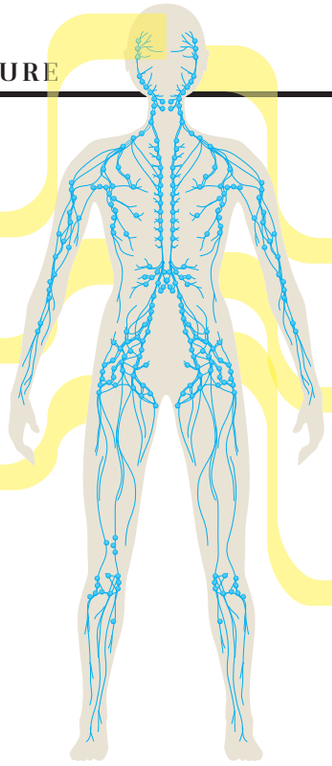
## TRANSMISSION AND SYMPTOMS

Ebola virus enters the patient through mucous membranes, broken skin, or parenterally. The virus exerts its effects directly, by causing cell necrosis, and indirectly, by causing apoptosis (programmed cell death). Apoptosis is prompted by the release of cytokines from infected cells. The virus infects many cell types, including monocytes, macrophages, dendritic cells, endothelial cells, fibroblasts, hepatocytes, adrenal cortical cells and epithelial cells. Although lymphocytes are not infected, they undergo apoptosis.



Fever, headache and chills are caused by the host mounting an overt immune (cytokine) response to the Ebola virus.

Impaired kidney and liver function is caused by death of renal and hepatic cells infected by the virus; there may also be some level of apoptosis in these tissues.

Muscle pain and weakness is likely to be due to the host immune (cytokine) response to the virus.

Haemorrhagic rash over the entire body, bruising, and oozing from venipuncture sites is caused by loss of vascular integrity due to endothelial cell death and dysregulation of clotting factors because of hepatocellular necrosis.

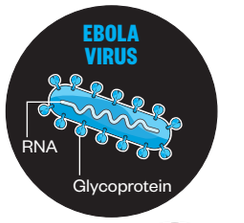
Bleeding from the eyes, ears and mouth is caused by loss of vascular integrity due to endothelial cell death and dysregulation of clotting factors because of hepatocellular necrosis.

The virus evades the immune response by causing rapid destruction of lymphoid tissue, including B and T cells, and disrupting the interferon response.

Severe watery diarrhoea, nausea, vomiting and abdominal pain is likely to be caused by necrotic infection of the gastrointestinal tract, resulting in loss of the ciliated cells required for absorption of nutrients. The physical damage leads to gastrointestinal bleeding and the other gastrointestinal symptoms.

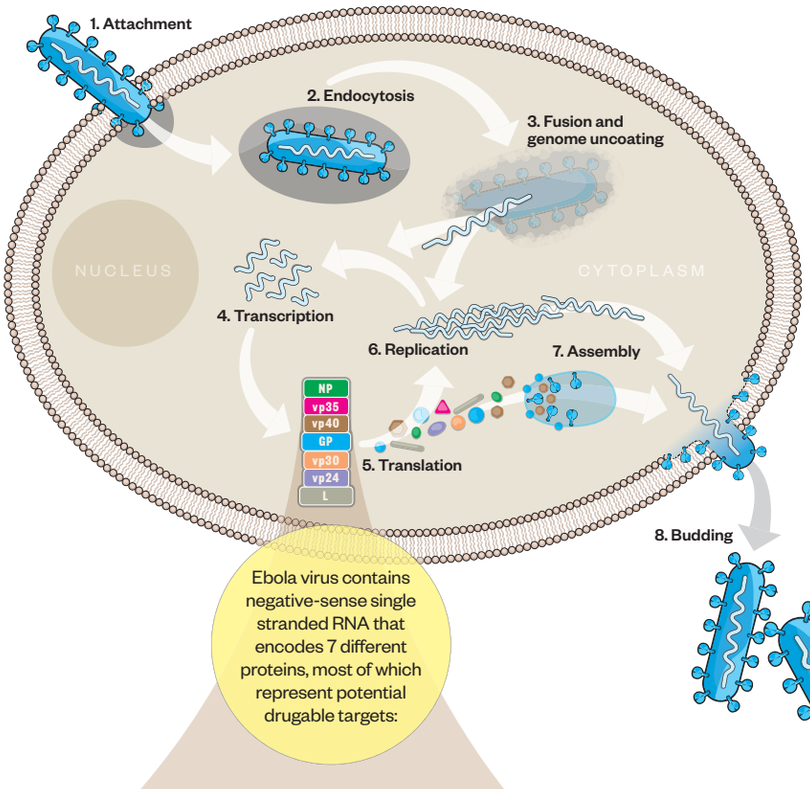
## THE BIOLOGY

Ebola virus attaches to the cell surface and is internalised, subsequently releasing its genetic material into the host cell cytoplasm. The RNA genome of the virus is transcribed into seven mRNAs, which are translated into the viral proteins. Some of these proteins then aid replication of the viral genome while others are destined to become the viral coating. New viral particles are then assembled from the replicated genome and new coat proteins and these bud from the cell.




**Monoclonal antibodies**
For example, ZMapp is a combination of three monoclonal antibodies which bind to three Ebola virus glycoprotein (GP) epitopes and neutralise the virus before attachment (**stage 1**).

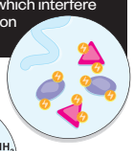
**Vaccines**
For example, a GSK vaccine uses chimpanzee adenovirus as a vector to deliver benign genetic material that allows the human cells to express Ebola surface glycoprotein prompting an immune response that neutralises the virus before attachment (**stage 1**).

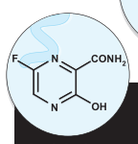



Ebola virus contains negative-sense single stranded RNA that encodes 7 different proteins, most of which represent potential drugable targets:

**There are a number of drug treatments and vaccines being developed to treat Ebola virus disease but none are yet licensed.**

**Small interfering (si)RNAs**
For example, siRNAs targeting the Zaire Ebola virus L polymerase (EK-1 mod), VP24 (VP24-1160 mod), and VP35 (VP35-855 mod) have been formulated by Tekmira, which interfere with translation (**stage 6**).






**Antivirals**
For example, viral RNA polymerase (L) inhibitor favipiravir (Avigan), currently licensed in Japan for influenza, inhibits viral gene replication (**stage 5**) within infected cells.

**VP35 – Polymerase cofactor**
Plays a part in catalysing RNA replication.

**VP30 – Transcription activator**
Essential for the initiation of transcription of Ebola virus mRNA.

**VP24 – Minor viral matrix protein**
Plays a major role in the subversion of the host immune response.

**NP – Nucleoprotein**
Associates with the viral genome to form helical nucleocapsid.


**L – RNA-dependent RNA polymerase**
Catalyses the replication and transcription of viral RNA.

**VP40 – Viral matrix protein.**
Plays a role in the formation and release of the enveloped virus particle.

**GP – Surface glycoprotein**
Forms spike-like projections on virions and plays a crucial role in virus entry into cells by mediating receptor binding and fusion. The G gene also encodes an additional protein that is secreted from the cells (secreted GP) and is an antibody decoy.