- Influenza virus

- Influenza virus
- 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 (2^{nd} & 3^{rd} 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