



## Swine flu: the present pandemic infectious disease

### Domuz gribi: Günümüzün pandemik enfeksiyon hastalığı

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Influenza virus infection is the well known respiratory tract infection. Swine flu is the newest atypical influenza virus infection that has just been reported since early 2009. This new disease becomes pandemic at present. In this specific article, epidemiology, symptomatology, pathology, diagnosis, treatment and prevention of swine flu disease are discussed and described in the light of current literature.

*Key Words:* Pandemic; prevention; swine flu.

Influenza virüsü enfeksiyonu iyi bilinen bir solunum yolu enfeksiyonudur. Domuz gribi, ilk olarak 2009 yılının erken dönemlerinde bildirilmiş olan en yeni atipik influenza virüs enfeksiyonudur. Bu yeni hastalık şu anda pandemik hale gelmiştir. Bu özel makalede, domuz gribi hastalığının epidemiyolojisi, semptomatolojisi, patolojisi, tanısı, tedavisi ve korunma yöntemleri güncel literatür bilgisi ışığında tartışılmış ve tanımlanmıştır.

*Anahtar Sözcükler:* Pandemik; korunma; domuz gribi.

#### INTRODUCTION TO NEW ATYPICAL INFLUENZA VIRUS INFECTION

Influenza virus is a well known virus in medicine that can cause problematic respiratory tract infection. There are several groups of influenza virus that can cause disease in human beings as well as other animals. In human beings, the influenza virus infection can be seen in any parts of the world causing illness of several people annually. Due to the nature of virus, the mutation within the influenza virus sequence can be expected. The mutation can be problematic if it is a sense mutation. The new atypical influenza virus can be the resulted of genetic mutation and this can be the cause of new disease,<sup>[1,2]</sup>

In medical history, there are many scenarios that are believed to be the cases of new atypical influenza virus infections. However, the proved

cases are the two scenarios, bird flu and swine flu, which are all described in the era with advent molecular diagnostic technologies. Bird flu is the new atypical influenza infection caused by H5N1 influenza virus.<sup>[3]</sup> while swine flu is the new atypical influenza infection caused by H1N1 influenza virus.<sup>[4]</sup> These two influenza virus infection are new infections described within this decade and become the public health threaten of the world.

Due to the nature of a new atypical influenza virus infection, a new emerging infection, there are limited data on its natural history. This usually brings the difficulty in diagnosis and treatment. In this specific article, the author will hereby discuss on the newest atypical influenza virus infection, swine flu, which has just been described to the medical society since April 2009.<sup>[4-6]</sup>

### FIRST REPORT ON SWINE FLU

It should be hereby clarified that influenza infection in pig can be seen. However, the case that human beings get the swine type influenza virus infection has never been reported before the outbreak of present swine flu. In early 2009, there are emerged cases of atypical infections in Mexico presently with the signs and symptoms of respiratory tract infection.<sup>[4-6]</sup> The exact pathogen of this infection was firstly unknown. After the molecular researches, the new pathogen was finally found. The new virus is the new influenza virus that is considered to the result from the genetic reassortment of components from three origins, classical human H1N1 influenza virus, classical swine influenza virus and avian influenza virus (mainly from swine influenza virus, hence, swine flu is named).<sup>[4-6]</sup> The sequence of this new pathogen has never been reported elsewhere and assigned to be the newest influenza virus.

The first report of swine flu is from Mexico. In April and May 2009, Mexico became the epidemic focus of this new emerging disease. Several hundreds of infected cases were reported. Also, there were several death cases. However, after the primary emerging in the primary site in Mexico, the disease widely spread to the new settings, from nearby countries to remote countries. At present, the World Health Organization already declares for level VI precaution for this infection

confirming the nature of world pandemic of this disease. Several thousands of infections are accumulated recorded from several countries around the world.<sup>[7-9]</sup>

### EPIDEMIOLOGY OF SWINE FLU

Swine flu can be seen in a person of any sex or age. In the first outbreak in Mexico, adult is the most affected group. When the disease spread to the other settings, the affected group is mainly the travelers to the epidemic area. However, after settled in the new setting, the disease crosses to non adult groups. The pediatric population becomes the main infected group in many countries such as Thailand. Since the pediatric group usually live in a crowded school, sharing facilities with others, the infection rapidly spread in the school.<sup>[5]</sup> Hence, school closing becomes the methods for disease control that is used in many countries.<sup>[5]</sup> Some vulnerable groups including to infant and pregnant<sup>[10]</sup> are also affected and becomes the focused topic at present (Table 1). Apart from general population, the disease emerges in some specific groups with underlying diseases such as those with diabetes mellitus and cardiovascular disease. It can be seen that these cases are highly risk for developing severe infection.<sup>[11,12]</sup>

At present, there are several possible risk factors for developing severe infections. These include diabetes mellitus,<sup>[11]</sup> cardiovascular disease,<sup>[12]</sup> human

**Table 1.** Considerations on swine flu infection in some specific groups

Groups	Descriptions
1. Infant	There are some sporadic cases of infantile infection. An unpublished possible vertical transmission is reported from Thailand. The infant becomes a susceptible group for severe disease. Due to non complete organ system, the extension of disease to the uncommon organ such as brain can be expected.
2. Pregnant	The pregnant can get the infection similar to the general population. The infection during pregnancy becomes a difficult case for treatment. The treatment has to focus on the possible teratogen effect of the antiviral drug. Also, the poor outcome among the pregnant case is usually observed.
3. Lactating mother	The lactating mother can pass the infection to their children but not from milk. The closed contact during breastfeeding can increase the chance of getting pathogen from respiration. It is suggested that the lactating mother if get swine flu should not perform breastfeeding at that period.
4. Elderly	Of interest, some elderly have the protective immunity to swine flu. This might reflect that the swine flu might ever emerge long time ago.
5. Diabetic case	Diabetes mellitus is confirmed for increasing morbidity and mortality due to classical influenza infection. This is expected to be similar in case of swine flu. However, there is no evidence that swine flu can deteriorate the blood sugar level among diabetic patients or lead to diabetic complication (hypo-or hyper-glycemia).

immunodeficiency virus infection, renal disease, liver disease, obesity and smoking. However, there is still no systematic assessment to decide whether factor is the exact risk factor.<sup>[3,4,7]</sup>

### SYMPTOMATOLOGY OF SWINE FLU

The signs and symptoms of swine flu are similar to other respiratory tract infection. High fever, coughing, sneezing, malaise and myalgia can be seen.<sup>[4-6]</sup> In the case that severe infection occurs, the lung manifestation can be seen. This can lead to the tachypnea and respiratory difficulty.<sup>[4-6]</sup> In addition to the respiratory manifestation, there are also other interesting manifestations. The gastrointestinal manifestation of swine flu should be mentioned. In infected case, diarrhea can be observed. This is the common nature of atypical influenza virus infection. The diarrhea in swine flu infected cases is usually the watery type without mucous or bloody appearance. The direct involvement of the intestinal epithelium is believed to be the cause of diarrhea in swine flu. In addition to diarrhea, liver involvement in swine flu is of interest. Indeed, hepatitis is an interesting clinical manifestation that has not presently been clarified for the correlation to swine flu.<sup>[3,4,7]</sup> Basically, hepatitis in influenza infection is mentioned in the literature. Kupffer cell dependant hepatitis is the well known condition.<sup>[13]</sup> Polakos et al.<sup>[13]</sup> noted that influenza-associated hepatitis was resulted from the formation of inflammatory foci which was the finalized result from apoptotic hepatocytes, antigen-specific CD8(+) T cells, and Kupffer cells This condition is expected to be existed in the case with swine flu, however, it has never been mentioned in the literature.

Focusing on other manifestations, there are few evidences. First, for the eye manifestation, although conjunctivitis is common in the classical influenza, there is no report that conjunctivitis is clinically significant in swine flu. Second, for the ENT manifestation, nose and throat manifestations are common as already described. But there is still limited report on ear manifestation. Third, for the cardiac manifestation, there is still no evidence. Although classical influenza can induce pericarditis and myocarditis, there is still no report in swine flu.<sup>[3,4,7]</sup>

Considering the complication of swine flu, the lower respiratory tract infection, lung involvement, is the most common complication as noted earlier.<sup>[14]</sup> This condition might lead to the respiratory distress and respiratory failure.<sup>[15]</sup> Also, in

the most serious case, death can be the outcome. It should be noted that respiratory distress is the most common cause of death among the cases with swine flu, either with or without underlying personal illnesses.

### PATHOLOGY OF SWINE FLU

Swine flu virus infected the respiratory tissue in upper respiratory tract and further cause infection (This lead to the easy transmission comparing to bird flu, of which the receptor is at lower respiratory tract). Similar to other viral infections the T cell system is the main immunological response to this viral infection.<sup>[16]</sup> The pathological change due to swine flu is expected to be similar to classical influenza. The severe manifestation is expected to be due to the lack for protective immunity.<sup>[16]</sup> Nevertheless, although there are hundreds of death cases and thousands of infected cases, there are no biopsy or autopsy reports showing the exact pathological change due to swine flu.

### DIAGNOSIS OF SWINE FLU

It is very hard to diagnosis swine flu by clinic. The clinical manifestation of swine flu cannot be differentiated from classical influenza and several other respiratory tract infections. Usually, it is recommended that any cases with high body temperature (more than 38.3 degree Celsius) who visited to the physicians during the outbreak of swine flu should get further diagnosis for swine flu. The first primary screening for influenza A/B infection by rapid test is suggested.<sup>[17]</sup> If the result from screening is positive, it is suggested to start the antiviral drug treatment and further confirmation test for swine flu should be done at the same time (There is no doubt for usefulness of antiviral treatment in this case, whether the identified influenza is swine flu or classical influenza). Focusing on the confirmation test, the gold standard technique is based on the molecular based diagnosis. Polymerase chain reaction (PCR)-based test is required.<sup>[18-19]</sup> At present, there is also the real time PCR system for shortening the waiting for finalized diagnosis.

For diagnosis of complication of disease, chest X-ray is useful for diagnosis o lung involvement, the common complication of swine flu. Normally, the chest X-ray usually shows the pattern of interstitial pneumonia in such case.<sup>[15]</sup> Generalization of infiltration in all lobes of the lung can be identified.<sup>[15]</sup>

**Table 2.** Possible causes of oseltamivir treatment failure

Causes	Descriptions
1. Late diagnosis and treatment	In many settings, the diagnosis of swine flu is usually late. This might be due to the lack of facilities for diagnosis. Also, this might be the consequence of limited resources, which is the common situation in developing countries getting attack by swine flu.
2. Poor quality of drug	It should also be noted that the availability of drug dose not means that such drug has good quality. In many settings, the local made drug comparable to the original drug, for the local usage, can be seen. Urgent drug production might be lack for complete good clinical trials and this can be the big problem.
3. Drug resistance	The problem of the drug resistance of the virus can be expected. This is expected to exist in the near future although there is no published report on oseltamivir resistance for swine flu at present.

### TREATMENT OF SWINE FLU

Although classical influenza can be self limited it is not recommended that the swine flu infected case should get no treatment. Indeed, a number of swine flu infected cases are expected to be self limited. However, the cases that visit to the physician and get finalized diagnosis of swine flu should get proper treatment. The treatment is useful for not only getting rid of the infection in the indexed case but also controlling of spreading of disease to the new case. The standard treatment for swine flu is similar to the classical influenza virus infection. The use of antiviral drug is recommended. The antiviral drug in the group of neuraminidase inhibitor is indicated in clinical practice.<sup>[20]</sup> The first line drug of choice is oseltamivir. Oseltamivir, which is generally known as Tamiflu, is an oral form antiviral drug.<sup>[20-21]</sup> Oseltamivir is proved to be effective in treatment. However, there are also some cases that oseltamivir treatment fails. The main reasons are usually late diagnosis and treatment (Table 2). The oseltamivir resistance is the present focused in treatment of swine flu.<sup>[22]</sup> At present, there is no published data but unpublished reports on less than 10 cases of drug resistance. Indeed, the oseltamivir drug resistance can be expected since the drug resistance in the case of classical influenza is already confirmed. With the increased usage of oseltamivir, if there is no strict control and surveillance of drug resistant virus, the emerging problem of oseltamivir resistance swine flu can be imagined. The good selection for proper case to get oseltamivir is very important.<sup>[23]</sup>

However, there might be some cases that oseltamivir is not effective. The second drug is the zanamivir. Zanamivir is an inhaler form antiviral

drug. Usually, this drug is reserved. In case that oseltamivir resistance emerges, zanamivir can be widely used.<sup>[20]</sup>

### PREVENTION OF SWINE FLU

Although there are thousands of accumulated infected swine flu cases at present the exact number of infection must be greatly higher.<sup>[24]</sup> The routine practice for prevention of respiratory tract infection can be effectively applied for prevention of swine flu. It should be noted that hand washing is still the low cost but effective mean for control of spreading of disease. Due to the nature that the virus usually blew out from the patient into the external environment during coughing and sneezing and laid down on external objects, the dirty hand after touching such objects can be the vehicles for transmission of disease. Indeed, hand washing is confirmed as an effective method for controlling of influenza. In addition, the use of face mask is recommended. The main question is "Which one should use the face mask?" It is recommended that everyone should use the face mask during the high epidemic state of the disease. All patients must wear the face mask. Also, the medical personnel must use the face mask.<sup>[25]</sup> For medical personnel, the N95 face mask is highly recommended. However, it can be seen that the influenza virus particle can still pass the nano-pore of this kind of face mask.<sup>[26]</sup>

Focusing on the pork safety, although the disease has its name relating to the pig there is no present evidence that ingestion of pork or contact with pork can cause the disease. However, there is also unpublished report that the pig can be infected with this new virus. Nevertheless, pork is still safe in the present status of swine flu outbreak if the standard pig farming is practiced.

Focusing on the vaccination for swine flu, there is still no present available specific vaccine. The presently available influenza vaccine for classical influenza cannot generate cross protective immunity to swine flu. It is presently accepted that the swine flu vaccine is the hope for successful controlling of the pandemic. There are several attempts to develop new swine flu vaccine with help of bioinformatics and biotechnology.<sup>[27]</sup> At present, the epitopes of new swine flu virus has already been explored and reported.<sup>[28]</sup> These epitopes are already used for production of the new swine flu vaccine. Several new alternatives are during the trials phase.<sup>[27]</sup> It is expected to get the swine flu vaccine within a few months.

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