

**SWINE FLU
EMERGING THREAT****NEW HORIZONS**

Infuenza A(H1N1) Vaccine-Current Status

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Influenza is rightly described as an "unvarying disease caused by a varying virus". No other febrile illness of respiratory origin is capable of such rapid spread and it is the endemicity that is hallmark of Influenza. At least four pandemics occurring in 18th Century and another three in 19th Century with 1918-1919 pandemic being the worst in terms of loss of life claiming estimated 20 million lives (1). Swine Influenza A (H1N1) Flu has managed to firmly establish its presence over a large part of globe quite rapidly since the outbreak started in Mexico on 18th March, 2009 (2,3,4). On June 11, 2009, the World Health Organization (WHO) declared a worldwide pandemic (5). Worldwide transmission of the novel influenza A (H1N1) virus has continued since then in both the Northern and Southern hemispheres and is likely to persist and might increase in the Northern Hemisphere during fall and winter (6). H1N1 has re-assorted itself with segments from four influenza viruses: North American Swine, North American Avian, Human Influenza and Eurasian Swine. Serologic studies suggest that a large majority of the population is susceptible to novel influenza A (H1N1) virus and substantial potential exists for widespread dissemination as the virus is antigenically distinct from other human influenza A viruses in circulation since 1977 (3). On the other hand, the novel influenza A (H1N1) viruses circulating worldwide appear to be antigenically similar (7). The pandemic has generated disproportionate panic and fear among populations. Lack of accurate information about the danger posed by the H1N1 coupled with misconceptions has further deteriorated the situation particularly in developing countries. The limitations in health services delivery system stands exposed. Notwithstanding the concerns listed above, almost all governments have responded to pandemic by putting in place various preventive measures including spreading awareness about the disease and use of personal protective equipment, early diagnosis & treatment and limiting mortality & disability. Vaccines do not find a place in the current array of strategies since an entirely new formulation need to be produced.

Vaccine Production- Process, Timeline, Availability and Implications: Vaccine manufacturing in general is a multi-step process. The identification of the novel virus (from routine surveillance e.g., Flu net of WHO) is followed by necessary modifications to produce the vaccine strain by mixing it with standard laboratory strain and the hybrid is allowed to grow together on hen's eggs (3 weeks). Another 3 weeks are required for verification before it can be delivered to vaccine manufacturers. Manufacturers then require 3 months to test the vaccine strain against standardized substances (reagents) provided by WHO collaborating centers. Further testing is undertaken to ascertain growth optimization (3 weeks) before bulk manufacturing can be done. Producing each batch, or lot, of antigen takes approximately two weeks, and a new batch can be started every few days. When one batch has been produced, the process is repeated as often as needed to generate the required amount of vaccine. The next step involves clinical trials to establish efficacy and safety of the vaccine. Following approval by regulatory authorities it is then licensed for widespread use. Vaccine safety then is carefully monitored through post-marketing surveillance. The full process, in a best case scenario, can be completed in five to six months. 70 % production capacity for manufacturing influenza vaccines for various forms of influenza is located in Europe and North America. Countries like Australia, Japan and China are supplementing the production. World Health Organization estimates that a maximum of 4.9 billion doses can be produced in a year time depending on using full manufacturing capacity and other consideration including dose sparing vaccine formulation. A more conservative estimate is 1-2 billion doses annually. As with seasonal influenza vaccines, neither of these vaccines will contain adjuvants. The Food and Drug Administration (FDA) and WHO have selected A/California/07/2009 (H1N1) for use as the strain for the vaccines currently being manufactured. Licensed vaccines are expected to be available in the United States by mid-October 2009 (8,9). The time lag between the

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production of the vaccine and its use allows the virus to continue spreading and keep establishing in new areas thus hampering control efforts.

Recommendations For use & Epidemiological impact:

Advisory committee on Immunization Practices (ACIP), 2009 recommends that vaccination efforts should focus initially on pregnant women, persons who live with or provide care for infants aged <6 months (e.g., parents, siblings, and daycare providers), health-care and emergency medical services personnel who have direct contact with patients or infectious material, children aged 6 months-24 years, persons aged 25-64 years who have medical conditions that put them at higher risk for influenza-related complications. The demand for vaccine and initial supply might vary considerably across geographic areas. If the supply of the vaccine initially available is inadequate to meet demand for vaccination, the target groups listed above may be prioritized depending on local epidemiological situation. The decision on the number doses required (not established yet), simultaneous use of seasonal (whole virus and subunit "split" vaccines) and novel influenza A (H1N1) vaccines is to be kept in mind while pursuing expansion of vaccination beyond initial target groups (10). It is important to keep in mind that the seasonal vaccines are not routinely used in India except in high risk groups.

ACIP 2009 Recommendations - Indian perspective:

Implementation of ACIP recommendations in India would mean delivering vaccine to a large population, undoubtedly a gigantic task. Apart from issues of production and availability (common to all countries), logistic and administrative issues would determine its feasibility for widespread use in India. Diversion of resources could seriously affect the performance of other national health programs. Does all this mean that we do not do anything to prevent morbidity and mortality from H1N1? The answer is both Yes and No.

We surely need to provide vaccination services to those at higher risk after careful consideration. Preventing deaths would help remove fear as well as establishing population confidence in health services. This also means that delivering preventive and promotive services are lot easier. However, it is important that a false sense of security is not allowed to gain ground. It follows that other measures like creating awareness by intensified IEC campaigns, personal protection, recognition of danger signs, timely referral and appropriate treatment are given due importance in order to prevent mortality. In fact many developing countries including India are unlikely to have adequate amount of vaccine till mid 2010 (11). Even after it is available, it is going to take some more time to administer it to such large population in India. What impact then we expect on the epidemiological situation in India? The influenza infections have already managed to establish

in large parts of India. The transmission shows no sign of abetting in near future and actually is likely to intensify further. That means more and more people will get exposed to infection in a natural manner and thus acquire immunity and in due course of time produce a so called "Herd Effect" (12). In contrast to seasonal influenza, current evidence indicates that relatively few severe cases of novel influenza A (H1N1) virus infection have occurred among older persons, and the highest hospitalization rates for illness caused by this virus have been among persons aged <65 years (13). Since the H1N1 influenza virus carry a low risk of death, and given that we are able to protect the high risk groups by identifying them earlier and putting them on treatment, a high proportion of deaths can certainly be averted even in the absence of vaccination.

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