H1N1 influenza A is a subtype of influenza virus. It was first detected in April 2009 in Mexico then subsequently in United States. In H1N1 influenza virus eight genes in the virus were similar to the influenza viruses circulating in pigs. Such swine influenza viruses do not normally cause infection in humans and even if they do, the infection is usually mild and not very transmissible. Pigs can become infected with influenza viruses from a variety of different hosts (such as birds and humans), and so can act as a "mixing vessel," facilitating the reassortment of influenza genes from different viruses resulting in a "new" influenza virus. The 2009-2010 pandemic, thought to have originated in swine, was caused by H1N1 influenza A virus representing a quadruple reassortment of two swine strains, one human strain and one avian strain of influenza, but largest proportion of genes came from the swine influenza virus that was able to spread easily among people and also cause disease. Since the 2009-2010 pandemic, H1N1 has caused seasonal outbreaks of illness in human populations and the current outbreak in India has resulted in more than 2000 deaths. The infection has its greatest impact on the pediatric and young adult population.

**Virology**

H1N1 influenza virus is a segmented and enveloped spherical RNA virus that belongs to the Family: Orthomyxoviridae and Genus: Influenza virus. There are three types based on nucleoprotein and M-capsid protein – Type A, Type B and Type C. H1N1 virus is a subtype in Type A, along with H5N1 (avian flu or ‘bird flu’ virus). Some of the characteristics of these viruses are seen in Table 1.

**Clinical Features**

Swine flu signs and symptoms in humans are similar to those of other flu strains. Flu-like illness must be suspected if there is:

1. Short duration fever (< 7 days) - seen in 93% of individuals
2. Temperature is >38° C/ 101°F
3. Symptoms of respiratory illness (cough, sore throat, runny nose) with no evidence of other cause (lobar pneumonia, bacterial pharyngitis etc.) - seen in approx 80-85% of individuals

The majority of infections is mild and requires no specific treatment. However there are certain groups...
H1N1 INFLUENZA (Swine Flu)

of people who are at risk of developing severe infection. Stratification of infections and management recommendations are given in the flow charts (Fig.2,3).

Severe pneumonia (in adults) is defined as:
1. Fever (Temp >101 °F or h/o fever) + respiratory symptoms + Chest x-ray infiltrates + any TWO of the following
2. Respiratory rate >30/min
3. Oxygen saturation <90% on room air
4. Blood pressure <90 mm Hg systolic
5. Confusion
6. Azotemia (blood urea >42 mg/dl)

(These features of severe pneumonia apply only to adults. The features of severe disease in children are given in Fig. 3.)

Table 1: Classification and characteristics of Influenza viruses

<table>
<thead>
<tr>
<th>TYPES</th>
<th>TYPE A</th>
<th>TYPE B</th>
<th>TYPE C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub Types or Sero types (based on hemagglutinin (H) and the neuraminidase (N))</td>
<td>The subtypes based on the combination of H and N proteins: H1N1, H1N2, H2N2, H3N1, H3N2, H3N8, H5N1, H5N2, H5N3, H5N8, H5N9, H7N1, H7N2, H7N3, H9N2, H10N7</td>
<td>No subtypes</td>
<td>No subtypes</td>
</tr>
<tr>
<td>Infectivity</td>
<td>Infect multiple species Human, avian, swine, equine</td>
<td>Infect humans</td>
<td>Infect humans and swine</td>
</tr>
</tbody>
</table>
| Public health importance | Causes Pandemics  
  - Spanish Flu [A (H1N1)] 1918-19;  
  - Asian Flu [A (H2N2)] 1957-59;  
  - Hongkong Flu [A (H3N2)] 1968-68;  
  - “Swine Flu” [A (H1N1)] 2009-10  
  Causes Epidemics, seasonal Influenza outbreaks and sporadic cases.  
  - Avian or bird flu [A (H5N1)] | Causes epidemics and seasonal influenza | Causes mild respiratory illness, does not cause epidemics. |

TRANSMISSION

There are two major modes of transmission
1. Inhalation of aerosols (droplets of respiratory secretions given out by coughing or sneezing)
2. Contact with infected material

Influenza virus is an air-borne illness that is spread through droplets given out while coughing or sneezing and inhalation of these aerosolized viruses. Infection may also be acquired by touching materials infected by droplets and then transferring these to the nose or mouth. Close contact with infected persons especially in crowded areas can result in spread of the disease. All respiratory, stools and body secretions from infected person are considered as potentially infectious.

H1N1 influenza virus is not spread through consumption of pork as long as the meat is washed well and cooked.

The incubation period for influenza is estimated to range from 1 to 4 days with an average of 2 days. Influenza virus shedding (the time during which a person might be infectious to another person) begins the day before illness onset and can persist for 5 to 7 days, although some persons may shed virus for longer periods, particularly young children and severely immunocompromised persons. The amount of virus shed is greatest in the first 2-3 days of illness and appears to correlate with fever, with higher amounts of virus shed when temperatures are highest. Most healthy adults may be able to infect other people beginning 1 day before symptoms
develop and up to 5 to 7 days after becoming sick. Children may pass the virus for longer than 7 days. Symptoms start 1 to 4 days after the virus enters the body.

Fig. 2: Flow chart for management of suspected cases of H1N1 influenza

**‘High-risk’ Groups**
(for developing complications of influenza)
1. Children <5 years old  
   a. Risk for severe complications highest among children <2 years old
2. Adults >65 years (for seasonal influenza)
3. Pregnant women
4. Persons with the following co-morbidities:
   a. Morbid obesity (BMI >40)
   b. COPD, asthma, Cystic fibrosis
   c. CAD, CHF
   d. CKD
   e. CLD
   f. Hematological conditions (including sickle cell disease)
   g. Neurologic, neuromuscular disorders
   h. Diabetes mellitus
   i. Immunosuppression (AIDS, long-term corticosteroid)

**Severe Influenza (Mnemonic TROPICAL)**
1. Temperature >101°F  
2. Respiratory rate >30/min
3. Oxygen saturation <90%  
4. Pressure (BP) <90 mm Hg systolic
5. Image (Chest Xray infiltrates)
6. Confusion (encephalopathy)
7. Azotemia (blood urea >42 mg/dl)
8. Lab test (RT-PCR for influenza) positive
**This recommendation is what is followed in CMC Vellore and differs from the Ministry of Health guidelines in that treatment in mild illness is advised only if the test is positive. In situations where diagnostic facilities are not available or cannot be made use of, it is recommended to start treatment in these patients.**

**LABORATORY TESTS**

### Influenza Diagnostic Tests

A number of different laboratory diagnostic tests can be used for detecting the presence of influenza viruses in respiratory specimens. These include:

1. Direct antigen detection tests (Rapid Influenza Diagnostic Tests)
2. Virus isolation in cell culture
3. Detection of influenza-specific RNA by reverse transcriptase-polymerase chain reaction (RT-PCR)
These tests differ in their sensitivity and specificity in detecting influenza viruses as well as in their commercial availability, the amount of time needed from specimen collection until results are available, and the tests’ ability to distinguish between different influenza virus types (A versus B) and influenza A subtypes (e.g. novel H1N1 versus seasonal H1N1 versus seasonal H3N2 viruses).

Rapid Influenza Diagnostic Tests provide results within 30 minutes however, they have limitations. Their sensitivity varies with commercial preparations and their ability to differentiate between types of Influenza viruses varies, though their specificity is high. RT-PCR is the diagnostic test that is commonly used and recommended.

Samples may be collected using nasal and throat swabs and bronchoalveolar lavage. All personnel working in laboratories and handling clinical samples related to Influenza A H1N1 Should use N95 respirators and adhere to hand hygiene practices.

*************************************

THERAPEUTIC MANAGEMENT

- Most cases of H1N1 influenza infection are mild and do not require antiviral medication.
- Antiviral medication is recommended only in individuals who have severe illness or those who have risk factors for developing complications (see flowcharts).
- Indiscriminate use can result in drug-resistance and is to be avoided.

Oseltamivir (Tamiflu/Fluovir) and Zanamivir (Relenza) are antivirals that are effective in the treatment of H1N1 influenza infection.

The neuraminidase inhibitor oseltamivir is available in India as capsules or oral suspension. The neuraminidase inhibitor zanamivir is formulated for oral inhalation. A third drug Peramivir also a neuraminidase inhibitor is formulated for intravenous (IV) administration but is still in the investigational phase and not approved.

a. Adults

The main stay of therapy is antivirals. Oseltamivir, zanamivir, and peramivir, are active against both influenza A and B. These shorten the duration of influenza symptoms by approximately one-half to three days if initiated within first 48 hours of onset of symptoms.

The adamantanes, amantadine and rimantadine, are active only against influenza A. These drugs are not recommended for H1N1 influenza due to high level of resistance.

Treatment initiation: Treatment should not be delayed while awaiting the results of diagnostic testing, nor should it be withheld in patients with indications for therapy who present >48 hours after the onset of symptoms, particularly sick and high risk patients.

Dosing: The usual dosing of oseltamivir for the treatment of influenza is 75 mg orally twice daily and of zanamivir is 10 mg (two inhalations) twice daily. Dosing of oseltamivir and peramivir must be modified for renal insufficiency.

Doubling the dose of oseltamivir to 150 mg orally twice daily has been suggested for some severely ill patients with H5N1 avian influenza. As there is no evidence that doubling the dose of oseltamivir is more effective, it is no longer recommended.

Duration: Recommended duration of antiviral therapy is five days. Longer therapy is considered in high risk individuals with worsening clinical and lab parameters.

b. Oseltamivir (Tamiflu) dosing in children:

Many patients who have had novel influenza (H1N1) virus infection, but who are not in a high-risk group have had a self-limited respiratory illness similar to
H1N1 INFLUENZA (Swine Flu)

typical seasonal influenza. For most of these patients, the benefits of using antivirals may be modest. Therefore, testing, and treatment efforts should be directed primarily at persons who are hospitalized or at higher risk for influenza complications.

<table>
<thead>
<tr>
<th>Agent, group</th>
<th>Treatment (5 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oseltamivir</strong></td>
<td></td>
</tr>
<tr>
<td>Adults *</td>
<td>75-mg capsule twice per day for 5 days</td>
</tr>
<tr>
<td>Children &gt; 12 months</td>
<td></td>
</tr>
<tr>
<td>15 kg or less</td>
<td>30 mg twice daily</td>
</tr>
<tr>
<td>16-23 kg</td>
<td>45 mg twice daily</td>
</tr>
<tr>
<td>24-40 kg</td>
<td>60 mg twice daily</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>75 mg twice daily</td>
</tr>
</tbody>
</table>

* For adult patients admitted to ICU, the dose of Oseltamivir is 75 mg twice daily for 7-10 days.

VACCINE AGAINST INFLUENZA A (H1N1)

The overwhelming majority of patients with pandemic influenza A H1N1 have mild symptoms and recover even without medical treatment.

**Vaccine Efficacy:** A recent Cochrane Review ⁴ has drawn the following conclusions:
1. Influenza vaccines have a modest effect in reducing influenza symptoms and working days lost.
2. There is no evidence that they affect complications, such as pneumonia, or transmission.
3. Inactivated vaccine adverse effect - an estimated 1.6 additional cases of Guillain-Barré Syndrome per million vaccinations.

**Vaccination in children**

The recommendation for vaccination in children is based on the Indian Academy of Pediatrics (IAP) recommendation ⁵ for influenza vaccination. Vaccination is recommended for persons with high-risk conditions (see Fig.2 - risk factors for complications).
- Minimum age: 6 months for trivalent inactivated influenza vaccine (TIV)
- First time vaccination: 6 months to below 9 years; two doses 1 month apart; 9 years and above: single dose
- Annual revaccination with single dose is recommended.
- Best time to vaccinate: As soon as the new vaccine is released and available in the market and just before the onset of rainy season

**Seasonal Influenza A (H1N1): Guidelines for Vaccination of Health Care Workers** ³

1. World Health Organization recommends vaccination of high risk groups with seasonal influenza vaccine.

<table>
<thead>
<tr>
<th>Age</th>
<th>Treatment (5 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 months</td>
<td>12 mg twice daily</td>
</tr>
<tr>
<td>3-5 months</td>
<td>20 mg twice daily</td>
</tr>
<tr>
<td>6-11 months</td>
<td>25 mg twice daily</td>
</tr>
<tr>
<td>&lt;3 months</td>
<td>12 mg twice daily</td>
</tr>
</tbody>
</table>

Table 2: Antiviral medication dosing recommendations for treatment of new influenza A (H1N1) infection.

Table 3: Dosing recommendations for antiviral treatment of children younger than 1 year using oseltamivir.
2. Vaccination is not recommended for the general public.
3. Health Care Workers working in close proximity to influenza patients are at higher risk of acquiring the disease. Hence, vaccination is recommended for them.
4. The vaccine should be used every year.
5. Influenza vaccination is most effective when circulating viruses are well-matched with vaccine viruses. Even with appropriate matching, efficacy of vaccine may be about 70% to 80%, especially in geriatric age group. In case the locally circulating virus is different from vaccine virus recommended by WHO, it may not be effective at all. Hence, vaccine should not give a false sense of security. The available vaccine takes about 2-3 weeks for development of immunity. The use of chemoprophylaxis during this period may be considered.

Chemoprophylaxis

Pre-exposure prophylaxis: To be given before contact with confirmed or suspected case of swine flu. Pre-exposure prophylaxis has a very limited role. There are concerns regarding supply of drug as well as emergence of resistance due to such practices. Hence decision should be taken as case by case basis and expert consultation is recommended.

Post-exposure prophylaxis: To be given after contact with confirmed or suspected case of swine flu. The decision to offer chemoprophylaxis to should be made on a case-by-case basis and should be based on the patient's individual risk for influenza complications, the risk of influenza acquisition from the specific exposure and clinical judgment. The chemoprophylaxis is not considered as alternative to vaccination. It could be considered for adults and children who have had close contact with a confirmed or suspected case AND who also belong to high risk group.

The drug of choice is oseltamivir 75 mg once a day. Data regarding duration of post-exposure prophylaxis is unclear; maximum duration suggested is no more than 10 days after the most recent exposure.

Infection Control Measures

In the community:

Since H1N1 influenza is an airborne illness, spread of the disease can be minimized by following some simple precautions.
1. Frequent hand washing with soap and water.
2. Covering the face while sneezing or coughing with a tissue paper.
3. Staying away from persons showing symptoms of influenza and crowded areas.
4. Avoiding contact greetings (eg. hand-shakes).
5. Masks are not advised for the general public as there is no evidence that wearing masks outside a hospital setting benefits.

In the hospital:

OPD: Information on cough etiquette should be provided.

Wards: All patients suspected to have severe influenza (as defined above) must be admitted to the Isolation Ward.

- Use alcohol-based hand rubs between patient contacts.
- Disposable triple layer surgical mask must be available for staff in all OPD areas.
- Information on cough etiquette should be provided.
- Isolation precautions to be followed: Standard precautions and droplet precautions:
- Patients should be admitted to a single room or cohorted.
- Disposable triple layer surgical masks to be worn by staff and visitors.
- Gowns not routinely necessary.
H1N1 INFLUENZA (Swine Flu)

- Use alcohol-based hand rubs or wash hands after touching the patient or potentially contaminated articles and before taking care of another patient.
- Should perform hand hygiene before putting on and after removal of personal protective equipments.
- Articles contaminated with infective material must be discarded or bagged and labeled before being sent for decontamination and reprocessing.
- Terminal cleaning as per present protocol after patient is discharged.
- No aerosol generating procedures (nebulisation, bronchoscopy, BAL) to be done on suspected patients. Can be done only if H1N1 negative on testing.
- Use MDI with spacer for inhaled bronchodilators; nebuliser chambers with tubing and mask to be purchased separately for individual children who need nebulisations.

Infection control practices to be followed

- Information on cough etiquette should be provided.
- Wear surgical mask for all care givers entering the room.
- No visitors for first 5 days; this can be overruled if patient is dying and relatives want to be at the bedside.
- No aerosol generating procedures (nebulisation, bronchoscopy, BAL) to be done on suspected patients. Can be done only if H1N1 negative on testing.
- Use MDI with spacer for inhaled bronchodilators; nebuliser chambers with tubing and mask to be purchased separately for individual children who need nebulisations.
- Ventilators to be fitted with device to exhaust exhaled gas to vacuum system.
- Use closed system for ET suctioning (surgical mask adequate).
- Oral suctioning – use N95 mask.
- Keep N95 mask for aerosol generating procedures if essential. Use N95 respirators after fit test and follow the correct procedure.
- Gowns and goggles must be worn for invasive procedure.

Intensive Care

All patients suspected to have severe influenza (as defined above) who need advanced life support or intensive monitoring will be admitted to the Intensive care units.

Sources and references:
1. WHO guidelines available at www.who.int
2. CDC guidelines available at www.cdc.gov/HINIflu/

PROCRUSTEAN SCIENCE

In Greek mythology, Procrustes was a rogue blacksmith who physically ‘modified’ people, stretching them or cutting off their legs so as to make them fit an iron bed’s size. In general, when something is Procrustean, different lengths or sizes or properties are fitted to an arbitrary standard. A Procrustean bed is an arbitrary standard to which exact conformity is forced.

A Procrustean solution is the undesirable practice of tailoring data to fit a conclusion. In a Procrustean solution in statistics, instead of finding the best fit line to a scatter plot of data, one first chooses the line one wants, then selects only the data that fits it, disregarding data that does not, in order to ‘prove’ some point.