甲型H1N1流感病毒
科技文献专辑(四)

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中国疾病预防控制中心

1 2005-2009 年间在美国分离出一株三源的甲型 H1 流感病毒

Triple-Reassortant Swine Influenza A (H1) in Humans in the United States, 2005-2009.

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This article (10.1056/NEJMoa0903812) was published at NEJM.org on May 7, 2009. It will appear in the July 2 issue of the Journal.

BACKGROUND: Triple-reassortant swine influenza A (H1) viruses - containing genes from avian, human, and swine influenza viruses - emerged and became enzootic among pig herds in North America during the late 1990s. METHODS: We report the clinical features of the first 11 sporadic cases of infection of humans with triple-reassortant swine influenza A (H1) viruses, occurring from December 2005 through February 2009, until just before the current epidemic of swine-origin influenza A (H1N1) among humans. These data were obtained from routine national influenza surveillance reports and from joint case investigations by public and animal health agencies. RESULTS: The median age of the 11 patients was 10 years (range, 16 months to 48 years), and 4 had underlying health conditions. Nine of the patients had had exposure to pigs, five through direct contact and four through visits to a location where pigs were present but without contact. In another patient, human-to-human transmission was suspected. The range of the incubation period, from the last known exposure to the onset of symptoms, was 3 to 9 days. Among the 10 patients with known clinical symptoms, symptoms included fever (in 90%), cough (in 100%), headache (in 60%), and diarrhea (in 30%). Complete blood counts were available for four patients, revealing leukopenia in two, lymphopenia in one, and thrombocytopenia in another. Four patients were hospitalized, two of whom underwent invasive mechanical ventilation. Four patients received oseltamivir, and all 11 recovered from their illness. CONCLUSIONS: From December 2005 until just before the current human epidemic of swine-origin influenza viruses, there was sporadic infection with triple-reassortant swine influenza A (H1) viruses in persons with exposure to pigs in the United States.

Although all the patients recovered, severe illness of the lower respiratory tract and unusual influenza signs such as diarrhea were observed in some patients, including those who had been previously healthy. Copyright 2009 Massachusetts Medical Society.

2 在人类中发现起源于猪的新型甲型 H1N1 流感病毒

Emergence of a Novel Swine-Origin Influenza A (H1N1) Virus in Humans.

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Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team.

The members of the writing group (Fatimah S. Dawood, M.D., Epidemic Intelligence Service, Office of Workforce and Career Development; and Seema Jain, M.D., Lyn Finelli, Dr.P.H., Michael W. Shaw, Ph.D., Stephen Lindstrom, Ph.D., Rebecca J. Garten, Ph.D., Larisa V. Gubareva, M.D., Ph.D., Xiyan Xu, M.D., Carolyn B. Bridges, M.D., and Timothy M. Uyeki, M.D., M.P.H, M.P.P., Influenza Division, National Center for Immunization and Respiratory Diseases - all at the Centers for Disease Control and Prevention, Atlanta) assume responsibility for the overall content and integrity of the article. This article (10.1056/NEJMoa0903810) was published at NEJM.org on May 7, 2009. It will appear in the July 2 issue of the Journal.

BACKGROUND: On April 15 and April 17, 2009, novel swine-origin influenza A (H1N1) virus (S-OIV) was identified in specimens obtained from two epidemiologically unlinked patients in the United States. The same strain of the virus was identified in Mexico, Canada, and elsewhere. We describe 642 confirmed cases of human S-OIV infection identified from the rapidly evolving U.S. outbreak. METHODS: Enhanced surveillance was implemented in the United States for human infection with influenza A viruses that could not be subtyped. Specimens were sent to the Centers for Disease Control and Prevention for real-time reverse-transcriptase-polymerase-chain-reaction confirmatory testing for S-OIV. RESULTS: From April 15 through May 5, a total of 642 confirmed cases of S-OIV infection were identified in 41 states. The ages of patients ranged from 3 months to 81 years; 60% of patients were 18 years of age or younger. Of patients with available data, 18% had recently traveled to Mexico, and 16% were identified from school outbreaks of S-OIV infection. The most common presenting symptoms were fever (94% of patients), cough (92%), and sore throat (66%); 25% of patients had diarrhea, and 25% had vomiting. Of the 399 patients for whom hospitalization status was known, 36 (9%) required hospitalization. Of 22 hospitalized patients with available data, 12 had characteristics that conferred an increased risk of severe seasonal influenza, 11 had pneumonia, 8 required admission to an intensive care unit, 4 had respiratory failure, and 2 died. The S-OIV was determined to have a unique genome composition that had not been identified previously. CONCLUSIONS: A

novel swine-origin influenza A virus was identified as the cause of outbreaks of febrile respiratory infection ranging from self-limited to severe illness. It is likely that the number of confirmed cases underestimates the number of cases that have occurred. Copyright 2009 Massachusetts Medical Society.

3 融合 C3d 与血凝素可增强对猪流感病毒免疫保护

Fusion of C3d with hemagglutinin enhances protective immunity against swine influenza virus.

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H1N1 and H3N2 are the dominant subtypes causing swine influenza in China and other countries. It is important to develop effective vaccines against both H1N1 and H3N2 subtypes of swine influenza virus (SIV). We examined the effects of a DNA vaccine expressing an influenza HA fused to three copies of murine complement C3d in mice. Plasmids encoding soluble HA (sHA), complete HA (tmHA), or a soluble fused form of HA (sHA-mC3d3) were constructed from the H3N2 subtype of SIV. The immune response was monitored by an enzyme-linked immunosorbent assay (ELISA), hemagglutination inhibition (HI) assays, and virus neutralization tests. Analysis of antibody titers indicated that immunization with HA-mC3d3 resulted in higher titers of anti-HA antibodies and higher antibody affinities, compared with serum from mice immunized with sHA or tmHA. Furthermore, the C3d fusion increased the Th2-biased immune response, by inducing IL-4 production. Splenocytes from mice immunized with sHA-mC3d3 produced about three-fold more IL-4 than did splenocytes from mice immunized with sHA or tmHA. Seven days post-challenge with homologous virus (H3N2), no virus was isolated from the mice immunized with HA-expressing plasmids. However, 10 days post-challenge with heterologous virus (H1N1), only mice immunized with sHA-mC3d3 had no virus or microscopic lesions in the kidneys and cerebrum. In conclusion, C3d enhanced antibody responses to hemagglutinin and protective immunity against SIV of different subtypes.

4 在美国爆发呼系统疾病的猪和乡村人中分离出的甲型流感病毒特性

Characterization of an influenza A virus isolated from pigs during an outbreak of respiratory disease in swine and people during a county fair in the United States.

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In August 2007, pigs and people became clinically affected by an influenza-like illness during attendance at an Ohio county fair. Influenza A virus was identified from pigs and people, and the virus isolates were characterized as swine H1N1 similar to swine viruses currently circulating in the U.S. pig population. The swine isolate, A/SW/OH/511445/2007 (OH07), was evaluated in an experimental challenge and transmission study reported here. Our results indicate that the OH07 virus was pathogenic in pigs, was transmissible among pigs, and failed to cross-react with many swine H1 anti-sera. Naturally exposed pigs shed virus as early as 3 days and as long as 7 days after contact with experimentally infected pigs. This suggests there was opportunity for exposure of people handling the pigs at the fair. The molecular analysis of the OH07 isolates demonstrated that the eight gene segments were similar to those of currently circulating triple reassortant swine influenza viruses. However, numerous nucleotide changes leading to amino acid changes were demonstrated in the HA gene and throughout the genome as compared to contemporary swine viruses in the same genetic cluster. It remains unknown if any of the amino acid changes were related to the ability of this virus to infect people. The characteristics of the OH07 virus in our pig experimental model as well as the documented human transmission warrant close monitoring of the spread of this virus in pig and human populations.

5 荷兰猪流感病毒种群动态分布:在未成年至成年牧群以及专门研究的特定牧群

Population dynamics of swine influenza virus in farrow-to-finish and specialised finishing herds in the Netherlands.

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Influenza virus infections with subtypes H1N1, H3N2 and H1N2 are very common in domestic pigs in Europe. Data on possible differences of population dynamics in finishing pigs in farrow-to-finish herds and in specialised finishing herds are, however, scarce. The presence of sows and weaned piglets on the same premises may, however, affect the exposure of finishing pigs to influenza viruses. In a longitudinal study on 14 farrow-to-finish herds and 15 finishing herds, groups of pigs were followed by repeatedly testing the same animals for antibodies against all three influenza virus subtypes (H1N1, H3N2 and H1N2). At the end of the finishing period, the seroprevalences in farrow-to-finish and specialised finishing herds were 44.3% and 62.0%, respectively for H1N1, 6.6% and 19.3%, respectively for H3N2, and 57.2% and 25.6%, respectively for H1N2. For all three subtypes, the incidence of influenza virus infections was highest at the beginning of the finishing period in farrow-to-finish herds, while the incidence of influenza virus infections was highest at the end of the finishing period in finishing herds. Respiratory disease, probably related to the influenza infections, was observed in five of these herds only, but also occurred at the beginning of the finishing period in farrow-to-finish herds and at the end of the finishing period in finishing herds. The observed differences of population dynamics of influenza virus may affect choice and timing of intervention measures.

6 建立一个健全合理的方法来管理 2009 年甲型 H1N1 流感

Towards a sane and rational approach to management of Influenza H1N1 2009.

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Gallaher WR.

ABSTRACT: Beginning in March 2009, an outbreak of influenza in North America was found to be caused by a new strain of influenza virus, designated Influenza H1N1 2009, which is a reassortant of swine, avian and human influenza viruses. Over a thousand total cases were identified with the first month, chiefly in the United States and Mexico, but also involving several European countries. Actions concerning Influenza H1N1 2009 need to be based on fact and science, following recommendations of public health officials, and not fueled by political, legal or other interests. Every influenza outbreak or pandemic is unique, so the facts of each one must be studied before an appropriate response can be developed. While reports are preliminary, through the first 4 weeks of the outbreak it does not appear to be severe either in terms of the attack rate in communities or in the virulence of the virus itself. However, there are significant changes in both the hemagglutinin and neuraminidase proteins of the new virus, 27.2% and 18.2% of the amino acid sequence, from prior H1N1 isolates in 2008 and the current vaccine. Such a degree of change qualifies as an "antigenic shift", even while the virus remains in the H1N1 family of influenza viruses, and may give

influenza H1N1 2009 significant pandemic potential. Perhaps balancing this shift, the novel virus retains more of the core influenza proteins from animal strains than successful human influenza viruses, and may be inhibited from its maximum potential until further reassortment or mutation better adapts it to multiplication in humans. While contact and respiratory precautions such as frequent handwashing will slow the virus through the human population, it is likely that development of a new influenza vaccine tailored to this novel Influenza H1N1 2009 strain will be essential to blunt its ultimate pandemic impact.

发送：中心甲型 H1N1 流感病毒防控领导小组成员

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