 1194 US military personnel exposed in a heavily tick-infested area of Arkansas in 1990. Seroconversions to spotted fever group rickettsiae occurred in 30 persons (2.5%), whereas seroconversion to *Ehrlichia* species occurred in 15 (1.3%) [107]. Chemoprophylaxis with daily doses of 100 mg of doxycycline for *Ehrlichia* infections has successfully prevented infection and clinical manifestations in dogs, but no data are available for the use of doxycycline in human chemoprophylaxis [108].

Tick-borne viruses. Approximately 100 viruses have been isolated from ticks, among which only 20 are considered to be pathogenic for humans. Tick-borne viruses are responsible for three main syndromes, classified according to their clinical manifestations: tick fever, tick haemorrhagic fever [2], and tick encephalitis. As tick-borne encephalitis, both Central Europe encephalitis and Russian spring–summer encephalitis, is now easily preventable by vaccination, this disease is no longer a problem. Viral tick fevers usually occur as a mild disease, characterized by a biphasic fever with frontal headache, myalgia, nausea, vomiting, and sometimes a rash. The most famous types are the Colorado tick fever transmitted by *Dermacentor andersoni* in the USA, and the Kemerovo tick fever transmitted by *Ixodes persulcatus* in Siberia. Other tick-borne viral fevers have been described both in tropical and in temperate areas, and could affect tick-exposed soldiers (e.g. Dugbe virus fever in Central Africa, or Banjha virus fever in the former Yugoslavia) [109].

Three main tick-borne viruses, all classified at biosafety level 4, may cause severe haemorrhagic disease: Crimean–Congo haemorrhagic fever (CCHF) virus, Omsk haemorrhagic fever (OHF) virus, and Kyasanur Forest disease (KFD) virus. CCHF was first noted in 1944–1945 among Soviet military personnel assisting civilians in the war-ravaged Crimea. Since then, CCHF has been considered to be an important vector-borne disease of humans in southern Europe, Asia, Africa, and the Middle East. Most of the outbreaks reported since this first description were linked to environmental changes due to war or to new agricultural practices [110]. However, the most recent outbreaks were clearly associated with contact with contaminated meat or infected sheep and goats subsequent to an initial *Hyalomma* tick bite [111]. Nosocomial and household transmission of CCHF has been commonly reported, and this must be taken into account for military personnel as well as healthcare workers [112]. Recently, Western forces engaged in Kosovo were confronted with an outbreak within the local population that resulted in additional countermeasures by military units to prevent transmission. Additionally, field hospitals prepared for potential outbreaks among soldiers [113,114]. In 2008, a CCHF epidemic involving at least 23 cases occurred among the Afghan population near Herat, Afghanistan [115]. In September 2009, a US soldier contracted the disease while stationed near Kabul, Afghanistan, subsequent to reporting a tick bite, and died at Landtuhl hospital, Germany, days later [116]. In the Middle East, besides CCHF, the Alkhurma virus, a recently discovered tick-borne flavivirus (biosafety level 4) responsible for several cases of severe haemorrhagic fever in Saudi Arabia, may be of special concern for deployed Western forces [60,117]. OHF occurs primarily in western Siberia and KFD is limited to northern India. KFD and OHF, both occurring in sylvatic enzootic foci, were always acquired by people who had gone into forests.

Flea-borne diseases. Fleas exist worldwide, from sea level to high altitudes [118]. They can affect human health in several ways: as biting pests, burrowing 'jiggers', parasite intermediate hosts, and vectors of pathogens, e.g. bubonic plague [119] and murine typhus [120].

Plague has affected military campaigns from antiquity to WWII. Outbreaks occurred in several Mediterranean towns and ports during 1943 and 1944. Thousands of cases occurred in the local civil population during the Vietnam War; however, beause of sanitation measures, systematic chemoprophylaxis of contacts, and immunization, only a few cases in military populations were recorded [121,122]. Since WWII, plague has not affected military campaigns, but military campaigns may contribute to the spread of plague, owing to displacement of rats and their fleas. An epidemic of 1005 cases in and around Dakar, Senegal, in 1943–1945, was initiated by WWII ship transport activities, and small outbreaks also occurred in France and Italy in 1945 [121]. During the Vietnam War, there were only five cases recorded in vaccinated US troops, whereas thousands of cases occurred in the local population. Subsequently, the disease expanded into unaffected areas of the country [122]. Of the five US military cases, one occurred in a returnee, who did not transmit the disease to others [123]. Of great concern during the later stages of the conflict was the prevention of plague importation into the USA via retrograde cargo. Enzootic plague is primarily an infection of rodents in natural foci. International forces can always be exposed to well-known natural foci, e.g. the French forces or the United Nation Organization forces in the east of the Republic of Democratic Congo [124,125].

Murine or endemic typhus. Endemic typhus, caused by *Rickettsia typhi*, is a natural infection in rats and rodents and is transmitted among rats by the rat flea [120]. Occasionally, fleas can transmit this infection to humans. During WWII, there were 786 cases in the US Army, leading to 15 deaths, with the majority of cases being recorded in the continental USA [126]. During the Indochina War, 90 cases were recorded among French soldiers in the Saigon arsenal [14]. In the Vietnam War, only a few cases were reported but, on the basis of serological investigations, the Armed Forces Epidemiological Board determined that 15% of FUOs acquired during the Vietnam conflict could be attributed to murine typhus [35,36,127]. During the first Gulf War, murine typhus was considered to be a threat before deployment into the endemic area of Kuwait [60]. The incidence of murine typhus in armed forces is probably underestimated.

Mite-borne diseases

Scrub typhus.. Scrub typhus, caused by *Orientia tsutsugamushi*, is transmitted to humans by the bite of numerous species of larval trombiculid mites (*Leptotrombidium* spp.), popularly known as 'chiggers'. It is an acute febrile rural zoonosis that is endemic in the Asian Pacific region from Korea to Australia, and from Japan to India and Afghanistan [94]. During WWII, with the deployment of Allied and Japanese forces into endemic areas, scrub typhus attack rates were very high, sometimes causing more casualties than those related to battles (18 000 cases and 20 000 cases, respectively, occurred among Allied forces and Japanese forces). The lethality rates at that time ranged from 1% to 60% [126].

Outbreaks occurred when troops were in field conditions associated with bivouacs or the establishment of camps. At the end of the war, mite-control regimens consisting of impregnation of clothing with repellents (initially dimethyl phthalate, later benzyl benzoate) and the preparation of camp sites (oiling, cutting and burning of the vegetation over an area of 100 yards around buildings or tents) significantly reduced the incidence rates. During the Indochina War, 6536 cases of scrub typhus and 158 deaths were recorded in French forces but this incidence was probably underestimated [15].

After the implementation of the generalized use of chloramphenicol in 1951, no more deaths due to scrub typhus among French forces were recorded. Although scrub typhus caused no known deaths among American troops during the Vietnam conflict, studies on the aetiology of FUOs conducted throughout the war indicated that 20–30% of such FUOs were due to scrub typhus [35,36]. These results and the reports of outbreaks at the beginning of the conflict suggest that scrub typhus was seriously under-reported and had a mission-compromising influence in Vietnam [128]. US forces have successfully conducted studies on the use of chloramphenicol or doxycycline for scrub typhus prophylaxis [129,130]. Regimens based on daily doses of 100 mg of doxycycline for malaria chemoprophylaxis have failed to prevent infection and clinical manifestations [131]. Presently, scrub typhus chemoprophylaxis is not recommended, because of the increase in the number of resistant *O. tsutsugamishi* strains [132]. Now, sporadic cases or outbreaks are regularly reported among forces on duty or in training in endemic areas [133]. Both early and recent attempts to develop a vaccine have been unsuccessful [134]. Scrub typhus is an enduring threat to the battle-readiness of troops in endemic areas and, because of some strains' low susceptibility to antibiotics, a threat to soldiers' lives. As at the end of WWII, PPMs and campsite sanitation measures will continue to be the rampart against mite bites.

Tsetse flies and human African trypanosomiasis

The Glossinidae, or tsetse flies, are found only in sub-Saharan Africa. *Glossina* spp. are vectors of sleeping sickness, or human African trypanosomiasis. Human trypanosomiasis is endemic in West and Central Africa (*Trypanosoma brucei gambiense*), where it manifests as a chronic disease leading to death after some years; in East Africa, however, *T. brucei rhodesiense* causes an acute disease leading to death in a few months [135]. No direct impact on war has been reported concerning this human trypanosomiasis, but the impact of colonial conquest, of WWI and of the African civil war on the extension of sleeping sickness is well documented [136–138]. Nevertheless, Western forces deployed in endemic areas, e.g. the European forces in the Democratic Republic of Congo in 2003 and 2006, could be affected by the spread of this life-threatening disease.

Kissing bugs

Among the 118 existing species of kissing bugs, or Triatominae, half have been shown, naturally or experimentally, to be susceptible to infection with *Trypanosoma cruzi*, the causative agent of Chagas disease [139]. Chagas disease can be transmitted by the faeces of domestic or sylvatic members of the Triatominae during a blood meal or by ingestion of food contaminated with kissing bug faeces. Chagas disease has not yet had a significant impact on military operations; only sporadic cases have been recorded in US forces deployed in Central America, and one acute case has been reported in French forces stationed in French Guiana [137] (F. Pagès, personal communication). In the Amazon, foodborne Chagas outbreaks are not infrequent; and severe and acute manifestations are more frequent in cases resulting from oral contamination [140]. Western forces involved in training exercises in the Amazon jungle must protect their food from insects and wild fauna, must avoid cooking under lights that attract kissing bugs, and must sleep under insecticide-impregnated nets. Military physicians must be informed of this risk to prevent its occurrence in the field and to take it into account in the medical follow-up of returnees.

Vector Control in Armed Forces

The burden of vector-borne diseases on armed forces could be very significant, and all Western armies have developed vector-control strategies [141–143]. Medical intelligence allows for the assessment of risks before deployment and for the planning of preventive countermeasures. In the past few years, military operations in rural or urban areas have permitted the creation of entomological and epidemiological risk models and maps of military settlements or theatres using remotely sensed data [144,145].

Preventive countermeasures include PPMs and unit protection measures (UPMs). PPMs consist of proper use of uniforms, the application of repellent to exposed skin, the application of permethrin to battledress uniforms, and the use of insecticide-impregnated bed-nets, curtains, tents, and window screens. UPMs include base camp selection, environmental management, larviciding, space spraying, aerial spraying, and indoor residual spraying. In a combat environment, PPMs are often the last line of protection for soldiers. For UPMs to be effective, there must be good knowledge of the entomological situation and the availability of certified persons to implement the chosen vector-control methods. Many of the tools currently used around the world in vector control and in personal protection derive from military research. Most modern dusting devices and repellents were developed by US forces. During WWII, aerosol bombs were perfected, research in repellents was conducted, and three repellents, dimethyl phthalate, Rutgers 612 (2-ethylhexane-1,3-diole), and indalone, were recommended to the US Army; moreover, DDT was developed, and the army, navy and air force developed and deployed aerosol spray systems [146]. Permethrin-impregnated battledress uniforms have proved their efficacy against arthropod bites in many studies of the field [147–151]. Since their first use in 2001, factory-based impregnated battledress uniforms have been developed by German and French forces for the protection of their soldiers. Synergistically combined with DEET skin repellent use, this PPM proved highly efficious during recent deployments [152,153]. Most of these recently developed measures are now currently used to effectively protect refugees and displaced populations who are threatened by vector-borne, especially louse-borne, diseases. Other protective measures, which include impregnated tents, curtains, and plastic sheeting, are, or will be, adapted for wider military use [154,155].

Entomological Studies in Armed Forces

To design an effective vector-control strategy, it is necessary to be highly knowledgeable about the entomological situation within deployment areas. Entomological studies are common tools in the assessment of health hazards before and during deployment for most Western armies [28,42,65,75,156,157]. For example, concerning malaria transmission, such studies provide information on the risk level according to the location of troops and on the insecticide susceptibility of vectors in the field. A recent study in the Côte d'Ivoire showed that the risk of malaria for soldiers in rural areas was very high (without protection, the number of infected bites for a soldier ranged from 30 to more than 300 during a 4-month tour of duty) and indirectly demonstrated the efficiency of the malaria-control schedule of the French forces [158]. Military research strategies are not only of special interest for the military community; study data may result in the transfer of important public health information concerning the epidemiology of vector-borne disease and trends for the local population, e.g. the first report of malaria transmission in downtown Dakar, the first identification of the *Kdr* mutation in *Anopheles gambiae* molecular form M, and the epidemiology of leishmaniasis and malaria in Afghanistan [159–162].

War, Vector-Borne Disease, and Civilian Populations

As vector-borne diseases have an impact on war, wars also have an impact on the development of vector-borne disease [163]. Infected or infested soldiers, returnees, migrants and refugees act as reservoirs and carriers of pathogens in areas where they were previously not present [164]. If competent vector populations exist in these areas, large-scale epidemics can occur in non-immune local populations, and vector-borne disease could become endemic. In the last century, WWI-related movements in Central Africa initiated the devastating spread of sleeping sickness in the 1920s, civil war in the Sudan led to visceral leishmaniasis and sleeping sickness outbreaks, the installation of Afghan refugees in Pakistan was followed by an increase in the global burden of malaria, and the influx of Somali refugees into Oman led to a malaria outbreak in a formerly malaria-free region [165–171]. At the same time, refugees and displaced people are often more vulnerable to vector-borne disease because of their poverty, their lack of immunity to the endemic diseases of their new location, the difficulty in gaining access to drugs, their poor nutritional status, their living conditions, and, sometimes, their installation into natural foci of zoonotic disease [172–174]. They are exposed to many arthropod-borne diseases, such as malaria, typhus, murine typhus, louse-borne typhus, plague, leishmaniasis, lymphatic filariasis, and sleeping sickness [122,175–180]. The destruction of vital infrastructure, including the health system, is another factor in the emergence or extension of vector-borne disease in a given region [181–183]. The return of refugees to their own land is another factor in the spread of vector-borne disease. For example, in Cameroon in 1916, refugees returning from Equatorial Guinea came back with sleeping sickness, and in Afghanistan, malaria is now present in new areas [138,159]. Clearly, the toll of wars should include both human lives lost in direct conflict and indirect deaths due to the loss of services and/or insufficient infrastructure [184,185].

Conclusions

Vector-borne disease and war are long-standing companions. Owing to commercially available immunization programmes, some diseases no longer pose a danger to military personnel and military operations (e.g. yellow fever and Japanese encephalitis), but others, old re-emerging diseases and newly emerging diseases, are still of concern in the absence of specific and efficient prophylaxis. Scientific progress has brought about a reduction in the impact of arthropod-borne diseases on military forces, but the threat is always present, and shortcomings in vector control or in the application of PPMs could cause these diseases to have the same impact as they did in the past.

Transparency Declaration

The authors declare that they have no competing interests.

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