Chapter

Introductory Chapter: Emerging Challenges in Filovirus Control

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1. Introduction

Infectious diseases in history have made a significant contribution to morbidity and mortality as well as disability worldwide. Nearly a quarter of the estimated 60 million reported deaths in the world each year are related to infectious diseases [1]. The influenza outbreak of 1918–1919 was the worst such incident in living memory during which nearly 40 million people died worldwide. The unprecedented *Black Death* plague outbreak in the mid 1300 equally killed millions of people. Filoviruses as emerging infections appear to be on the same path, with an ever-increasing significant global impact on public health, human traffic and commerce. The recent West African Ebola outbreak which affected 10 countries in West Africa, Europe and the USA has demonstrated its capacity to be a global threat with profound psychological, emotional and mental repercussions. Its highly virulent nature over the years and the recent West African Ebola outbreak generated considerable panic and unprecedented global public health emergency [2]. Filoviruses are comprised of the Marburg and Ebola viruses. Since the discovery of the Marburg virus disease in the 1967, and the Ebola virus disease in 1976, over 50 filovirus disease outbreaks due to *Marburgvirus and Ebolavirus* have occurred. Some 37 Ebola virus disease and 14 Marburg virus disease outbreaks occurred mostly in Africa. The recent 2013–2016 outbreak in West Africa was so far the largest and most devastating. At the end of the epidemic, about 28,000 cases and 11,000 deaths were recorded. The case fatality for both viruses is very high (34–90%). There is yet no known cure. Since July 2018, the second largest EBOV outbreak is devastating Eastern Democratic Republic of the Congo with over 1600 cases and 1000 deaths reported by October 2019 [3]. New data from the West African epidemic suggests an expansion of our understanding on ecology and geographical scope of these viruses. The pattern of occurrence and its negative impact on the economy, society and development is emerging.

2. Perspectives on ecology and transmission

Understanding the ecology and virology of filoviruses helps in designing strategies for prevention and control. Filoviruses are non-segmented negative-stranded RNA viruses. They belong to the family *Filoviridae* in the order *Mononegavirales.* There are five genera in the filovirus family: the *Marburgvirus*, *Ebolavirus*, *Cuevavirus*, *Striavirus*, and *Thamnovirus.* The Marburg virus and the Ebola virus are the most virulent to humans, while TAFV cause very limited disease and RESTV only asymptomatic infections. The *Ebolavirus* has five species known to cause disease in humans: *Zaire ebolavirus* (EBOV), *Sudan ebolavirus* (SUDV), *Tai Forest ebolavirus* (TAFV), *Reston ebolavirus* (RESTV), and the *Bundibugyo ebolavirus* (BDBV). In addition the *Bombali ebolavirus* was recently discovered in fruit bats in

Sierra Leone and Kenya. Also a new distinct filovirus, the *Dianlovirus* genus, has been proposed following the recent discovery of the *Měnglà virus* (MLAV) in fruit bats in China [4], demonstrating further the expanding geographical scope of the Ebola virus ecology. It is yet to be fully determined whether the impact of population pressures such as deforestation and forest encroachment or subsequent climate change has also leveraged the ecosystems for transmission.

The origin of the infection and its life cycle is partly elusive. It is generally accepted that the infection is a zoonosis linked to wildlife reservoirs principally fruit bats and non-human primates. Studies indicate that such bats may be the ultimate reservoirs of this infection. Epizootics in wildlife have also been reported prior to outbreaks. It is also suggested that in endemic countries, non-human primates and other animals including pigs, dogs, duikers and even arthropods may be involved in the cycle linking wildlife infection to humans [5]. Direct contact during hunting and eating bush meat facilitates rapid spread. At community level, funeral ceremonies of the victims amplify further transmission. In reported outbreaks of Marburg virus infection in Kenya, Angola, the Congo Republic and the DRC, Uganda has demonstrated cave-dwelling fruit bats as the source of infection. Serological ecological studies also have showed sero-positivity in asymptomatic individuals in selected communities in the DRC. Among the pigmy population nearest to the forest, the sero-positivity for EBOV is high and nearly 10-fold. Sexual transmission of Ebola infection among survivors raises concerns. Questions remain on the role linking these observations particularly the role of asymptomatic individuals in the community outbreak initiation.

3. Challenges on case detection

The clinical features of Ebola virus disease and Marburg virus disease have been consistent and the basis for the case definition in the detection of cases and contact tracing. The clinical features are typically high-grade fever associated with severe bleeding tendencies and followed by a rapid descent to multiple organ failure, shock and death within days. However these symptoms are nonspecific and mimic several many tropical conditions such as malaria which is so endemic and responsible for up to a quarter of the patient load in typical low-resource settings. This may undermine the timely detection of cases in outbreak management and affect the implementation of contact tracing using the WHO syndrome based on the case definition and criteria. The WHO has outlined the case definition criteria of an *alert* case, a *suspected* case, a *probable* case and a *confirmed* case. The first three are based on clinical symptom assessment, and only the confirmed case depends on laboratory confirmation with RT-PCR or IgG antibody and virus antigen for Ebola virus and Marburg virus. However, the specificity and the positive predictive values in reported laboratory tests have not been accurately determined. The challenge in making a diagnosis is that the positive predictive value of the criteria may differ from outbreak to outbreak. Studies are therefore needed for concurrent validation of the case definition at localised field conditions and identification of cross-reactions in asymptomatic individuals. Concurrent validation studies should be carried out during outbreak management and containment. Therefore the search for new and accurate diagnostic methods needs to be addressed.

The factors behind the emergence of new pathogens are complex but are facilitated partly by the enabling interaction between the host and the agent in the supported by conducive environmental factors. Apparently for emerging infections, pathogens evolve and create new phenotypic properties that adapt infectious agents to new or old hosts. The genetic variation may lead to increased virulence

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and infectivity. Understanding these factors including the immunology and the interactions between the filovirus and the host immune system is critical. Such knowledge will support the development of better diagnostics and tools. These tools will facilitate surveillance and outbreak management. It will provide evidence for the development of effective drugs and vaccines against the infection.

This book reviews and discusses known filovirus outbreak experiences. In particular, it examines opportunities and the missing links in the ecology, the natural history, immunology and the interactions with the host innate immune systems and other infections. It examines the potential benefits that would shape future research priorities. Such efforts could lead to quality and timely outbreak detection. Early detection and early action appear to be best approach, but such strategies should use evidence for prevention and control.

4. Conclusion

The epidemiology and the ecology together with the life cycle remain elusive. Studies are required to improve early detection to facilitate quick action. The unpredictability of the outbreaks suggests that basic epidemiological research for prevention and control should be carried out before, during and after outbreaks. Understanding the gaps in the ecology and the natural cycles of the filoviruses as well as its reservoirs will lead to the development of better strategies for prevention, control and management of future outbreaks. Campaigns directed at communities and tourists would be of benefit. Studies are needed to improve future forecasting of outbreaks. The impact of these viruses on the economy and society in general is an important area for future research. There is therefore a need for a strong global strategy that ensures international and interagency collaboration. International efforts are required to coordinate research to develop preventive strategies and tools. Support is required to support national efforts to build health systems for surveillance and emergency disease preparedness. A Global Health framework for coordination and financing of research into emerging infections will support and facilitate containment at national and global levels. The chapters in this book have tried to discuss some of these challenges and made suggestions for future research.

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