Vaccines for Swine Flu

Updated 1 May 2009

What is swine flu?

Swine flu is formally known as "swine influenza A(H1N1)".

What is the history of swine influenza in humans?

Strains of swine influenza have co-circulated with the more common human influenza A (H3N2) strain throughout the 20th Century and have been isolated occasionally. Variants of H1N1 caused the 1918 Spanish Flu and a much less severe pandemic in 1977.[1] In 1977, most persons over 20 years old had immunity to the virus, so illness was confined to children and adolescents.

What is this new swine flu?

The majority of genes in this new swine flu virus are similar to those of influenza swine viruses that have circulated in US pigs since approximately 1999; however, two genes (coding for proteins NA and M) are similar to those of a different swine flu variant.[2] This particular combination of H1N1 genes appears to be new.

Will the current annual ("seasonal") vaccine protect against swine flu?

A vaccine for H1N1 variants exists. The seasonal "flu shot" FLUVAX® contains protein from an influenza A (H1N1) variant (strain A/Brisbane/59/2007).[3] The selection of which strain to include in the seasonal vaccine is based on recommendations from the World Health Organisation (WHO), using best-available scientific information at the time of the recommendation.[4] The current WHO recommendation for the 2009/2010 northern hemisphere influenza season is also for H1N1 strain A/Brisbane/59/2007.[5]

A bioinformatics comparison of the main protein (HA) from the new strain of swine flu (A/California/04/2009, from a 10 y.o. boy in San Diego) and the vaccine strain (A/Brisbane/59/2007) shows they are approximately 30% different. There are significant regions of difference, suggesting that the current H1N1 vaccine will not protect well against the new swine influenza A(H1N1) variant.

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[1] 1 Oxford, J.S. (2000). Rev. Med. Virol., 10, 119-133.
[2] www.cdc.gov/mmwr/preview/mmwrhtml/mm58d0421a1.htm
[3] FLUVAX® Datasheet
[4] http://www.who.int/csr/disease/influenza/recommendations2009south/en/index.html
[5] http://www.who.int/csr/disease/influenza/recommendations2009_10north/en/index.html

What non-seasonal vaccines may become available?

The Australian Health Management Plan for Pandemic Influenza[6] defines two main nonseasonal vaccine types that might be able to respond to pandemic threat:
(1) candidate influenza vaccines, and
(2) customised influenza vaccines.

Candidate vaccines are unlikely to be an exact match to the pandemic strain but may nevertheless offer some protection until a customised vaccine becomes available. Customised vaccines are specific and based on genetic information about the actual pandemic virus strain.

How are influenza vaccines made?

In Australia, influenza vaccines are made using old technology based on the use of embryonated chicken eggs. The production process using egg-based technology takes months.[7]

Internationally, influenza vaccines are being made using modern cell culture technology.[8] Novartis produces the Optaflu® seasonal vaccine using cell culture; the vaccine has received regulatory approval for use in humans.[9][10]

Other leading companies such as Baxter International Inc. and Sanofi Pasteur have cell-culture influenza vaccine technology. Cell culture manufacturing offers significant advantages over egg-based technology in the face of pandemic threat (see "What about new vaccine technologies?").

When will a vaccine be available in Australia?

It will take months for the first doses of vaccine to become available in Australia. The Australian plan for pandemic influenza states that it will take up to 12 months before there is enough vaccine for all Australians to receive a full course, and develop immunity, once production of a customized pandemic vaccine starts.[11]

CSL has announced it will shortly receive isolates of swine flu and will start developing a vaccine for swine flu.[12] The key first step will be to establish a strain that is able to be cultivated in eggs. CSL will reportedly use conventional techniques for egg adaptation, as well as modern genetic synthesis techniques that are well established in the

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[6] http://www.flupandemic.gov.au/internet/panflu/publishing.nsf
[7] http://www.gsk.com/press_archive/press2005/flu_backgrounder.pdf
[8] http://www.ifpma.org/Influenza/index.aspx?56
[9] http://www.medscape.com/viewarticle/558192_print
[10] http://www.novartis-vaccines.com/press-room/news/20070427_Optaflu.shtml
[11] Australian Health Management Plan for Pandemic Influenza 2008
[12] http://www.news.com.au/heraldsun/story/0,21985,25401869-664,00.html

biotechnology industry. CSL hopes to have a vaccine in full manufacturing mode by early July, consistent with the timing in the Australian pandemic plan for the first doses to become available within months, with complete vaccination within 12 months.

CSL's virus adaptation work will give critical information about the possible speed of supply and likely vaccine effectiveness, which are currently unknown. Adaptation will determine how closely matched the vaccine can be to the actual swine flu strain. Many influenza viruses do not grow well in eggs and so the process of adaptation (or/and genetic synthesis) makes them compatible with the production technology. It also makes the vaccine less like the harmful virus (i.e. more like a *candidate vaccine* and less like a *customised vaccine* – see Australian definitions above).

In developments that may help CSL, the US CDC in collaboration with a leading biotechnology company (Medimmune, Maryland USA) has reportedly found that the swine flu virus grows slowly in eggs.[13] In response, the CDC has started creating a reference virus strain which they aim to ship to manufacturers in the second week of May. However, Dr. Ruben Donis from the CDC cautioned that all timelines are approximate as "This is biology, not mathematics".

The US Government is still deciding whether to order production of a swine flu vaccine.[14] Customised manufacture may interrupt ongoing work to create the seasonal vaccine for the northern hemisphere influenza season (containing vaccine strain A/Brisbane/59/2007). An alternative approach may be to reconfigure the seasonal vaccine so that it might contain swineflu vaccine components.[15] This approach will not impact Australia until next year's flu season.

What about new vaccine technologies?

Internationally, vaccine technology has moved forward quickly in recent years, motivated by the threat of avian influenza and SARS.

Cell culture techniques that use modern biomanufacturing technology have been developed for the manufacture of pre-pandemic and seasonal vaccines (see above). Instead of using eggs, cell-culture techniques move from small flasks to engineered bioreactors that produce thousands of litres of material at a time. This is a common process used, for example, to produce polio vaccines, and is now being used and developed for influenza vaccine manufacture.[16]

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[13] http://news.yahoo.com/s/ap/20090428/ap_on_he_me/us_med_swine_flu_vaccine
[14] www.breitbart.com/article.php?id=D97QUM385&show_article=1
[15] http://www.latimes.com/features/health/la-sci-swine-vaccine29-2009apr29,0,4276069.story
[16] http://www.gsk.com/press_archive/press2005/flu_backgrounder.pdf

Cell culture techniques can significantly reduce, to 3-6 months, the time needed to manufacture large amounts of vaccine against an emergent virus such as swine flu. Cell culture techniques also reportedly have other advantages:

> "Virus cultivation utilizing the Novartis proprietary cell [culture] line as an exclusive host offers the possibility of more robust virus proliferation since most circulating viral strains are unable to replicate in chicken eggs. In a next generation of products, it also offers the possibility for vaccine seed strain development that more closely matches the original "wild" virus because cell culture technology eliminates the need for passage through eggs where the virus may be forced to adapt in order to replicate. As a result, the antigen included in the vaccine may express more authentically the surface of the wild type virus, potentially translating into a better immunogenic and effective response."[17]

Cell culture techniques are expected to become the preferred manufacturing method for influenza vaccines. It has been reported that the US Centre for Disease Control and Prevention has begun sharing the seed virus with vaccine manufacturers who use cell culture.[18]

Next-generation cell culture techniques based on Baculovirus technology are also being used in the US to develop next-generation particle vaccines and those based on recombinant protein. These vaccines are already being trialed in humans and show both effectiveness and simplified manufacturing routes. Baculovirus technology is used by GSK to manufacture a cervical cancer vaccine approved for use in humans.

Beyond cell-culture techniques, new methods including those based on vaccine particles and nanotechnology promise to be able to deliver scaled amounts of vaccine within days or weeks, in response to emerging viruses such as swine flu. These methods will provide vaccine precisely matched to the threat strain, without the complexity of egg adaptation or cell-line development (for cell-culture techniques). These methods will radically change the way in which the world reacts to, and ultimately overcomes, the ongoing threat of pandemic viral disease.

Professor Anton PJ Middelberg FIChemE FTSE
Australian Institute for Bioengineering and Nanotechnology
Centre for Biomolecular Engineering
The University of Queensland, Australia
Telephone: 0434-603-093
a.middelberg@uq.edu.au

[17] http://www.novartis-vaccines.com/press-room/news/20070427_Optaflu.shtml
[18] http://www.guardian.co.uk/world/2009/apr/27/us-swine-flu-cdc