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disease, a finding that, although not previously noted in influenza, has been reported for some viral diseases.\(^5\)

During the influenza pandemic of 1957, which was caused by the H2N2 subtype, individuals who had previously been infected with the H1N1 virus were less likely to be infected with H2N2 influenza than were those who had not.\(^6\) The low incidence of severe H5N1 infections in elderly compared with younger people might be related to the presence of cross-protective antibodies to neuaminiadase that are induced by seasonal influenza A H1N1 viruses.\(^7\)

Overall, we postulate that antibodies to pre-1957 influenza A H1N1 viruses protected elderly people against pandemic A H1N1 virus infection, but consequently affected the development of heterosubtypic immunity and the disease outcome of H7N9 virus infections. The rate and timing of pandemic A H1N1 virus infections might have revealed the differences in H7N9 disease outcome, by contrast with historical infections with seasonal influenza A H3N2 viruses. This counterproductive imprinting of immunity might increase susceptibility to H7N9 virus infection. For that reason, older individuals should be given priority for vaccination if sustained person-to-person transmission of H7N9 viruses emerges. To obtain a better understanding of the role of imprinting of the adaptive immune system in H7N9 disease severity, prospective cohort studies in which cross-reactive T-cell immunity and virus-specific serum antibodies are tested for are imperative before possible wider spread of the virus.

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1. Gao R, Cao B, Hu Y, et al. Human infection with a novel avian-origin influenza A (H7N9) virus. N Engl J Med 2013; 368: 1888–97.
2. WHO. Number of confirmed human cases of avian influenza A(H7N9) reported to WHO. http://www.who.int/influenza/human_animal_interface/influenza_h7n9/08_ReportWebH7N9Number.pdf (accessed July 3, 2013).
3. MCEIRS. http://www.cidrap.umn.edu/sites/default/files/public/downloads/topics/mceirs_h7n9_graphs.pdf (accessed July 5, 2013).
4. Anjma’Y, Zo R, Murhekar M, Vong S, Shimaeda T. Human infections with avian influenza A(H7N9) virus in China: preliminary assessments of the age and sex distribution. WPSAR 2013; 4: 1–3.
5. Li Q, Zhou L, Zhou M, et al. Preliminary report: epidemiology of the avian influenza A(H7N9) outbreak in China. N Engl J Med 2013; published online April 24. DOI:10.1056/NEJMoA1304617.
6. Meyer KC. The role of immunity in susceptibility to respiratory infection in the aging lung. Respi Physiol Neurobiol 2001; 128: 23–31.
7. Smits SL, de Lang A, van den Brand JM, et al. Exacerbated innate host response to SARS-CoV in aged non-human primates. PLoS Pathog 2010; 6: e1000756.
8. Garten RJ, Davis CT, Russell CA, et al. Antigenic and genetic characteristics of swine-origin 2009 A(H1N1) influenza viruses circulating in humans. Science 2009; 325: 197–201.
9. Hancock K, Yeguilla V, Lu X, et al. Cross-reactive antibody responses to the 2009 pandemic H1N1 influenza virus. N Engl J Med 2009; 361: 1945–52.
10. Itoh Y, Shinya K, Kiso M, et al. In vitro and in vivo characterization of new swine-origin H1N1 influenza viruses. Nature 2009; 460: 1021–25.
11. Skountzou I, Koutsonanos DG, Kim JH, et al. Immunity to pre-1950 H1N1 influenza viruses confers cross-protection against the pandemic swine-origin 2009 A (H1N1) influenza virus. J Immunol 2010; 185: 1642–49.
12. Hillaire ML, van Trierum SE, Bodewes R, et al. Characterization of the human CDB(+) T cell response following infection with 2009 pandemic influenza H1N1 virus. J Virol 2011; 85: 11257–61.
13. Bodewes R, Fraaij PL, Geelhoed-Miers MM, et al. Annual vaccination against influenza virus hampers development of virus-specific CDB(+) T cell immunity in children. J Virol 2011; 85: 11995–2000.
14. Bodewes R, Fraaij PL, Kreijtz JH, et al. Annual influenza vaccination affects the development of heterosubtypic immunity. Vaccine 2012; 30: 7407–10.
15. Huisman W, Martina BE, Rimmelzwaan GF, Gruters RA, Osterhaus AD. Vaccine-induced enhancement of viral infections. Vaccine 2009; 27: 50–12.
16. Epstein SL. Prior H1N1 influenza infection and susceptibility of Cleveland family study participants during the H2N2 pandemic of 1957: an experiment of nature. J Infect Dis 2006; 193: 49–53.
17. Sandbulte MR, Jimenez GS, Boon AC, Smith LR, Treanor J, Webby RJ. Cross-reactive neuaminiadase antibodies afford partial protection against H5N1 in mice and are present in unexposed humans. PLoS Med 2007; 4: e59.

Point-of-care testing for community-acquired pneumonia

Community-acquired pneumonia is a life-threatening disease. An estimated 8% of patients are admitted to intensive care and overall estimated 30 day mortality is 4–11%. Many bacteria and viruses cause community-acquired pneumonia (and can co-infect), and the causative pathogen (or pathogens) cannot be predicatively identified by any clinical, radiological, or biological methods. Accordingly, antibiotic treatment is empirical, and guidelines recommend a combination of a β-lactam with a macrolide. Identification of the causative pathogen is usually delayed because clinical specimens are processed in a core laboratory, which is often in a different centre from the patient and the doctor. Culturing, if done, can also take several days.
To avoid this delay, we introduced point-of-care (POC) microbiology laboratories near emergency departments where patients with community-acquired pneumonia are seen first. POC laboratories have a rapid turnaround time (<1.5 h) and deliver results as text messages directly to doctors’ mobile phones. POC testing could be implemented in medical centres in large cities, where specimen transport delays diagnosis, and in remote areas without full microbiological facilities. However, it should be noted that not all pathogens that can cause community-acquired pneumonia can be detected by POC tests, and molecular tests for Staphylococcus aureus have not been approved by the US Food and Drug Administration (FDA) or the European Conformity (CE).

In the emergency department, community-acquired-pneumonia POC kits, comprising a plastic bag containing prelabelled tubes for clinical samples, prelabelled laboratory forms, and an informed consent form, can be used to take nasal or pharyngeal swabs and urine and serum samples. These samples can be used for the entire panel of POC tests. POC diagnosis of community-acquired pneumonia relies on immunochromatographic assays for the rapid antigen detection of pathogen-specific antigen and real-time PCR tests detecting pathogen-specific genomic sequences. Three RT-PCR-based POC tests have been approved by the FDA—GeneXpert Flu A/B (Cepheid, Sunnyvale, CA, USA), Simplexa Flu A/B&RSV (Focus Diagnostics, Cypress, CA, USA), and FilmArray RVP (Biofire, Salt Lake City, UT, USA). The appendix lists FDA-approved and CE-approved tests.

Procalcitonin, a useful biomarker in bacterial community-acquired pneumonia, can be rapidly semiquantified (in 30 min) in serum via immunochromatographic testing. Urinary rapid antigen detection of Legionella pneumophila serotype 1 and Streptococcus pneumoniae can be done in 20 min. A meta-analysis showed that urinary detection of L pneumophila had a pooled sensitivity of 0.74 and a specificity of 0.99. Urinary detection of S pneumoniae had a specificity of 0.96 and positive predictive value of 0.88–0.96, allowing clinicians to use a narrower spectrum of antibiotics. Rapid antigen detection of the influenza virus in nasal or pharyngeal swabs (done in 30 min) has a low sensitivity of less than 0.60; sensitivity correlates with viral load. However, specificity is around 1.00, resulting in a positive predictive value of more than 0.98—high enough to make a positive result reliable for medical decisions. A negative result does not rule out the presumptive diagnosis of the physician, which should be checked by a second-line molecular test in a core laboratory.

POC tests have to be operator-independent, and thus we do not recommend implementation of microscope-based tests, such as direct fluorescent antibody tests, for which skilled microscopists are needed. However, a liquid direct fluorescent antibody format (Fast-Point; Diagnostic Hybrids, Athens, OH, USA) is available for POC testing (appendix). It has not been approved by the FDA or the CE, but detects influenza virus, respiratory syncytial virus, adenovirus, coronavirus, and parainfluenza virus in 25 min. The latest generation real-time PCR kits can complete molecular testing of swabs for bacterial and viral pathogens in 60 min. New generation real-time PCR kits are typically multiplexed assays testing as many as 22 potential pathogens in parallel. This new capacity of POC tests increases the number of diagnoses and underscores that community-acquired pneumonia can result from co-infection with several pathogens, which will challenge common notions about causation and management. For example, we propose that influenza and S pneumoniae have to be tested for in parallel irrespective of which one is the presumed causative pathogen. Furthermore, detection by POC testing of an abnormal increase in group A streptococci might suggest co-infection with influenza. Procalcitonin concentrations greater than 0.5 ng/mL suggest bacterial co-infection in influenza—a major risk factor for death.

POC results could affect the major decisions that doctors have to make in emergency departments—eg, whether to admit the patient (the usual action for community-acquired pneumonia), which antibiotic (such as balancing the advantages of β-lactam and macrolides) or antiviral to prescribe, isolation of contagious patients. Although barriers to the implementation of POC tests in developing countries have been identified, POC tests have been successfully implemented in remote areas—eg, rural Senegal, where patients and health-care providers are in close contact. Furthermore, assessment of the numbers of POC tests done on a weekly basis could help to predict epidemics even before the causative organism is known.
Exposure of HIV-positive sex workers in Greece

In May, 2012, on the Attorney General’s order, the police publicised photos and identity details of 18 women working illegally as sex workers in Athens, Greece, who had been arrested and found to be HIV positive. The rationale for this decision was presumably protection of the public—people who had had sexual intercourse with these sex workers might recognise them and seek medical advice and HIV testing, whereas people who pay for sex could avoid contact with these particular workers. Five of the sex workers were prosecuted for intentional grievous harm—ie, transmission of HIV. The case drew media attention and sparked controversy for a brief period, but was forgotten amid pressing problems related to the economic crisis. On March 11, 2013, the five women were acquitted, but this news did not make headlines. Some important ethical issues were raised, which need to be adequately addressed both in Greece and internationally.

Sex work in Greece is legal and regulated; sex workers must register at their local prefecture and carry a medical card that is updated every 2 weeks. However, fewer than 1000 women are estimated to be legally employed as sex workers, whereas roughly 20,000 women, mostly of foreign origin, are thought to be engaged in illegal sex work. Greece is not unique in this regard—and large, the sex industry evades control worldwide. Notwithstanding the diversity of sex work settings and its many problematic aspects, such as human trafficking, sex workers’ health has gained the attention of policy makers, which is shown by a growing body of published guidelines and strategies. Is the aim of these strategies to protect sex workers or to protect public health via protection of sex workers? If the outcome is the same either way, does the intent make a difference?

The Greek authorities’ handling of the 18 HIV-positive sex workers shows an obvious difference between the two aims. Researchers from other countries have already pointed out that public health officials are concerned less about the health of sex workers than about that of the sex workers’ clients or the larger community. The public health response to sex workers is often one sided. In breach of key...