

Antiviral Drug Resistance of Influenza Viruses in Europe, Winter 2007/2008

Preliminary results of surveillance (1) of the antiviral drug susceptibility of influenza viruses circulating in Europe has revealed that a significant proportion (13%) of the A(H1N1) viruses, currently the predominant viruses, are resistant to oseltamivir (Tamiflu), the most widely used anti-influenza drug, but retain sensitivity to zanamivir (Relenza) and amantadine/rimantadine.

Although early in the influenza season, the presence of oseltamivir-resistant viruses circulating in the community in at least 4 European countries (Denmark, France, Norway and the United Kingdom) is in marked contrast to the previous winter seasons of 2004/2005, 2005/2006 and 2006/2007, when little or no evidence of oseltamivir resistance was detected in over nine hundred isolates from 24 countries (1).

A total of 148 influenza A(H1N1)viruses isolated during November and December have been tested so far this winter from ten European countries (2). Twelve of 16 Norwegian isolates (75%), 4 of 19 (21%) French isolates, 2 of 75(3%) United Kingdom isolates and 1 of 10 (10%) of Danish isolates carry the same mutation, substituting histidine by tyrosine at residue 274 (H274Y) of the neuraminidase, which confers high level resistance to oseltamivir. All of these viruses remain sensitive to the other anti-neuraminidase drug zanamivir and to the anti-M2 drugs amantadine and rimantadine.

The resistant viruses have been isolated from both adults and children, ranging from 1 month to 53 years in age, with the majority of viruses being isolated from adults. So far, there is no information that any of these viruses, in any country, has been obtained from a person who has either been treated or been in close contact with another individual who has been treated with oseltamivir. We, therefore, conclude that the identification of this oseltamivir resistance mutation in a substantial proportion of circulating viruses, particularly in Norway, is the first clear evidence that influenza A(H1N1) virus with the H274Y mutation can readily transmit between individuals. More extensive surveillance globally is required to establish the relative prevalence and geographical distribution of these resistant viruses and to evaluate their potential impact on the effectiveness of drug use.

As of week 03/08, 13 European countries have reported significant influenza activity (Austria, Bulgaria, France, Hungary, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Slovenia, Spain, Switzerland and the UK (3)). The predominant virus circulating in most countries has been A(H1N1) similar to the A/Solomon Islands/3/2007 vaccine strain, although limited circulation of influenza A(H3N2) and influenza B is also reported in several countries). Over three thousand influenza isolates have been identified within Europe so far this winter season, although most of them have not yet been tested for antiviral susceptibility.

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(1) Surveillance of antiviral susceptibility of circulating influenza strains in Europe has been established since 2004 through the EU funded VIRGIL programme in collaboration with EISS and WHO. Testing of virus isolates is carried out at the Health Protection Agency in London

(2) Methodology used for establishing *in vitro* susceptibility of influenza virus strains to oseltamivir and zanamivir is described by the Neuraminidase Inhibitor Susceptibility Network (NISN) in J Clin Micro (2003) 41 742-50

(3) European Influenza Surveillance Scheme. The influenza season has started in a number of European countries. EISS Weekly Electronic Bulletin 2008. 18 Jan 2008: 249 available at <http://www.eiss.org>
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