

# Contribution of the French army health service in support of expertise and research in infectiology in Africa

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## Abstract

Historically, infectious diseases have caused more casualties than battle. The French military health service therefore developed a range of research on vector-borne diseases such as malaria and arboviruses, antibiotic resistance, infectious agents that can be used as biological weapons and vaccines. The main objective is to control naturally acquired or provoked infectious diseases and limit their impact on armed forces as well as on civilian populations in France or abroad, particularly in Africa and anywhere French armies may be deployed. The expertise of the military health service teams in manipulating agents requiring high level of biosafety precautions and in organizing and providing medical care in unnatural conditions, including the battlefield, associated with complementarity staff experience (physicians, biologists, epidemiologists, researchers, pharmacists, logisticians), has been used in the management of the Ebola outbreak in Guinea.

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## Introduction

Infectious diseases historically cause more casualties than fighting. As an example of the potential burden of infectious diseases during military expeditions, in 1894–1895 in Madagascar, about a third of 15 000 French soldiers died, mainly of malaria, dysentery and typhoid fever; only 25 of them died from enemy fire. The infectious threat still remains high, is responsible for loss of duty days and deaths, may greatly affect the military operational capacity and justifies medical measures for prevention, diagnosis, treatment and evacuation that have a

significant logistics burden. In a recent multicentre prospective survey in military primary care units deployed abroad in operation, infectious diseases represented 41% of all health problems for which soldiers consulted general practitioners, while combat-related injuries only represented 0.65% of them [1]. In response to this threat, the French military health service is developing a range of research. Their objective is to control naturally acquired or provoked infectious diseases and limit their impact on armed forces as well as on civilian populations in France or abroad, particularly in Africa and anywhere French armies may be deployed.

## Recent achievements in vector-borne diseases

Vector-borne diseases constitute a major threat to the operational capacity of armed forces personnel operating outside or stationed overseas. In past years, the military health service participated in monitoring the entomologic status of French

military bases in sub-Saharan Africa (Gabon, Ivory Coast, Republic of Central Africa, Senegal, Djibouti) and focused on French Guiana [2–8]. This surveillance included the identification of vectors, the study of behaviour and the evaluation of insecticide resistance and enabled the development or improvement of new tools for vector trapping [9,10], vector identification such as molecular and proteomic methods [11,12], pathogen identification in vectors [13,14] or identification of markers of resistance to insecticides [2,3]. New tools to map vector distribution by using remote sensing or meteorologic data have also been developed [15,16].

Among infectious diseases, malaria remains the first cause of aeromedical evacuation of French soldiers and the first cause of death by infection. The parasitology unit of the military health service, involved also as laboratories associated with the French reference centre for malaria, conducts epidemiologic, biological and clinical studies on imported malaria cases and in malaria-endemic areas where French soldiers are staying or may stay in future, particularly in Africa and French Guiana. Its research on the *in vitro* susceptibility of *Plasmodium falciparum* (ex vivo and molecular markers) and on clinical efficacy in patients have led to the adaptation of chemoprophylaxis and malaria treatment for the French armed forces and civilian travelers [17–21]. Additionally, a traveler database can be used as a surveillance system to assess and monitor the emergence of drug resistance in endemic African areas where information is limited [22]. The resistance of malaria to most antimalarial drugs has developed in Southeast Asia and has spread to Africa. The parasitology unit has identified new molecular markers of resistance to doxycycline (*pfmt* and *pftetQ*) [23] and participates in identification, development and/or validation of resistance markers to quinine, quinolones and artemisinin [24–27]. It also participates in the identification of new antimalarial drugs by *in vitro* screening in collaboration with several international departments of medical chemistry and international pharmaceutical laboratories. The development of these antimalarial drugs is based on evaluation of *in vitro* activity against *P. falciparum* clones, evaluation of ex vivo activity against field isolates from several areas, evaluation of *in vivo* activity in experimental models and identification of the mode of action and potential resistance mechanisms [28–30].

Arboviroses are other major threats for soldiers. A team of the military health service coordinates the French reference centre for arboviruses. It conducts a large number of studies in collaboration with clinicians, entomologists and epidemiologists [31–35]. For example, it detected for the first time the emergence of chikungunya in the Americas at the end of 2013 with the Asian lineage, enabling public health authorities at the international level to be alerted [36]. As early as 2013, with the emergence of Zika virus in French Polynesia, it was also involved in the development of fundamental data for public

health on genomic, clinical and transmission aspects of Zika virus infection [37–41]. French military physicians have also conducted retrospective and prospective studies on continuous rheumatic or musculoskeletal pains that persist after chikungunya infection. They allowed a better understanding of their clinical evolution, their prognostic factors and their pathophysiologic basis. Their results enabled the design of a diagnostic and therapeutic algorithm to help physicians deal with chronically infected patients and to limit both functional and economic impacts, which is useful both for militaries and civilians [42].

In order to better characterize the risk of naturally acquired infections, epidemiologic studies are conducted in French armies and their neighbourhood. For example, investigations have been conducted after the occurrence of malaria outbreaks among French forces involved in missions to control illegal gold mining in French Guiana [7]. The epidemiologic and entomologic studies conducted in these remote and dangerous areas have demonstrated that illegal gold mining sites must be considered to be high-level malaria transmission areas. This challenges the present organization and the effectiveness of the malaria control programme in French Guiana and in neighbouring countries because of the huge mobility of the gold miners [43,44].

## Recent achievements in vaccinology

With more than 500 000 injections per year, armies are the main vaccination operator in France. Their health service is conducting numerous studies as well as extensive research and development in order to improve the immune protection of soldiers and the quality of the vaccination process. Because data arising from the surveillance of pertussis in the French armed forces had shown a shift of pertussis to young adults, and because military personnel are highly exposed because of their collective lifestyle, the military vaccination schedule has been adapted to more appropriately prevent this infectious disease. A subsequent study has demonstrated the effectiveness of the new vaccination practice [45]. New electronic communication technologies have a disruptive potential in public health, including against infectious diseases and in the vaccination process. With the help of collaborators, a military medical doctor has developed MesVaccins.net, a new immunization information system approved by the World Health Organization [46]. It will be part of the information system of the French military health service. It aims at creating an immunization registry, at collecting factual data in real time, at aiding decisions of health professionals, at focusing on the patient's active role and responsibility and at fighting vaccine hesitancy through

holistic approach to personalizing and synchronizing health information.

### Recent achievements in antibiotic resistance

In the face of rising antibiotic resistance, a team of the French military health service coordinates a multicentre European phase 1/2 clinical trial known as PhagoBurn, which is the first large-scale test of phages under modern regulatory standards [47]. Phages are bacteria-killing viruses discovered a century ago which are possible alternatives to conventional antibiotic treatments for drug-resistant bacterial infections. This project, funded by the European Commission under the 7th Framework Program for Research and Development, aims at evaluating phage therapy for the treatment of burn wounds that are infected with bacteria. Despite many obstacles, the study has attempted to demonstrate the safety and efficacy of phages and to provide a basis for the optimization of current regulatory guidelines in phage therapy.

### Recent achievements in infectious agents that can be used as weapons

Biological toxins or infectious agents such as bacteria, viruses and fungi can be used with the intent to kill or incapacitate humans as an act of war. The military health service is conducting research aimed at preventing or controlling diseases that could be provoked by such weapons. For example, it has developed monoclonal antibodies against some toxins and has conducted research on some bacteria, like *Burkholderia pseudomallei* and *Bacillus anthracis*, which cause melioidosis [48] and anthrax, respectively. Some of this research work explores the pathophysiology of the disease [49–51] and the potential ways for improving its prevention or treatment [52,53]. Research is also being conducted on poxvirus for improving or developing new vaccines against smallpox [54–56] and on viruses that cause haemorrhagic fever, particularly for the development of treatments [57].

### Conclusions

The expertise of military health service teams in manipulating agents requiring high levels of biosafety precautions and in organizing and providing medical cares in constrained conditions, including the battlefield, associated with complementarity experience of staff (physicians, biologists, epidemiologists,

researchers, pharmacists, logisticians), has been used for the deployment in Guinea of a new type of hospital for treating caregivers infected by Ebola virus, a caregiver treatment centre. Within a few weeks, the structure, organization, training and several technical innovations were developed by the military team and made possible the provision of intensive medical care to highly contagious patients in single-patient rooms despite the context of an epidemic in a low-income country. All patients were monitored by continuous video surveillance and through the use of radios. A specific protocol was developed to standardize Ebola virus disease therapy, with particular emphasis on rehydration, including by central venous catheter. Supportive critical care interventions were delivered according to the medical team's collective clinical judgement, available resources and workload. The objective was to maximize the utility of the interventions while not putting the healthcare workers at increased risk. Laboratory facilities enabled the diagnosis of Ebola virus infection and the measurement of a panel of biological and biochemical parameters [58]. The caregiver treatment centre offered conditions for the care and study of Ebola virus-infected patients never previously available in developing countries or in an epidemic context. That has allowed a number of clinical, pathophysiologic, therapeutic, diagnostic and epidemiologic studies to provide original and valuable results [59–62].

This experience of the French military health service in building from nothing the capacity of diagnosing, isolating and treating patients with highly contagious diseases in conditions preserving the security of the caregivers and allowing a high quality of care may also be valuable in developed countries. For example, under the exceptional conditions of an epidemic of a severe, highly contagious airborne infectious disease, specially equipped transportable structures might be useful for permanent hospitals that are overwhelmed or that appear to be inappropriate for the management of such patients.

### Conflict of interest

None declared.

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