

Avian influenza (H5N1) and human influenza (Novel Flu-A H1N1) current threats and Research agenda in Kenya

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By

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CRISIS

Temperature is key swine flu symptom

High fever is a key symptom that distinguishes A(H1N1) swine flu from regular human seasonal flu, with others including swollen glands, lethargy, lack of appetite, coughing, sore throat, nausea, vomiting and diarrhoea. Infected people shed the virus – and remain infectious to others – for five to seven days after symptoms appear

FEVER: Temperature rises from normal 37°C (98.6 °F) to up to 40°C (104°F).

Sustained fever above 38.3°C necessary for positive diagnosis

CHILDREN: Babies and small children with flu can also display the following symptoms: **Drowsiness, unresponsiveness, limpness, poor feeding, vomiting, diarrhoea**

■ Cover your nose and mouth when you cough or sneeze

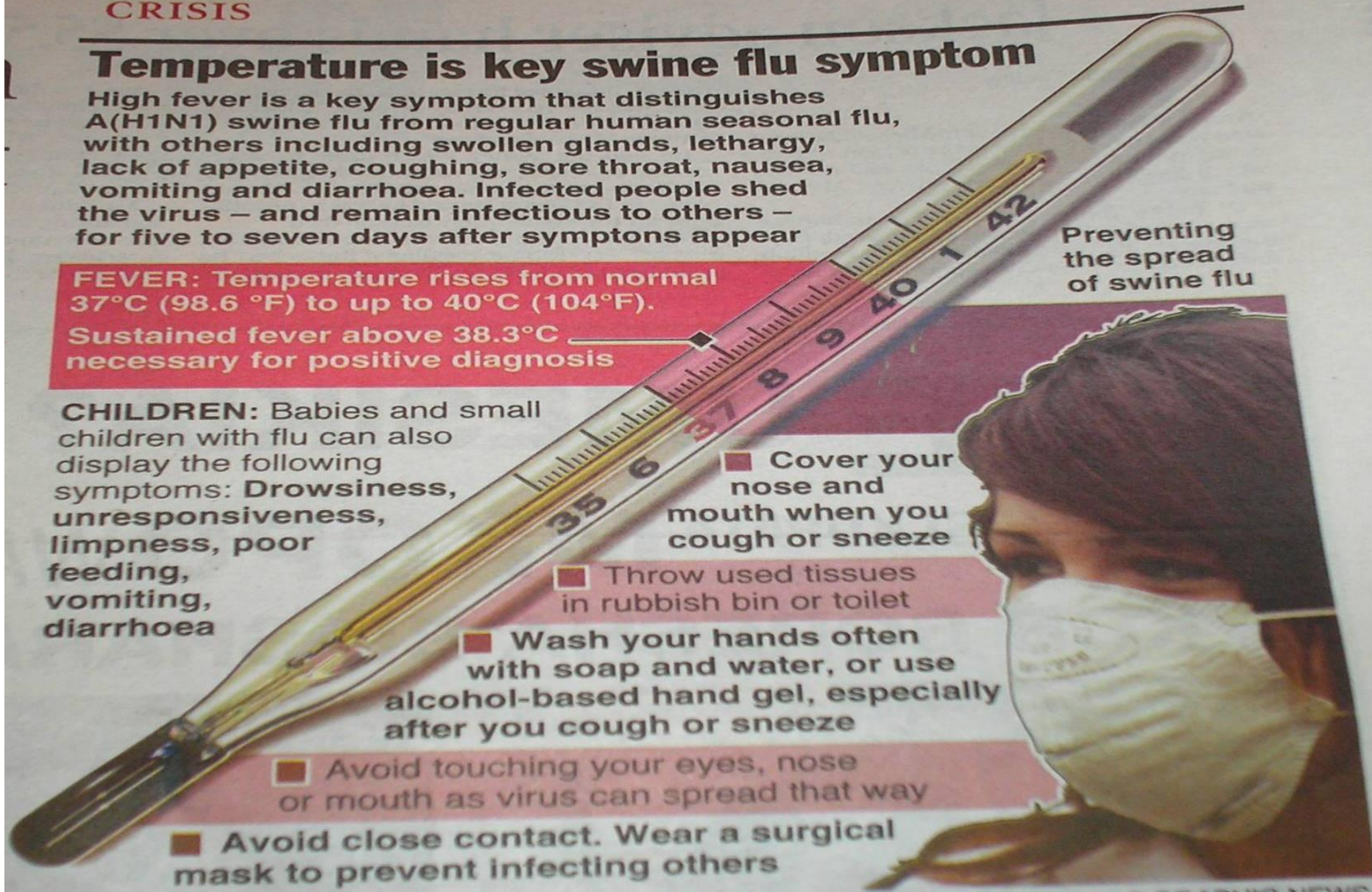
■ Throw used tissues in rubbish bin or toilet

■ Wash your hands often with soap and water, or use alcohol-based hand gel, especially after you cough or sneeze

■ Avoid touching your eyes, nose or mouth as virus can spread that way

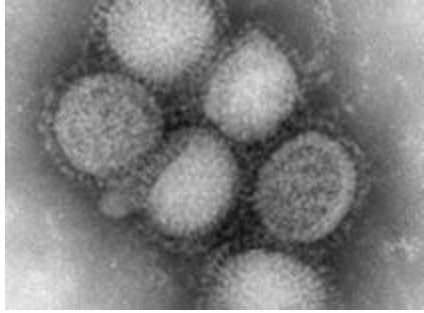
■ Avoid close contact. Wear a surgical mask to prevent infecting others

Preventing the spread of swine flu

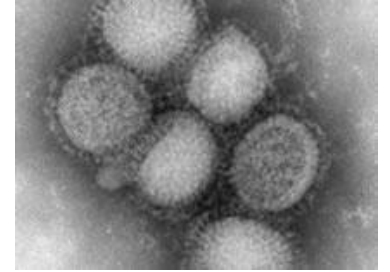


Avian flu deaths pic





Influenza in birds



- “ Representatives of all known influenza A subtypes have been isolated from aquatic birds
- “ Largest number of isolates from wild birds were from waterfowl: ducks, geese, terns, gulls.
- “ Domestic poultry isolates from: turkeys, chickens, quail, pheasants, geese and ducks.
- “ In waterfowl virus multiplies in the lungs and the gut and releases large quantities of virus in faeces into the environment. Virus survives the acid in the gizzard to multiply in the intestines

Influenza in birds

- “ Waterfowl may not show overt disease
- “ Subtypes that infect humans(H1N1, H2N2, H3N2) will replicate in duck gut cells.
- “ But if given intra-nasally only multiply in the lungs
- “ Avian influenza may reassort with swine or human viruses and infect humans
- “ They may cross species barrier and infect humans directly (e.g. H5N1 of 1997, 2003)
- “ Avian viruses from wild birds of low pathogenicity infect domestic birds as low pathogenic but soon change to high virulence and cause severe disease

Change of virulence (**LPAI to HPAI**)

- “ Avian influenza viruses **produce little or no disease in wild ducks** (Low Pathogenic Avian influenza strains - **LPAI**)
- “ After circulating in the poultry for some time which may be short or long, they, under yet unknown influence, change to highly pathogenic avian influenza - **HPAI** and produce severe systemic infection, disease and very high mortalities in poultry.
- “ **Examples of these Strains: H5, H7 subtypes (H9)** with different N combinations, e.g. H5N2, H5N1, H7

Influenza gene constellations

There are (**NOT one but many = 8**) genes:

1. RNA segments coding for the external spike proteins:

- . (**HA**= hemagglutinin, **NA**= neuraminidase, and **M2**= matrix protein 2)

2. RNA segments coding for the internal proteins:

- . (**PB2, PB1, PA**) = polymerase
- . **NP** = nucleoprotein
- . **M1** = matrix protein-2
- . **NS** = non structural proteins)

Virus receptors

- “ Alpha 2-3 = avian affinity
- “ Alpha 2-6 = human affinity

- “ Pigs have both types of receptors
- “ And can therefore allow propagation of swine, human, and avian virus to occur in their trachea.

Influenza in swine

Influenza subtypes in swine

Classic swine influenza subtypes:

1. H1N1 (first observed in 1918 Spanish pandemic); 1976 one man who died; man and pig from the same farm . genetically indistinguishable isolate recovered from both.
2. H1N2 (Europe and Japan). reassortants of H1N1 and H3N2
3. H3N2 swine (Isolated from swine during a human of disease in humans in Taiwan 1970); and **H3N2** variants of humans replicate in swine ; ---1998 ONE* pig isolates containing:
 - A. 1995 human H3N2 genes= (**HA, NA, PB1**),
 - B. Classic swine genes = (**NP, M, and NS**)
 - C. Avian genes = (**PB2, PA**)The other isolate had:
 - A. Humans genes = (**HA, NA, PB1**)
 - B. Classic swine genes = (**NP,M,NS,PB2,PA**)

* = widespread in swine populations in USA.

Could H1N1 % swine flu+have arisen in similar manner silently in some pig herds?

Influenza subtypes in swine

4. H3N1.

Recovered but not established disease status

” H1H7

” H9N2

The pandemic novel Swine Flu = FluA H1N1
has not been isolated from pigs yet , 2009.

Pig influenza viruses ecology

- “ Viruses of the classical H1N1 lineage were virtually the exclusive cause of swine influenza from the time of their initial isolation in 1930 through 1998.
- “ **Antigenic drift variants** of these H1N1 viruses were isolated in 1991-1998,
- “ but a much more dramatic **antigenic shift occurred with the emergence of H3N2 viruses in 1997-1998.**
- “ In particular, H3N2 viruses with genes derived from **human, swine and avian viruses have become a major cause of swine influenza in North America.**
- “ In addition, **H1N2 viruses that resulted from reassortment between the triple reassortant H3N2 viruses and classical H1N1 swine viruses** have been isolated subsequently from pigs in at least six USA states.
- “ Finally, **avian H4N6 viruses crossed the species barrier to infect pigs in Canada in 1999.**
- “ Fortunately, these H4N6 viruses have not been isolated beyond their initial farm of origin.

“ Transmission of avian influenza viruses to swine in Europe in 1979 has resulted in the appearance of human-avian reassortant influenza viruses in pigs in Italy and in children in the Netherlands

Why is novel H1N1 virus sometimes called “swine flu”?

”

This virus was originally referred to as “swine flu” because laboratory testing showed that many of the genes in this new virus were very similar to influenza viruses that normally occur in pigs in North America.

”

But further study has shown that this new virus is very different from what normally circulates in North American pigs.

”

It has two genes from flu viruses that normally circulate in pigs in Europe and Asia and avian genes and human genes.

”

Scientists call this a “quadruple reassortant” virus.

Generation of Influenza pandemic strain in swine

- “ Triple-reassortant swine influenza A (H1) viruses, containing genes from **avian, human, and swine influenza viruses**, emerged and became an outbreak among humans worldwide.
- “ **Pigs are susceptible to avian, human and swine** influenza viruses, they potentially may be infected with influenza viruses from different species (e.g., ducks and humans) **at the same time hence the possibility of the tripple reassortants arising**. The new strain would be having and **antigenic shift** with the potential to generate a pandemic !!! --- location of shift genesis not know !!!
- “ This became true with the current world wide human flu pandemic
- “ **Note** : humans and chickens **also have the** two receptor types in the trachea **and may have the potential to generate antigenic shift** through concurrent subtype infections

Influenza in swine

- “ Influenza A viruses are found in many different animals, including ducks, chickens, pigs, whales, horses and seals.
- “ Pigs can be infected with both human and avian influenza viruses in addition to swine influenza viruses.
- “ Infected pigs get symptoms similar to humans, such as cough, fever and runny nose.
- “ Because pigs are susceptible to avian, human and swine influenza viruses, they potentially may be infected with influenza viruses from different species (e.g., ducks and humans) at the same time.
- “ If this happens, it is possible for the genes of these viruses to mix and create a new virus.
- “ This type of major change in the influenza A viruses is known as **antigenic shift**.
- “ Antigenic shift results when a new influenza A subtype to which most people have little or no immune protection infects humans.
- “ If this new virus causes illness in people and can be transmitted easily from person to person, an influenza pandemic can occur

Influenza in swine

“ **Can humans catch swine flu?**

Swine flu viruses do not normally infect humans. However, sporadic human infections with swine flu have occurred. Most commonly, these cases occur in persons with direct exposure to pigs (e.g. children near pigs at a fair or workers in the swine industry). In addition, there have been documented cases of one person spreading swine flu to others. For example, an outbreak of apparent swine flu infection in pigs in Wisconsin in 1988 resulted in multiple human infections, and, although no community outbreak resulted, there was antibody evidence of virus transmission from the patient to health care workers who had close contact with the patient.

“ **How common is swine flu infection in humans?**

In the past, CDC received reports of approximately one human swine influenza virus infection every one to two years in the U.S., but from December 2005 through February 2009, 12 cases of human infection with swine influenza have been reported.

“ **What are the symptoms of swine flu in humans?**

The symptoms of swine flu in people are expected to be similar to the symptoms of regular human [seasonal influenza](#) and include fever, lethargy, lack of appetite and coughing. Some people with swine flu also have reported runny nose, sore throat, nausea, vomiting and diarrhea.

Case study

- “ **What do we know about swine -to-human spread of classic swine flu?**
- “ In September 1988, a **previously healthy 32-year-old pregnant woman** was hospitalized for pneumonia and died 8 days later. **A classic swine H1N1** flu virus was detected in her tissues. **Four days before getting sick, the patient visited a county fair swine exhibition where there was widespread influenza-like illness among the swine.**

What medications are available to treat “Swine flu” infections in humans?

- “ There are four different antiviral drugs that are licensed for use in the US for the treatment of influenza:
 - “ amantadine,
 - “ rimantadine,
 - “ oseltamivir and
 - “ zanamivir.
- “ While most swine influenza viruses have been susceptible to all four drugs, the most recent seven swine influenza viruses isolated from humans are **resistant to amantadine and rimantadine**.
- “ At this time, CDC recommends the use of **oseltamivir or zanamivir for the treatment and/or prevention** of infection with swine influenza viruses.

CONFIRMATION OF INFECTION WITH

- “ Only RT-PCR or viral culture can confirm infection with swine-origin influenza A (H1N1) virus.
- “ The test performance of rapid antigen tests and immunofluorescence tests for detection of swine-origin influenza A (H1N1) virus is unknown.
- “ Persons who might have swine-origin influenza A (H1N1) virus and who test positive for influenza A using one of these tests should have confirmatory RT-PCR or viral culture testing to confirm the presence of swine-origin influenza A (H1N1) virus.
- “ A negative rapid antigen or immunofluorescence test cannot be used to rule out swine-origin influenza A (H1N1) virus infection.

Treatment and antiviral Resistance

- “ This **swine** influenza A (H1N1) virus is sensitive (susceptible) to the neuraminidase inhibitor antiviral medications zanamivir and oseltamivir.
- “ It is resistant to the adamantane antiviral medications, amantadine and rimantadine.

Table 1. Swine-origin influenza antiviral medication dosing recommendations.
 (Table extracted from [IDSA guidelines for seasonal influenza](#).)

| Agent, group | | Treatment | Chemoprophylaxis |
|--|---------------|--|---|
| Oseltamivir | | | |
| Adults | | 75 - mg capsule twice per day for 5 days | 75 - mg capsule once per day |
| Children (age, 12 months or older), weight: | 15 kg or less | 60 mg per day divided into 2 doses | 30 mg once per day |
| | 15-23 kg | 90 mg per day divided into 2 doses | 45 mg once per day |
| | 24-40 kg | 120 mg per day divided into 2 doses | 60 mg once per day |
| | >40 kg | 150 mg per day divided into 2 doses | 75 mg once per day |
| Zanamivir | | | |
| Adults | | Two 5 - mg inhalations (10 mg total) twice per day | Two 5 - mg inhalations (10 mg total) once per day |
| Children | | Two 5 - mg inhalations (10 mg total) twice per day (age, 7 years or older) | Two 5 - mg inhalations (10 mg total) once per day (age, 5 years or older) |

Table 2. Dosing recommendations for antiviral treatment of children younger than 1 year using oseltamivir.

| Age | Recommended treatment dose for 5 days |
|-------------|--|
| <3 months | 12 mg twice daily |
| 3-5 months | 20 mg twice daily |
| 6-11 months | 25 mg twice daily |

Table 3. Dosing recommendations for antiviral chemoprophylaxis of children younger than 1 year using oseltamivir.

| Age | Recommended prophylaxis dose for 10 days |
|-------------|---|
| <3 months | Not recommended unless situation judged critical due to limited data on use in this age group |
| 3-5 months | 20 mg once daily |
| 6-11 months | 25 mg once daily |

| Seasonal influenza: | Pandemic influenza: |
|--|---|
| <i>Human routine viral respiratory infection</i> | <i>Global outbreak of new strain of human influenza virus</i> |
| <i>Self-limiting, but can be serious and fatal in the elderly and the very young</i> | <i>Causes increased illness and death worldwide</i> |
| <i>Causes an estimated 250,000-500,000 deaths each year</i> | <i>Rare event; has occurred every 11-42 years over the past two centuries; could cause millions of deaths</i> |
| <i>Occurs seasonally every year; occurs in winter in temperate areas</i> | <i>Three pandemics in the past 100 years: 1968, 1957 and 1918</i> |
| <i>Routine vaccines available</i> | <i>Vaccines can only be developed once we know the strain of the virus.</i> |

Does Flu differ from common cold ?

| Symptoms | Cold | Flu |
|--------------------------------|---------------------------------------|--|
| <i>Fever</i> | <i>Rare</i> | <i>Usual; high (100°F to 102°F; occasionally higher, especially in young children); lasts 3-4 days</i> |
| <i>Headache</i> | <i>Rare</i> | <i>Common</i> |
| <i>General aches, pains</i> | <i>Slight</i> | <i>Usual; often severe</i> |
| <i>Fatigue, weakness</i> | <i>Sometimes</i> | <i>Usual; can last up to 2-3 weeks</i> |
| <i>Extreme exhaustion</i> | <i>Never</i> | <i>Usual; especially at the beginning of the illness</i> |
| <i>Stuffy nose</i> | <i>Common</i> | <i>Sometimes</i> |
| <i>Sneezing</i> | <i>Usual</i> | <i>Sometimes</i> |
| <i>Sore throat</i> | <i>Common</i> | <i>Sometimes</i> |
| <i>Chest discomfort, cough</i> | <i>Mild to moderate hacking cough</i> | <i>Common; can become severe</i> |

- “ severe pneumonia was reported in conjunction
- “ with the concurrent isolation of a novel swine-origin influenza A (H1N1) virus
- “ a novel swine-origin influenza A (H1N1) virus (S-OIV), isolated recently , widely known as swine flu, in Mexico.
- “ Influenza A (H1N1) subtype viruses have rarely predominated since the 1957 pandemic. The analysis of epidemic pneumonia in the absence of routine diagnostic tests can provide information about risk factors for severe disease from this virus and prospects for its control

- “ From March 24 to April 29, 2009, a total of 2155 cases of severe pneumonia, involving
- “ 821 hospitalizations and 100 deaths, were reported to the Mexican Ministry of Health.
- “ During this period, of the 8817 nasopharyngeal specimens that were submitted to the National Epidemiological Reference Laboratory, 2582 were positive for S-OIV.
- “ We compared the age distribution of patients who were reported to have severe pneumonia with that during recent influenza epidemics to document an age shift in rates of death and illness.

The symptoms of Influenza A H1N1

ADULTS:

- “ Temperature rise from 38.3 to 40°C
- “ Sustained High fever necessary for diagnosis $\geq 38.3^{\circ}\text{C}$
- “ Swollen glands
- “ Lethargy/malaise
- “ Body aches
- “ Lack of appetite
- “ Coughing
- “ Sore throat
- “ Nausea
- “ Vomiting
- “ diarrhoea
- “ Severe pneumonia
- “ Virus shedding 5-7 days after signs appear

The symptoms of avian influenza H5N1 in humans

(be considered in countries with poultry avian H5N1)

- “ Fever $\geq 38^{\circ}\text{C}$
- “ Cough
- “ Running nose
- “ Headache
- “ Sore throat
- “ Pneumonia
- “ Swollen lymph nodes(lymph depletion)
- “ Vomiting
- “ Abdominal pain
- “ Diarrhoea

Ages affected

“ Features of this epidemic were similar to those of past influenza pandemics in that circulation of the new influenza virus was associated with an off-season wave of disease affecting a younger population

Source : Daily Nation 27th July, 2009 pg 21

CRISIS

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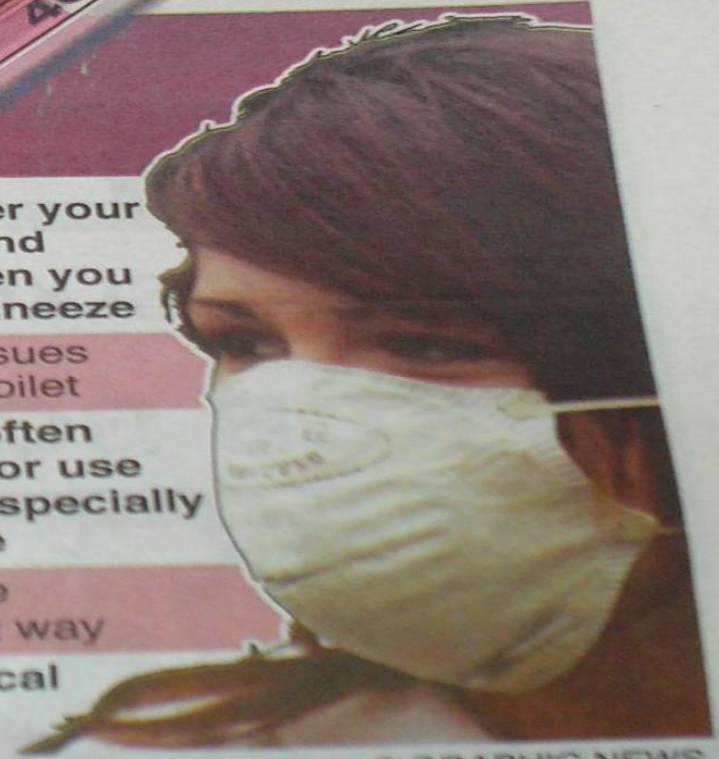
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■ Avoid close contact. Wear a surgical mask to prevent infecting others

Preventing the spread of swine flu



Media report in Kenya on safety steps to take when %swine influenza+

Flu A H1N1 in Mexico shifts illness pattern

| Deaths, pneumonia at ages 5-59 years and time of epidemic occurrence | | | |
|---|-----------|------------------|-----------------------|
| | Deaths(%) | Pneumonia (%) | Time of occurrence |
| Flu-A H1H1 | 87 | 71 | Off flu season |
| Seasonal influenza | 17 | 32 | In flu season |

How does Influenza A H1N1 spread?

- “ Influenza viruses are mainly spread from one person to another through droplets released during coughing or sneezing;
- “ Sometimes people may become infected by touching surfaces or holding objects contaminated with influenza viruses (e.g., hands, door handles, handkerchiefs, tissue paper) and then touching their own mouth, nose or eyes.



Does novel Flu A H1N1 spread from person to person less or more effectively than other flu viruses

- “ A team from the Massachusetts Institute of Technology (MIT) and the Centers for Disease Control and Prevention found that the H1N1 strain, which circled the globe recently has a form of surface protein that binds inefficiently to receptors found in the human respiratory tract.

Inability of H1N1 virus to spread easily among humans

- “ Virus binds human respiratory cell alpha 2-6 glycan receptors, not to alpha 2-3 glycan receptors and appears to be restricted,
- “ A genetic variation in the novel FluA H1N1 viral RNA polymerase known as PB2 which is critical for efficient influenza transmissibility, further adds to the explanation why the virus has not spread as efficiently as seasonal flu does.
- “ Flu viruses mutate rapidly, so there is great cause for concern if H1N1 undergoes mutations that improve its binding affinity.. it will establish itself as an effective seasonal influenza flu virus worldwide.
- “ Pandemic status:
Countries in more than four continents now exposed

Alpha 2-3, alpha 2-6 binding



Avoiding being infected?

- “ Regular washing of hands with soap and water (or with an alcohol-based handrub, if available) is strongly recommended;
- “ Keep a distance of at least **two metres (six feet)** from the infected person to avoid coming into contact with the **influenza droplets**;
- “ If contact with a sick person or with potentially infected surfaces or objects occurs, those involved must not **touch their eyes, nose or mouth with unwashed hands**;

How can an individual avoid being infected?

- “ Avoid close contact with a sick person;
- “ Refrain from handshaking, kissing or hugging during an outbreak;
- “ Those taking care of a sick person should use a face mask in accordance with guidelines provided by national health authorities;
- “ Be physically active, drink plenty of fluids, eat well, reduce stress and have enough sleep to boost their immunity.
- “ Use approved disinfectants to decontaminate hands and appliances





What can infected individuals do to prevent spreading Influenza A H1N1 to others?

- “ Cover the mouth with a piece of cloth or tissue paper when sneezing or coughing;
- “ Properly dispose used tissue paper; ????
- “ Cloth used be washed with soap, dried and replaced as often as required;
- “ The infected person should wear a mask when in contact with others;
- “ Tissue paper, cloth, a handkerchief or other material used by the sick person for wiping his nose or mouth, must not be used by others; ???

What can infected individuals do to prevent spreading Influenza A H1N1 to others?

- “ If there is no tissue paper or cloth, the sick person should sneeze or cough into his elbow, ??? and not into his hands ??? which can contaminate surfaces or things that may be touched or held;
- “ Hands be washed with soap and water especially after sneezing, or coughing, and before touching ??? door handles and other objects or surfaces so as to prevent contamination with droplets;
- “ Sick persons should stay at home and limit contact with others as much as possible.
- “ People should seek treatment immediately if infection is suspected, if symptoms occur or when advised by a health worker.

What should communities do to help prevent the spread of Influenza A H1N1?

- “ Ensure community members know how to prevent the spread of influenza, the symptoms of the disease and what to do if infection occurs;
- “ Ensure provision of care for those infected;
- “ Support social distancing, isolation or quarantine when requested by a health worker (or as determined by health authorities);
- “ Establish contact with the nearest health facility that will provide support in managing the disease;
- “ Report suspected cases and deaths to a health worker or other relevant authority.

Case study: Danish cases: 1999-2006

- “ RESULTS: H3N2 was the prevalent strain in Denmark during the study period, but H1N1 dominated the 2000-2001 season.
- “ H1N2 viruses were first observed in Denmark in 2002-2003.
- “ After years of little genetic change in the H1N1 viruses the 2005-2006 season presented H1N1 of greater variability than before.
- “ This indicates that H1N1 viruses are evolving and that H1N1 soon is likely to be the prevalent strain again.
- “ Generally, the influenza A haemagglutinin (HA) of H3N2 viruses formed seasonal phylogenetic clusters.
- “ Different lineages co-circulating within the same season
- “ Could we expect more changes?

“ Data are presented on structural variability of individual genes of selected variants of epidemic influenza viruses H1N1 (1977-1979) and H3N2 (1968-1979) in the course of antigenic drift obtained by oligonucleotide mapping. Six out of 8 genes of H1N1 viruses were found to be more variable than the corresponding genes of H3N2 viruses. Only HA and NS genes of H3N2 viruses underwent greater structural changes as compared with the analogous genes of H1N1 viruses. In viruses of both serotypes, most variable were the genes coding for hemagglutinin and matrix protein. Possible causes of greater structural variability of the matrix protein gene in the course of antigenic drift are discussed.



TRY THIS



OR ANY OF THESE



AND HAVE A FLU FREE COUNTRY

THANK YOU

THE END