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Prepandemic" immunization for novel influenza viruses, "swine flu" vaccine, guillain-barré syndrome, and the detection of rare severe adverse events

Evans D, Cauchemez S, Hayden FG
J Infect Dis. 2009 Aug 1;200(3):321-8

The availability of immunogenic, licensed H5N1 vaccines and the anticipated development of vaccines against "swine" influenza A(H1N1) have stimulated debate about the possible use of these vaccines for protection of those exposed to potential pandemic influenza viruses and for immunization or "priming" of populations in the so-called "prepandemic" (interpandemic) era. However, the safety of such vaccines is a critical issue in policy development for wide-scale application of vaccines in the interpandemic period. For example, wide-scale interpandemic use of H5N1 vaccines could lead to millions of persons receiving vaccines of uncertain efficacy potentially associated with rare severe adverse events and against a virus that may not cause a pandemic. Here, we first review aspects of the 1976 National Influenza Immunization Programme against "swine flu" and its well-documented association with Guillain-Barré syndrome as a case study illustration of a suspected vaccine-associated severe adverse event in a mass interpandemic immunization setting. This case study is especially timely, given the recent spread of a novel influenza A(H1N1) virus in humans in Mexico and beyond. Following this, we examine available safety data from clinical trials of H5N1 vaccines and briefly discuss how vaccine safety could be monitored in a postmarketing surveillance setting.

Swine influenza A (H1N1) strikes a potential for global disaster

Galwankar S, Clem A
J Emerg Trauma Shock. 2009 May;2(2):99-105

As of April 25(th)2009, 11.00 AM, eight human cases of swine influenza A virus infection have been identified in the United States in California and Texas. There is also established evidence of similar cases across the United States border in Mexico. Experts from the Centers for Disease Control and Prevention in cooperation with World Health Organization and public health experts from Canada and Mexico are leading an exhaustive investigation to find the source of infection and infected people. We present a profile of this illness from the available literature.

Emergence and pandemic potential of swine-origin H1N1 influenza virus

Neumann G, Noda T, Kawaoka Y
Nature. 2009 Jun 18;459(7249):931-9

Influenza viruses cause annual epidemics and occasional pandemics that have claimed the lives of millions. The emergence of new strains will continue to pose challenges to public health and the scientific communities. A prime example is the recent emergence of swine-origin H1N1 viruses that have transmitted to and spread among humans, resulting in outbreaks internationally. Efforts to control these outbreaks and real-time monitoring of the evolution of this virus should provide us with invaluable information to direct infectious disease control programmes and to improve understanding of the factors that determine viral pathogenicity and/or transmissibility.

Novel swine-origin influenza A virus in humans: another pandemic knocking at the door

Michaelis M, Doerr HW, Cinatl J Jr
Med Microbiol Immunol. 2009 Jun 20

Influenza A viruses represent a continuous pandemic threat. In April 2009, a novel influenza A virus, the so-called swine-origin influenza A (H1N1) virus (S-OIV), was identified in Mexico. Although S-OIV originates from triple-reassortant swine influenza A (H1) that has been circulating in North American pig herds since the end of the 1990s, S-OIV is readily transmitted between humans but is not epidemic in pigs. After its discovery, S-OIV rapidly spread throughout the world within few weeks. In this review, we sum up the current situation and put it into the context of the current state of knowledge of influenza and influenza pandemics. Some indications suggest that a pandemic may be mild but even "mild" pandemics can result in millions of deaths. However, no reasonable forecasts how this pandemic may develop can be made at this time. Despite stockpiling by many countries and WHO, antiviral drugs will be limited in case of pandemic and resistances may emerge. Effective vaccines are regarded to be crucial for the control of influenza pandemics. However, production capacities are restricted and development/production of a S-OIV vaccine will interfere with manufacturing of seasonal influenza vaccines. The authors are convinced that S-OIV should be taken seriously as pandemic threat and underestimation of the menace by S-OIV to be by far more dangerous than its overestimation.

The 2009 H1N1 influenza outbreak in its historical context

Gatherer D
J Clin Virol. 2009 Jul;45(3):174-8

Of the 16 known serotypes of influenza A haemagglutinin, 6 have been isolated from humans at the molecular level (H1, H2, H3, H5, H7, H9). 3 of these have been involved in past pandemics (H1, H2, H3). Traditional pandemic surveillance has focussed on monitoring antigenic shift, meaning the re-assortment of novel haemagglutinins into seasonal human influenza A viruses during rare events of double infection with seasonal and zoonotic strains. H5, from avian H5N1 influenza, has been the major cause for concern in recent years. However, the 2009 H1N1 zoonotic event demonstrates that even serotypes already encountered in past human pandemics may constitute new pandemic threats. The protein sequence divergence of the 2009 zoonotic H1 from human seasonal influenza H1 is around 20-24%. A similar level of divergence is found between the 2009 H1 and European swine flu. By contrast, its divergence from North American swine flu strains is around 1-9%. Given that the divergence between H1 and its nearest serotype neighbour H2 is around 40-46%, the 2009 H1 may be broadly considered as halfway towards a new serotype. The current situation is one of antigenic pseudo-shift.

Detection of novel (swine origin) H1N1 influenza A virus by quantitative real-time RT-PCR

Wang R, Sheng ZM, Taubenberger JK
J Clin Microbiol. 2009 Jun 24

A novel H1N1 subtype influenza A virus, derived by reassortant between two known circulating swine influenza strains, has now been declared a human pandemic influenza A virus.

Unraveling the mystery of swine influenza virus

Wang TT, Palese P

Cell. 2009 Jun 12;137(6):983-5

Influenza virus outbreaks occur with regularity, but the severity of outbreaks is not consistent. The recent flu epidemic caused by an H1N1 swine influenza virus presents an opportunity to examine what is known about virulence factors and the spread of infection to better prepare for major influenza outbreaks in the future.

Origins of the new influenza A(H1N1) virus: time to take action

Nava GM, Attene-Ramos MS, Ang JK, Escorcia M

Euro Surveill. 2009 Jun 4;14(22)

To gain insight into the possible origins of the 2009 outbreak of new influenza A(H1N1), we performed two independent analyses of genetic evolution of the new influenza A(H1N1) virus. Firstly, protein homology analyses of more than 400 sequences revealed that this virus most likely evolved from recent swine viruses. Secondly, phylogenetic analyses of 5,214 protein sequences of influenza A(H1N1) viruses (avian, swine and human) circulating in North America for the last two decades (from 1989 to 2009) indicated that the new influenza A(H1N1) virus possesses a distinctive evolutionary trait (genetic distinctness). This appears to be a particular characteristic in pig-human interspecies transmission of influenza A. Thus these analyses contribute to the evidence of the role of pig populations as "mixing vessels" for influenza A(H1N1) viruses.

Characterization of triple reassortant H1N1 influenza A viruses from swine in Ohio

Yassine HM, Khatri M, Zhang YJ, Lee CW, Byrum BA, O'Quin J, Smith KA, Saif YM

Vet Microbiol. 2009 May 3

An H1N1 influenza A virus, A/swine/Ohio/24366/07, was isolated from pigs in an Ohio county fair. Twenty-six people who came in contact with the infected pigs developed respiratory disease and two of these people were laboratory confirmed as H1N1 by the Centers for Disease Control and Prevention (CDC). The A/swine/Ohio/24366/07 virus we isolated from swine was shown at the CDC to have 100% identical genome sequence to the human virus associated with the county fair. This prompted us to characterize three swine and two human origin H1N1 influenza A viruses isolated at different time points in the State of Ohio. The three swine viruses were shown to be triple reassortant viruses harboring genes of human (PB1), swine (HA, NA, NP, M, and NS), and avian (PB2 and PA) lineage viruses. Although viruses evaluated in this study were isolated during a short time interval (3 years), genetic drift was observed within the HA and NA genes, including changes at the receptor binding and antigenic sites of HA1 protein. Nevertheless, all viruses exhibited antigenic similarity as evaluated with hemagglutination inhibition and virus neutralizing tests. Internal genes were similar to other reassortant viruses of various subtypes currently circulating in the United States. Interestingly, two of the swine viruses including the 2007 isolate replicated well in human airway epithelial cells, however, another virus isolated in 2006 showed very little replication.

Lessons From Outbreaks of H1N1 Influenza

Stein RA

Ann Intern Med. 2009 Jul 7;151(1):59-62

A new H1N1 triple-reassortant "swine" influenza virus was recently described in individuals from the United States and Mexico who presented with respiratory symptoms, and the same virus was subsequently confirmed in patients from several countries around the world. The circumstances surrounding the emergence of this pathogen, and the factors that facilitated the initial cross-species transmission, are still incompletely understood. It became apparent in the early days of the outbreak that the virus can be directly transmitted between humans. Pathogens that originate in animal reservoirs and subsequently acquire the potential for human-to-human transmission have caused outbreaks throughout human history. Although each outbreak is marked by its own particularities, it is important to remember the teachings that emerge from previous epidemics and pandemics. Integrating the important lessons of the past will provide the best opportunity to understand host-pathogen interaction and the most powerful approach to implementing effective prophylactic and therapeutic measures.

April 2009: an outbreak of swine-origin influenza A(H1N1) virus with evidence for human-to-human transmission

Naffakh N, van der Werf S

Microbes Infect. 2009 May 12

A swine-origin influenza A(H1N1) virus is currently responsible for an outbreak of infections in the human population, with laboratory-confirmed cases reported in several countries and clear evidence for human-to-human transmission. We provide a description of the outbreak at the end of April 2009, and a brief review of the zoonotic potential of swine influenza viruses.