

months of age and were potentially preventable by MenB vaccine vaccination.

During 2012–13 through 2014–15, a total of 25 (67.5%) of 37 MenW cases in infants were confirmed by culture; 18 (49%) of these cases were phenotypically characterized as MenW:2a, a surrogate phenotypic marker for the hypervirulent ST11 MenW strain. Ten (48%) of the 21 isolates from infants during 2014–15 were MenW:2a, compared with 1 (25%) of 4 during 2012–13 (Figure, panel B). Final diagnoses reported for 20 infants included meningitis (n = 10 [50%]), septicemia (n = 3 [15%]), both meningitis and septicemia (n = 5 [10%]), and septic arthritis (n = 1 [2%]). From 1998–99 through 2014–15, six infants died of MenW IMD (case-fatality rate 3.4%). Four of those deaths occurred during the Hajj outbreak; only 1 death attributed to MenW occurred during the 3 most recent epidemiologic years.

The rapid increase in MenW cases among infants, particularly most recently (2014–15), is cause for concern, and the contemporaneous introduction of MenB vaccine into the national immunization schedule is timely. Although this vaccine is licensed for prevention of MenB disease, the antigens are not specific to this capsular group and could protect against other meningococcal capsular groups that share the same antigens as those in the vaccine. Infants and toddlers immunized with MenB vaccine are expected to develop bactericidal antibodies against ST11 MenW. Data on age distribution suggest that ≈70% of MenW cases in infants could be prevented by MenB vaccination at 2 and 4 months of age. Beginning in mid-2016, the MenB vaccine booster for children 1 year of age is also expected to protect toddlers, for whom MenW cases have also rapidly increased (3).

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## Novel Reassortant Avian Influenza A(H5N6) Viruses in Humans, Guangdong, China, 2015

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**To the Editor:** Avian influenza A(H5N6) influenza viruses have circulated among poultry in southern (Jiangxi, Guangdong) and western (Sichuan) provinces of China since 2013 (1,2). In 2014, outbreaks of H5N6 virus infection occurred among poultry in China, Laos, and Vietnam (1). In April 2014, the first case of highly pathogenic H5N6 infection among humans was detected in Sichuan Province (3); the second case was detected on December 3, 2014, in Guangdong Province (4). In December 2015, 4 humans in Guangdong Province were infected with H5N6 influenza (5,6).

To study the genetic basis of continuing human infections with this avian influenza subtype, we sequenced the complete genomes of 2 of the 4 human H5N6 isolates obtained in December 2015 in Guangdong Province. We compared these sequences with those of 1 H6N6 and 8 H5N6 influenza viruses isolated from birds in live poultry markets in this region during 2013–2015 (online Technical Appendix, <http://wwwnc.cdc.gov/EID/article/22/8/16-0146-TechApp1.pdf>) and other published genomes of H5, H6N6, and H9N2 avian influenza viruses (online Technical Appendix Table). Phylogenetic analyses of the hemagglutinin (HA) genes showed that all human H5N6 isolates belonged to clade 2.3.4.4 (online Technical Appendix Figure 1, panel A). HA and neuraminidase (NA) genes of some H5N6 viruses isolated in Guangdong Province during 2013–2014 were in the Sichuan-like lineage, but all of those from 2015 were in the Jiangxi-like lineage (online Technical Appendix Figure 1, panels A, B).

Despite the similarities of the HA and NA genes, the 6 internal genes from the 2 human isolates from 2015, A/Guangdong/ZQ874/2015 (H5N6) and A/Guangdong/SZ872/2015 (H5N6) were different from 2 human H5N6 isolates from 2014, A/Sichuan/26221/2014 (H5N6) and A/Guangzhou/39715/2014 (H5N6). The polymerase basic (PB) 2 gene from isolate A/Guangdong/ZQ874/2015 (H5N6) appears to have derived from an H6N6 virus isolated from a duck; all other genes in this isolate were derived from H5N6 viruses that have been circulating among poultry since 2013 (online Technical Appendix Figure 1, panel C; online Technical Appendix Figure 2). This isolate showed high nucleotide identity to 6 of the 8 genes (HA, 96.5%; NA, 98.2%; nucleoprotein (NP), 98.5%; polymerase acidic (PA), 98.3%; PB1, 98.1%; PB2, 98.4%) of the isolate A/chicken/Guangdong/FG594/2015 (H5N6); the identities of the matrix (M) and nonstructural protein (NSP) genes were 76.2% and 79.8% similar, respectively. This finding suggests that undetected reassortants of H5N6 may exist. The other human isolate, A/Guangdong/SZ872/2015 (H5N6), showed high nucleotide identity with A/Yunnan/0127/2015 (H5N6), an isolate collected from a person in Yunnan Province (GenBank accession nos. KT963053–60; online Technical Appendix Table), for all 8 genes (HA, 97.2%; M, 97.7%; NA, 96.8%; NP, 98.3%; NSP, 93.2%; PA, 95.9%; PB1, 96.9%; PB2, 94.0%). The 6 internal genes of A/Guangdong/SZ872/2015 (H5N6) appear to have come from the enzootic H9N2 (ZJ-HJ/07) virus lineage (online Technical Appendix Figure 1, panel C). These

**Table.** Molecular analyses of 5 influenza A(H5N6) virus isolates from humans in China, 2014 and 2015\*

Phenotypic consequences	Mutations	A/Sichuan/ 26221/2014	A/Guangzhou/ 39715/2014	A/Yunan/ 0127/2015	A/Guangdong/ SZ872/2015	A/Guangdong/ ZQ874/2015
<b>HA gene</b>						
Altered receptor specificity	S128P	T	P	P	P	P
Increased $\alpha$ 2,6-SA recognition	S137A	A	A	A	A	A
Removal of the 158N glycosylation	T160A	A	T	A	A	A
Cleavage site sequence	Q226L	Q	Q	Q	Q	Q
	Not applicable	REKRRKR↓G	REKRRKR↓G	REKRRKR↓G	REKRRKR↓G	REKRRKR↓G
<b>NA gene</b>						
59–69 del	TIINNHPQNNF	No	Yes	Yes	Yes	Yes
Osetamivir resistance	H274Y N294S	H N	H N	H N	H N	H N
<b>PB2</b>						
Increased pathogenicity in mice	L89V E627K	V E	V K	V K	V E	V E
Increased virulence and replication in mice	G309D, T339K R477G, I495V	DMGV	DTGV	DKGV	DKGV	DKGV
Enhanced transmission	D701N	N	D	D	D	N
<b>NS1</b>						
Increased virulence in mice and pigs	D92E	E	E	D	D	E
PDZ-motif	Not applicable	ESEV	ESEV	KPEV	KPEV	ESEV
Increased virulence in mice	P42S	S	S	S	S	S
<b>M2</b>						
Antiviral resistance (amantadine)	S31N	S	S	N	N	S

\*HA, hemagglutinin; M2, matrix protein 2; NA, neuraminidase; NS1, nonstructural protein 1; PB2, polymerase basic 2 amino acid.

findings show that the circulating H5N6 virus in southern China has reassorted with enzootic H6N6 and H9N2 viruses, resulting in new H5N6 viruses that are capable of infecting humans.

We compared the 2 newly sequenced genomes with 3 available genomes of human influenza virus strains in public databases to determine if they had attained key molecular features associated with increased virulence in mammals, mammalian transmissibility, and antiviral resistance (Table). The HA gene cleavage site encoded by all 5 isolates from humans showed a multiple basic amino acid motif (REKRRKR↓G), which indicates high pathogenicity in poultry. The viruses isolated from humans in 2014 had no mutations associated with reduced sensitivity to adamantane antiviral drugs, but 2 of the 3 viruses isolated in 2015 have the 31N amino acid in M2, suggesting that those 2 viruses have acquired resistance. Thus, this virus lineage could be a great threat to public health.

Although H9N2 is not highly pathogenic in poultry, it provides internal genes for the recent emergence of many novel avian influenza viruses that infect humans, such as the H5N6 virus in this study, as well as the H7N9 (7,8) and H10N8 (9) viruses. Infection with H6 subtype viruses results in no clinically significant signs of disease in poultry (10), but co-circulation of these viruses with other subtypes among poultry results in transfer of internal genes. This reassortment has resulted in a major increase in genetic diversity among the H5N6 viruses that cause human infections; therefore, low-pathogenicity viruses in poultry should also be controlled in poultry.

In summary, we isolated 2 novel reassortant H5N6 viruses from 2 patients in Guangdong Province, China. The internal genes of these strains are different from those found in the first wave of H5N6 infections in 2014. The PB2 of 2 human isolate A/Guangdong/ZQ874/2015 (H5N6) appears to have been derived from a duck H6N6 virus, and all other genes of this virus originated in circulating H5N6 viruses. In contrast, the 6 internal genes of the other human isolate, A/Guangdong/SZ872/2015 (H5N6), were derived from enzootic H9N2 viruses. Although human infection has been sporadic, the co-circulation and reassortment of this virus with other enzootic low pathogenicity influenza viruses has resulted in new reassortant viruses. Further surveillance of birds is needed to monitor the spread of this novel virus.

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