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YOUR FREE BIOLOGICAL SCIENCES REVIEW UPDATE

The Ebola story

Liz Sheffield discusses why a disease first identified in the 1970s still lacks a cure

Ebola kills up to 90% of those infected. The most recent outbreak has already killed more than 5500 people. This deadly disease was first identified in 1976 in people who lived in a town near the Ebola river in the Congo, Africa. We cannot be sure of the source of the disease, which affects several other mammals including bats, pigs and primates, but those first affected included workers in a factory where bats roosted.

Since the first outbreak, Guinea's rainforests have been reduced by 80%, Liberia has sold logging rights to over half its forests, and within the next few years Sierra Leone is predicted to become completely deforested. The removal of forest has reduced the habitat for animals, and brought them into closer contact with ever-increasing populations of humans. The most recent outbreak of Ebola has been attributed to bushmeat (e.g. illegally obtained bats and monkeys killed and sold for human consumption) or to fruit contaminated by fruit-bat saliva.

What causes the disease?

Ebola is a virus (see Figure 1). Normally when viruses invade the body they trigger cells in the immune system to fight off the infection. The Ebola virus, however, infects and cripples immune cells, taking out this first line of defence. These dying immune cells trigger a destructive flood of chemicals called cytokines. The cytokine storm kills the cells that normally make antibodies.

The Ebola virus also attacks the spleen and kidneys, where it destroys cells that help the body to regulate its fluid and chemical balance, and cells that make proteins which help blood to clot. At its worst, the virus causes the liver, lungs and kidneys to shut down, other organs to fail and the blood vessels to leak fluid into surrounding tissues. This often proves fatal.

Fabio Basone/MSF

An MSF doctor working on the Ebola frontline in Sierra Leone

What hope of a cure?

Now that the disease is killing people in the developed world, governments and pharmaceutical companies have started to invest seriously in finding vaccines and a cure. Several avenues are being pursued, one of which is the production of antibodies in plants — plantibodies. Amid much controversy, ZMapp — an unlicensed drug made from plantibodies — was given to people who had contracted the disease last summer. Although two American aid workers and a British volunteer recovered after the treatment, a Liberian doctor and a Spanish priest died.

ZMapp had only been tested on monkeys before it was given to the Ebola sufferers. It had not been through clinical trials in healthy people — the step required to get a drug licensed for clinical use. The production

Next page

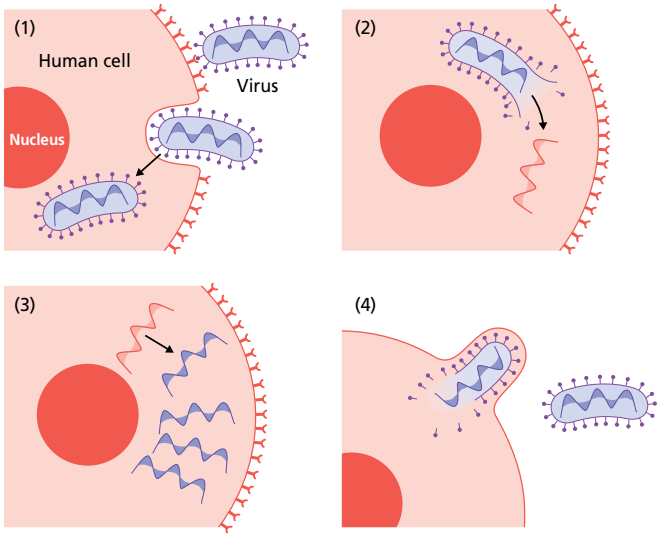

Figure 1 How the Ebola virus replicates. (1) Virus fuses with cell surface. (2) Virus releases its genetic material — RNA — into the cell. (3) The viral RNA is replicated by the host cell. (4) The host cell makes viral coat proteins and new viruses are released back into the host bloodstream

of the drug started by infecting mice with the Ebola virus. Antibodies were extracted from the blood of the mice and humanised. This process involves removing the genes coding for any parts of proteins that would trigger an attack from the human immune system. The relevant genetic sequences were then inserted into a virus which infects tobacco plants, and plants grown indoors in tightly controlled conditions were infected with the virus. In the same way that Ebola forces its host to make more viral genes, the tobacco virus forces the plants to make antibodies.

With clinical trials of a range of experimental Ebola treatments set to begin in December, public-health officials face an ethical quandary. Should some participants, who will necessarily have to be at risk of contracting the disease, be put in control groups? These people would only get the standard care — such as provision of intravenous fluids — but no drugs. 'The idea that there's no need for randomised, controlled trials presupposes that the drugs have zero side effects, that they are efficacious, and that there's no substantial variability from patient to patient,' says Clifford Lane, deputy director for clinical research and special projects at the US National Institute of Allergy and Infectious Diseases in Bethesda, Maryland. 'I don't think any of that is true.'

With at least 2 million people currently living in quarantined conditions because of Ebola, we have to hope that trial participants will come forward and that a cure emerges.

Things to do

- Discuss with your friends whether you would volunteer to take part in trials for a drug to treat a disease that had 1, 10, 50 or 90% mortality rates.
- Find out which other diseases are currently being treated with plantibodies.

Weblinks to follow up

In 60 seconds: what is Ebola:
www.bbc.co.uk/news/health-28105531

How the Ebola drug ZMapp is made:
http://tinyurl.com/l66a68d (Note: the movie mentions 'Ebola cells' but viruses are not cellular).

Ethical dilemma for Ebola drug trials, *Nature*:
http://tinyurl.com/onh5hkg

Fighting Ebola with ZMapp:
http://tinyurl.com/pgya2pn

How saving West African forests might have prevented the Ebola epidemic. *Guardian*:
http://tinyurl.com/lq7w87l

Ebola treatments: how far off?:
www.bbc.co.uk/news/health-29613902