

SWINE FLU AND ITS POSSIBLE THERAPY

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ABSTRACT

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. The novel H1N1 strain which is responsible for the current outbreak of Swine origin influenza was first recognized at the border between Mexico and in almost span of 2 months became first pandemic of 21st century. The most frequently reported symptoms in this are fever, cough, and sore throat; 25% of patients report diarrhoea, and a further 25% report vomiting. Myalgia and joint pains may also be present. Patients have radiologically confirmed pneumonia, of each type that includes pneumomediastinum, necrotizing pneumonia, and empyema. S-OIV is susceptible to oseltamivir and zanamivir, neuraminidase inhibitor antiviral medications, which target the early phase of the infection. However, this strain is resistant to adamantanes, such as amantadine and rimantadine. The possible herbal therapy includes drugs like Elderberry (*Sambucus nigra*), Japanese wasabi (*Wasabia japonica*), *Solanum tuberosum* ssp. *tuberosum* and *Solanum tuberosum* ssp. *andigena* and various immunoenhancers like *Ocimum sanctum* (holy basil), *Glycyrrhiza glabra*, *Allium sativum*, *Melissa officinalis* etc. This article collects the brief information about this particular disease and about their method of prevention which directly or indirectly provides help to the peoples of various countries.

Keywords: Elderberry, Swine Flu, Tami flu

1. INTRODUCTION

Swine flu, also known as Influenza A (H1N1), pig influenza, swine flu, hog flu and pig flu is a new influenza virus causing illness in people¹. It infects the respiratory tract and results in nasal secretions, a barking like cough, decreased appetite and listless behaviour. It has been found that this new virus has gene segments from the swine, avian and human flu virus genes, hence named "swine flu". The scientists call this a 'quadruple reassortant' virus and hence this new (novel) virus is christened "influenza-A (H1N1) virus." Influenza A H1N1 is a circulating seasonal influenza virus first reported in Mexico on 18th March, 2009 and then spread to neighbouring United States and Canada. As on 8th June, 2009, World Health Organization has reported 25,288 laboratory confirmed cases of influenza A/H1N1 infection with 139 deaths from 73 countries spread over America, Europe, Asia and Australian continent.

2. TRANSMISSION OF VIRUS TO HUMAN

Transmission of the virus from pigs to humans is not common and does not always lead to human influenza, often resulting only in the production of antibodies in the blood. If transmission does cause human influenza, it is called zoonotic swine flu. People with regular exposure to pigs are at increased risk of swine flu infection. The meat of an infected animal poses no risk of infection when properly cooked.

3. SYMPTOMS OF SWINE FLU

The U.S Centres for Disease Control and Prevention (CDC) includes following symptoms for Swine-Flu infection^{2,3}.

- Fever (94%)
- Cough (92%)
- Sore throat (66%)
- Diarrhoea (25%)
- Vomiting (25%)
- Myalgia and joint pains

Infants and elderly are more susceptible for serious infection. Pregnant women, people with chronic medical problems such as asthma, cardiovascular diseases, and diabetes are at high risk. The most common causes of death due to Swine-Flu are:

- Respiratory failure
- Pneumonia
- Sepsis
- Dehydration (from excessive vomiting)
- High fever
- Electrolyte imbalance.

4. INFECTION PERIOD

It should be considered that persons with Influenza H1N1 infection potentially infectious from 1 day before to 7 days following illness onset or until symptoms resolve. Children, patients with lower respiratory tract infections, elderly and immunocompromised patients might be infectious for up to 10 days or longer^{5,6}. This is due to low cytotoxic T-lymphocyte activity which is responsible for viral clearance and recovery from infection⁷. Cytotoxic T-

lymphocyte activity declines in the elderly as well as in immunocompromised individuals so that viral shedding could persist longer in them⁸. The potential for persons with asymptomatic infection to be the source of infection to others is unknown but should be investigated.

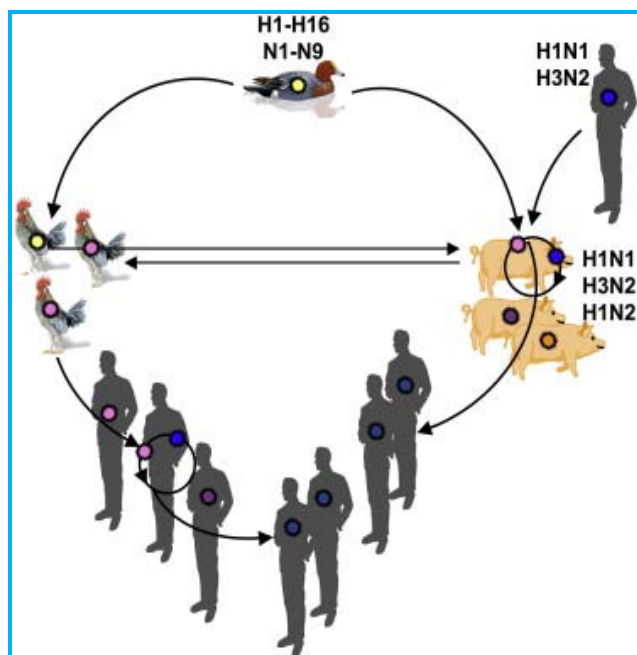


Figure 1: Models for the role of pigs in interspecies transmission and adaptation of influenza viruses. Pigs serve as reservoirs of H1N1, H3N2 and H1N2 influenza viruses which can be transmitted to humans.

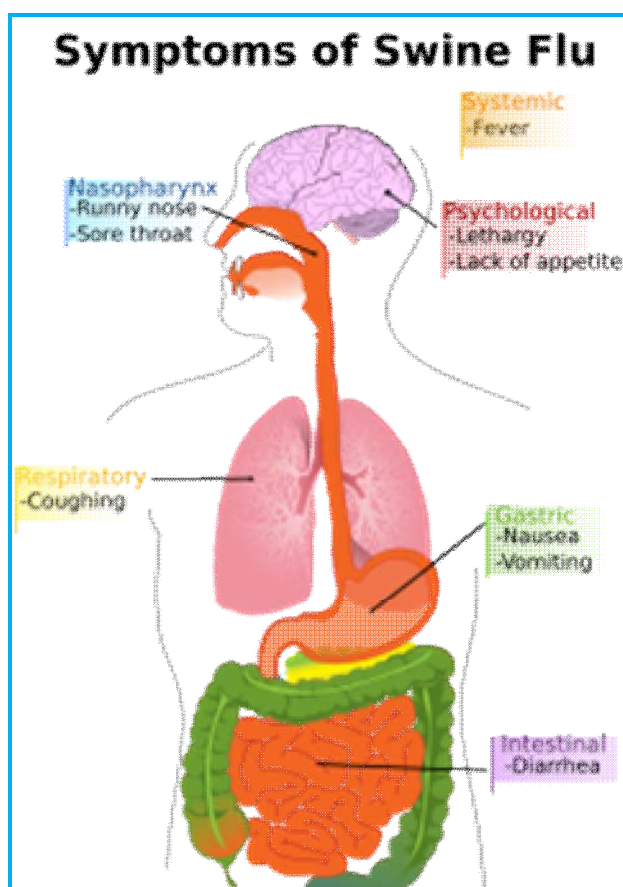


Figure 2: Main symptoms of swine flu in humans⁴.

5. DIAGNOSIS OF SWINE FLU

The Centers for Disease Control and Prevention (CDC) recommends real time RT-PCR as the method of choice for diagnosing H1N1⁹. This method allows a specific diagnosis of novel influenza (H1N1) as opposed to seasonal influenza. Near-patient point of care tests are in development¹⁰. The major tests that are being used for the diagnosis of Swine-Flu are:

- ✓ Nasopharyngeal swab for viral culture
- ✓ The gold standard test
- ✓ Typing using haem
- ✓ Agglutination inhibition and immunofluorescence
- ✓ Rapid immune fluorescence test
- ✓ Viral culture
- ✓ Real-time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)

Usually, a quick test (for example, nasopharyngeal swab sample) is done to see if the patient is infected with influenza A or B virus. If the test is positive for type B, the flu is not likely to be Swine-Flu (H1N1). If it is positive for type A, the person could have a conventional flu strain or Swine-Flu (H1N1).

The current protocols (As per WHO guidelines revised on 23 November, 2009) are available for testing and detection of virus¹¹:

- Influenza A type –Specific Conventional and Real time –PCR
- Pandemic (H1N1)2009, Virus Specific Conventional and Real time PCR
- CDR Real time (RT-PCR) Protocol for detection and characterization of Pandemic (H1N1) 2009
- Seasonal influenza (H1N1 and H3N2) and Avian Influenza A (H5, H7, H9) Real time RT-PCR

6. MECHANISM OF VIRAL INFECTION

It can be represented by the diagram which is given below as:

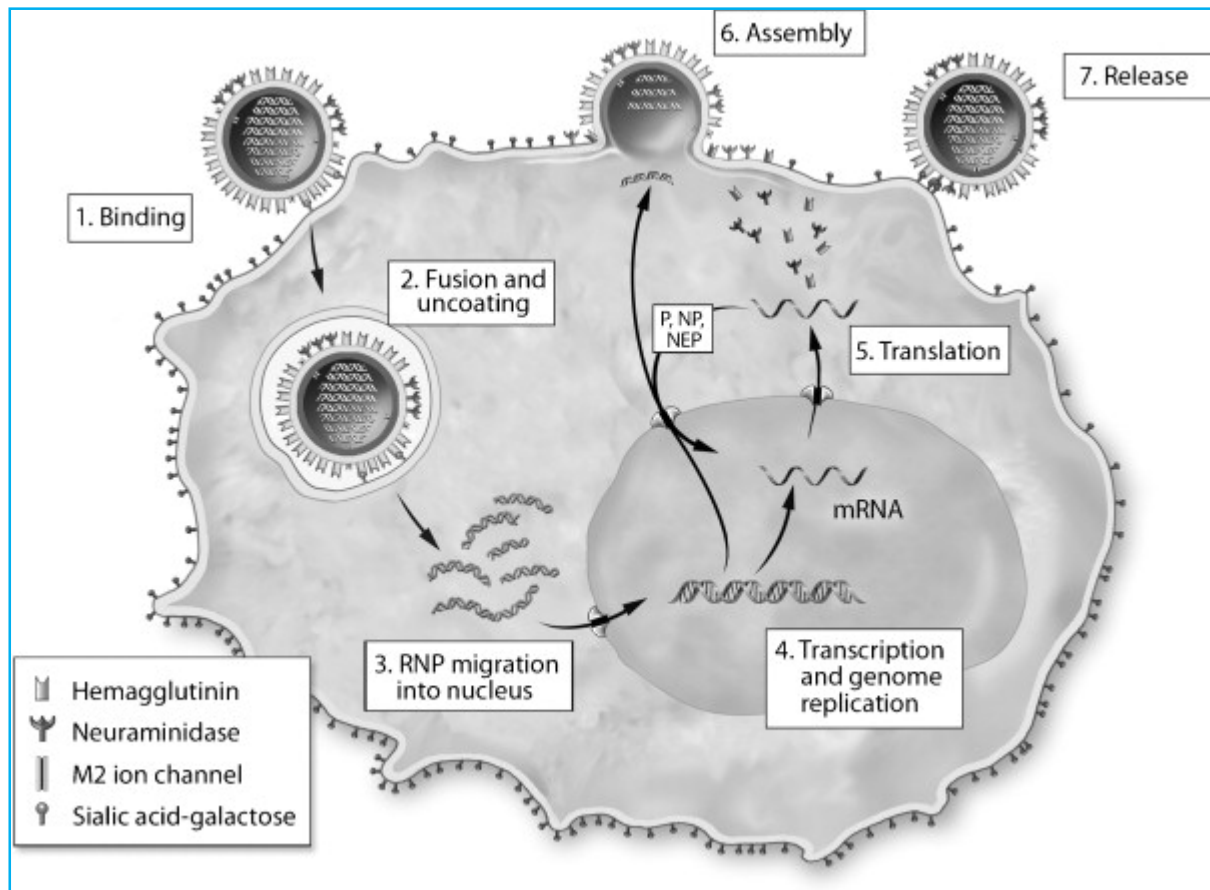
The 469 amino acid long neuraminidase (NA) protein is essential for release of the viral particle from the outer membrane of infected cells by cleaving sialic acid from host glycoproteins that are recognized by the viral hemagglutinin. As a type II transmembrane protein, it is N-terminally attached to the membrane. It consists of a tiny cytoplasmic tail at the N-terminus (residues 1 to 6) followed by the transmembrane region (residues 7 to 34) that is also responsible for translocation of the protein. Next, a presumably unstructured linker region (residues 35 to 82) connects the membrane anchor to the catalytic neuraminidase domain. Such unstructured linker regions are rich in small and polar residues and often harbour sites for posttranslational modifications. Probable posttranslational modification sites in the neuraminidase of the new strain are glycosylation motifs involving N88, N146 and N235, which correspond to residues that are also glycosylated in other subtype neuraminidases. However, the minimal and non-specific consensus motif of glycosylation sites (Nx [ST]) is found in total 8 times in the new strain sequence with an apparent clustering (50%) in the unstructured linker region. Interestingly, another

putative novel glycosylation site N386, which is unique to the new strain, would be accessible on the surface, as seen in the structural models.

Comparing among all strains, the sequence variation is largest in the linker region, including large deleted segments. Nevertheless, this region harbours a cysteine that can be aligned over multiple NA subtypes and is

conserved in N1-N5 and N8, but not in N6, N7 and N9. Earlier reports assume that, at least in related viruses, cysteines in the non-globular region could be involved in intermolecular disulfide bridges. Alternatively, by analogy to other influenza proteins such as hem agglutinin and M2 protein, it cannot yet be excluded that cysteine C49 is palmitoylated and that the anchor localizes the protein to lipid rafts.¹²

Figure 3: Viral infection cycle



7. PREVENTION OF TRANSMISSION TO HUMANS

Transmission occurs mainly in swine farms where farmers are in close contact with live pigs. The use of vaccines on swine to prevent their infection is a major method of limiting swine to human transmission. Risk factors that may contribute to swine-to-human transmission include smoking and, especially, not wearing gloves when working with sick animals -- thereby increasing the likelihood of subsequent hand-to-eye, hand-to-nose or hand-to-mouth transmission¹³. Few precautions to be taken by humans so as to prevent transmission are given below as:

- ✓ Cover your nose and mouth with a tissue when you cough or sneeze. Throw the tissue in the trash after you use it.
- ✓ Wash your hands often with soap and water, especially after you cough or sneeze. Alcohol-based hand cleaners are also effective.

- ✓ Avoid touching your eyes, nose or mouth. Germs spread this way.
- ✓ Try to avoid close contact with people having respiratory illness.
- ✓ If one gets sick with influenza, one must stay at home, away from work or school and limit contact with others to keep from infecting them. However, if one is having any respiratory distress, one should report to a nearby hospital.

A new vaccine against 2009 H1N1 strain is being developed soon by ICMR and is expected to provide adequate protection.

Steps taken by the Government of India to prevent outbreak of this flu in India

- The government has taken steps to detect early cases among the passengers coming from the affected countries either by air, road or ship.
- It has launched a massive mass media campaign to inform and educate people.
- Sharing information with public through media.

8. TREATMENT

The Government has in the designated hospitals stored medicines if required. It is strongly advisable not to take medicines of your own, as it will lower your immunity. The different ways of its treatment are as follows:

- i. Neuraminidase inhibitor antiviral medications (example, Oseltamivir, Zanamivir)¹⁴
- ii. Immunization by vaccines¹²
- iii. Possible herbal therapy (example, Elderberry, Japanese wasabi leaves, Tulsi etc.)¹⁵⁻¹⁹

(i) Neuraminidase inhibitor antiviral medications

These medications target the early phase of the infection. However, this strain is resistant to adamantanes, such as amantadine and rimantadine¹⁴.

Oseltamivir (Tamiflu): It is a prodrug that is hydrolyzed by the liver to its active metabolite, oseltamivir carboxylate, with an elimination half-life of about 6–10 h. The mechanism of action is by a neuraminidase inhibitor, serving as a competitive inhibitor of sialic acid, found on the surface proteins of normal host cells. By blocking the activity of the neuraminidase, oseltamivir prevents new viral particles from being released by infected cells²⁰. Adverse effects occur more commonly in children and adolescents which are nausea (severity is less, if oseltamivir taken with food), vomiting, transient neuropsychiatric events (self-injury or delirium)²¹.

Dose: Tamiflu (75-mg capsule) should be taken twice a day for 5 days.

Zanamivir (Relenza): The bioavailability of the drug is 10–20% by inhalation, compared with 2% by oral administration. The elimination half-life in serum of zanamivir is about 2–5 h. The mechanism of action is similar to oseltamivir. The later may be preferred over zanamivir for young children because zanamivir therapy requires the patient to voluntarily inhale through the device, so it is quite difficult for the children to administer this drug by this route. The main adverse effect includes Cough, diarrhoea, dizziness, headache, nausea, sinus inflammation, sore throat, stuffy nose and vomiting.

Dose: Two inhalations (5mg each) of Relenza should be administered twice in a day (i.e. 20mg/day) for 5 days.

Precaution: It is not recommended for treatment for patients with chronic airway disease or asthma as it can induce bronchospasm²².

In the U.S., on April 27, 2009, the FDA issued Emergency Use Authorizations to make available Relenza and Tamiflu antiviral drugs to treat the swine influenza virus in cases for which they are currently unapproved²³.

(ii) Immunization by vaccines

Vaccines are the most powerful public health tool for control of influenza. The U.S. Food and Drug Administration (FDA) approved the new swine flu vaccine for use in the United States on September 15, 2009. Studies by the National Institutes of Health (NIH) show that a single dose creates enough antibodies to protect against the virus within about 10 days²⁴. A lot of progress

has been going on and currently a candidate reassortment virus vaccine has been developed by the World Health Organization (WHO) essential regulatory laboratory at the centre for biologics evaluation and research, USA by using reverse genetic technology²⁵.

(iii) Possible herbal therapy: There are a lot of herbs have evaluated for the beneficial effects in swine flu which are described below as:

(a) Tulsi (*Ocimum sanctum*)



Figure 4: Tulsi

In some countries, though, vaccines are not as available and people are using traditional herbs to help protect against H1N1. Holy basil (*Ocimum sanctum*), called Tulsi in India, are being used in countries worldwide to help protect against swine flu. The main chemical constituents isolated from leaves are Ursolic acid, apigenin and luteolin. Several formulations are available in the market. It enhances the immunity and metabolic functions as well as in the management of respiratory problems (Shwas –Kasa)^{18,19}.

(b) Elderberry



Figure 5: Elderberry

Elderberry (*Sambucus nigra*), an herb with anti-viral properties is a wonderful remedy for flu symptoms when taken in the form of tincture, cordial or syrup to fight off the flu virus. It makes itself even more useful since these remedies can be made from dry or fresh berries.

Chemical constituents are:

- Flavonoids (natural antioxidants that work to protect the body's cells from the potential damage caused by free radicals)
- Anthocyanins (remarkable ability to stimulate the body's immune system by increasing the production of cytokines)

Formulation: Example, Sambucol, the syrup available in most health-food stores.

It shows the antifu activity by binding with viruses before penetrating into the walls of cells, thus prevents the spreading of viruses^{15,16}.

(c) Japanese wasabi



Figure 6: Japanese wasabi leaves

It has been found that the summer leaves of Japanese wasabi (*Wasabia japonica*) shows anti-influenza virus activity while winter leaves and rhizomes are generally used as a spice and for processed foods such as pickled wasabi. Since the leaf area of summer leaves is far greater than that of winter leaves, they are not used for food, and are discarded. Thus, on investigation anti-influenza virus activity was found in these summer leaves as a new function. Seventy percent ethanol extracts of leaves harvested in July exhibited a high replication inhibition rate (98% or higher) in the type A strain (AH1N1, A/shimane/48/2002), its subtype (AH3N2, A/shimane/122/2002), and type B strain (B/shimane/2/2002). Therefore, such extracts are expected to be a promising source of a novel anti-influenza virus agent¹⁷.

Other herbal plants used around the world to protect against swine flu are enlisted as below:

- Liquorice (*Glycyrrhiza glabra*)
- Lemon Balm (*Melissa officinalis*)
- Garlic (*Allium sativum*)
- Juniper (*Juniperus*, various species)
- Shiitake (*Lentinus edodes*)
- Ginger (*Zingiber officinale*)
- Red fleshed potatoes (*Solanum tuberosum* ssp. *tuberosum* and *S. tuberosum* ssp. *Andigena*)²⁵

CONCLUSION

Influenza H1N1 virus is spreading rapidly through sustained human-to-human transmission in multiple countries. Infected person may be able to infect others beginning one day before symptoms develop and up to seven or more days after becoming sick. However, with efficient human to human transmission established and more than 48 countries involved, so a series of actions need to be put in place to contain the outbreak. Few of the antiviral drugs are available in the market for treating this wide spread infecting disease but due to their immense side effects, scientists are now, turn their attention towards herbal therapy. So through this article we tried to collect the brief information about this particular disease. We can play main role in the prevention of the transmission of this disease by following the main factors enlisted in the article.

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