Epstein-barr virus: It causes mono and maybe MS. Is a vaccine near?

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The mononucleosis virus, Epstein-Barr, has become a major suspect in

the search for what causes multiple sclerosis.

Now researchers are raising the next logical question—can we *stop* both MS and mononucleosis by preventing Epstein-Barr infections, which occur in 95% of adults?

Epstein-Barr vaccines currently under development by the U.S. National Institutes of Health (NIH) and the pharmaceutical company Moderna could provide an answer.

But experts warn it's going to be years before any of the vaccine candidates are proven effective, and years more before studies will show that vaccination could prevent MS.

"Ultimately, a study to look at the effect of a vaccine on MS susceptibility would require a rather large study with extensive follow-up," said Dr. Eric Klawiter, an associate neurologist at Massachusetts General Hospital in Boston. "It may be some time before we have a good idea related to the long-term safety and efficacy of these types of vaccines to reduce the likelihood not just of MS but other diseases that have been linked to Epstein-Barr virus."

It can take as long as a decade before some people infected with Epstein-Barr develop multiple sclerosis, said Dr. Jeffrey Cohen, chief of the Laboratory of Infectious Diseases at the NIH, a group that has developed two potential EBV vaccines.

"If it's seven or 10 years between the time people get infected with EBV and get multiple sclerosis, one would have to follow those people for a long time to find out whether the vaccine prevented MS," Cohen said.

What is MS?

Nearly 1 million Americans have multiple sclerosis, a neurodegenerative disease that disrupts nerve signals from the brain to the body. MS causes people to develop symptoms such as numbness, muscle spasms, walking difficulties, speech problems and paralysis.

A pair of studies last month provided fresh evidence tying Epstein-Barr to MS:

- A study of more than 10 million U.S. military personnel found that MS risk skyrockets 32-fold after a person is infected with Epstein-Barr. The paper in *Science* found EBV present in all but one out of 801 MS cases that occurred among that group over 20 years.
- EBV is linked to MS in some by tricking their immune system into attacking the body's own nerve cells, according to a second paper published in *Nature*. A review of nine MS patients found the virus contains proteins that mimic a protein found in myelin, the fatty insulating sheath that coats nerve fibers; antibodies developed against the virus could damage nerves as well in some people. (Inflammation of the sheath and the nerve fibers that it surrounds is a hallmark of MS.)

Together, the two studies checked some boxes essential to proving a link between MS and EBV, said Bruce Bebo, executive vice president for research with the National MS Society.

"The final piece of evidence you would need to show in order to prove causation" is to do a study showing that an effective vaccine prevents MS, he said.

"If you have a way to prevent the infection, and that would be most likely a vaccine, then would you be able to reduce or prevent MS? That would be the final box you'd need to check in order to prove causation,"

Bebo continued.

The NIH has been leading the effort to develop an Epstein-Barr vaccine, Bebo said.

One vaccine candidate will enter phase 1 clinical trials within the next couple of months, Cohen said, while another should be ready for human testing next year. Phase 1 trials test vaccine candidates for safety, and look for early signs that they produce a significant antibody response in humans.

The NIH vaccines are similar to the vaccine for human papillomavirus (HPV), in that they provoke an immune response by exposing the body to protein particles derived from the original Epstein-Barr virus, Cohen said.

The first NIH vaccine to be tested targets a major protein on the surface of the virus called gp350.

An experimental Epstein-Barr vaccine developed and abandoned years ago used the same target and "reduced the rate of infectious mononucleosis by 78%, but it did not prevent infection with EBV," Cohen said. "People still got infected, but they had a much lower rate of developing disease.

"We've used the same protein that was in that vaccine, but we've put it onto a particle such that there are 24 copies of the protein on this particle," so it is expected to provide an even stronger immune response, Cohen said.

Moderna—famously the creator of an mRNA vaccine for COVID-19—recently used that technology to create another Epstein-Barr virus vaccine candidate.

A phase 1 clinical trial for the Moderna vaccine recently kicked off, said Dr. Katherine Luzuriaga, the study's principal investigator and chair of biomedical research for UMass Memorial Health Care in Worcester, Mass.

Moderna's vaccine incorporates four different proteins found on the surface of EBV, providing more potential targets for antibodies, said Luzuriaga.

Any EBV vaccine's main goal will be to prevent infectious mononucleosis, the main disease caused by the virus, researchers said.

About 30% of young adults get to college without having been infected with Epstein-Barr, Luzuriaga said. About half of those students will wind up with infectious mono during their college years.

"There's a big need, and we're excited to have a vaccine that could potentially address that need," Luzuriaga said.

Epstein-Barr also has been linked to several types of cancer, Cohen added. Each year, there are about 200,000 new cases of cancer associated with the virus.

"If we could prevent EBV infection, we think we would prevent a lot of those cancers," Cohen said. "On the other hand, our vaccine might not prevent infections. It might prevent mononucleosis but not infection with EBV.

"What we don't know is if we prevented mononucleosis or if the vaccine was partially effective, would that prevent multiple sclerosis and would that prevent these EBV-associated cancers?" Cohen continued.

Are there risks?

Part of the safety testing for any EBV vaccine also will have to examine whether the jab itself increases risk for MS, Bebo said.

"You would absolutely want to take care that whatever targets you are using to increase an immune reaction to fight the virus wasn't in some way accidentally triggering an autoimmune reaction," Bebo said.

Cohen thinks that shouldn't happen with the NIH's first candidate because it targets a protein on EBV that's different from the one that allegedly causes the immune system mix-up resulting in MS.

If one of the vaccines does get approved, there are ways that could potentially speed up follow-up studies to prove whether or not vaccination prevents MS, experts said.

For one thing, researchers could simply keep tracking the patients tested with the vaccine, to see how many wind up developing MS in the long run, Luzuriaga said.

Future multiple sclerosis prevention trials also could be more tightly focused by identifying people at increased risk for MS due to their family history, genetics and other early markers for the disease, Bebo and Klawiter said.

For example, neurofilament light chains (NfL) are nerve filaments that, when found in blood, provide an early and reliable marker for future MS. Looking for NfL levels at all stages of vaccine testing could "not only further ensure that a vaccination didn't contribute to a risk of MS," but could also be used to sort patients for future prevention trials, Klawiter said.

More information: There's more about multiple sclerosis from the U.S. National Institutes of Health.