

Does Rabies Regimen Include Vaccination?

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Mini Review

The use of rabies vaccination as a post-exposure preventative measure makes it special. This is a result of the lengthy incubation period, which is often measured in months but can occasionally be measured in years, between exposure and the onset of the disease. Although it is yet unclear what the virus does during this time, it does present a chance for treatment to be applied. Despite intensive research, there is now no antiviral treatment; nevertheless, there is still time to immunise with a variety of approved inactivated virus vaccines, which trigger a powerful immune response that prevents the virus from progressing to infection of the central nervous system. All fine and good, but what happens if no steps are done after being exposed to a rabid animal bite? Here, the rabies virus exhibits its vicious side. There is limited chance of survival for individuals who go from exposure by a bite to the development of the disease, an overwhelming encephalomyelitis, according to unreliable statistics. The creation of therapeutic coma as a kind of treatment for patients exhibiting rabies symptoms is one effort to address that. Dr. Rodney Willoughy devised this strategy after successfully using it to treat a teen who contracted rabies after being bitten by a bat [1]. The approach, which has been developing over the past seven years as more experience is acquired from its use, lacks models for evaluation, hence the treatment is still regarded as controversial. Nevertheless, the bulk of the cases in which the treatment has been used have not resulted in success, despite the limited number of successes. Although survivors tend to be younger and have contracted the bat variant of the virus rather than the more common dog variant, they also develop high titres of neutralising antibodies early in the disease and this is found in both the blood and cerebrospinal fluid. However, there are no clear indicators of what determines a successful outcome. A rabies diagnosis must be made quickly in order to start treatment, and the patient needs to be watched closely while under anaesthesia. High quantities of rabies virus have been found throughout the brains of individuals who have died after therapy, indicating the requirement for antiviral treatment via an antiviral or immune-mediated response to support therapeutic coma [2].

The creation of vaccine candidates based on the reverse genetics technique has been one strategy that might provide some support. Since

Conzelmann and Schnell initially announced the first recovery of the rabies virus from a cloned genome, it has been over 20 years. Since then, the strategy has been developed by a number of labs in Europe and the US in an effort to better understand the biology of the virus and create attenuated viruses that could be potential vaccine candidates [3]. One well-liked strategy has been to insert genes that control mammalian innate immunity into the rabies virus genome, typically between the L polymerase gene and the glycoprotein gene. When examined in a mouse model, the effect of these introductions attenuates the virus by overstimulating the innate immune response, avoiding infection of the central nervous system. Following inoculation with a recombinant virus that shows no signs of virulence, this manifests as high levels of circulating anti-rabies virus antibodies and increased recruitment of dendritic cells into lymph nodes. One research team has gone one step further and developed a type of vaccination therapy using a modified rabies virus that contains the gene for Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF). They have demonstrated the prevention of death from a fatal infection by first infecting mice with a virulent strain and then reinfecting the mice with the attenuated strain. Up to 5 days after intracerebral infection with a virulent rabies virus strain, this impact was shown in mice given the modified virus. Increased levels of neutralising antibodies and inflammatory cell infiltration into the brain were seen in infected mice [4].

There is still much work to be done before this can be thought of as a potential therapeutic strategy, though, because mice are not men. But aside from therapeutic coma, there is no cure for rabies at the moment. Vaccination before and after exposure is quite efficient at preventing disease, but it is not sufficient. While there are still rabid dogs and bats in the world, there will always be people who have this illness and escape the public health system due to ignorance or a lack of resources [5]. For people who contract rabies, any medication that can be developed that has either direct or indirect antiviral efficacy would be encouraging.

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