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Early onset of protection against lethal HPAIV H5N1 infection – what is possible?

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In light of the widespread occurrence of highly pathogenic avian influenza (HPAIV) H5N1 and the consistent failure of eradication attempts in many countries in Asia and Africa, additional tools for its prevention are indispensable. Most important tools are safe and efficacious vaccines. We therefore used a novel neuraminidase-deleted apathogenic variant of the HPAIV H5N1 strain R65 (“H5N1del”) for a series of immunization/challenge experiments. In a first trial, it could be demonstrated, that a complete protection from lethal HPAIV H5N1 challenge infection was induced after a single intramuscular application of $10^{4.5}$ TCID₅₀ per chicken. The animals developed high titres of hemagglutinin-specific antibodies shortly after immunization, but no neuraminidase-specific reactivity was seen in an N1-specific ELISA test. Furthermore, there was no indication of a generalized infection, and no viral RNAs were detected in brain and lung samples or cloacal swabs, and only tracheal samples revealed a limited replication of challenge virus. Interestingly, the same level of protection could be achieved in a second trial with the H5N1del strain, when six-week-old chickens were immunized seven and three days before challenge infection, respectively. In contrast, immunization only one day before HPAIV H5N1 challenge infection could not prevent clinical symptoms and death, but resulted in a delay in the onset of disease. In addition, the mutant allowed a neuraminidase-based marker strategy.

In conclusion, a very early onset of immunity against HPAIV seems feasible using a modified live vaccine prototype and should be taken into consideration for future developments and control strategies.

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