Validation of diagnostic tests for detection of avian influenza in vaccinated chickens using Bayesian analysis

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Vaccination is an attractive tool for the prevention of outbreaks of highly pathogenic avian influenza in domestic birds. It is known, however, that vaccination does not always provide perfect protection against infection, and that the detection of infection in vaccinated birds can be problematic. This implies that there is a risk of silent spread of virus in vaccinated populations (Savill et al., 2006). Therefore, it is increasingly believed that vaccination programs should always be accompanied by active surveillance.

Surveillance programs can be based on the use of serological DIVA (differentiating infected from vaccinated animals) tests. However, validation of serological DIVA tests is difficult to perform, because there is no gold standard test, and the true disease status of the animals is unknown. Here, we investigate the characteristics of three serological tests for avian influenza (immunofluorescent antibody test (iIFAT), neuraminidase inhibition (NI) assay, and NS1 ELISA) that are able to differentiate infected from vaccinated animals. To this end, data of H7N7 infection experiments are analyzed using Bayesian methods of inference (Enoe et al., 2000; Engel et al., 2008). These Bayesian methods enable validation of the tests in the absence of a gold standard, and allow one to take into account that infected birds do not always develop antibodies after infection.

The results show that the N7 iIFAT and the NI assay have sensitivities for detecting antibodies of 0.95 (95% CI: 0.89-0.98) and 0.93 (95% CI: 0.78-0.99), but substantially lower sensitivities for detecting infection: 0.64 (95% CI: 0.52-0.75) and 0.63 (95% CI: 0.49-0.75). The NS1 ELISA has a low sensitivity for both detecting antibodies (0.55 (95% CI: 0.34-0.74)) and infection (0.42 (95% CI: 0.28-0.56)). The estimated specificities of the N7 iIFAT and the NI assay are 0.92 (95% CI: 0.87-0.95) and 0.91 (95% CI: 0.85-0.95), and 0.82 (95% CI: 0.74-0.87) for the NS1 ELISA. Additionally, our analyses suggest a strong association between the duration of virus excretion of infected birds and the probability to develop antibodies.

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