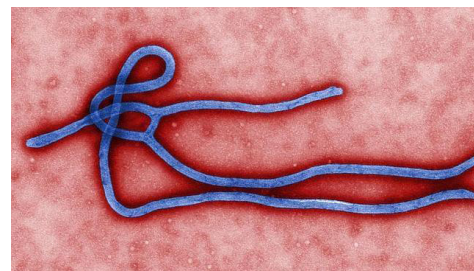




ÉBOLA, LO QUE DEBEMOS SABER

EBOLA VIRUS DISEASE: WHAT WE MUST KNOW



La entidad conocida como ébola, recibe esa denominación por el nombre del río más cercano al distrito africano, donde se presentaron los primeros casos del brote en la década de los setenta del siglo XX (1). Esta zoonosis que está afectando a África y actualmente extendiéndose a otros continentes, llama la atención de las autoridades sanitarias a nivel mundial. Los virus pertenecen a la familia *Filoviridae*, género *Ebolavirus* (EBOV) y están divididos en las especies *Bundibugyo ebolavirus*, *Reston ebolavirus*, *Sudan ebolavirus*, *Tai Forest ebolavirus* y *Zaire ebolavirus* (2).

El origen de la entidad es desconocido, el primer brote de EBOV se reportó en Sudán en 1976 y tres semanas más tarde en Zaire, hoy República Democrática del Congo [RDC] (3). Luego la frecuencia de casos disminuyó, reportándose pequeños brotes, hasta que en 1994 el virus inició recorrido en dirección oriental, con incremento progresivo de casos desde Gabón hacia RDC y Uganda (4-6). Actualmente existe un nuevo brote que no ha podido ser contenido. Para el 4 de septiembre del año en curso, se habían reportado 3707 casos, incluyendo 1848 muertes (7), distribuidas entre Guinea (771 casos y 494 muertes), Liberia (1698 casos y 871 muertes), Sierra Leona (1216 casos y 476 muertes), Nigeria (21 casos y 7 muertes) y Senegal (1 caso). Sumado a lo anterior el pasado 26 de agosto el Ministerio de Salud de la RDC notificó a la OMS un nuevo brote en su provincia ecuatorial (8).

En un intento por entender la historia natural de la enfermedad se han realizado estudios en vertebrados (murciélagos y roedores) y artrópodos, relacionados con el caso índice o sitio del brote, sin conseguir aislamiento viral o anticuerpos anti-EBOV (9,10). Debido a que los monos desarrollan una sintomatología hemorrágica similar a la de los humanos con posterior fallecimiento, no son considerados portadores asintomáticos (11). Se ha señalado que un murciélago aloja el virus, también al parecer los antílopes y el puercoespín. Existe un vacío importante de conocimiento al respecto.

En 1999 se estudiaron 242 mamíferos pequeños, detectando la glicoproteína del EBOV y secuencias del gen de la polimerasa, en animales pertenecientes a dos géneros de roedores y una especie de musaraña (12), señalados como reservorios de la enfermedad.

Falta mucho por esclarecer en lo referente a manifestaciones clínicas y vías de transmisión. Se informa de nueve días promedio de sintomatología, tanto para desenlaces fatales como para sobrevivientes. Existe predominio de: diarrea no disintérica (81%), náuseas y vómitos (65%), cefalea intensa (81%), astenia (77%), mialgia (65%), dolor abdominal (62%), disfagia (58%), pérdida del apetito (58%), conjuntivitis (50%) y fiebre (42%). Son frecuentes las erupciones cutáneas, insuficiencia renal, hepática y las hemorragias tanto externas como internas. La entidad se adquiere por contacto directo con sangre infectada, sudor o secreciones corporales, incluidas las genitales, por

tanto es de riesgo el contacto sexual con persona infectada. También se puede adquirir al manipular cadáveres u objetos infectados.

El manejo es inespecífico, se debe centrar en soportar la función circulatoria, realizar sustitución de los factores de la coagulación, plaquetas y el uso de anticoagulantes. Enfrentar los síntomas, corregir las alteraciones electrolíticas e instaurar antibióticos en el caso de shock séptico o infecciones bacterianas secundarias, suelen hacer parte del abordaje terapéutico (13).

Se están desarrollando investigaciones que permitan aumentar la terapéutica contra la infección por EBOV. Los inhibidores de la vía del factor tisular (rNAPc2), que bloquean el primer paso en la cascada de coagulación, en primates no humanos inducen reducción de la mortalidad en 33% (14). Fármacos antivirales de amplio espectro como el interferón α y la ribavirina, activos contra virus de tipo ARN, no tienen ningún efecto en la infección por EBOV; sin embargo, tratamientos basados en la intervención en el ciclo de replicación del virus, están siendo diseñados para atacar la expresión del mismo en el hospedero (15). No se dispone de herramientas terapéuticas consideradas exitosas ni se han definidos líneas de elección.

Se han realizado distintos abordajes y propuestas para el desarrollo de vacunas. Los resultados son promisorios *in vitro*, pero aún sin pruebas de efectividad y seguridad en humanos. No obstante, por el elevado número de casos y la alta tasa de letalidad del actual brote, el pasado 11 de agosto un panel de expertos autorizó el uso de intervenciones con biológicos aún en vía de aprobación, lo cual no deja de plantear interrogantes referentes a principios bioéticos y riesgo/beneficio. El ébola es una entidad de elevado y creciente riesgo en salud pública.

Para octubre del 2014 se consideró que estaba fuera de control, un brote sin precedentes por el número de casos y la dispersión geográfica, se recomendó no viajar a Liberia, Sierra Leona, Senegal ni Guinea y los que fueran a dichos países debían tomar precauciones. La Organización Mundial de la Salud (OMS) decretó el estado de emergencia sanitaria internacional. En todos los aeropuertos de América carteles informativos alertaban a los viajeros, se buscaban a enfermos sospechosos que eran sometidos a cuarentena e incluso bajo guardias armados y también se hacía un llamado para evitar el pánico y la histeria.

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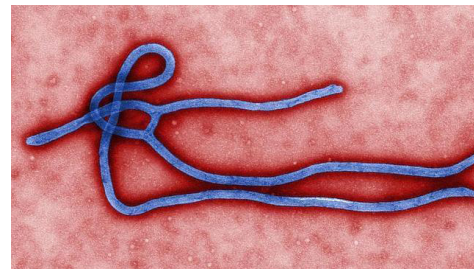
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EBOLA VIRUS DISEASE: WHAT WE MUST KNOW

The disease known as ébola receives this denomination for the name of the closer river to the African district, where the first cases of the outbreak were presented in the decades of the seventies of the 20th century (1). This zoonosis that is affecting Africa and currently spreading itself to other continents, attracts attention of the sanitary authorities worldwide.



The virus belongs to the family *Filoviridae*, genus *Ebolavirus* (EBOV) and they are divided in the species *Bundibugyo ebolavirus*, *Reston ebolavirus*, *Sudan ebolavirus*, *Tai Forest ebolavirus* y *Zaire ebolavirus* (2).

The origin of the disease is unknown, the first outbreak of EBOV was reported in Sudán in 1976 and three weeks later in Zaire, today named Democratic Republic of the Congo [DRC] (3). Then the frequency of cases decreased, being reported small outbreaks until that in 1994 the virus began tour in oriental direction, with progressive increase of the cases since Gabón to DRC and Uganda (4-6). At this moment, a new outbreak exists that could not have been contained. For September 4th of the year in process, 3707 cases had been reported, including 1848 deaths (7), distributed between Guinea (771 cases and 494 deaths), Liberia (1698 cases and 871 deaths), Sierra Leona (1216 cases and 476 deaths), Nigeria (21 cases and 7 deaths) and Senegal (1 case). Added to the previous information, the last August 26 the Ministry of Health of the DRC notified to the WHO a new outbreak in its equatorial province (8).

In an attempt for understanding the natural history of the disease, studies in vertebrates (bats and rodents) and arthropods related to the index case or site of the outbreak have been carried out, without viral isolation or antibodies anti-EBOV obtained (9,10). Due to the fact that the monkeys develop a hemorrhagic symptomatology similar to that of the human beings with later death, they are not considered to be asymptomatic carriers (11). It has been indicated that a bat lodges the virus, also apparently the antelopes and the porcupine. An important emptiness of knowledge exists in the matter.

In 1999, 242 small mammals were studied, detecting the EBOV glycoprotein and sequences of the gene of the polymerase in animals belong to two genres of rodents and a specie of shrew (12), indicated as reservoir of the disease.

A lot of information needs to be clarified in what concerns to clinical manifestations and routes of transmission. An average of nine days of symptomatology are informed as much for fatal as for surviving outcomes. There is predominance of: Non-dysenteric diarrhea (81%), nausea and vomiting (65%), intense headache (81%), asthenia (77%), myalgia (65%), abdominal pain (62%), deglutition disorders (58%), eating disorders (58%), conjunctivitis (50%) and fever (42%). The exanthema, renal and hepatic failure and external and internal hemorrhages are frequent. The disease is acquired by direct contact with infected blood, sweat or body secretions, including the genital ones; therefore the sexual contact with an infected person is of risk. Also it could be acquired on having manipulated cadavers or infected objects.

The management is unspecific, it should be centered in supporting the circulatory function, doing substitution of the blood coagulation factors, platelets and the use

of anticoagulants. To face the symptoms to correct the electrolytic alterations and to establish antibiotics in the case of septic shock or secondary bacterial infections, usually are part of the therapeutic management (13).

Researches are in process that will allow to increase the therapeutic against to the EBOV infection. The tissue factor pathway inhibitors (rNAPc2) that block the first step in the coagulation cascade in nonhuman primates induce the reduction of the mortality in 33% (14).

Antiviral drugs of wide spectrum as the alpha interferon and the ribavirin, active against RNA virus, do not have effect in the EBOV infection; nevertheless, treatments based in the intervention in the replication cycle of the virus are being designed to attack the expression of the same in the host (15). There are not therapeutic tools considered as successful and attention lines have not been defined.

Different proposals for the development of vaccines have been carried out. The results are promising in vitro, but still without tests of efficiency and safety in humans. Nevertheless, due to the high number of cases and the elevated lethality index of the current outbreak, the last August 11th a panel with experts authorized the use of interventions with biological substances still in routes of approval, which does not stop raising questions relating bioethical principles and risk/benefit. The Ebola is a disease of high and increasing risk in public health.

For October of 2014 it was considered that it was out of control, an outbreak without precedents for the number of cases and the geographical dispersion, and it was recommended not to travel to Liberia, Sierra Leone, Neither Senegal nor Guinea and those who were to the above mentioned countries had to take precautions. The World Health Organization (WHO) decreed the state of international sanitary emergency. In all the airports of America, informative cartels were alerting the travelers, suspicious patients were looked who were submitted to quarantine and even under armed police officers and also a call to avoid the panic and the hysteria was done.

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