* Influenza virus
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* Orthomyxoviridae family of viruses
* RNA enveloped viruses that make up three genera
* Influenzavirus A
* Influenzavirus B
* Influenzavirus C
* The type A viruses are the most virulent among the three, genetically diverse and infecting human, birds and animals
* It is often confused with common cold, influenza is a more severe disease than the common cold and is caused by a different type of virus
* Structure
* RNA enveloped
* RNA is segmented with eight pieces
* The envelope is studded with 2 different types of glycoprotein spikes
* Heamagglutinin binds to the sialic acid receptors on cells in respiratory tract allowing adsorption of virus. (Antibodies against this prevent adsorption and are protective)
* Neuraminadase cleaves neuraminic acid allowing exit of virus from cell (antibodies against this are also protective)
* Nomenclature
* Strains are designated according to the site of origin, isolate number, year of isolation, and subtype—for example, influenza A/Hiroshima/52/2005 (H3N2).
* Influenza A has 16 distinct H subtypes and 9 distinct N subtypes.
* Influenza B and C viruses are similarly designated, but H and N antigens do not receive subtype designations, since variations in influenza B antigens are less extensive than those in influenza A viruses and may not occur with influenza C virus.
* Q: If antibody to the NA and HA are protective, why do we continually get epidemics & pandemics of flu?
* Ans: Antigenic Variation
* The most extensive and severe outbreaks are caused by influenza A viruses, in part because of the remarkable propensity of the H and N antigens of these viruses to undergo periodic antigenic variation
* Minor antigenic variations are called drifts
* Major antigenic variations are called shifts
* Antigenic drifts
* Antigenic drift causes slight mutations in HA and NA, year on year, from which humans have partial, but not complete, immunity.
* These mutations occur during person to person spread
* The resulting new strains are only partially attacked by our immune system, resulting in milder disease in adults who have previously acquired antibodies.
* Drifts result in localized outbreaks and epidemics
* Localized outbreaks take place at variable intervals, usually every 1–3 years
* Antigenic shift
* With antigenic shift there is a complete change of the HA, NA, or both.
* This can only occur with influenza type A because it infects both humans and animals and undergoes a phenomenon called genetic reassortment
* When 2 influenza types co-infect the same cell( usually in pigs), RNA segments can be mispackaged . The new virus now yields a new HA or NA glycoprotein that has never been exposed to a human immune system anywhere on the planet. , leading to devastating pandemics.
* Latest flu pandemics
* An **influenza pandemic** is an epidemic of an influenza virus that spreads on a **worldwide scale** and infects a large proportion of the human population.
* **Influenza A subtype H5N1  
  (Bird Flu or avian influenza virus)**
* Is highly pathogenic strain found in birds
* So far 499 human cases had been recorded of which 295 died
* These cases resulted from intense human to poultry contact; human to human transmission is limited an inefficient
* It is feared that as a result of mixing with human flu viruses (genetic reassortment) a new strain will emerge with efficient human to human transmisssion🡪a pandemic and a high mortility similar to spanish flu
* 2009 H1N1 flu(swine flu)
* It contained reassorted genes from five different flu viruses:
* North American swine influenza,
* North American avian influenza,
* human influenza,
* and two swine influenza viruses found in Asia and Europe.
* Virulance and mortality rates were very low, killed about 18,000 people worldwide
* Partial immunity in older adults were detected may be due to previous exposure to similar seasonal influenza viruses,
* On 10 August 2010, WHO announced the end of H1N1 pandemic
* Pathogenesis
* The initial event in influenza is infection of the respiratory epithelium
* The cells eventually become necrotic and desquamate
* The degree of viral replication is an important factor in pathogenesis
* Despite systemic signs and symptoms such as fever, myalgias, influenza virus has only rarely been detected in extrapulmonary sites
* Pathogenesis of systemic symptoms in influenza is related to inflammatory mediators(cytokines)
* Clinical features
* Spectrum of clinical presentations is wide, ranging from a mild, illness similar to the common cold to severe prostration
* Usually there is abrupt onset of symptoms, such as headache, fever(100-105 F), chills, myalgia, or malaise, and accompanying respiratory tract signs,cough and sore throat,sneezing
* In uncomplicated influenza, the acute illness generally resolves over 2–5 days, and most patients recover in 1 week, although cough may persist 1–2 weeks longer
* Complications
* Pneumonia
* Primary viral
* Secondary bacterial
* Mixed viral & bacterial
* Reye's syndrome(with aspirin)
* Cases of influenza by avian A/H5N1 virus are associated with high rates of pneumonia (>50%) and extrapulmonary manifestations such as diarrhea and CNS involvement. Deaths have been associated with multisystem dysfunction
* High risk for complications
* >64 years old
* those with chronic disorders, like
* cardiaopulmonary diseases, diabetes , renal dysfunction, and immunosuppression
* Pregnant (2nd & 3rd trimester)
* Infants
* Lab diagnosis
* Samples include throat swabs, nasopharyngeal washes, or sputum
* Serology. Fourfold or greater titer rise in antibody titre in serum as detected by Heamagglutination, compliment fixation,ELISA
* RT- PCR
* Isolation of virus in cell cultures
* Viral antigen detection by immunoflorescence or ELISA
* Treatment
* Symptomatic
* Rest, drink plenty of fluids, cough suppressants, antipyritics but no aspirin
* Anti virals:These drugs can reduce the severity of symptoms if taken soon after infection.Two classes of drugs available
* Neuraminidase inhibitors zanamivir and oseltamivir
* inhibitors of the viral M2 protein(uncoating inhibitors), amantadine and rimantadine (90 % viruses now resistant to this category).Only for Inf A
* Prophylaxis
* Recommended for high risk individuals
* Vaccination
* Chemoprophylaxis
* Prophylaxis
* Vaccination
* Killed vaccine. The vast majority of currently used vaccines are"killed" preparations derived from influenza A and B viruses that circulated during the previous influenza season. 50–80% protection would be expected
* A live attenuated vaccine administered by intranasal spray . The vaccine is generated by reassortment between currently circulating strains of influenza A and B virus and a cold-adapted, attenuated master strain (92% protective)
* Chemoprophylaxis
* Antiviral drugs Neuraminadase inhibitors may also be used as prophylactics in half the dose recommended for treatment
* For high-risk individuals who have not received influenza vaccine or in a situation where the vaccines previously administered are relatively ineffective because of antigenic changes in the circulating virus
* Prevention
* Hand washing
* Respiratory etiquettes