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Review

# Viral bioterrorism: Learning the lesson of Ebola virus in West Africa 2013–2015

Orlando Cenciarelli[a,b,*,1], Valentina Gabbarini[c,1], Stefano Pietropaoli[d], Andrea Malizia[a,b], Annalaura Tamburrini[c], Gian Marco Ludovici[c], Mariachiara Carestia[a,b], Daniele Di Giovanni[a,b], Alessandro Sassolini[b], Leonardo Palombi[b,e], Carlo Bellecci[a,b], Pasquale Gaudio[a,b]

[a] Department of Industrial Engineering, University of Rome Tor Vergata, Rome, Italy
[b] Didactical Board of the International Master Courses in Protection Against CBRNe events, Department of Industrial Engineering and School of Medicine and Surgery, University of Rome Tor Vergata, Rome, Italy
[c] International Master Courses in Protection Against CBRNe events, Department of Industrial Engineering and School of Medicine and Surgery, University of Rome Tor Vergata, Rome, Italy
[d] Department of Science, University of Roma 3, Rome, Italy
[e] Department of Biomedicine & Prevention, School of Medicine and Surgery, University of Rome Tor Vergata, Rome, Italy

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ABSTRACT

Among the potential biological agents suitable as a weapon, Ebola virus represents a major concern. Classified by the CDC as a category A biological agent, Ebola virus causes severe hemorrhagic fever, characterized by high case-fatality rate; to date, no vaccine or approved therapy is available. The EVD epidemic, which broke out in West Africa since the late 2013, has got the issue of the possible use of Ebola virus as biological warfare agent (BWA) to come to the fore once again. In fact, due to its high case-fatality rate, population currently associates this pathogen to a real and tangible threat. Therefore, its use as biological agent by terrorist groups with offensive purpose could have serious repercussions from a psychosocial point of view as well as on closely sanitary level. In this paper, after an initial study of the main characteristics of Ebola virus, its potential as a BWA was evaluated. Furthermore, given the spread of the epidemic in West Africa in 2014 and 2015, the potential dissemination of the virus from an urban setting was evaluated. Finally, it was considered the actual possibility to use this agent as BWA in different scenarios, and the potential effects on one or more nation's stability.



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* Corresponding author at: Department of Industrial Engineering, University of Rome "Tor Vergata", Via del Politecnico 1, 00173 Rome, Italy.
*E-mail address:* orlando.cenciarelli@uniroma2.it (O. Cenciarelli).
[1] These authors contributed equally to the manuscript.

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## 1. Introduction

### 1.1. Bioterrorism

Bioterrorism is a criminal act that provides the deliberate use of biological agents such as viruses, bacteria or toxins as harmful means, causing diseases or death in humans, animals or plants (Centers for Disease Control and Prevention (CDC), 2015a). Biological agents can be spread through air, water or food and they could be modified to improve their capability to cause disease and to make them resistant to drugs. Depending on the severity of disease that they cause and on their ability to spread, biowarfare agents (BWA) are classified by the Centre for Disease Control and Prevention (CDC) into three categories: A–C (Centers for Disease Control and Prevention (CDC), 2015a). Category A pathogens would produce the greatest risk during a bioterrorism attack (Bray, 2005a) because they can be easily spread and transmitted from person to person; their release might cause public panic and require special actions for public health (Centers for Disease Control and Prevention (CDC), 2015a). *Bacillus anthracis, Brucella spp., Clostridium botulinum, Yersinia pestis, Francisella tularensis*, Variola virus and Ebola virus are the most likely biological agents to be used with bioterrorism aims. The phenomenon of bioterrorism represents a growing major threat of modern civilization, although examples of the use of biological agents as weapons date back thousands of years ago (Cenciarelli et al., 2013). In fact, if on one hand scientific and technological progress in molecular biology and genetic engineering fields has brought important benefits for mankind, on the other hand new knowledge could be exploited with terrorist purposes, determining serious repercussions on international communities (Bray, 2005b; Van Aken and Hammond, 2003). In recent times, the use of biological agents by terrorist organizations has become a worrying reality. Therefore, an assessment of the risks associated with the use of pathogenic microorganisms is required in order to develop countermeasures to limit unexpected scenarios, characterized by mass destruction, and to assure a ready response to them (Cenciarelli et al., 2013; Bray, 2003).

Biological warfare and bioterrorism are very complex issues because many agents can be used and widespread, affecting environment and people. Two are the main factors in a biological event: one or more pathogens implied during the attack and the vehicle for their dissemination. Immediate diagnosis is very difficult due to the high spread ability, lethality, invisibility and difficulty in short-term detection (Cenciarelli et al., 2013). This is why the most effective resources to avoid critical bioterrorist episodes are prevention and collaboration. Both health intelligence and specialized medical units should cooperate to ensure rapid and effective response (Morse, 2007).

A bioterrorist attack requires a large amount of biological agent to cause diseases in a target population (Cenciarelli et al., 2013). To be an effective weapon, a microorganism must first be highly pathogenic to humans. In addition, it should have a number of features including the ability to cause serious and predictable diseases in a short time and to resist outside the host organism for a sufficient period to infect a victim (Utgoff, 1993). Moreover, it should be easy to disseminate and difficult to detect through currently available techniques (Carus, 1991).

The potential use of bioweapons represents a great concern, due to the serious impact that may cause and the lack of effective tools for detection and identification of the biological agent used (Cenciarelli et al., 2013; Carestia et al., 2014; Cenciarelli et al., 2014a). Bioterrorism detection represents a major issue: a possible bioterrorist attack may be announced or unannounced. In the first case primary health care providers and law enforcement agencies should be on alert, preparing isolation facilities and improving rapid response to contain the infection and take care of the victims; but if a bioterrorist attack occurs without any announcement, depending on the incubation period, the infectivity and the lethality of the biowarfare agent utilized, unusual diseases and death could spread in the community before anyone can really understand the situation (Üstun and Özgurler, 2005). Part of government policy in biological warfare and in terrorist groups is the manipulation and release of pathogens (Jansen et al., 2014). The real threat of a large-scale bioterrorist attack makes the defense against bioweapons a priority in terms of security.

### 1.2. Ebola virus

Ebola virus is the etiological agent of a hemorrhagic fever (EHF) in humans and non-human primates (monkeys, gorillas and chimpanzees) and in other wild animals; EHF is endemic in central Africa regions. Ebola virus, together with Marburg virus, is a *Filovirus* belonging to the family of *Filoviridae,* order of *Mononegavirales* (Feldmann and Geisbert, 2011). Ebola virus was first recognized in 1976, when in the Northern Zaire (actual Democratic Republic of Congo) and in the Southern Sudan EHF appeared. Five species of Ebola virus have been identified: Ebola virus (EBOV) and Sudan virus (SUDV), discovered in 1976; Reston virus (RESTV), discovered in 1989; Taï Forest virus (TAFV), discovered in 1994 and Bundibugyo virus (BDBV), discovered in 2007 (Bukreyev et al., 2014). All species of Ebola viruses are harmful to humans with the exception of Reston species: it originated in the Philippines and it does not cause disease in humans; however it can be fatal to monkeys and some evidences suggest also a pig-to-human transmission through contact, with the opportunity to become more communicable, by mutating in susceptible people (i.e. immune-compromised) (Morris, 2009). Filovirus viral particles are pleomorphic, thus they can take different shapes: long, branched, circular, as well as filaments shaped like “6” or “U” (Centers for Disease Control and Prevention (CDC), 2015b). Viral particles show a common diameter of 80 nm, while their length is variable, reaching 14 μm. Viruses are enveloped by a lipid membrane that encloses the ribonucleoprotein complex, including four of the seven structural proteins (NP, VP30, VP35, L protein) and viral genome, which is composed by a non-segmented, negative-stranded RNA, approximately 19 Kb long. It consists of seven genes linearly arranged (Feldmann and Klenk, 1996) encoding 11 proteins. VP40 in association with VP24 serves as the matrix protein and mediates particle formation. GP (glycoprotein) is the only transmembrane surface protein of the virus; it is important to mediate binding to cellular receptors, such as β1-integrins, and subsequent fusion with cellular membranes and it is the major viral antigen (Feldmann and Geisbert, 2011). Moreover, four soluble glycoproteins are produced during the infection by Ebola virus: sGP, delta peptide (Δ-peptide), $GP_1$, and $GP_{1,2\Delta}$. These proteins seem to be involved in viral pathogenesis, mainly during the target cell activation phases (Wahl-Jensen et al., 2005).

Viruses survival is closely related to the presence of a specific host (the natural virus reservoir) that allows viral replication