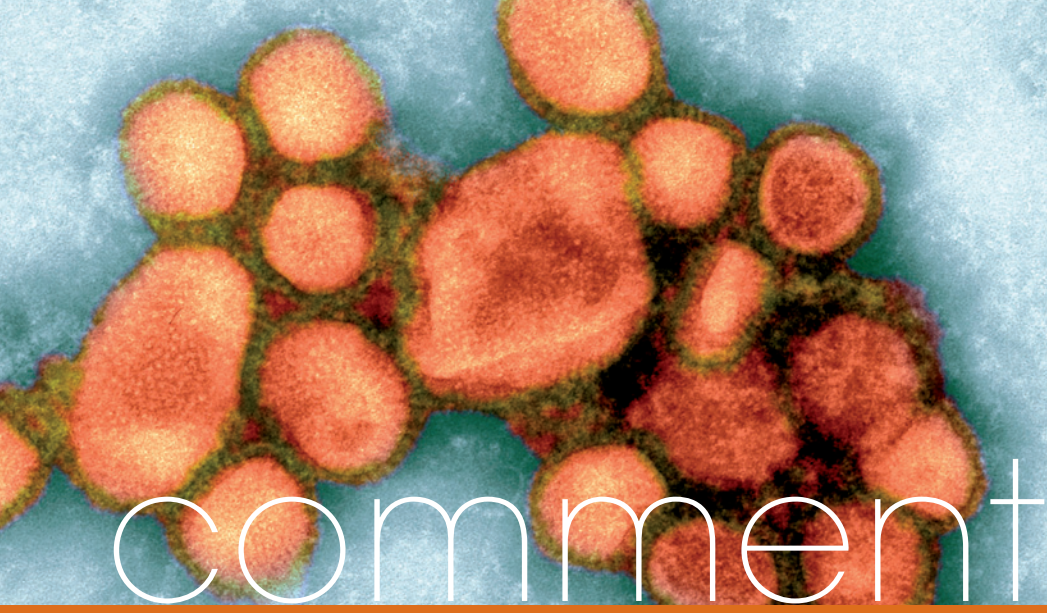

comment

Sw-HINI-ng on about 'flu again

Hot on the heels of bird 'flu comes a novel influenza A H1N1 strain to cause fears of a worldwide pandemic. Influenza virologist **Wendy Barclay** ponders on how effectively we are prepared to cope if disaster strikes..

In the spring of 2009 we have once again had a pertinent reminder of the aleatoric behaviour of influenza virus evolution. As if pulling the handle of the reassortment slot machine, Nature has rung up a viral genetic constellation that is an octagenic 'jackpot' in terms of posing the latest pandemic threat to man. Swine-origin influenza H1N1 has crossed a species barrier in Mexico from pigs to people and then spread beyond, stealing across the border to the US and hitching on air travel routes to new continents. Causing a mild upper respiratory illness with case fatality of around 0.1%, why should we be worried about swine 'flu? At least this is not the dreaded H5N1 bird 'flu pandemic that influenza virologists have been wittering on about for a decade!

If the events of the recent months reinforce any one thing about influenza, that is its unpredictability. If the virus survives the unfavourable summer climate, and our Lilliputian attempts to restrain its circulation by administering the antiviral drug Tamiflu to cases and their contacts, it may infect many more of us during the winter months. Moreover, every additional human infection increases the potential for the virus to gain mutations that enhance its replicative capacity in human cells. This might be achieved by the accumulation of point mutations in swH1N1 viral genes, or by acquiring whole gene segments from a human influenza virus by reassortment with a circulating seasonal strain. The nature of such swH1N1 derivatives is unknown at present, but is of significant consequence to those involved in planning appropriate public health measures. Does this virus, like currently circulating strains of human H1N1, have the capacity to tolerate mutations that render it resistant to Tamiflu? If the virus acquires a set of polymerase genes by reassorting with seasonal human H3N2 or H1N1 subtype influenzas, will its replication and transmissibility in humans increase? Such questions could be addressed in advance by employing the technique of reverse genetics to create these viral possibilities inside high containment laboratories so we can study their behaviour before nature throws them at us. This type of approach was employed last year by workers at the CDC in Atlanta USA to assess whether the highly pathogenic avian influenza virus H5N1 had the potential to recombine with a circulating human strain of virus. The same technique can also allow the rapid generation of a tailor-made swine 'flu vaccine and the development of important diagnostic reagents that will help to differentiate between infections with swine 'flu and other human circulating strains in the coming months.

The swine 'flu zoonosis has served as a timely dress rehearsal of pandemic plans under a situation that could not have been kinder. Has the intense research focus on H5N1 avian influenza virus been worth anything in our ability to deal with this new event? Ten years ago we would not be considering a 'pre-pandemic' vaccine because we did not believe that there would be adequate cross protection with related but non-identical strains. Now we know that by using different formulations for influenza immunization such as incorporating new adjuvants, these issues can be overcome. Nonetheless, vaccine manufacturers still lack capacity to deal with the increased demand that results from a pandemic threat, and difficult decisions about interrupting seasonal vaccine manufacture and prioritizing target groups for the monovalent (pre-) pandemic vaccines will be necessary. The realization that we still cannot supply sufficient vaccine to immunize the world's population may prompt a re-look at live-attenuated flu vaccines as a 21st century strategy to deal with the inevitable but unpredictable influenza pandemics of the future.

▲ Coloured TEM of H1N1 virus particles from the April 2009 outbreak. *AMI Images / Science Photo Library*

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Further reading

Chen, L.M., Davis, C.T., Zhou, H., Cox, N.J. & Donis, R.O. (2008). Genetic compatibility and virulence of reassortants derived from contemporary avian H5N1 and human H3N2 influenza A viruses. *PLoS Pathog* 4(5), e1000072. doi:10.1371/journal.ppat.1000072

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