TNT’s “The Last Ship” shadows Ebolavirus crisis: How realistic is a contagious vaccine?

On the TNT hit series, *The Last Ship*, a global pandemic has killed most of humanity, but a scientist has developed a vaccine, along with a cure. The vaccine and cure are breathable and also contagious.

There are a lot of details about the science that either were overlooked or did not survive the script writing process any better than the bulk of humanity survived the fictional plague, but there is also a really cool element.

With the second season of *The Last Ship* now at a close, the cure-vaccine is airborne. Initially, it had to be injected, just like most of the immunizations that we all get routinely. But later, the scientist, Dr. Rachel Scott (Rhona Mitra), succeeded in nebulizing the treatment, so it could be released from an aircraft and inhaled by large numbers of people all at once. It sounds like science fiction–it’s a sci-fi show, after all–but it also hints at real-life developments. This includes the fight against Ebolavirus, where inhalable vaccines are on on-deck.

The Last Ship writers also have imagined the vaccine, or cure (it’s not clear whether the fictional treatment contains two separate entities, or one molecular component that immunizes as well as undoes damage in those already sick) that is not only aerosolized, but also contagious. It enters a person’s body through the lungs, then reproduces just like the plague virus does, leading to the synthesis of daughter vaccine particles. These particles then go out through the person’s lungs to infect, and thus cure or immunize, those who are not yet exposed to the disease.

It’s wildly imaginative and the science breakthroughs and clinical development of the treatment happen all too quickly on the show to be realistic. And yet, at the foundation of the story are some concepts that make real sense and could foretell a new era in vaccines and genetic medicine.

First, the fiction

Before delving into the science that *The Last Ship* got right, the mistakes should be pointed out for those who have been watching the show and may be wondering “Wait, is that true? Could that really happen?”. This will be the biomedical equivalent of critiques that others analyzing the show may write concerning accuracy of plot elements related to sonar, torpedoes, or other naval matters.

Here is the elephant in the room: To make her new cure-vaccine contagious, Dr. Scott used DNA scissors (special enzymes that cut and paste particular DNA segments and include CRISPRs, TALENs and ZFNs) from shell-fish-inhabiting bacteria to remove a genetic stability sequence from the lungs of another scientist, Niels Sørensen (Ebon Moss-Bachrach). Experimenting on himself several months earlier, using the stability sequence, the virus, and one of his own genes, Sørensen had rendered himself immune, but this had made the virus worse and made him a carrier, amplifying the number of deaths from millions to billions.

Once liberated from Sørensen's lung cells, Scott made her her vaccine-cure do in her own lungs what the virus did in Sørensen's lungs; she became contagious with the cure. Removal of the stability sequence from the virus within Sørensen also ended his immunity. The virus spread from his lungs to the rest of his body and he developed the usual late-stage symptoms within minutes and died, making it the fastest virus ever. It made for a very complex story line, complete with a murder investigation that exposed Scott.

Just one problem, though. Scientifically, it makes no sense.

As with Ebolovirus, the fictional "Red Flu" virus of *The Last Ship* causes an immune response. Whether the person lives or dies depends largely on how quickly the immune system learns to recognize the virus compared with how quickly the virus wreaks havoc on body tissues. With the fictional Red Flu, the wreaking havoc dominates over the development of immunity. In Sørensen's case, he is a carrier, because the virus–which, in sharp contrast to Ebolavirus, is airborne and is spread by people breathing on one another–is held in his lungs. According to Scott and another scientist working with her, this also is why Sørensen is immune. But that's not how immunity works.

Sørensen had made himself into a carrier, unwittingly, by injecting himself with the altered virus, not by breathing it. The virus had gone through his body, reaching all of his tissues and presenting itself to his immune system. Somehow, the extra gene from his own genome that he'd attached to the virus had allowed him to live long enough for his own immune system to adapt. That's why he was immune, not because the virus was concentrated in his lungs. Thus — in real life — giving Sørensen the DNA scissors to snip out the stability sequence might have cured him of his carrier status, but would not have killed him.

Breathable vaccines

Other than being airborne, the fictional Red Flu virus of *The Last Ship* is eerily similar to the Ebolavirus strain of the current West African outbreak (Ebola Zaire). This is because of the high death rate and the symptom profile. Also, as with the fictional virus, Ebolavirus may be fought soon with a breathable vaccine. On *The Last Ship*, the benefits of a breathable vaccine (or vaccine-cure) related only to the logistics of delivering it to populations. By dropping the treatment from a helicopter as a nebulized mist, the good guys were able to immunize and treat tens of thousands of people in one city. We can imagine scenarios of real-life diseases, including Ebolavirus, where such an option would be an advantage. Furthermore, avoidance of needles is a benefit, because of the risk of needle injury to health workers, which is amplified by the protective suits and equipment they must wear.

But in the case of Ebola research, there may be an additional advantage to the breathable strategy. In a study published recently in the journal *Molecular Pharmaceutics*, researchers from the University of Texas, Canada's national Microbiology Laboratory, and the University of Pennsylvania presented evidence that their vaccine (made from an adenovirus modified with selected Ebola virus genes to make Ebola viral coat proteins) is more effective in monkeys when inhaled than when given by either by intramuscular injection or a sublingual (by mouth) route. With the breathable form, immunity to Ebolavirus lasts longer than with the injectable and sublingual forms and improves survival.

“While [the results of the sublingual route study] were disappointing, it is important to realize that the primary goal of this project was to develop an adenovirus-based vaccine that could be given by either the respiratory or the oral route,” the researchers noted in the discussion in their paper.

Using a technological innovation called nanoparticles, other researchers also are developing breathable vaccines against several other conditions, such as influenza and pneumonia.

Contagious cure?

The breathable vaccines under study today would be administered through devises similar to inhalers that asthmatics use for their bronchodilator drugs. With some future developments, we also can imagine such vaccines being optimized for release into the air to immunize large groups of people at once, similar to the release of the vaccine-cure from a helicopter on the the season 2 finale of *The Last Ship*.

But on the show the other delivery system is neither an aircraft nor an inhaler, but the lungs of other people. It’s called a contagious cure, because you’re exposed to it when someone breathes it onto you. In real-life, there actually have been contagious vaccines already, notably the Sabin oral polio vaccine (OPV). This was live attenuated virus used from 1963-1999 and it could spread to close contacts of those immunized and confer immunity. OPV was discontinued, because occasionally it would revert to a form of the virus strong enough to cause actual disease so now only the killed vaccine (Salk) is used, and while OPV did end up spreading immunity, the route of spread was fecal-to-oral, which is different from a contagious vaccine that spreads through the lungs.

There’s a rationale for a contagious vaccine through the lungs as well, but as even *The Last Ship* writers seem to be aware, creating a vaccine that would live in people’s lungs and is released in their breath sufficiently to immunize others they breathe on would be an ambitious goal. Thus, compared with the deadly virus itself, from which un-immunized characters are in danger simply by being in the same room with an infected person, the fictional vaccine-cure is somewhat less contagious. Thus, Scott tells other characters that to spread the treatment they must get within centimeters of a person’s face.

There are more problems with the fictional biology. Firstly, to acquire the contagious vaccine-cure in order to distribute it to sick or about-to-be sick people, crew members of *The Last Ship*‘s protagonist naval vessel *USS Nathan James* must receive a “booster” via injection of a vaccine that they’ve already received. However, once those people receive it from the injected people breathing on them, somehow they have the vaccine-cure in their lungs, after no injection, and that cure is ready to spread to others, also with no injection.

Second, although Scott made such a contagious cure using the very same genetic stability sequence that enabled the deadly virus to be extra contagious by residing in Sørensen's lungs and not his body fluids, once given the contagious vaccine cure, the *Nathan James* crew has the treatment both in their breathand their body fluids. Thus, they can spread the cure both by breathing on people and by sharing bottledwater infected with their saliva. That's very convenient for the story, but also illustrative of the many contradictions.

None of this is meant to poke fun at the writing of *The Last Ship*, which actually is prime for any science fiction show, or for that matter any TV drama. Rather, the idea here is to promote discussion — not only discussion about which technologies are too far-fetched, but also what is really possible. If we are willing to put aside the various errors of the biological details, we're left with a general concept that in itself is an excellent idea: very soon, we'll be able to make breathable vaccines that we can spread through populations with much greater speed and efficiency than have been possible to this point.

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