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Oseltamivir-resistant pandemic A(H1N1) 2009 influenza viruses detected through enhanced surveillance in the Netherlands, 2009-2010.

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Enhanced surveillance of infections due to the pandemic A(H1N1) influenza virus, which included monitoring for antiviral resistance, was carried out in the Netherlands from late April 2009 through late May 2010. More than 1100 instances of infection with the pandemic A(H1N1) influenza virus from 2009 and 2010 [A(H1N1) 2009] distributed across this period were analyzed. Of these, 19 cases of oseltamivir-resistant virus harboring the H275Y mutation in the neuraminidase (NA) were detected. The mean 50% inhibitory concentration (IC(50)) levels for oseltamivir- and zanamivir-susceptible A(H1N1) 2009 viruses were 1.4-fold and 2-fold, respectively, lower than for the seasonal A(H1N1) influenza viruses from 2007/2008; for oseltamivir-resistant A(H1N1) 2009 virus the IC(50) was 2.9-fold lower. Eighteen of the 19 patients with oseltamivir-resistant virus showed prolonged shedding of the virus and developed resistance while on oseltamivir therapy. Sixteen of these 18 patients had an immunodeficiency, of whom 11 had a hematologic disorder. The two other patients had another underlying disease. Six of the patients who had an underlying disease died; of these, five had received cytostatic or immunosuppressive therapy. No indications for onward transmission of resistant viruses were found. This study showed that the main association for the emergence of cases of oseltamivir-resistant A(H1N1) 2009 virus was receiving antiviral therapy and having drug-induced immunosuppression or an hematologic disorder. Except for a single case of a resistant virus not linked to oseltamivir therapy, the absence of detection of resistant variants in community specimens and in specimens from contacts of cases with resistant virus suggested that the spread of resistant A(H1N1) 2009 virus was limited. Containment may have been the cumulative result of impaired NA function, successful isolation of the patients, and prophylactic measures to limit exposure.

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