particularly when term approaches. The imbalance in T-cell immunity (Th1/Th2) has been proposed to be implicated in the progression of chronic HEV infection in immunocompromised pigs (7). This imbalance may explain the absence of cytolysis during pregnancy and the increased viral load observed despite discontinuation of infliximab. Conversely, after delivery, restoration of cellular immunity is commonly observed (11) and may have contributed to efficient clearance of the virus by hepatic cytolysis along with the reduced immunosuppression resulting from infliximab discontinuation. Despite reintroduction of infliximab when HEV RNA was still detectable, we observed spontaneous resolution of chronic hepatitis E, although immunosuppressive treatment at that time was identical to that previously implicated in the chronicity of infection.

The risk for HEV vertical transmission seems dependent on viral load (12). In a model of HEV infection in pregnant rabbits, Xia et al. reported severe outcomes and a high level of transmission to offspring (13). In the case we report, despite high viral loads in the mother’s plasma throughout pregnancy, we found no HEV RNA in the newborn’s plasma. Of note, although mothers in the rabbit model were negative for HEV IgG throughout pregnancy, in the case we report, the mother was IgG positive before pregnancy, which may have helped protect the fetus from infection, although this protective role is inconsistent in previous reports of HEV genotype 3 (HEV3) infection of humans (2–4). Furthermore, despite a high sequence similarity to HEV3, rabbit HEV cross-species infections are restricted to nonhuman primates, and pathogenesis may differ from that of HEV3. In conclusion, our results and those reported by Mallet et al. (5) indicate that chronic HEV3 infection in pregnant women might resolve after pregnancy.

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Multiple Introductions of Influenza A(H5N8) Virus into Poultry, Egypt, 2017


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After high mortality rates among commercial poultry were reported in Egypt in 2017, we genetically characterized 4 distinct influenza A(H5N8) viruses isolated from poultry. Full-genome analysis indicated separate introductions of H5N8 clade 2.3.4.4 reassortants from Europe and Asia into Egypt, which poses a serious threat for poultry and humans.

In Egypt, highly pathogenic avian influenza A(H5N1) clade 2.2.1 virus was introduced to poultry via migratory birds in late 2005 (1) and is now endemic among poultry in Egypt (2). Also in Egypt, the number of H5N1 infections in humans is the highest in the world, and low pathogenicity influenza A(H9N2) virus is widespread among poultry and has infected humans (2). Despite extensive vaccination, H5N1 and H9N2 viruses are co-circulating and frequently reported (2). In 2014, highly pathogenic avian influenza A(H5N8) virus clade 2.3.4.4 was isolated, mostly from wild birds, in several Eurasian countries and was transmitted to North America. However, in 2016 and 2017, an unprecedented epidemic was reported in Asia, Africa, and Europe (3). In Egypt, during November 30–December 8, 2016, a total of 3 H5N8 viruses were isolated from common coot (Fulica atra) (4) and green-winged teal (Anas carolinensis) (5). To provide data on the spread of the virus in poultry, we genetically characterized 4 distinct H5N8 viruses isolated from commercial poultry in Egypt in 2017.

During February–May 2017, a high mortality rate was observed for 48 poultry flocks in the Nile Delta, Egypt. Up to 20 tracheal and cloacal swab samples were collected from each flock for initial diagnosis by reverse transcription PCR and virus isolation at the Faculty of Veterinary Medicine, Damanhour University (Damanhour, Egypt). Results were positive for H5N8 virus in samples for 4 flocks not vaccinated for H5 in 3 governorates (Figure). Sudden deaths also occurred in 3 broiler chicken flocks (Ck12, Ck15, Ck21) and 1 duck flock (Dk18); mortality rates were 29%–52% (online Technical Appendix 1 Table 1, https://wwwnc.cdc.gov/EID/article/24/5/17-1935-Techapp1.pdf). No epidemiologic links between farms were observed.

Positive samples were spotted onto FTA cards (6) and submitted to Friedrich-Loeffler-Institut (Insel Riems-Greifswald, Germany), where H5N8 virus was confirmed.

Figure. Characterization of highly pathogenic avian influenza A(H5N8) viruses of clade 2.3.4.4 from Egypt, 2017. A) Phylogenetic relatedness of the HA gene and schematic representation of potential precursors of different H5N8 viruses. The maximum-likelihood midpoint rooted tree was constructed by using MrBayes (http://mrbayes.sourceforge.net/). Gray indicates viruses from this study. Scale bar indicates nucleotide substitutions per site. B) Putative ancestors of the different gene segments of H5N8 viruses from Egypt characterized in this study compared with reference viruses. C) Governorates in Egypt where H5N8 viruses had been reported in domestic birds (circles) and where viruses in birds had been previously reported (stars). Inset shows study location in Egypt. Ck, chicken farm; Dk, duck farm; HA, hemagglutinin; M, matrix; NA, neuraminidase; NP, nucleocapsid protein; NS, nonstructural; PA, polymerase acidic; PB, polymerase basic.
by reverse transcription PCR and full-genome sequences (7) from 4 viruses (GISAID [https://www.gisaid.org/] accession nos. EPI1104268–EPI1104299) (online Technical Appendix 2, https://wwwnc.cdc.gov/EID/article/24/5/17-1935-Techapp2.pdf). We retrieved sequences with high similarity and all H5N8 virus sequences from GISAID and GenBank and aligned them by Multiple Alignment using Fast Fourier Transform (https://mafft.cbrc.jp/alignment/server/index.html). The most highly related viruses are summarized in online Technical Appendix 1 Table 2. We calculated sequence identity matrices in Geneious (https://www.geneious.com/) (online Technical Appendix 1 Figure 1) and studied phylogenetic relatedness to H5N8 virus isolated in Eurasia and in Egypt by using IQtree (http://www.iqtree.org/). Representative viruses were selected for generation of maximum-likelihood midpoint rooted trees by MrBayes (http://mrbayes.sourceforge.net/) using a best-fit model (GTR+G) (8) and were further edited using FigTree (http://tree.bio.ed.ac.uk/software/figtree/) and Inkscape (https://inkscape.org/en/).

The hemagglutinin (HA) and neuraminidase (NA) genes of the 4 viruses shared 95.8%–99.2% nt and 93.1%–99.4% aa identity and shared 96.5%–99.2% nt and 94.2%–99.7% aa identity with viruses from wild birds in Egypt (4,5). Other segments showed 92.6%–99.6% nt and 96%–99.7% aa identity, where the polymerase acidic (PA) genes and proteins of viruses from Dk18 showed the lowest similarity to those of other viruses (online Technical Appendix 1 Figure 1).

All viruses possess the polybasic HA cleavage site PRRRRRKR/G and contain mammal-adaptation and virulence markers (9) in polymerase basic (PB) 2 (T63I, L89V, G309D, T339K, Q368R, H447Q, R477G), PB1 (A3V, L13P, K328N, S375N, H436Y, M677T), PA (A515T), HA (T156A, A263T; H5 numbering), matrix (M) 1 (N30D, T215A), and nonstructural (NS) 1 (P42S, T127N, V149A) proteins. Therefore, protection of humans and risk assessment of bird-to-human transmission is crucial. The NS1 protein from viruses from Ck15 and Ck18 is 217 aa long because of truncation in the C-terminus, whereas NS1 protein from viruses from Ck12 and Ck21 (from chickens in the same governorate, February and May 2017) clustered together, and the same genes from viruses from Dk18 and Ck15 (from ducks and chickens in 2 governorates) clustered in 2 distinct phylogenetic groups. However, viruses from Ck12 and Ck15 have similar but not identical PA gene segments (online Technical Appendix 1 Figure 3).

These data suggest 4 different introductions of H5N8 virus into poultry in Egypt, independent of viruses isolated from captive birds (4,5). Multiple separate introductions of H5N8 virus into Europe also occurred (10). Further studies are needed to identify the source(s) of introduction. The separate introductions of different reassortants of H5N8 clade 2.3.4.4 virus from Europe and Asia into Egypt indicate a serious threat for poultry and human health.

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In most locations except for Russia, tick-borne encephalitis is mainly caused by the European virus subtype. In 2015, fatal infections caused by European and Siberian tick-borne encephalitis virus subtypes in the same Ixodes ricinus tick focus in Finland raised concern over further spread of the Siberian subtype among widespread tick species.