China experienced a large-scale H7N9 influenza outbreak during 2013–2014. Within 2 months after the first report, 132 patients were infected and 37 died. The case fatality (CF) rate was ~25% (1). The log-log plot of cases versus fatality on the x- and y-axes, however, yielded a slope of 0.66, indicating that the CF rate gradually decreased during the epidemic. The plot was approximated by postulating that the epidemic consisted of the original H7N9 strain with a high-virulence variant (HVV) and attenuated low-virulence variant (LVV) that spread much more rapidly than the former (2). The faster spread of LVV was expected because lower virulence allows for higher mobility of the patients that spread the virus (3). The second waves in Shanghai/Zhejiang/Jiangsu/Anhui and in Guangdong/Fujian/Hunan were reconstituted. The plots were well approximated by postulating that the LVV had a CF rate of 14% and spread twice as rapidly as did the HVV with the CF rate 80% (4).

Three years later in 2017, China experienced resurgence of H7N9. The available information is ProMed data distributed by umin.ac.jp <tani-kkr@umin.ac.jp> (Table 1). The number of the patients and that of deaths were plotted in Fig. 1. The slope was 45° suggesting homogeneous virus population and CF rate of the 2017 H7N9 epidemic obtained by extrapolating the plots to the x-axis was 17% (= [1/6] × 100). It was close to the CF rate, 14%, estimated for the LVV (by simulation) in the second wave of 2013–2014 epidemics. Had the virus continuously spread in the human communities since 2013–2014, a much lower CF rate could have been reached in comparison to 2009 with AH1pdm2009 (3). It was as if H7N9 stopped adaptation to human community since 2014.

Several pieces of data, however, indicated that a low-virulence H7N9 variant had arisen and spread among human communities by 2017 without being noticed. On the basis of serological data between December 2013 and April 2014, Lin et al. found that in Guangzhou in China, the overall age-standardized cumulative infection rate was 0.50%, corresponding to 64,000 H7N9 human infections, and the infection fatality risk was 3.6 deaths per 10,000 cases (5). Yang et al. found that, whereas none of 1,129 of the general population was seropositive, >6% of 396 apparently healthy poultry workers were HI antibody positive (HI ≥ 80), indicating the presence of a subclinical infection with H7N9 among poultry workers (6). Subclinical spread of H7N9 throughout the human population was already suggested by Watanabe et al. (7). A similar observation was made regarding H5N1: Shimizu et al. found that 84% of the serum samples obtained from workers in a live poultry market in Indonesia were A (H5N1) HI antibody positive although none of them had experienced an acute respiratory illness in previous years (8).

The plot for the 2017 H7N9 epidemic in Fig. 1 is thus compatible with the notion that the overwhelming presence of asymptomatic or subclinical H7N9 human infections went unnoticed and only the symptomatic infections were reported. This observation is consistent with the first simulation in 2013, under the assumption that the LVV with the CF rate 0.1% spread 5-fold faster than did the HVV with the CF rate 50% (2). The symptomatic infection with H7N9 in China in 2017 was due to direct exposure to birds (see the bottom of Table 1). HVV H7N9 will be maintained among the birds without being noticed because natural infections with H7N9 in chickens, ducks, and other birds are asymptomatic (1). The sequence of events proposed above is hypothetical.

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On the Case Fatality Rate: H7N9 Influenza Resurgence in China in 2017

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respiratory tracts of the influenza patients may shed light on this issue.

If selective propagation of the LVV in the human population is the rule, then the best countermeasures against the coming influenza pandemic will be to increase the transmission barrier against the HVV, as was done by the WHO in 2009.
Conflict of interest  None to declare.

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