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Cuprins

INFECȚIA UMANĂ CU VIRUSUL GRIPAL A(H7N9)
– World Health Organization. Global Alert and Response (GAR)
– The Global Early Warning System „GLEWS“

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HUMAN INFECTION WITH INFLUENZA A(H7N9) VIRUS IN CHINA - UPDATE

World Health Organization

7 APRIL 2013 - As of 7 April 2013 (16:30 CET), the Chinese health authorities notified WHO of an additional three laboratory-confirmed cases of human infection with influenza A(H7N9) virus.

The first patient is a 59-year-old man resident of Shanghai, who became ill on 25 March 2013, and is now in critical condition. The second patient is a 55-year-old man from Anhui who became ill on 28 March 2013, and is now in stable condition. The third patient is a 67-year-old man from Shanghai who became ill on 29 March 2013, and is considered a mild case.

To date, a total of 21 cases have been laboratory confirmed with influenza A(H7N9) virus in China, including six deaths, 12 severe cases and three mild cases.

More than 530 close contacts of the confirmed cases are being closely monitored. In Jiangsu, investigation is ongoing into a contact of an earlier confirmed case who developed symptoms of illness.

The Chinese government is actively investigating this event and has heightened disease surveillance. Retrospective testing of recently reported cases with severe respiratory infection may uncover additional cases that were previously unrecognized. An inter-government task force has been formally established, with the National Health and Family Planning Commission leading the coordination along with the Ministry of Agriculture and other key ministries. The animal health sector has intensified investigations into the possible sources and reservoirs of the virus.

WHO is in contact with national authorities and is following the event closely. The WHO-coordinated international response is also focusing on work with WHO Collaborating Centres for Reference and Research on Influenza and other partners to ensure that information is available and that materials are developed for diagnosis and treatment and vaccine development. No vaccine is currently available for this subtype of the influenza virus. Preliminary test results provided by the WHO Collaborating Centre in China suggest that the virus is susceptible to the neuraminidase inhibitors (oseltamivir and zanamivir).

At this time there is no evidence of ongoing human-to-human transmission.

WHO does not advise special screening at points of entry with regard to this event, nor does it recommend that any travel or trade restrictions be applied.

BACKGROUND AND SUMMARY OF HUMAN INFECTION WITH INFLUENZA A(H7N9) VIRUS– AS OF 5 APRIL 2013

World Health Organization

Background and summary of human infection with influenza A(H7N9) virus– as of 5 April 2013

In the past few weeks, WHO has received from China reports of human infection with influenza A(H7N9) virus. The influenza A(H7N9) virus is one subgroup among the larger group of H7 viruses, which normally circulate among birds.

Human infections with other subgroups of H7 influenza viruses (H7N2, H7N3, and H7N7) have previously been reported in the Netherlands, Italy, Canada, United States of America, Mexico and the United Kingdom. Most of these infections occurred in association with poultry outbreaks. The infections mainly resulted in conjunctivitis and mild upper respiratory symptoms, with the exception of one death, which occurred in the Netherlands.

These recent reports from China are the first cases of human infection with H7N9 viruses.

EPIDEMIOLOGY

The reported laboratory-confirmed cases have come from several different provinces in eastern China and are not known to be linked. All patients so far have been severely ill, and some have died (for the latest information on cases and outcomes, see Disease Outbreak News.

Two family clusters have been reported. Beyond these two clusters, no cases have been reported among contacts or in health care workers associated with confirmed cases.

The source of infection and the mode of transmission are currently unknown. No association with outbreaks of disease among animals or clear exposure to animals has been established. Some of the confirmed cases had contact with animals or with environments in which animals were located. The virus has been found in a pigeon in a market in Shanghai. The possibility of animal-to-human transmission is being investigated, as is the possibility of human-to-human transmission. The family cluster raises the possibility of human-to-human transmission, but two of the cases in that cluster have not been laboratory confirmed and there is no other evidence pointing toward sustained transmission among people.

CLINICAL PRESENTATION

The main clinical feature among most patients is respiratory diseases resulting in severe pneumonia. Symptoms include fever, cough and shortness of breath. Patients have required intensive care and mechanical ventilation. Information is, however, still limited about the full spectrum of disease that this infection might cause.

VIROLOGY

The HA gene is genetically distinct from the HA gene of other H7 viruses. The six internal genes are derived from influenza A(H9N2) viruses circulating in birds in eastern Asia. The NA gene is similar to the NA genes from influenza A(H11N9) viruses detected in birds in previous years.

We do not know why cases of influenza A(H7N9) virus infection are being detected now , as we do not know how these persons were infected. Sequence analyses have shown that the genes of the influenza A(H7N9) viruses from the first human cases in China are of avian (bird) origin. However, these genes also show signs of adaption to growth in mammalian species. These adaptations include an ability to bind to mammalian cell receptors, and to grow at temperatures close to the normal body temperature of mammals (which is lower than that of birds).

TREATMENT

Laboratory testing conducted in China has shown that the influenza A(H7N9) viruses are sensitive to the anti-influenza drugs known as neuraminidase inhibitors (oseltamivir and zanamivir). When these drugs are given early in the course of illness, they have been found to be effective against seasonal influenza virus and influenza A(H5N1) virus infection. There is no experience yet with the use of these drugs for the treatment of H7N9 infection.

PREVENTION

No vaccine for the prevention of influenza A(H7N9) infections is currently available, although viruses have already been isolated and characterized from the initial cases. The first step in development of a vaccine is the selection of candidate viruses that could go into a vaccine. WHO, in collaboration with partners, will continue to characterize available influenza A(H7N9) viruses to identify the best candidate viruses. These candidate vaccine viruses can then be used for the manufacture of vaccine should this become necessary.

While the source of infection and the mode of transmission have not yet been determined, it is prudent to follow good hygiene practices to prevent infection. For advice on infection prevention, contact with animals and food preparation, see:http://www.who.int/influenza/human_animal_interface/faq_H7N9/en/. Guidance for infection prevention and control in health care settings is available athttp://www.who.int/csr/resources/publications/swineflu/WHO_CDS_EPR_2007_6/en/index.html.

Current activities

WHO has closely monitored the situation since detection of the first case and has been working with partners to ensure a high degree of preparedness should the new virus be found to be sufficiently transmissible to cause community outbreaks. We have also been working with animal health partners to investigate possible circulation in animals. Some viruses are able to cause limited human-to-human transmission under condition of close contact, as occurs in families, but are not transmissible enough to cause larger community outbreaks.

Actions taken by WHO in coordination with national authorities and technical partners include the following:

• Information is being provided to countries under the International Health Regulations (IHR).

• Enhanced surveillance for pneumonia cases of unknown origin to ensure early detection and laboratory confirmation of new cases.

• Epidemiological investigation, including assessment of suspected cases and contacts of known cases.

• Close collaboration with animal health partners, specifically the World Organization for Animal Health (OIE), the Food and Agriculture Office of the United Nations (FAO) and the OIE/FAO Network of Expertise on Animal Influenza (OFFLU), to investigate possible circulation of this virus in animals and to ensure that materials and information, including laboratory test reagents, are shared between animal health and public health laboratories.

• Continuous risk assessment of the situation in collaboration with the WHO Global Influenza Surveillance and Response System (GISRS), which is comprised of WHO Collaborating Centres for Reference and Research on Influenza, National Influenza Centres and Essential Regulatory Laboratories (seehttp://www.who.int/influenza/gisrs_laboratory/en/); in animal health laboratories, coordinated by the WHO-OFFLU collaboration; and with other technical partners.

WHO RECOMMENDATIONS

Based on the current situation and available information, WHO advises the following:

• When laboratories testing for influenza viruses detect an influenza A virus by RT-PCR assays using primers for the conserved M genes and then find that tests using currently available H1, H3 and H5 primers are negative, such unsubtypable influenza A viruses should be sent urgently to a WHO Collaborating Centre for further analysis (seehttp://www.who.int/influenza/gisrs_laboratory/collaborating_centres/en/).

• When a laboratory or Member State finds such an unsubtypable influenza A virus, the finding should be reported to WHO through the International Health Regulations national focal point as is required under the IHR.

• The same surveillance strategy applies as for human infections with highly pathogenic avian influenza A (H5N1) virus.

• Clinicians and laboratory specialists should consider the possibility of human infection with influenza in any person presenting with severe acute respiratory disease.

• Clinicians are reminded of standard guidance for infection control and contact tracing around such cases.

• Standard guidance should also be applied for vigorously investigating clusters of severe respiratory infections and such infections in health care workers who have been caring for patients with severe acute respiratory disease.

• WHO does not advise special screening at points of entry with regard to this event nor does it recommend that any travel or trade restrictions be applied.

SUMMARY

Any animal influenza virus that develops the ability to infect people can theoretically cause a pandemic.

However, whether the influenza A(H7N9) virus could actually cause a pandemic is unknown. Experience has shown that some animal influenza viruses that have been found to occasionally infect people have not gone on to cause a pandemic while others have done so. Surveillance and the investigations now underway will provide some of the information needed to make this determination.

WHO continues to work closely with national authorities and technical partners to gain a better understanding of this disease in humans and will continue to provide updated information. WHO will continue to reassess the situation as it evolves. As more information becomes available WHO will revise its guidance and actions accordingly.

FREQUENTLY ASKED QUESTIONS ON HUMAN INFECTION WITH INFLUENZA A(H7N9) VIRUS, CHINA

World Health Organization

Update as of 5 April 2013

Note that this document supersedes the previous version. Updates will be posted as new information becomes available.

1. What is the influenza A(H7N9) virus?

Influenza A H7 viruses are a group of influenza viruses that normally circulate among birds. The influenza A(H7N9) virus is one subgroup among the larger group of H7 viruses. Although some H7 viruses (H7N2, H7N3 and H7N7) have occasionally been found to infect humans, no human infections with H7N9 viruses have been reported until recent reports from China.

2. What are the main symptoms of human infection with influenza A(H7N9) virus?

Thus far, most patients with this infection have had severe pneumonia. Symptoms include fever, cough and shortness of breath. However, information is still limited about the full spectrum of disease that infection with influenza A(H7N9) virus might cause.

3. How many human cases of influenza A(H7N9) virus have been reported in China to date?

New cases that are reported are now being compiled and posted daily. The most current information on cases can be found in Disease Outbreak News.

4. Why is this virus infecting humans now?

We do not know the answer to this question yet, because we do not know the source of exposure for these human infections. However, analysis of the genes of these viruses suggests that although they have evolved from avian (bird) viruses, they show signs of adaption to growth in mammalian species. These adaptations include an ability to bind to mammalian cells, and to grow at temperatures close to the normal body temperature of mammals (which is lower than that of birds).

5. What is known about previous human infections with H7 influenza viruses globally?

From 1996 to 2012, human infections with H7 influenza viruses (H7N2, H7N3, and H7N7) were reported in the Netherlands, Italy, Canada, United States of America, Mexico and the United Kingdom. Most of these infections occurred in association with poultry outbreaks. The infections mainly resulted in conjunctivitis and mild upper respiratory symptoms, with the exception of one death, which occurred in the Netherlands. Until now, no human infections with H7 influenza viruses have been reported in China.

6. Is the influenza A(H7N9) virus different from influenza A(H1N1) and A(H5N1) viruses?

Yes. All three viruses are influenza A viruses but they are distinct from each other. H7N9 and H5N1 are considered animal influenza viruses that sometimes infect people. H1N1 viruses can be divided into those that normally infect people and those that normally infect animals.

7. How did people become infected with the influenza A(H7N9) virus?

Some of the confirmed cases had contact with animals or with an animal environment. The virus has been found in a pigeon in a market in Shanghai. It is not yet known how persons became infected. The possibility of animal-to-human transmission is being investigated, as is the possibility of person-to-person transmission.

8. How can infection with influenza A(H7N9) virus be prevented?

Although both the source of infection and the mode of transmission are uncertain, it is prudent to follow basic hygienic practices to prevent infection. They include hand and respiratory hygiene and food safety measures.

Hand hygiene:

• Wash your hands before, during, and after you prepare food; before you eat; after you use the toilet; after handling animals or animal waste; when your hands are dirty; and when providing care when someone in your home is sick. Hand hygiene will also prevent the transmission of infections to yourself (from touching contaminated surfaces) and in hospitals to patients, health care workers and others.

• Wash your hands with soap and running water when visibly dirty; if not visibly dirty, wash your hands with soap and water or use an alcohol-based hand cleanser.

Respiratory hygiene:

• Cover your mouth and nose with a medical mask, tissue, or a sleeve or flexed elbow when coughing or sneezing; throw the used tissue into a closed bin immediately after use; perform hand hygiene after contact with respiratory secretions.

9. Is it safe to eat meat, i.e. poultry and pork products?

Influenza viruses are not transmitted through consuming well-cooked food. Because influenza viruses are inactivated by normal temperatures used for cooking (so that food reaches 70°C in all parts—"piping" hot — no "pink" parts), it is safe to eat properly prepared and cooked meat, including from poultry and game birds.

Diseased animals and animals that have died of diseases should not be eaten.

In areas experiencing outbreaks, meat products can be safely consumed provided that these items are properly cooked and properly handled during food preparation. The consumption of raw meat and uncooked blood-based dishes is a high-risk practice and should be discouraged.

10. Is it safe to visit live markets and farms in areas where human cases have been recorded?

When visiting live markets, avoid direct contact with live animals and surfaces in contact with animals. If you live on a farm and raise animals for food, such as pigs and poultry, be sure to keep children away from sick and dead animals; keep animal species separated as much as possible; and report immediately to local authorities any cases of sick and dead animals. Sick or dead animals should not be butchered and prepared for food.

11. Is there a vaccine for the influenza A(H7N9) virus?

No vaccine for the prevention of influenza A(H7N9) infections is currently available. However, viruses have already been isolated and characterized from the initial cases. The first step in development of a vaccine is the selection of candidate viruses that could go into a vaccine. WHO, in collaboration with partners, will continue to characterize available influenza A(H7N9) viruses to identify the best candidate viruses. These candidate vaccine viruses can then be used for the manufacture of vaccine if this step becomes necessary.

12. Does treatment exist for influenza A(H7N9) infection?

Laboratory testing conducted in China has shown that the influenza A(H7N9) viruses are sensitive to the anti-influenza drugs known as neuraminidase inhibitors (oseltamivir and zanamivir). When these drugs are given early in the course of illness, they have been found to be effective against seasonal influenza virus and influenza A(H5N1) virus infection. However, at this time, there is no experience with the use of these drugs for the treatment of H7N9 infection.

13. Is the general population at risk from the influenza A(H7N9) virus?

We do not yet know enough about these infections to determine whether there is a significant risk of community spread. This possibility is the subject of epidemiological investigations that are now taking place.

14. Are health care workers at risk from the influenza A(H7N9) influenza virus?

Health care workers often come into contact with patients with infectious diseases. Therefore, WHO recommends that appropriate infection prevention and control measures be consistently applied in health care settings, and that the health status of health care workers be closely monitored. Together with standard precautions, health care workers caring for those suspected or confirmed to

have influenza A(H7N9) infection should use additional precautions (http://www.who.int/csr/resources/publications/swineflu/WHO_CDS_EPR_2007_6/en/index.html).

15. What investigations have begun?

Local and national health authorities are taking the following measures, among others:

• Enhanced surveillance for pneumonia cases of unknown origin to ensure early detection and laboratory confirmation of new cases;

• Epidemiological investigation, including assessment of suspected cases and contacts of known cases;

• Close collaboration with animal health authorities to determine the source of the infection.

16. Does this influenza virus pose a pandemic threat?

Any animal influenza virus that develops the ability to infect people is a theoretical risk to cause a pandemic. However, whether the influenza A(H7N9) virus could actually cause a pandemic is unknown. Other animal influenza viruses that have been found to occasionally infect people have not gone on to cause a pandemic.

17. Is it safe to travel to China?

The number of cases identified in China is very low. WHO does not advise the application of any travel measures with respect to visitors to China nor to persons leaving China.

18. Are Chinese products safe?

There is no evidence to link the current cases with any Chinese products. WHO advises against any restrictions to trade at this time.

INFLUENZA AT THE HUMAN-ANIMAL INTERFACE

World Health Organization

Influenza viruses circulating in animals pose threats to human health. Humans can be exposed to these viruses, such as avian influenza virus subtypes H5N1 and H9N2 and swine influenza virus subtypes H1N1 and H3N2, in many ways, such as:

- when people's work brings them in contact with infected animals.
- when people contact infected animals during their everyday lives, such as when visiting live animal markets or when these animals are kept as part of the household.
- when people handle or slaughter infected animals, or work with raw meat and by-products from infected animals.
- when people contact things around them, such as animal housing areas and equipment, ponds and other water sources, faeces, and feathers, if these things are contaminated with influenza viruses.

In some cases these zoonotic infections (infections in humans acquired from an animal source) result in severe disease or even death in humans, but often these infections result in only a mild illness or appear to cause no illness at all. All human infections with animal influenza viruses are of concern, not only because of the cases of disease and deaths in individual people, but also because if these viruses become able to spread from human to human they could spark a pandemic. All of the past four pandemic influenza viruses have contained gene components originating in animals.

The actual public health risks posed by influenza viruses circulating in bird, swine, and other animal populations are not completely understood. Recent findings suggest that influenza viruses in animals and humans increasingly behave like a pool of genes circulating among multiple hosts, and that the potential exists for novel influenza viruses to be generated in swine and other animals. This situation reinforces the need for close monitoring and close collaboration between public health and veterinary authorities. WHO continues to work vigilantly with national ministries of health and animal health sector partners globally to identify and mitigate these influenza public health risks at the human-animal interface.

Most avian influenza viruses do not cause disease in humans. However, some are zoonotic, meaning that they can infect humans and cause disease. The most well known example is the avian influenza subtype H5N1 viruses currently circulating in poultry in parts of Asia and northeast Africa, which have caused human disease and deaths since 1997.

Other avian influenza subtypes, including H7N7 and H9N2, have also infected people. Some of these infections have been very severe and some have resulted in deaths, but many infections have been mild or even subclinical in humans.

Because birds play an important role as source of food and livelihoods in many countries affected by avian influenza viruses, WHO and animal health sector partners are working at the human-animal interface to identify and reduce animal health and public health eisks within national contexts.

SWINE INFLUENZA IN HUMANS

World Health Organization

Most swine influenza viruses (SIVs) do not cause disease in humans. However, some countries have reported cases of human infection with SIVs. Most of these human infections have been mild and the viruses have not spread further to other people. The H1N1 virus that caused the influenza pandemic in 2009-2010, thought to have originated in swine, is an example of an SIV that was able to spread easily among people and also cause disease.

Because pigs can become infected with influenza viruses from a variety of different hosts (such as birds and humans), they can act as a "mixing vessel," facilitating the reassortment of influenza genes from different viruses and creating a "new" influenza virus. The concern is that such "new" reassortant viruses may be more easily spread from person to person, or may cause more severe disease in humans than the original viruses. WHO and animal health sector partners are working at the human-animal interface to identify and reduce animal health and public health risks within national contexts.

THE GLOBAL EARLY WARNING SYSTEM (GLEWS)

Collect, verify, analyse and respondto information from a variety of sources, including unofficial media reports and informal networks. In addition, the OIE and WHO mandates include official notification of disease or infection outbreaks to the international community within conditions determined by their Member Countries. FAO has a broad mandate to diseminate information, including all agricultural statistics, to Member Countries.

The Global Early Warning System for Major Animal Diseases, including Zoonoses (GLEWS), builds on the added value of combining the alert mechanisms of the different organizations, enhacing the Early Warning capacity for the benefit of the international community. Through sharing of information on disease alerts, unjustified duplication of efforts will be avoided and the verification processes of the three organizations will be combined and coordinated. For zoonotic events, alerts of animal outbreaks can provide direct early warning so that human surveillance could be enhanced and preventive action taken. Similarly, there may be cases where human surveillance is more sensitive and alerts of human cases precede known animal occurrence of disease.

On the other hand, sharing assessments of an ongoing outbreak will enable a joint and comprehensive analysis of the event and its possible consequences. Joint dissemination will furthermore allow harmonized communication by the three organizations regarding disease control strategies.

Disease intelligence generated by GLEWS directly feeds into and informs the respective mechanisms of the three organizations, wich will be able to respond to a larger number and cover a wider range of outbreaks or exceptional epidemiological events with the provision of a wider range of expertise. This will improve international preparedness for epidemies and provide rapid, efficient and coordinated assitance to countries experiencing them.

GLEWS is based on the notion that infection does not recognize geographical nor species borders. For its zoonotic component it takes a stand in the shift in paradigm from independence to interdependence of agencies and professions in zoonotic control.

ABOUT GLEWS

The **Global Early Warning System (GLEWS)** is a joint system that builds on the added value of combining and coordinating the alert and disease intelligence mechanisms of OIE, FAO and WHO for the international community and stakeholders to assist in prediction, prevention and control of animal disease threats, including zoonoses, through sharing of information, epidemiological analysis and joint risk assessment.

Early warning of outbreaks and the capacity for prediction of spread to new areas is an essential pre-requisite for the effective containment and control of epidemic animal diseases, including zoonoses. As experienced throughout much of the globe, weaknesses of disease surveillance systems and the inability to control major diseases at their source have contributed to the spread across geographical borders of diseases confined to livestock, such as foot-and-mouth disease, as well as diseases with a zoonotic potential, e.g. BSE and avian influenza.

Early Warning is based on the concept that dealing with a disease epidemic in its early stages is easier and more economical than having to deal with it once it is widespread. From a public health perspective, early warning of outbreaks with a known zoonotic potential will enable control measures that can prevent human morbidity and mortality. Also, new previously unknown human infectious diseases have emerged and will continue to emerge from the animal reservoir.

The GLEWS team during a daily outbreak debriefing in the operation room.

Several initiatives, at national and regional level have already been developed in the field of early warning. At the international level FAO, OIE and WHO have each developed Early Warning Systems that systematically collect, verify, analyse and respond to information from a variety of sources, including unofficial media reports and informal networks. In addition, the OIE and WHO mandates include official notification of disease or infection outbreaks to the international community within conditions determined by their Member Countries. FAO has a broad mandate to disseminate information, including all agricultural statistics, to Member Countries.

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