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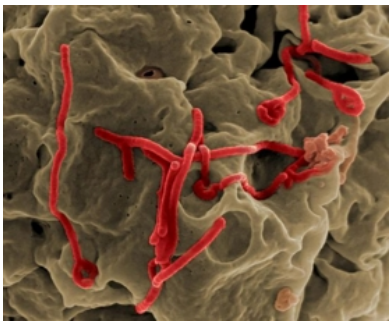
Infection Secrets of Ebola Explained

By attacking the body's first responders, the virus cripples the immune system before it can mount an effective defense

November 7, 2014 | By Helen Branswell | Véalo en español |

Researchers often describe the battle between the Ebola virus and the humans it occasionally infects as a race—one that people win only if their immune systems manage to pull ahead before the virus destroys too many of their internal defenses. What they may not know is that the virus is a cheat.



Although it contains only seven genes, Ebola is an exquisitely effective killer of humans and other primates once it enters a body. Unlike the spiky sea urchin that is influenza, or the golf-ball shaped poliovirus, Ebola resembles noosed ropes under the electron microscopes used to capture viral images. *Credit: NIAID via Wikimedia Commons*

The Ebola virus gives itself a head start when it first slips into a human body by disabling parts of the immune system that should be leading the charge against the invader. It hijacks the functions of certain defense warriors known as dendritic cells—whose primary function is to alert the immune system to the incoming threat. Other targets include monocytes and macrophages, types of white blood cells whose job is to absorb and clear away foreign organisms.

These are the first cells Ebola infects and bends to the process of making more Ebola viruses. The maneuver is the viral version of invading a country by hypnotizing the army and turning it against its own people. Then, having kicked the immune system's feet out from under it, Ebola takes off in a run.

Seven Deadly Genes

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Classified as a filovirus, Ebola is one of two members of that family; the other is Marburg virus, named after the German city where it was first seen in researchers who caught it from imported non-human primates. Both pathogens are among the most lethal viruses that afflict people, but it is Ebola that has become the recognized and dreaded face of the filovirus family.

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Marburg tends not to provoke the same fear in the general public as Ebola, although it is deserves equal billing. Daniel Bausch, a filovirus expert at Tulane University School of Public Health and Tropical Medicine in New Orleans, La., recalls preparing to head to a

Marburg outbreak in the Democratic Republic of Congo in the late 1990s when he was contacted by a journalist. The reporter had heard there was an Ebola outbreak. "And I said 'No, it's Marburg.' And he said 'Oh, thanks anyway' and he hung up the phone." The outbreak that the journalist had so nonchalantly dismissed killed 83 percent of known cases.

Ebola was previously known as a viral hemorrhagic fever, a description that is falling from use because of the erroneous implication that it kills by exsanguination or bleeding out. In fact, most patients do not hemorrhage or ooze blood, at least not externally, Bausch says. Ebola virus disease is now the preferred terminology.

Few autopsies have been performed on people who have died from Ebola virus disease, because of the high risk posed by the procedures. In fact, a scientific review published in October 2014 identified only 30 human cases where an autopsy or post-mortem biopsies were performed. But here is what's known about the way the disease takes off in the body: The early infection of–or recruitment of—the monocytes, macrophages and dendritic cells is believed to speed spread of the virus to the lymph nodes, liver, spleen and elsewhere in the body. In the liver, the presence of the virus appears to trigger a sharp decline of lymphocytes, white blood cells that help fight infections. The reason for their decline is unknown, but the result helps the virus; lymphocytes typically would increase in number in the face of an infection.

Decoy Strategy

Meanwhile, Ebola employs a second dastardly trick, another cheat. It releases large amounts of something called secreted glycoprotein – sGP – into the bloodstreams of its victims. A decoy, sGP looks like the glycoprotein on the exterior of the virus, GP, which should be the immune system's chief target. By tricking the immune system into seeing it, not GP as the invader, sGP undermines the system's ability to react effectively to stem the infection.

As the amount of virus in a person's system starts to rise, symptoms begin to appear. They start with low-grade fever, which can come and go, and is sometimes missed. Severe headache and abdominal pain are followed by vomiting and diarrhea, which lead to profound loss of fluids.

Doctors at Emory University Hospital, who have treated four repatriated medical workers infected with Ebola in the current outbreak, found at times their patients excreted between six and eight liters of diarrhea a day – a loss that triggers electrolyte imbalances, says Marshall Lyon, an infectious disease physician on the Emory Ebola team. It has been known for some time that keeping Ebola patients hydrated is the main battle to be waged – at least until drugs proven to be effective are available. But the experience at Emory and other hospitals treating med-evaced health-care workers also suggests that when patients have profound diarrhea, replenishing electrolytes such as potassium may be something doctors should consider, even in low-resource settings where laboratory support is minimal and electrolyte levels cannot be monitored.

Back in the body, the accumulating damage in the liver leads to something called disseminated intravascular coagulation or DIC, where blood over-coagulates in some locations, but cannot thicken in others, creating a situation where blood vessels become leaky. That is what results in the bleeding – mostly internal – for which Ebola is known.

The leakiness of blood vessels compromises blood supply to key organs like the liver and the kidneys. Bausch employs the analogy of trying to use a hose full of holes to water your garden – the water does not get to where it is needed. Likewise, bacteria from the gastrointestinal tract can slip into the bloodstream, causing sepsis. The result in the worst cases: blood pressure plummets, vital organs begin to fail, the patient goes into shock and dies.

Where and How Much?

The speed and degree to which Ebola manages to overcome an individual depends on a couple of factors, scientists who study the virus say. If you are unlucky enough to be infected with Ebola, the amount (or dose) of virus to which you are exposed and the route by which the virus makes its way into your body could mean the difference between whether you live or die.

In the world of Ebola, less is better but even a very little is bad. Scientists have differing views on the sometimes cited claim that a single virion – just one virus – is sufficient to trigger infection. While that may, or may not be the true figure for the minimum infectious dose for humans, it is likely that infection can occur from contact with small amounts of virus, Bausch says.

"We think that it's very low — a little dab will do you," he notes, playing on a 1960s advertisement for a men's hair pomade, Brylcreem. "You don't need much of this virus to get infected." Nevertheless, a low-dose exposure may prove less lethal if it allows the immune system to get into gear before the viruses have a chance to disable too many of the early responders.

How you get infected likely also plays a role in how sick you become. An exposure that delivers the virus into the blood stream – for example a needlestick injury, dreaded in the filovirus research world – is more damaging than when viruses are introduced via the mucus membranes surrounding the eyes, nose and in the mouth. Onset of symptoms is quickest with direct-to-blood exposures; they typically account for the short end of the incubation period range, two to 21 days. Most infections become apparent within eight to 10 days of exposure.

"If you get a direct injection with a lot of virus particles, I don't think anything's going to save you, because you're just overwhelmed," says Thomas Geisbert, a microbiologist at the University of Texas Medical Branch at Galveston. Geisbert notes that in the 1976 Ebola epidemic that brought the disease to the attention of the world, 85 people were known to have been infected through the reuse of contaminated syringes. All 85 died, along with nearly 200 others in and around Yambuku, in the former Zaire (now the Democratic Republic of Congo).

Two other features that may play into the outcome of the life or death struggle between humans and Ebola are age and genetic predisposition. A recently published study which tracked case outcomes in Sierra Leone during the current West African outbreak showed a higher survival rate for patients under the age of 21 compared to those over the age of 45. Earlier, a study done based on blood samples from people who had been infected during a 2000 outbreak of Ebola Sudan in Uganda found that certain people were more likely to have milder disease and survive. Another recently published paper looking at the spectrum of disease in mice also suggests genetics play a role in survival.

Geisbert is one of the discoverers of an Ebola species known as Ebola Reston, unique among the five types of the viruses because it does not originate in Africa and so far it has not been seen to sicken people. Reston viruses come from the Philippines; on six occasions research monkeys imported from that country have triggered animal outbreaks. It has also been found in pigs, though the animals do not show signs of infection. Ebola Reston is lethal in primates.

Research done after animal outbreaks shows that several people have developed antibodies (or "seroconverted") to Ebola Reston, but did not become noticeably ill. Still, it is too soon to assume Reston is harmless in humans, Geisbert says. "Some people have seroconverted but we don't really know much about that. All you can say is there hasn't really been any human that has gotten really sick or died from it. But the 'n' [number infected] is quite small."

The other species of Ebola are: Zaire, the most lethal and the virus responsible for the current West African outbreak, Sudan, Bundibugyo and Ivory Coast (sometimes called Tai Forest). The fatality rates for the first three range from 70 percent to 90 percent, about 50 percent and 25 percent, respectively. The Ivory Coast virus has only been seen once, in 1994. The infected person survived, but was very ill.

Geisbert works with a variety of bad bugs. But it is Ebola and the Marburg strain responsible for the 2004 outbreak in Uije, Angola – case fatality rate, 90 percent – that make him extra cautious. "It's always in the back of your mind that you're working with something that can kill you."