End-of-Season Influenza Outbreaks and Possible Waning Vaccine Immunity

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BACKGROUND

We report on 3 hospital-based influenza outbreaks during the 2016 and 2017 seasons. Traditional epidemiological and viral sequencing methods were used to investigate the outbreaks, as well as influenza vaccination history.

METHODS

The outbreaks included in this study took place as follows:

Outbreak 1. Feb 2016 (Fig. 1): The first outbreak occurred during a 2-week period on an adult haematology ward, and was associated with the death of 3 patients infected with influenza A/H1N1. A total of 18 patients (mean age 58.7 years, s.d. 16.4), were potentially involved, only 3 of whom were symptomatic, with another 15 testing positive for A/H1N1dpm09.

Outbreak 2. Mar 2016 (Fig. 2+inset): an influenza A/H1N1pdm09 outbreak occurred on the adult respiratory and cystic fibrosis ward, involving 8 patients (mean age 56.1 years, s.d. 14.8), with one patient death. Diagnostic respiratory swabs were taken and patients were isolated where possible.

Outbreak 3. Mar 2017 (Fig. 2+inset): an outbreak, involving influenza A/H3N2, occurred on the same ward, involving 9 patients (mean age 58.7 years, s.d. 21.8), with one patient death.

All influenza A positive samples were sequenced and analysed for any epidemiological linkage between the patients' viruses.

RESULTS

Outbreak 1 (Fig. 3). Sequencing was successful (with whole genome, HA and NA sequences) or partially successful (with just HA and or NA partial sequences) in all but 2 out of the 20 samples (2 patients had 2 samples sequenced). The viruses from 3 patients who died had whole or partial sequences that were available for analysis. Phylogenetic sequence analysis showed that these viruses were all related to A/H1N1pdm09 subgroups 6B (S84N)/ 6B.1 (S84N, S162N, I216T), which were good matches to that season's influenza A/California/7/2009-like vaccine virus. However, there were 5-6 possible introductions of slightly different viral strains, with two main clusters of patients showing the majority of the infections with 2 of these different strains. No seasonal influenza vaccination histories were obtained for these patients.

Outbreak 2: Sequencing results showed that in the 2016 outbreak, all the patient A/H1N1pdm09 viruses were virtually identical and identified as H1N1pdm09 group 6B, with a good antigenic match to that season's influenza A/California/7/2009-like vaccine virus. Out of these 8 patients, 3 had a history of influenza vaccination, with an average interval between the date of vaccination and the positive influenza swab result of 147.7 days (s.d. 15.3 days). The patient who died in this 2016 outbreak had not been vaccinated against influenza.

Outbreak 3: Similarly, for the 2017 outbreak of A/H3N2, all the viruses were virtually, genetically identical and a match to the A(H3N2) strain (subclade 3C.2a)-like virus contained in the vaccine (i.e. the A/Hong Kong/4801/2014 (H3N2)-like virus). Out of these 9 patients, 5 had a history of influenza vaccination, with an average interval between the date of vaccination and the positive influenza swab result of 155 days (s.d. 18.2 days). It was unknown if the patient who died had had influenza vaccination.

Only Outbreaks 2 and 3 (for which vaccine histories were obtained) are discussed further below

DISCUSSION

Several previous studies from UK and Europe have described possible intra-seasonal waning vaccine effectiveness (VE) of the A/H3N2 component of the 2011/2012 trivalent inactivated seasonal influenza vaccine, but this was also in the context of a poor vaccine match to this virus that season [1-3]. Despite this, some intra-seasonal waning of vaccine immunity may have contributed to the generally poor protection against the A/H3N2 virus for that season.

Time since vaccination is an important factor in assessing the waning of vaccine immunity. Pebody et al. [3] demonstrated, using a time-stratified analysis, an adjusted VE of 53% for those vaccinated less than three months, and 12% for those vaccinated three months or more before onset of influenza-like illness (ILI). Similarly, Sullivan et al. [4] reported an A/H3N2 VE of 37% in patients vaccinated <93 days before presenting to their GPs ILI, and a VE of 18% in those presenting with ILI ≥93 days after vaccination.

An age-related effect on VE is also well-recognised. Kissling et al. [2] reported an adjusted VE of 25% among all ages (n=1,014), with a VE of 63% in adults aged 15-59 years and 15% in those aged 60 years and over.

Although this was a retrospective study, given the mean age of our patients, the long interval between influenza vaccination and ILI, and the presence of likely good antigenic and/or genetic vaccine matches for both 2016 and 2017 season locally circulating influenza viruses, intra-seasonal waning of vaccine immunity is a likely contributor to these outbreaks.

As a result of these findings, in the coming influenza season for this patient population, we will be extending our influenza immunisation program to the end of December to maintain the vaccine-induced immunity and protection of our staff and patients for as long as possible [5].

References

1. Castilla et al. Euro Surveill. 2013;18 pii: 20388.
2. Kissling et al. Euro Surveill. 2013;18 pii: 20390.
3. Pebody et al. Euro Surveill. 2013:18 pii: 20389.
4. Sullivan et al. J Med Virol. 2014;86:1017-25.
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Fig. 1. Map of main adult haematology ward involved in Feb 2016 influenza A/H3N2 outbreak. Epidemic curve is also shown (inset).

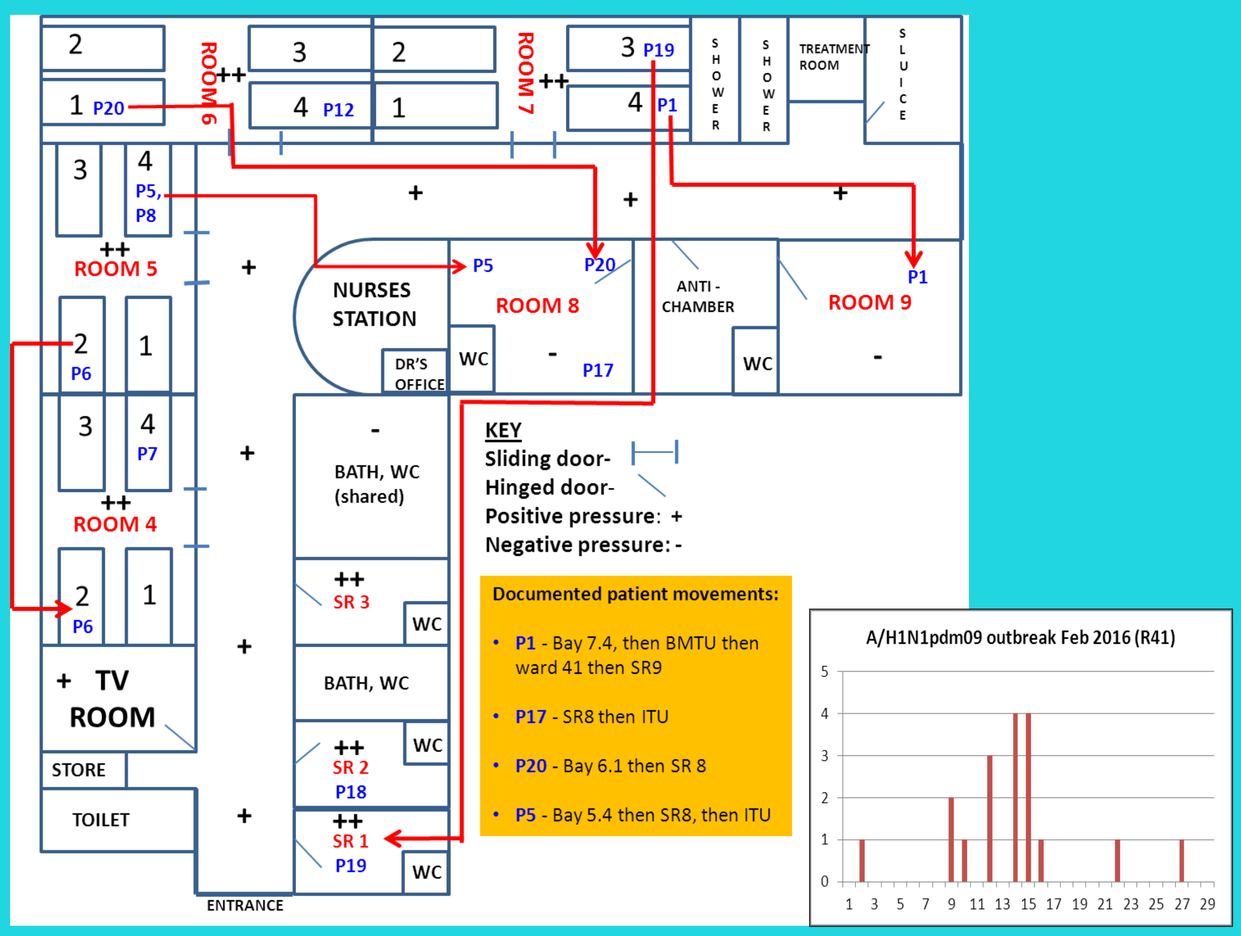

Fig. 2 (above). Map of adult respiratory/ cystic fibrosis ward with influenza outbreaks in two consecutive years: Mar 2016 (A/H1N1pdm09) and Mar 2017 (A/H3N2) . Epidemic curves of each outbreak are also shown (inset).

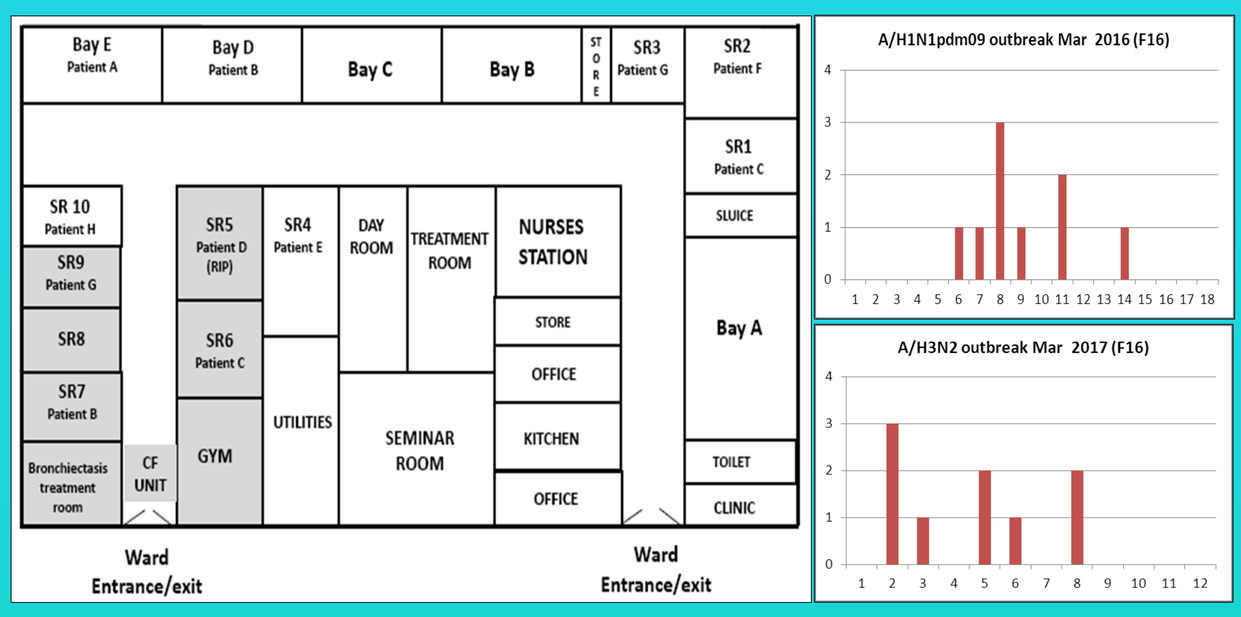

Fig. 3 A neighbour-joining phylogenetic tree of whole genome A.H1N1pdm09 sequences from the adult haematology Feb 2016 outbreak, drawn using Mega 6. Two main clusters (A and B are seen, with several outlying sequences, which were probably not part of the main outbreak. Patient code numbers are the same as in **Fig. 1.**