

New influenza A(H1N1) vaccination

Influenza A and B viruses cause annual outbreaks of 'seasonal flu'. The respiratory infection may cause fever, cough, pains and weakness. Immunity is built up either by natural infection or by vaccination. However, the virus evades this immunity with minor changes so annual updates of the vaccine are necessary. Each year, between 250,000–500,000 people around the globe die of seasonal flu.

Every now and then a new variant emerges against which humans have no immunity. In April 2009 a new influenza A(H1N1) virus was recognised. The virus contains a combination of genes of swine, avian and human influenza viruses, apparently has circulated in the swine population, crossed the species barrier to humans and can be transmitted from human to human. Deaths were reported in several countries. In June 2009 the WHO declared a pandemic, the hunt was on to protect the general public.

By August 2009 the virus had been characterised with respect to virulence [1]. More efficient human-to-human transmission was shown than currently circulating H1N1 viruses. The virus replicates in lungs, causing viral pneumonia with considerable pathogenicity. By early November 2009 WHO estimated the worldwide deaths attributable to the new virus at around 6,250.

Modern pharmaceutical research and technology has brought us a safe vaccine to protect the general public against the new influenza virus – at least in the short term – within barely six months. What an achievement! Since the outbreak of avian H5N1 flu in 1997, the industry had been preparing to mass produce pandemic vaccines. The challenges are impressive. How could sufficient antigen be produced in a short time? At the same time as the seasonal flu vaccine, hundreds of millions of extra vaccine doses had to be produced. For those vaccines produced on eggs, e.g. Focetria and Pandemrix, each dose requires two sterile fertilised GMP-certified chicken eggs. The new influenza A(H1N1) has poor antigenicity and two strategies have been followed to increase protection: 1) addition of adjuvant and 2) booster vaccination [2]. With these antigen-sparing strategies the production of sufficient vaccines became feasible. Novartis has experience with more than 45 million seasonal flu vaccine doses with their MF59 adjuvant, GSK lags somewhat behind with their AS03 adjuvant [3, 4].

As the vaccine is distributed in most cases as a multi-dose vial, a preservative is needed. Thiomersal has a strong track record for this, notwithstanding some rumours regarding its potential neurotoxicity [5]. Methylmercury, which may accumulate and will be excreted very slowly, differs from ethylmercury in thiomersal, which has a short half-life with little retention. A large Cochrane analysis has confirmed the safety of the preservative, as did a 14-year, 1.4 million-participant Finnish clinical study. So, it seems warranted for the EMEA to license Celvapan, Focetria and Pandemrix at high speed. However, debate around the safety of the vaccine will continue, because there will be considerable mortality and morbidity in these large cohorts anyway, regardless of vaccination [3]. But now these events will occur after vaccination, so many will assume a relationship. Governments will need top communication skills to explain that the epidemiology of death is very unlikely to be affected by the large number of vaccinations.

In October 2009 a first clinical trial was published [7] and the outcome confirmed expectations. So, if a new wave of 'swine flu' strikes, protection will be required. With this new influenza not only the usual risk groups but young children and pregnant women are at risk. The first wave of the pandemic was relatively mild in Europe. Pandemics are characterised by their recurrence, so it is possible that a new wave of infection is reaching your country, where it may possibly coincide with seasonal flu.

Why did EJHP not discuss the pandemic earlier? At first only limited information was publicly available, kept changing, and differed by country. It was not feasible to add value in a low-frequency publication like EJHP on top of the excellent websites from the EMEA, WHO and the local websites in your country. However, given a debate around the vaccination strategy I hope that the references will provide you with sufficient information to participate with objective and scientifically valid information [8].

On behalf of the editorial board of *EJHP Practice* and the staff of the publishing house, we wish you all a pleasant Christmas and hope you will enjoy reading your journal.

References

1. Itoh Y, et al. *Nature*. 2009;460:1021.
2. De Jong M, Sanders RW. *BMJ*. 2009;339:B4014.
3. Podda A, Del Giudice G. *Expert Rev Vaccines*. 2003;2(2):197-203.
4. Vogel FR, et al. *Expert Rev Vaccines*. 2009;8:483-92.
5. Coombes R. *BMJ*. 2009;338:1528-31.
6. Black, et al. *Lancet*. 2009. doi:10.1016/S0140-6736(09)61877-8.
7. Zhu FC, et al. *N Engl J Med*. 2009;361. doi:10.1056/NEJMoa0908535.
8. Rappuoli R, et al. *Science*. 2009;326:50.



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