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Influenza: A Challenge?

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ABSTRACT

Ignorance is rectifiable but knowingly ignoring is suicidal and this what Influenza is? The three Influenza pandemics of the last century have high morbidity world wise and high mortality; 50 -100 millions, an unheard figure for any single disease the world population has suffered. Suffering, morbidity & mortality, all are warning to human life and this Influenza means. A hanging fear, all the time for a castrophy outbreak is the alternative name of the disease Influenza. Last century the three Influenza pandemic is not only a warning but an eye opener (1918-19; 1957 & 1967-68: with 50-100M deaths) due to one disease, is singular. The pH1N1 Mexican swine flu of this century (2009) is an eye-opener reminder of this. Today there not one strain but few more lurker influenza strains and could possible cause of future pandemics. Bird flu H5N1 was the anticipated strain for the pandemic ever since 1997 but a swine strain unexpected from Mexico made history as human Influenza pandemic of this century. Ever since influenza was known this virus always gave surprise.

INTRODUCTION

It is paradoxical as we all have suffered with influenza infection but yet we ignore this as common cold. Influenza is not just common cold, and if ignored specially in risk person could end fatally. The preventive vaccine is available from over sixty years but very much underused in developing countries. Last century during the three influenza pandemics over 50- 100 million people died all over the globe. The 1918-1919, is the worst pandemic known as Swine Flu affected almost one fifth of the world population, killing almost 50 million people. India was worst affected and it is estimated over 20 million people died. There were two more flu pandemics in the last century (1957; 1967-68). The

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best prevention of influenza is Influenza vaccine, the single most cost effective.

Anthrax? Ebola? No, the real killer is… Flu. This unpredictable virus kills approx. 500,000 people each year and goes un-noticed. USA uses preventive influenza vaccine in old/ young and risk population and yet each year over 35,000 people die due to influenza and influenza complications.

During 2014-15 Ebola killed 11,000 worldwide and influenza kills between 250,000 to 500,000 in a year. (Ref.: Book: Khan; the Next Pandemic, Peruses Book Group (2016).

The infection is self limiting and the recovery is in couple of weeks in uncomplicated case. This is one reason that the infection gets ignored. The vaccine is the best prevention. But, this also ignored very conveninately. There is just couple of human strains but the host virus is genetically mutating all the time and the vaccine needs to be repeated yearly to update the host system with the new virus stain.

Both the H & the N surface antigens of influenza A virus mutates either individually or, seen as in both the antigens. The mutation decides the seriousness of infection depending of the change from OB to pandemic. Interestingly the viral infection due to this characteristic influenza A virus from other host especially from pigs to birds has been observed as a living threat all the time.

Influenza is a common cause for acute upper and lower respiratory tract infection (ARI & LRI). The disease starts suddenly and spreads like wild fire among contacts. Since it is a respiratory infection due to inhalation of infectious virus particles, it is difficult to avoid. The incubation is short, 1-2 days and the disease subsides in 5-7 days, and poses difficulty in isolation & hospitilation in normal course, when there is no complication. Superimposed influenza complications in risk group, is serious and ends fatally in many cases. This, therefore, becomes a reason for concern.

http://www.fotosearch.com/

DISEASE LOAD

The seasonal influenza, estimated globally causes 250,000 to 500,000 deaths each year.

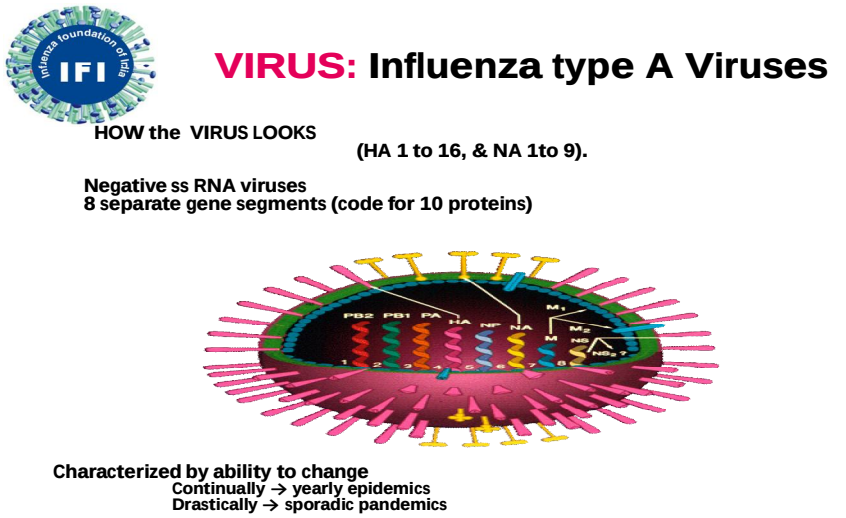
CLASSIFICATION

Influenza viruses belong to the Orthomyxoviridae family and are divided into types A, B and C. Influenza types A and B are responsible for epidemics of respiratory illness that are often associated with increased rates of hospitalization and death. Influenza type C is not discussed here as it causes a subclinical to a mild infection of insignificant illness. It does not cause epidemics, like influenza types A and B viruses.

VIRUS

All influenza viruses has negative strand RNA with a segmented genome. Influenza type A and B viruses have 8 genes that code for 10 proteins, including the surface proteins hemagglutinin (HA) and neuraminidase (NA). In the case of influenza type A viruses, further subdivision can be made into different subtypes according to differences in these two surface proteins.

Till date, 16 HA subtype and 9 NA subtypes have been identified. However, during the last century, the human influenza A subtypes that circulated extensively were A (H1N1); A (H1N2); A (H2N2); and A (H3N2). All other known subtypes of influenza type A viruses have been isolated from birds and can affect a range of mammal species. As with humans, the number of influenza A subtypes that have been isolated from other mammalian species is limited. Influenza type B viruses almost exclusively infect humans.



ANIGENIC DRIFT AND SHIFT

The characteristics of influenza viruses is their ability to undergo antigenic change, which occurs as **antigenic drift** –a gradual process and is continuous change in the viral HA and NA proteins. This results in OB and small epidemics. This also necessitates the use of influenza preventive seasonal vaccine as an annual event to up gate the protective capability for the drifted strain.

Antigenic shift is a total change in either H or, N or, both influenza surface proteins from the existing in virus in circulation.

(1)A virus bearing new HA and NA proteins can arise through the genetic reassortment of non-human and human influenza viruses;

(2) An influenza virus from other animals (e.g. birds or pigs) can infect a human directly without undergoing genetic reassortment; or

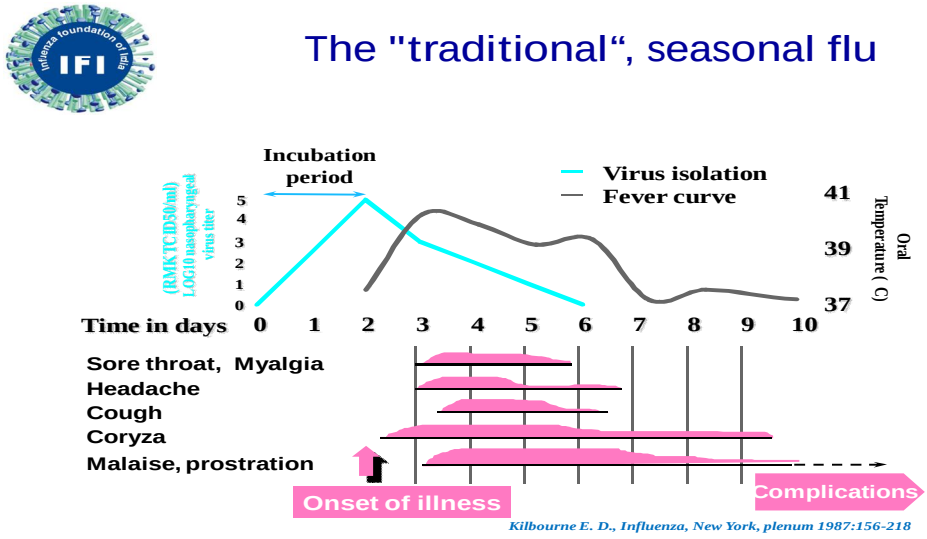
(3) A non-human virus may be passed from one type of animal (e.g. birds) through an intermediate animal host (such as a pig) to humans.

Antigenic drift – is a process of gradual and relatively continuous change in the viral HA and NA proteins. It results from the accumulation of point mutations in the HA and NA genes during viral replication. Both influenza type A and B viruses undergo antigenic drift, leading to new virus strains. The emergence of these new strains necessitates the frequent updating of influenza vaccine virus strains. Because antibodies to previous influenza infections may not provide full protection against the new strains resulting from antigenic drift, individuals can have many influenza infections over a lifetime.

Out breaks and influenza epidemic generally occur each year or every alternate year due to drift in the surface H & N antigen. The severity depends upon the amount of drift. But, when there is a shift in the surface H & N antigen the infection spreads globally in absence of any protective antibody in the world population. There is no vaccine as the change is unpredictable and the pandemic strain is not available.

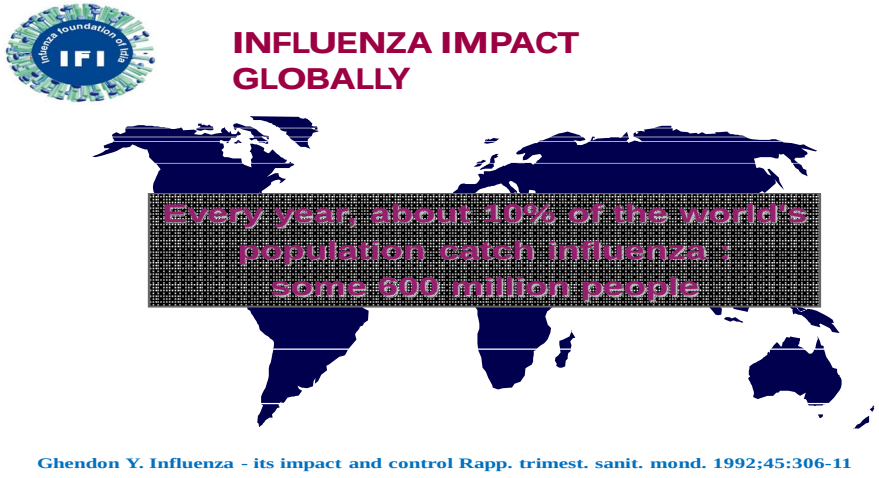
PERIOD OF CONTAGIOUSNESS

The disease has a short incubation period 1-2 days and normally recedes in 5-7 days as self limiting infection. A person recovers in 2-4 weeks time in uncomplicated cases. The sick person is infectious from a day before the onset of symptoms and till 1-2 weeks post infection.



CHRACTRIST FEATURES OF INFECTION

Sudden symptoms characterized by fever, headache, myalgia, and sore throat, followed by dry or running nose, comatose, feeling of weakness in leg, pressure in eye and anorexia occurs. One observes a sudden increase in similar cases in the OPD. In case of School going children there will be large absentees with similar symptoms.



PANDEMIC INFLUENZA

During the last, 20th century, the only influenza A subtypes that circulated extensively in humans were A(H1N1); A(H1N2); A(H2N2); and A(H3N2). The hallmark of human influenza viruses is their ability to undergo antigenic change, which occurs in the following two ways:

1919 – The "Spanish flu" A (H1N1) pandemic led to more than 40 million deaths worldwide (Palese, 2004). Nearly half of these deaths were among people 20–40 years of age, and case-fatality rates of 30% were reported among pregnant women.

1957–1958 – the "Asian flu" A (H2N2) pandemic was associated with a total excess mortality of more than 1 million deaths globally (Lipatov et al., 2004).

1968–1969 – despite the lack of well-established estimates, the global excess mortality caused by the "Hong Kong flu" A(H3N2) pandemic has been calculated at around 1 million (Lipatov et al., 2004).

In all cases, the pandemic spread throughout the world within a year of its initial detection. Outbreaks of the Asian flu were first reported in late February 1957 in China and spread to other parts of Asia by April–May. Quarantine efforts were not helpful in curtailing the spread.

Although the highest rates of seasonal influenza-related illness occur among school-age children, the highest rates of associated hospitalizations occur among: children under 2 years of age; people of any age with certain chronic medical conditions (including chronic heart disease, lung disease such as asthma, diabetes, and renal failure or immunocompromising conditions); those aged 65 years or older; and pregnant women.

For example, one study from the United States (Izurieta et al., 2000) estimated that healthy children under 2 years of age have 12 times the risk of influenza-related hospitalization as healthy children aged 5–17 years. Influenza-associated hospitalization rates are also higher among those with chronic medical conditions than among otherwise healthy people of the same age group. At both extremes of the age spectrum, however, rates of influenza-related hospitalization are elevated, even among those without chronic medical conditions. Rates of seasonal influenza-associated hospitalization are highest for people aged 85 years or older. The rates are lower for children and young adults, but children younger than 5 years old have hospitalization rates similar to people aged 50–64 years. Pregnant women also appear to be at increased risk of complications from influenza. One study of pregnant women enrolled in the Tennessee Medicaid Program in the

Timing of regional influenza activity

The timing of influenza activity around the world varies depending upon the climate of each region. In temperate climates, the onset and peak of influenza activity may vary substantially from one influenza season to the next but activity generally begins to increase in late autumn. In temperate regions of the northern hemisphere, influenza viruses are frequently isolated in the autumn, winter and spring. Periods of peak influenza activity typically occur between December and March and last for 6–8

weeks. In temperate regions of the southern hemisphere, influenza activity typically peaks in May to September. Although temperate regions of the world experience such seasonal peaks in influenza activity, influenza viruses can be isolated sporadically throughout the year, usually associated with outbreaks in closed environments such as nursing homes and summer camps.

The timing of seasonal peaks in influenza activity in tropical and subtropical countries also varies by region, and in some areas more than one peak of activity may occur in the same year. Such variability in influenza seasonal peaks in tropical and subtropical countries illustrates the importance of country-specific and regional epidemiological and virological data including decisions on timing of vaccination programmes. Influenza viruses in tropical and subtropical regions can circulate at low levels at any time of the year and can cause isolated cases of influenza as well as outbreaks outside the peak periods of activity.

The Pandemic influenza in addition to the annual seasonal epidemics of influenza seen in some regions, pandemics of influenza have occurred infrequently and at irregular intervals.

In all age groups, influenza infection rates are generally higher during pandemics than during annual epidemics. As with epidemics, school-age children play an important role in the spread of pandemic influenza in the community.

The Pandemic (H1N1) 2009 was even more rapid due to the high mobility and interconnectedness of 21st century societies. Within 6 weeks of first being described, it had affected all regions resulting in the declaration of a pandemic. Once again schools appeared to play an important role in the amplification of virus transmission.

The overall rates of severe disease, however, were considerably lower than those recorded for the pandemic of 1918. The rapidity with which the pandemic (H1N1) 2009 virus spread highlighted the need for timely and effective surveillance systems to detect emerging viruses with pandemic potential, and the need for standard platforms for data sharing and dissemination.

Impact of influenza

Increases in the circulation of influenza viruses are associated with increases in acute respiratory illnesses, physician visits, hospitalizations and deaths. In general, rates of primary influenza illness are highest among school-age children (exceeding 30% in some years) and are lower among adults. During non-pandemic years, influenza infection rates among adults are estimated to generally range from 1% to 15%.

Morbidity

Although the highest rates of seasonal influenza-related illness occur among school-age children, the highest rates of associated hospitalizations occur among: children under 2 years of age; people of any age with certain chronic medical conditions (including chronic heart disease, lung disease such as asthma, diabetes, renal failure or immunocompromising conditions); those aged 65 years or older; and pregnant women.

Influenza control

Influenza vaccines

Annual vaccination is the primary means of reducing the impact of seasonal influenza. Vaccination is associated with reductions in: influenza-related respiratory illness and physician visits among all age groups; hospitalizations and deaths among people at high risk; otitis media among children; and work absenteeism levels among adults.

Currently, seasonal influenza vaccines contain a mixture of four inactivated strains of the influenza viruses (two type influenza A and two influenza B viruses, likely to circulate during the next influenza season. Because influenza viruses are constantly changing, the seasonal influenza vaccines are updated and administered annually to provide the necessary protection.

Live attenuated and inactivated seasonal influenza vaccines

Live attenuated seasonal influenza vaccines have been advised for healthy people aged 2–49 years to avoid influenza infection themselves or if they are in close contact with people at high risk of developing serious complications from influenza infection.

Inactivated seasonal influenza vaccines are similar in many respects to live attenuated influenza vaccines. They both contain similar strains of influenza viruses representative of the recommended strains. The virus strains for both types of vaccine are selected annually, and one or more of these may be changed based on the results of global influenza surveillance and the emergence of new strains.

ANTIVIRAL DRUGS

Amantadine and Rimantadine are chemically related drugs that specifically inhibit the replication of Influenza types A viruses – but not influenza type B viruses.

The mechanism of action of adamantine derivatives is not completely understood, but it is believed that they interfere with the function of the transmembrane domain of the M2 protein of influenza type a viruses. They also interfere with influenza type a virus assembly during viral replication. as a result they prevent the release of infectious influenza a viral particles from the host cell.

Influenza Burden:

The burden of influenza, not only from a clinical but also from an economic perspective, is mostly underestimated. The annual epidemics are deadly and costly occurrences and the pandemic events are devastating. Annual influenza vaccination prevents incidence impact, reduces disease complications and deaths. Government due to resource crunch and pressure for other more pressing diseases is not able to lay emphasis for influenza. Although, very young children, old adults and persons with conditions, pregnant women in influenza season needs protection.