Ebola virus disease – a global threat

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Editor-in-Chief

Ebola and Marburg viruses belong to the same family –*Filoviridae*– and both have filamentous structures. Ebola virus has a single-stranded nonsegmented RNA, sharing certain similarities with rhabdoviruses as well as paramyxoviruses regarding genome organization and replication mechanisms.

The *Ebolavirus* genus is made up of five species: Zaire, Sudan, Ivory Coast, Bundibugyo and Reston. Of these, Reston species appear to be non-pathogenic in humans.

The reservoir for Ebola virus is represented by fruit bats, which display long-term chronic infection with no clinical impact.

From here, the virus can pass to different primate species (gorilla, chimpanzee and macaques). From bats or apes the virus reaches humans, who develop viral hemorrhagic fever after a variable incubation period of 2 to 21 days. At this point, person-to-person transmission may occur.

As soon as the virus reaches the human body, it establishes a specific strategy, by eliminating the cells it has no use for –lymphocytes– through so-called "bystander" apoptosis, sustaining the useful cells –monocyte/macrophages, dendritic cells and endothelial cells– and activating the tissue factor.

Both Ebola and Marburg viruses use multiple entry mechanisms via receptors such as: hepatocyte receptor asialoglycoprotein, folate receptor α, dendritic-cell-specific intercellular adhesion molecule-3-grabbing nonintegrin (DC-SIGN), DC-SIGN-related factors, β1 integrin receptors and human macrophage galactose- and N-acetylgalactosamine-specific C type lectin.

As a result of viral impact on the human body, after the incubation period, the clinical onset is abrupt, with fever, chills, extreme malaise, myalgia of the trunk and lower back, headache, followed after 48-72 hours by the hemorrhagic syndrome. Fever may be accompanied by relative bradycardia.

Laboratory tests reveal leukopenia with lymphopenia and relative neutrophilia with immature forms, as well as thrombocytopenia, all due to the pathologic mechanisms used by Ebola virus. Cytolysis, renal impairment and coagulation abnormalities can also be identified. For etiological diagnosis a PCR test can be performed.

If so far no specific therapy has been available, the European Medicines Agency has recently presented the research status for Ebola therapeutic candidates evaluated in preclinical/clinical studies. These include monoclonal antibodies, RNA-polymerase inhibitors, small interfering RNAs targeting RNA-polymerase, inhibitors of viral mRNA translation, or hyper-immune horse serum.

Ebola vaccines are also well underway in preclinical research, through non-replicating viral vectors platforms (chimpanzee adenovirus Ad3), viral-vectored vaccines (vesicular stomatitis virus, or modified vaccinia Ankara), recombinant adenovirus vector platform (Ad 26 & Ad 35), or adjuvanted virus-like particles.

As the West-African Ebola outbreak continues, access to high-quality up-to-date information remains essential, and a thorough knowledge of the viral mechanisms of action during human infection can identify potential therapeutic targets to be studied in preclinical and clinical trials.

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