

Is the first cure for advanced rabies near?

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Rabies virus is incurable and almost always fatal once it has invaded the central nervous system, with the victim doomed to suffer a horrible death.



But researchers now think they've found an effective and simple treatment that can cure even advanced cases of rabies.

A monoclonal antibody injected into <u>lab mice</u> successfully protected them from a lethal dose of rabies <u>virus</u>, researchers reported in a World Rabies Day article published online Sept. 28 in *EMBO Molecular Medicine*.

"I would say this is the first practical therapy for rabies," said senior researcher Brian Schaefer, a professor of immunology at Uniformed Services University of the Health Sciences in Bethesda, Md.

The antibody was created using Australian bat lyssavirus, a close cousin of rabies virus.

The researchers designed the antibody to block the rabies virus and prevent its spread.

"This antibody is specific for the <u>cell surface protein</u> on all those lyssaviruses that enables the lyssavirus to attach to target cells and infect those cells," Schaefer said.

Prior efforts to treat advanced rabies have failed because treatments have been unable to pass through the blood-brain barrier, the study authors noted.

But this antibody, even though it's too big to slip into the nervous system and treat rabies directly, appears to prime the immune system to effectively fight the virus in the brain and spinal cord, Schaefer said.

The researchers were surprised to find that a single dose of the antibody effectively reversed rabies infection even after it had reached the nervous system, preventing death.



This antibody appears to spur the <u>immune system</u> to create smaller immune cells that can pass through the <u>blood-brain barrier</u> and into the <u>nervous system</u>, where they effectively target and destroy <u>rabies virus</u>, the findings showed.

"It seems like what the antibody is doing is acting in the periphery, acting outside of the brain to change the immune response in such a way that the immune cells that go into the brain are now successfully able to fight the infection," Schaefer said.

Low levels of the virus remained in the mice that received the antibody, but those levels didn't increase and signs of rabies did not immediately return, the results showed.

The next step would be to create a version of this antibody for humans and to test it in <u>clinical trials</u>, but that's a huge next step, Schaefer said.

Rabies virus kills virtually no one in the United States, given Americans' access to immediate therapies that prevent advanced disease, he noted.

Rabies does kill about 60,000 people around the world each year, mostly in developing countries, so it's there that clinical trials would have to take place.

"Probably the best place for this would be someplace like India where they have a pretty advanced health care system, but they also still have a lot of cases of advanced-stage rabies," Schaefer said. "It would take something like a drug company or maybe a government to put a lot of money behind it to actually do the human testing."

Dr. William Schaffner, a professor of infectious diseases and <u>preventive</u> <u>medicine</u> at Vanderbilt University in Nashville, Tenn., emphasized that these are "early days" for this potential treatment.



"Mouse studies are one thing. Studies in people are something else," Schaffner said. "But nonetheless, if you could see me, I would be jumping up and down in my chair a little bit. Because until now, there's really been no reliable treatment for rabies once that infection has become established. Given its success in mice, it certainly deserves further investigation in other animals."

This potential cure for advanced rabies is particularly promising because it could be distributed easily to places that need it, Schaffner said.

"Monoclonal antibodies can be produced fairly readily now and could be widely distributed around the world," he said. "We could treat those cases, and they're 100% fatal now. Once this disease gets established, there are only a literal handful of cases that have been treated and have survived rabies."

The need for therapy is evident, Schaffner said.

"If this pans out, it would clearly advance what it is that we could do to mitigate the impact of this terrible disease," he added.

More information: Kate E Mastraccio et al, mAb therapy controls CNS-resident lyssavirus infection via a CD4 T cell-dependent mechanism, *EMBO Molecular Medicine* (2023). <u>DOI:</u> 10.15252/emmm.202216394

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