

An influenza smiley

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In recent years hundreds of scientists, epidemiologists, virologists, and other microbiologists have been conducting investigations, creating models, and making predictions in the field of emerging infectious diseases. Despite this, and to the best of my knowledge, none of them ever foresaw the establishment of West Nile virus in North America, the SARS outbreak, the spread of chikungunya across the Indian Ocean and, more recently, the new influenza A H1N1 swine virus. After this virus emerged in humans the WHO concluded that an influenza pandemic was unavoidable; apparently everyone has already forgotten avian influenza. In view of recent events, do we still need to worry about this chicken virus?

Influenza H5N1 is a serial killer when it infects humans or other mammals, and for this reason deserves our highest respect. Still, like any other entity, it also has its weaknesses, the chief one being that it is not transmitted efficiently from one human to another. Avian influenza has circulated among animals for more than 12 years now and, in the final analysis, has infected humans only episodically or accidentally; the small epidemics we have observed are far removed from a catastrophic pandemic. Lack of transmissibility is the sole reason we have been spared an avian pandemic, for otherwise this virus has all the weapons required: easy airway transmission; a high viral load in infected cases; and lack of previous immunity in humans. The recipe for a catastrophic pandemic is there, but one essential ingredient is lacking; fondue without cheese.

In 2009 avian H5N1 virus is still an animal virus, ill-equipped to infect humans. Its ability to mutate, to exchange genes and adapt, however, is phenomenal and this represents a potential threat. Whether we can cease to regard this virus as a threat is a matter of faith and not of scientific evidence. It is a magician with plenty of tricks in its bag; animals and humans are its playground, and it can escape from much of the immune response. But is efficient human-to-human transmission among its bag of tricks? Some experts no longer believe that the H5N1 influenza will jump the species barrier, while others consider that continued vigilance is necessary. I would argue that it is not because a pig has shown up in the front yard that we should ignore the chicken coop at the back. Though, admittedly, it is difficult to

be in front and at the back of the house at the same time.

What is this swine H1N1? Pigs are known hosts for all kinds of different influenza viruses, including human and avian varieties. They are often depicted as ideal "mixing vessels" for influenza, where all types of different influenza viruses can mix together with the potential to form new combinations – a reservoir for emerging viruses. The H1N1 genes code for the surface glycoproteins of the virus and are the main target of the immune response. The present virus's H1N1 genes are predominantly porcine in origin, but they also contain pieces related to human and avian influenza viruses and thus represent a previously unknown subtype. Human and porcine H1N1 viruses are close relatives but, thanks to a number of differences distributed along the genome, they can be easily distinguished. These differences cause subtle phenotypical changes resulting in either specific adaptation to swine or humans or, for some, in the potential ability to cross the species barrier. After a time period of unknown duration in swine, the present H1N1 virus has just crossed this barrier, and by so doing, in contrast to the H5N1 avian virus, it has also acquired the ability to be transmitted by respiratory droplets between humans and to establish a human reservoir. A question mark remains: why was this virus not previously identified in surveillance systems in animals? Identification of the initial animal reservoir may only be a question of time: H1N1 has recently been identified in Canadian pigs. However, given the very rapid pace of events, we need more observations and epidemiological data before definite conclusions can be drawn.

Fortunately, at the moment, the virulence of the virus seems to be limited and at worst similar to severe seasonal human influenza. Again, this is not certain, and the observed mortality in Mexico is disturbing. The age distribution of hospitalised cases is also peculiar, since the median age seems to be approximately 15 to 20 years. We must also bear in mind that most proven cases in the United States or Europe have been treated by neuraminidase inhibitors, an intervention that may change the course of the disease and prevent complications. At present we have a flood of incomplete information and few evidence-based

conclusions. Hints do not equal proof. The pessimists will say “Yes, the mortality is low, but given the virus’s capacity to mutate it might well become more virulent”; but the opposite could also easily occur and there are no scientific reasons at present to make assumptions either way. Since the virus was isolated only a few weeks ago, our knowledge of it is still limited. Animal models, *in vitro* studies etc. are lacking. Two points are not presumptive, however: the first is the fact that the strain is sensitive to neuraminidase inhibitors, the only antiviral agents available against this virus; and the second is that only one mutation can lead to resistance. This has already occurred in the human H1N1 virus, in the absence of strong selective drug pressure. Given the number of oseltamivir pills distributed recently, the rapid emergence of resistant strains will not be surprising (and may indeed even be expected).

Another issue is the immune response. It appears that the current H1N1 vaccine affords no protection against this new swine strain, but whether previous H1N1 infection with other natural strains could provide some kind of protection requires investigation. Certainly the present outbreak will complicate the design of new vaccines. In addition to the usual human strains, this new swine strain will need to be added to new vaccines, at least for the foreseeable future. At the diagnostic level this will also complicate the life of any microbiologist, since we will need to design new tests specifically adapted to the emerging strain.

For centuries influenza has managed to persist, both in animals and humans, and thus there is

nothing surprising in the present events. Quite simply, Mr Public Health has been dating a girl, Miss Avianflu, for the last 12 years. After so many years, he has finally succeeded in inviting her over for dinner. The chicken noodle soup was ready when the bell rang. With a beating heart, he ran to open the door ... and in walked a corpulent Texas farmer with a broad grin on his face and a tequila bottle in his hand, asking “Where’s the pork barbecue party?”

References

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