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Abstract

Emergence and Selection of a Highly Pathogenic Avian Influenza H7N3 Virus †

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Abstract: Low pathogenic avian influenza (LPAI) viruses of subtypes H5 and H7 have the ability to spontaneously mutate into highly pathogenic (HPAI) variants, causing high mortality in poultry. The switch to high pathogenicity is poorly understood, and evidence from the field is scarce. This study provides direct evidence for LPAI to HPAI mutation from a turkey farm during an H7N3 outbreak in the Netherlands. At the farm, only mild clinical symptoms were reported, but the intravenous pathogenicity index measured for the virus isolated from the infected turkeys was consistent with a highly pathogenic virus. Using deep-sequencing, we showed that a minority of HPAI virus (0.06%) was present in the virus preparation. Analysis of different organs of the infected turkeys showed the highest percentage of HPAI virus was present in the lung (4.4%). The HPAI virus contained a 12-nucleotide insertion in the hemagglutinin (HA) cleavage site that was introduced by a single event, as no intermediates with shorter inserts were identified. The HPAI virus was rapidly selected in chickens, after both intravenous and intranasal/intratracheal inoculation with the mixed virus preparation. Full-genome sequencing revealed that both pathotypes contained a deletion in the stalk region of the neuraminidase protein. We identified mutations in HA and polymerase basic protein 1 (PB1) in the HPAI virus, which were already present as minority variants in the LPAI virus. Our findings provide more insight into the molecular changes and mechanisms involved in the emergence of HPAI viruses. This knowledge may be used for the timely identification of LPAI viruses that pose a risk of becoming highly pathogenic in the field.

Keywords: avian influenza virus adaptive mutations; pathotypes; virulence determinants