

A(H1N1) virus resistance to Oseltamivir in the Southern Hemisphere – 2008 Influenza season September 12, 2008

An [article](#) published in the *New England Journal of Medicine* dated 04/09/09 describes a severely immunocompromised patient who died with concurrent infection with an oseltamivir-resistant A(H1N1) influenza strain (H274Y mutation on the neuraminidase gene). Recently available data on oseltamivir-resistant A(H1N1) strains are presented below:

1. NORTHERN HEMISPHERE

- In January 2008, several European countries notified and documented oseltamivir-resistant A(H1N1) influenza strains (cf. [WHO/ECDC](#) and [BHI](#)).
- Cases documented at the time and since that date suggest a clinical presentation in patients with resistant A(H1N1) strains which does not differ significantly from that of patients infected with non-resistant strains ([WHO/ECDC](#)).

2. SOUTHERN HEMISPHERE

High proportions of oseltamivir mutation-resistance in A(H1N1) strains have been found during the 2008 influenza season in the southern hemisphere ([WHO](#)).

2.1. In South Africa

- As of 11/08/08, according to [NICD](#), a total of 283 A(H1N1) strains have been tested, 129 of which were documented for the H274Y mutation (PCR and sequencing).
- All 129 (100%) strains showed a mutation resistance to oseltamivir.
- Treatment with oseltamivir was documented in only one of the 129 sampled patients.
- These strains were all collected by a community-physician - based influenza-like illness surveillance network.
- These sampled patients are all documented for clinical signs. None of the sampled patients with oseltamivir-resistant A(H1N1) presented signs of severe influenza.
- South African health authorities plan to develop a specific surveillance system for severe influenza in the future.
- Available data from surveillance systems in South Africa show that the 2008 epidemic began earlier than in 2007 (peaking during the second week of July).
- In August 2008, South-African authorities reported 413 influenza isolates tested: 356 (86%) were influenza A and 38 (9%) influenza B. Among 224 influenza A samples tested, 218 (97%) were A(H1N1).

2.2. In Australia

- From 01/01/2008 to 29/08/2008, 3,458 cases of influenza have been reported. A total of 8,327 biologically-confirmed influenza cases were reported during the same period in 2007 (see Figs. 1 and 2).
- In 2008, 30% of cases notified and tested were influenza A and 65% influenza B.
- As of 20/08/2008, 10 of 10 (100%) A(H1N1) strains tested showed mutation resistance to oseltamivir.

Figure 1. Number of notifications of laboratory-confirmed influenza, NNDSS, Australia, 01/01/2003 – 29/08/2008, by week of diagnosis ([source](#)).

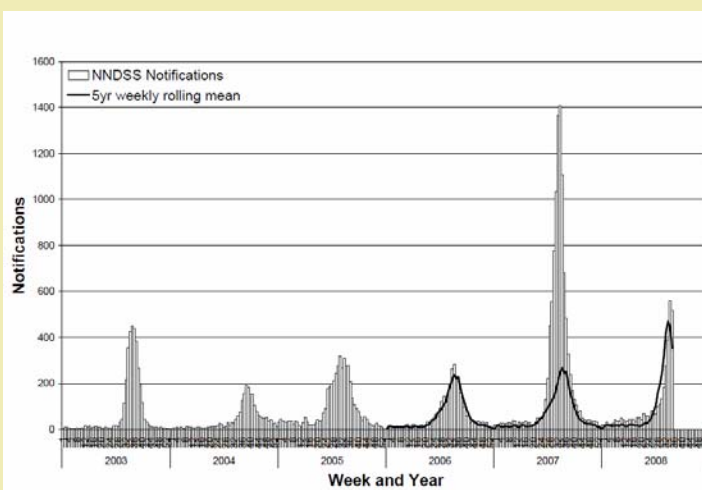
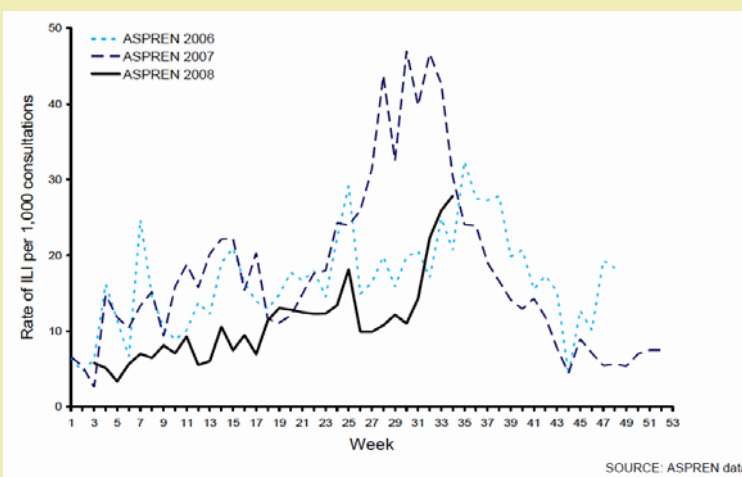


Figure 2. Rate of ILI reported from ASPREN in Australia from 01/01/2006 to 24/08/08, by week ([source](#)).

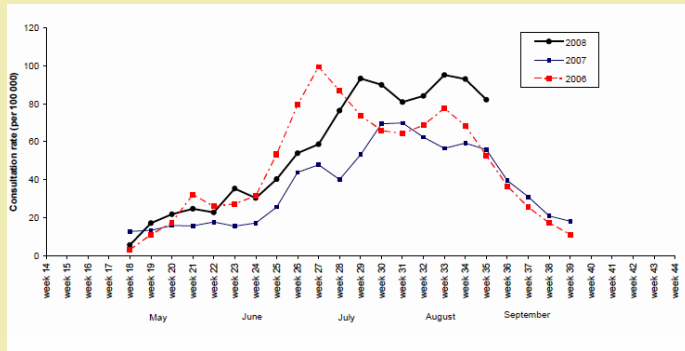


SOURCE: ASPREN data

2.3. In New-Zealand

- The 2008 epidemic seems more active than in 2007 (Fig 3).
- Among 566 strains analyzed during week 33 (ending 15/08/08), 158 (28%) were influenza A (typing ongoing), 175 (31%) were A(H3N2) and 232 (41%) were influenza B.

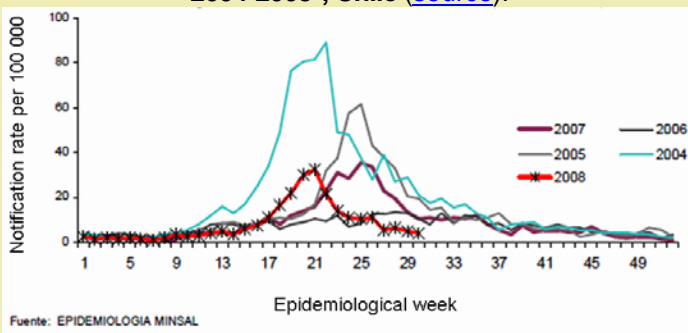
Figure 3. Weekly consultation rates for influenza-like illness in New Zealand, 2006-2008 ([source](#))



2.4. In Chile

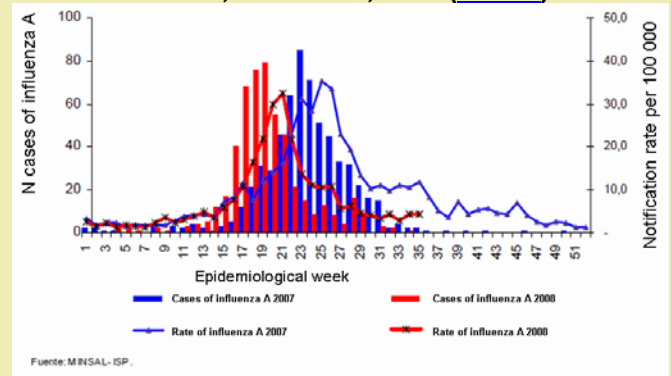
- Data collected by a community-based surveillance system shows a 2008 epidemic which began earlier but with a comparable dynamic to that of 2007 (Fig. 4 and 5).
- Among 54 strains typed in 2008, 53 (98%) were influenza A and one was influenza B.
- According to [WHO](#), 4 of 32 (12.5%) A(H1N1) strains tested presented mutation H274Y.

Figure 4. Rate of ILI notification in a sentinel network, 2004-2008*, Chile ([source](#)).



* As of epidemiological week 35.

Figure 5: Number and rate of ILI notification in a sentinel network, 2007-2008*, Chile ([source](#)).



* As of epidemiological week 35.

3. COMMENTS

The death of a patient associated with influenza infection is not an unexpected event, especially in a severely immunocompromised patient. The causal link between the oseltamivir-resistance of the strain and the patient's death remains unclear.

Available data on the circulation of influenza during the 2008 season in the southern hemisphere show a varying profile in terms of strains, chronology and intensity. Data from South Africa (a majority of A(H1N1) circulating strains) and Australia (a majority of B strains associated with A(H3N2)) show a very high proportion (100%) of A(H1N1) strains with *in vitro* resistance to oseltamivir.

This case, therefore, raises the issue of treatment in patients with a severe form of influenza due to an oseltamivir-resistant strain. Available surveillance data, however, do not reflect an increase in the intensity of the seasonal influenza epidemic or a higher proportion of clinically severe forms during the 2008 season in the Southern Hemisphere.