

Susceptibility to antiviral drugs of influenza A viruses circulating in Germany between 1998 and 2007

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Knowledge about the susceptibility to antiviral drugs of seasonal influenza viruses is important, since influenza A viruses with reduced sensitivity were even detected in untreated immunocompetent patients. Moreover, several countries have stockpiled neuraminidase inhibitors (NAI) and M2 channel protein blocker within their influenza pandemic preparedness programmes.

Using genotypic assays (pyrosequencing and cycle sequencing) as well as phenotypic assays (neuraminidase activity and plaque reduction assays) representatively selected human and avian influenza A viruses of subtype A/H3N2, A/H1N1, and A/H5N1 circulating in Germany from October 1998 to May 2007 were analysed.

The neuraminidase of subtype A/H1N1 and A/H5N1 viruses (NA-N1) showed a significant lower phenotypic susceptibility to NAI than NA-N2 (A/H3N2 viruses). No mutation known to confer resistance to NAI was detected in genotypic assays.

All analysed viruses showed full susceptibility to NAI, whereas a high incidence of influenza A viruses of subtype A/H3N2 with resistance to M2 channel protein blocker was observed. Resistance occurred due to the S31N substitution, which leads to a more than 100-fold reduced phenotypic susceptibility to M2 channel protein blocker. However, after a dramatic increase from 12% resistant viruses (2005) to 81% in the following season, a regressive trend in prevalence of resistant viruses (45%) has been detected for the last season (2007).

In view of stockpiling and a possible wider application of antiviral drugs, monitoring the emergence and spread of resistant influenza A viruses should be included as part of the ongoing influenza surveillance.

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