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Review Article

SWINE FLU PANDEMIC INFLUENZA VIRUSES A (H1N1)

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Abstract

Influenza viruses are able to infect humans, swine, and avian species, and swine have long been considered a potential source of new influenza viruses that can infect humans. Swine have receptors to which both avian and mammalian influenza viruses' bind which increases the potential for viruses to exchange genetic sequences and produce new reassortant viruses in swine. A number of genetically diverse viruses are circulating in swine herds throughout the world and are a major cause of concern to the swine industry. Control of swine influenza is primarily through the vaccination of sows, to protect young pigs through maternally derived antibodies. However, influenza viruses continue to circulate in pigs after the decay of maternal antibodies, providing a continuing source of virus on a herd basis. Measures to control avian influenza in commercial poultry operations are dictated by the virulence of the virus. The WHO declared the H1N1 pandemic on June 11, 2009, after more than 70 countries reported 30000 cases of H1N1 infection. In 2015 the instances of Swine Flu substantially increased to five year highs with over 10000 cases reported and 774 deaths in India. The CDC recommends real time PCR as the method of choice for diagnosing H1N1. Prevention of swine influenza has three components: prevention in swine, prevention of transmission to humans, and prevention of its spread among humans. They may also prevent serious flu complications. The CDC recommends the use of Oseltamivir (Tamiflu) or Zanamivir (Relenza) for the treatment.

Keywords: H1N1 influenza, Virology, diagnosis, vaccine, CDC.

Introduction

Influenza ("flu") is a contagious disease that spreads around the World or India every winter, usually between October and May. There are three types of Influenza viruses A, B and C. The subtypes of type A Influenza virus is determined by haemagglutinin and neuraminidase. Both A and B viruses are responsible for seasonal influenza epidemics, and out-of season sporadic cases and outbreaks. Three worldwide (pandemic) outbreaks of influenza occurred in the 20th century: in 1918, 1957, and 1968. The latter 2 were in the era of modern virology and most thoroughly characterized. All 3 have been informally identified by their presumed sites of origin as Spanish, Asian, and Hong Kong influenza, respectively. They are now known to represent 3 different antigenic subtypes of influenza A virus: H1N1, H2N2, and H3N2, respectively. Swine influenza is an acute respiratory disease caused by influenza A viruses that circulate among pigs [1-6]. The morbidity rate is usually high, and the case fatality rate low, but more severe outbreaks may be seen,, and reduced growth rates in young pigs can cause economic losses [1-5,7-8]. Swine influenza viruses occasionally affect other species including turkeys, mink, ferrets and humans. In people, clinical cases have tended to resemble human influenza [1-3,6,9].

VIROLOGY

The types of influenza virus found in pigs are known as swine influenza generally called swine flu or swine-origin influenza virus (S-OIV) . Swine Influenza is a respiratory disease of pig caused by Type A influenza viruses that causes regular outbreak in pigs. Influenza virus belongs to the genus Orthomyxovirus in the family

Orthomyxoviridae which consists of influenza A, B and C viruses and has an envelope, single-stranded, negatively sensed RNA, eight separate segments and pleomorphic appearance with an average diameter of 120nm[17-18].

ETIOLOGY

Swine influenza viruses belong to the species influenza A virus, genus Influenzavirus A, and family Orthomyxoviridae. Other influenza A viruses infect birds (avian influenza viruses), horses and other equids (equine influenza viruses), people (human influenza A viruses) or dogs (canine influenza viruses). Influenza A viruses are classified into subtypes based on two surface proteins, the hemagglutinin (HA) and neuraminidase (NA). A virus that has a type 1 HA and type 2 NA, for example, would have the subtype H1N2. At least 16 types of hemagglutinins (H1 to H16), and 9 neuraminidases (N1 to N9) are known to exist in birds, and two additional HA and NA types occur in bats, while small subsets of avian subtypes circulate in other mammals [9-14]. The HA, and to a lesser extent the NA, are major targets for the immune response, and there is ordinarily little or no cross-protection between different HA or NA types [15-20]. Influenza A viruses are very diverse, and two viruses that share a subtype may be only distantly related. The high variability is the result of two processes, mutation and genetic reassortment. Mutations cause gradual changes in the HA and NA proteins of the virus, a process called ‘antigenic drift.’3 Once these proteins have changed sufficiently, immune responses against the former HA and NA may no longer be protective [20].

TRANSMISSION

In mammals, influenza viruses are transmitted in droplets and aerosols created by coughing and sneezing, and by contact with nasal discharges, either directly or on fomites.1,3,5,6 While most viruses are thought to enter the body through the respiratory tract, the eye might act as an additional entry point, based on evidence from humans and laboratory animals. Close contact and closed environments favor transmission [21-22].

The relative importance of the various routes in each host species is still incompletely understood, but swine influenza viruses are thought to be transmitted between pigs mainly during direct contact, and to a lesser extent on fomites. Virus shedding can begin within 1-3 days after infection, and typically continues for 4-5 days and up to 7 days [5-6]. While there are rare reports of pigs that shed viruses for as long as four months, this is unusual and long-term carrier pigs do not seem to exist or play any role in virus maintenance. There is some evidence that aerosol transmission might be possible, at least within densely populated pig barns, and possibly over longer distances in swine-dense regions. Swine influenza viruses have been isolated from air samples inside barns and immediately outside exhaust fans. Based on RNA quantification, the amount of virus decreases significantly with distance outside the barn, although small amounts of viral RNA could be found up to 2 km downwind [23-25].

Transmission to humans

People are usually infected with viruses from other species during close contact with the living host or its tissues, although indirect contact via fomites or other means is also thought to be possible [1-2]. During recent cases associated with fairs, many (though not all) patients had been exposed to pigs for more than one day. Person-to-person transmission of swine influenza viruses has occasionally been reported to family members or other close contacts, and a limited outbreak occurred on a military base; however, most viruses were not transmitted to other people [1-2, 26-27].

CLINICAL SIGNS

Most laboratory-confirmed, symptomatic swine influenza virus infections have been characterized by upper respiratory signs that resemble human influenza, including gastrointestinal signs in some patients, although acute parotitis was reported in a 6-year-old with H3N2 influenza, and one young patient had only fever and vomiting [1-2,7]. In a recent series of infections caused by North American triple reassortant H3N2 viruses, redness of the eyes or eye irritation appeared to be more common than with seasonal influenza viruses. The illness was mild in most healthy people, although young children were sometimes hospitalized for dehydration. Pneumonia, serious illnesses and deaths have also been seen, generally though not always in people who had underlying health conditions or were immunocompromised by illnesses or pregnancy. Serological evidence suggests mild or asymptomatic cases might also occur among people who are occupationally exposed [9, 26-27].

DIAGNOSTIC TESTS

Tests used to detect influenza virus infections in humans can include RT-PCR, virus isolation and assays to detect influenza virus antigens. Many recent swine influenza cases were diagnosed by genetic methods, particularly RT-PCR. Routine diagnostic tests used to detect human influenza viruses, including commercial rapid test kits, do not necessarily detect

zoonotic viruses [28-29]. One indication that a novel, possibly zoonotic influenza, virus might be present is the detection of influenza A virus, but not the hemagglutinins in seasonal human influenza viruses. Zoonotic influenza virus infections are occasionally diagnosed retrospectively by serology, but serological diagnosis can be complicated by cross-reactivity with human influenza viruses. A further difficulty is that the HA and NA of some swine influenza viruses (the main targets of antibody responses) originally came from human influenza viruses, to which people may have already been exposed. Testing for novel influenza viruses is generally performed by state, regional or national public health laboratories [30-31].

TREATMENT

Supportive care for uncomplicated influenza in humans includes fluids and rest. Additional adjunct and supportive treatments for more severe cases vary, and can include various drugs, including antibiotics to treat or prevent secondary bacterial pneumonia, and mechanical ventilation. Two groups of antiviral drugs-: the adamantanes (amantadine, rimantadine), and neuraminidase inhibitors (zanamivir, oseltamivir, peramivir and laninamivir) – are used to treat some cases of influenza, although some of these drugs (peramivir and laninamivir) are not licensed in all countries [32-36]. Both groups of drugs are effective against some influenza A viruses, although they may have some side effects. Antiviral drugs are most effective if they are started within the first 48 hours after the clinical signs begin, although they may also be used in severe or high risk cases first seen after this time [32, 34]. Antiviral resistance can develop rapidly, and may emerge during treatment [32-, 37-38]. One recent study reported resistance to neuraminidase inhibitors in 9% of swine influenza viruses that contained the N2 neuraminidase (H1N2, H3N2 and H9N2) [34]. Zanamivir and Oseltamivir are members of a new class of drugs called neuraminidase inhibitors and are active against both influenza type A and type B. Zanamivir is provided as a dry powder that is administered by inhalation. It is approved for treatment of uncomplicated acute influenza A or B in persons 7 years of age and older who have been symptomatic for no more than 48 hours. Oseltamivir is provided as an oral capsule. It is approved for the treatment of uncomplicated influenza A or B in persons 1 year of age and older who have been symptomatic for no more than 48 hours. Zanamivir is approved for prophylaxis of influenza in persons 5 years and older. Oseltamivir is approved for prophylaxis of influenza infection among persons 1 year of age and older [38].

In 2007-08, a significant increase in the prevalence of Oseltamivir resistance was reported among influenza A (H1N1) viruses worldwide. During the 2007-08 influenza seasons, 10.9% of H1N1 viruses tested in the U.S. were resistant to Oseltamivir. During 2008 more than 90% of H1N1 viruses were resistant to Oseltamivir. For the 2008-09 influenza seasons CDC recommends that persons who test positive for influenza A should receive only zanamivir if treatment is indicated. Oseltamivir should be used alone only if recent local surveillance data indicate that circulating viruses are likely to be influenza A (H3N2) or influenza B viruses, which have not been found to be resistant to Oseltamivir [39].

Antiviral agents for influenza are an adjunct to vaccine and are not a substitute for vaccine. Vaccination remains the principal means for preventing influenza related morbidity and mortality [40]. Presently government of India recommends Tamiflue as a drug of choice which is available at all government health bodies. Human influenza A is susceptible to both Oseltamivir and zanamivir, two antiviral medications approved for the prevention and treatment of influenza in the United States [41].

Oseltamivir: Oseltamivir is the recommended drug both for prophylaxis and treatment. In the current phase, if a person conforms to the case definition of suspect case, then he would be provided Oseltamivir [35].

Table: 1. Dose for treatment

By Weight	For Infants
• For weight <15kg 30 mg BD for 5 days • 15-23kg 45 mg BD for 5 days • 24-<40kg 60 mg BD for 5 days • >40kg 75 mg BD for 5 days	• < 3 months 12 mg BD for 5 days • 3-5 months 20 mg BD for 5 days • 6-11 months 25 mg BD for 5 days • It is also available as syrup (12mg per ml) • If needed dose & duration can be modified as per clinical condition.

Adverse Reactions: Oseltamivir is generally well tolerated, gastrointestinal side effects (nausea, vomiting) may increase with increasing doses, particularly above 300 mg/day. Occasionally it may cause bronchitis, insomnia and vertigo. Less commonly angina, pseudo membranous colitis and peritonsillar abscess have also been reported. There have been rare reports of anaphylaxis and skin rashes.

PREVENTION

Protective measures for zoonotic influenza viruses include sanitation and hygiene (e.g., frequent hand washing), avoidance of contact with sick animals or animals known to be infected, and the use of personal protective equipment when working with infected pigs. Depending on the circumstances, recommended personal protective equipment may include masks to reduce droplet transmission or respirators, as well as other barriers such as protective clothing and gloves [42].

CONCLUSION

Swine flu refers to swine influenza or the viral infection caused by any of the several types of swine influenza virus. Only people who used to have direct contact with pigs were observed to get swine flu in the past. But, H1N1 virus is a new swine flu virus and it contains the genetic material of swine, bird and human influenza virus. H1N1 is an Influenza A virus. Swine Flu is caused by influenza viruses, and is spread mainly by coughing, sneezing, and close contact. Prevention and control measures for swine influenza are based on our understanding of seasonal human influenza and consideration of potential modes of transmission.

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REFERENCES

1. Acha PN, Szyfres B (Pan American Health Organization 146). Zoonoses and communicable diseases common to man and animals. Volume 2. Chlamydiosis, rickettsioses and viroses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Influenza; p. 155-72.
2. Heinen P. Swine influenza: a zoonosis. Vet Sci Tomorrow [serial online]. 2003 Sept 15. Available at: http://www.vetscite.org/publish/articles/000041/print.html.* [Accessed 26 Feb. 2015].
3. Fenner F, Bachmann PA, Gibbs EPJ, Murphy FA, Studdert MJ, White DO. Veterinary virology. San Diego, CA: Academic Press Inc.; 1987. Orthomyxoviridae; p. 473-84.
4. Taubenberger JK, Morens DM. 1918 influenza: the mother of all pandemics. Emerg Infect Dis. 2006; 12:15–22.
5. World Organization for Animal Health [OIE]. Manual of diagnostic tests and vaccines for terrestrial animals [online]. Paris;OIE; 2010. Swine influenza. Available at: http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.08.08_SWINE_INFLUENZA.pdf. [Accessed: 26 Feb, 2015].
6. Brown IH. The epidemiology and evolution of influenza viruses in pigs. Vet Microbiol. 2000;74(1-2):29-46.
7. Schultz-Cherry S, Olsen CW, Easterday BC. History of swine influenza. Curr Top Microbiol Immunol. 2013;370:21-8.
8. Vincent AL, Ma W, Lager KM, Gramer MR, Richt JA, Janke BH. Characterization of a newly emerged genetic cluster of H1N1 and H1N2 swine influenza virus in the United States. Virus Genes. 2009;39(2):176-85.
9. Olsen CW, Brammer L, Easterday BC, Arden N, Belay E, Baker I, Cox NJ. Serologic evidence of H1 swine Influenza virus infection in swine farm residents and employees. Emerg Infect Dis. 2002;8(8):814-9.
10. Swayne DE. Avian influenza. In: Foreign animal diseases. Boca Raton, FL: United States Animal Health Association; 2008. p. 137-46.
11. Centers for Disease Control and Prevention [CDC]. Avian flu [Website online]. CDC; 2014 Jan. Available at: http://www.cdc.gov/flu/avianflu/. [Accessed 26 Feb. 2015].
12. World Organization for Animal Health [OIE]. Manual of diagnostic tests and vaccines for terrestrial animals [online]. Paris; OIE; 2008. Avian influenza. Available at: http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.03.04_AI.pdf. Accessed 26 Feb 2014.
13. Tong S, Li Y, Rivailler P, Conrardy C, Castillo DA, Chen LM et al. A distinct lineage of influenza A virus from bats. Proc Natl Acad Sci U S A. 2012;109(11):4269-74.
14. Tong S, Zhu X, Li Y, Shi M, Zhang J, Bourgeois M et al. New world bats harbor diverse influenza A viruses. PLoS Pathog. 2013;9(10):e1003657.
15. Grebe KM, Yewdell JW, Bennink JR. Heterosubtypic immunity to influenza A virus: where do we stand? Microbes Infect. 2008;10(9):1024-9.
16. Swayne DE. Principles for vaccine protection in chickens and domestic waterfowl against avian influenza: emphasis on Asian H5N1 high pathogenicity avian influenza. Ann N Y Acad Sci. 2006;1081:174-81.

17. Adeola OA, Adeniji JA, Olusaga BO. Isolation of influenza A viruses from pigs in Ibadan, NigeriaVet. Ital. 2009; 45(3): 383-90.
18. Ohwada, K., Kitame, F., Sugawara, K., Nishimura, H., Homma, M., and Nakamura, K. Distribution of the antibody to influenza C virus in dogs and pigs in Yamagata Prefecture, Japan. Microbiol. Immunol.1987; 31(12):1173-1180Kapczynski DR, Swayne DE. Influenza vaccines for avian species. Curr Top Microbiol Immunol. 2009;333:133-52.
19. Lee CW, Saif YM. Avian influenza virus. Comp Immunol Microbiol Infect Dis. 2009;32(4):301-10.
20. Aamir UB, Naeem K, Ahmed Z, Obert CA, Franks J, Krauss S, Seiler P, Webster RG. Zoonotic potential of highly pathogenic avian H7N3 influenza viruses from Pakistan. Virology. 2009;390(2):212-20.
21. Belser JA, Gustin KM, Pearce MB, Maines TR, Zeng H, Pappas C, Sun X, Carney PJ, Villanueva JM, Stevens J, Katz JM, Tumpey TM. Pathogenesis and transmission of avian influenza A (H7N9) virus in ferrets and mice. Nature. 2013;501(7468):556-9.
22. Janke BH. Clinicopathological features of swine influenza. Curr Top Microbiol Immunol. 2013;370:69-83.
23. Corzo CA, Culhane M, Dee S, Morrison RB, Torremorell M. Airborne detection and quantification of Swine influenza a virus in air samples collected inside, outside and downwind from Swine barns. PLoS One. 2013;8(8):e71444.
24. Torremorell M, Allerson M, Corzo C, Diaz A, Gramer M. Transmission of influenza A virus in pigs. Transbound Emerg Dis. 2012 [Epub ahead of print].
25. Dacso CC, Couch RB, Six HR, Young JF, Quarles JM, Kasel JA. Sporadic occurrence of zoonotic swine influenza virus infections. J Clin Microbiol. 1984;20(4):833-5.
26. Olsen CW, Karasin AI, Carman S, Li Y, Bastien N, Ojkic D, Alves D, Charbonneau G, Henning BM, Low DE, Burton L, Broukhanski G. Triple reassortant H3N2 influenza A viruses, Canada, 2005. Emerg Infect Dis. 2006;12(7):1132-5.
27. Centers for Disease Control and Prevention [CDC]. Seaonal influenza. Information for health care professionals [Website online]. CDC; 2014. Available at: http://www.cdc.gov/flu/professionals/index.htm. [Accessed 26 Feb. 2015].
28. Cong YL, Pu J, Liu QF, Wang S, Zhang GZ, Zhang XL, Fan WX, Brown EG, Liu JH. Antigenic and genetic characterization of H9N2 swine influenza viruses in China. J Gen Virol. 2007;88(Pt 7):2035-41.
29. Centers for Disease Control and Prevention [CDC]. Avian flu [Website online]. CDC; 2014 Jan. Available at: http://www.cdc.gov/flu/avianflu/. [Accessed 26, Feb. 2014].
30. Uyeki TM. Human infection with highly pathogenic avian influenza A (H5N1) virus: review of clinical issues. Clin Infect Dis. 2009;49(2):279-90.
31. Couch RB. Orthomyxoviruses [monograph online]. In: Baron S, editor. Medical microbiology. 4th ed. New York: Churchill Livingstone; 1996.
32. Smith NM, Bresee JS, Shay DK, Uyeki TM, Cox NJ, Strikas RA. Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morb Mortal Wkly Rep. 2006; 55(RR-10):1-42.
33. Public Health Agency of Canada. Pathogen Safety Data Sheet – Influenza A virus type A. Pathogen Regulation Directorate, Public Health Agency of Canada; 2012 (www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/influenza-a-eng.php) [Accessed: 27, Feb. 2015].
34. National Institute of Allergy and Infectious Diseases 279, National Institutes of Health 279. Flu drugs [online]. NIAID, NIH; 2003 Feb. (www.niaid.nih.gov/factsheets/fludrugs.htm) Accessed: [Ffeb.27, 2015].
35. Thorlund K, Awad T, Boivin G, Thabane L. Systematic review of influenza resistance to the neuraminidase inhibitors. BMC Infect Dis. 2011; 11:134.
36. Acha PN, Szyfres B (Pan American Health Organization 146). Zoonoses and communicable diseases common to man and animals. Volume 2. Chlamydiosis, rickettsioses and viroses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Influenza; p. 155-72.
37. Orozovic G, Orozovic K, Lennerstrand J, Olsen B. Detection of resistance mutations to antivirals oseltamivir and zanamivir in avian influenza A viruses isolated from wild birds. PLoS One. 2011;6(1):e16028.
38. Centers for Disease Control and Prevention (CDC) Update: Influenza activity – United States, September 28, 2008April 4, 2009, and composition of the 200910 influenza vaccine. MMWR Morb Mortal Wkly Rep. 2009;58:369–74.
39. Epidemiology and Prevention of Vaccine Preventable Diseases The Pink Book: Course Textbook 12th Edition Second Printing (May 2012)

(http://www.cdc.gov/vaccines/pubs/pinkbook/flu.html).[Accessed: 2, March 2015].

40. Centers for Disease Control and Prevention (CDC) Update: Drug susceptibility of swine origin influenza A (H1N1) viruses, April 2009. MMWR Morb Mortal Wkly Rep. 2009;58:433–5.
41. Centers for Disease Control and Prevention [CDC]. Information on swine influenza. CDC; 2014. Available at: http://www.cdc.gov/flu/swineflu/index.htm. [Accessed 2, March 2015].