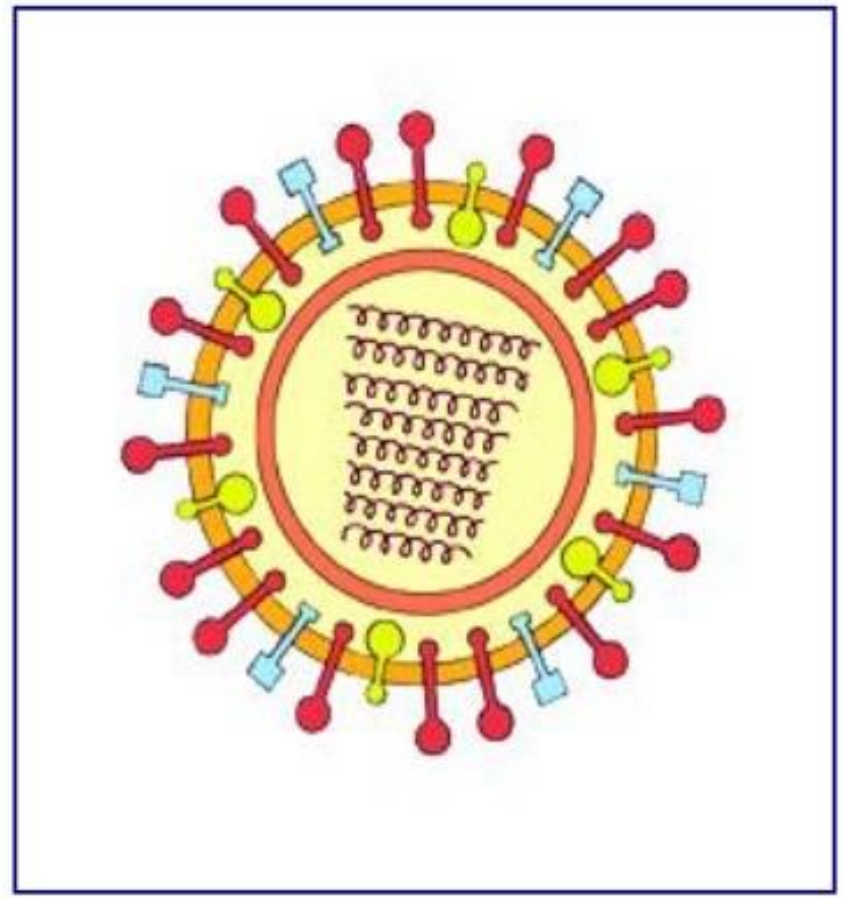
Lesson 23.

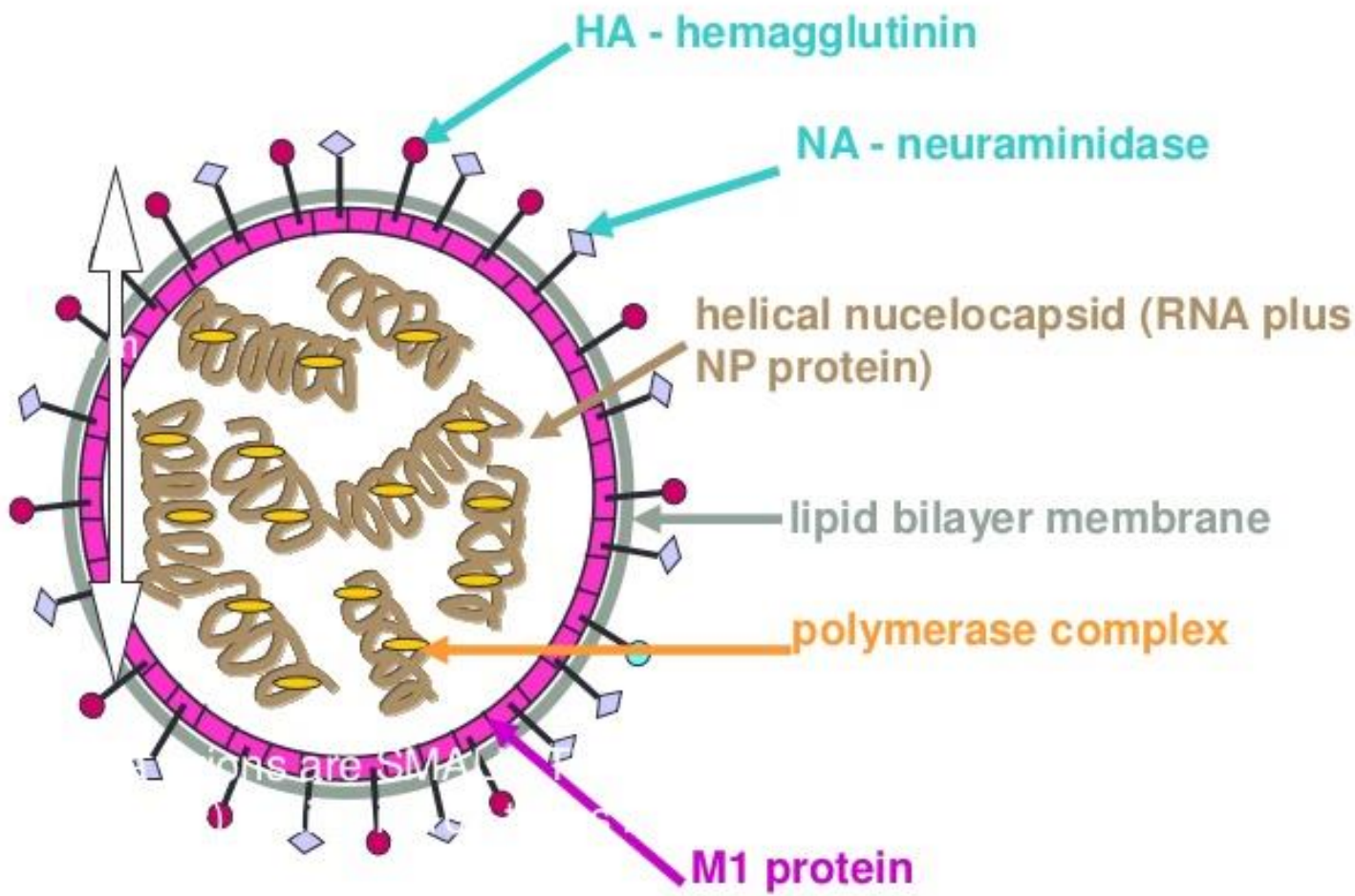
Introduction to basic virology. Microbiology diagnosis of respiratory viral infections (families of Orthomyxoviridae, Paramyxoviridae, Coronaviridae, Picornaviridae, Rhabdoviridae)

Influenza Virus

- Virus are spherical in shape
- Size is 80 -120 nm
- Pleomorphism is common with variant forms

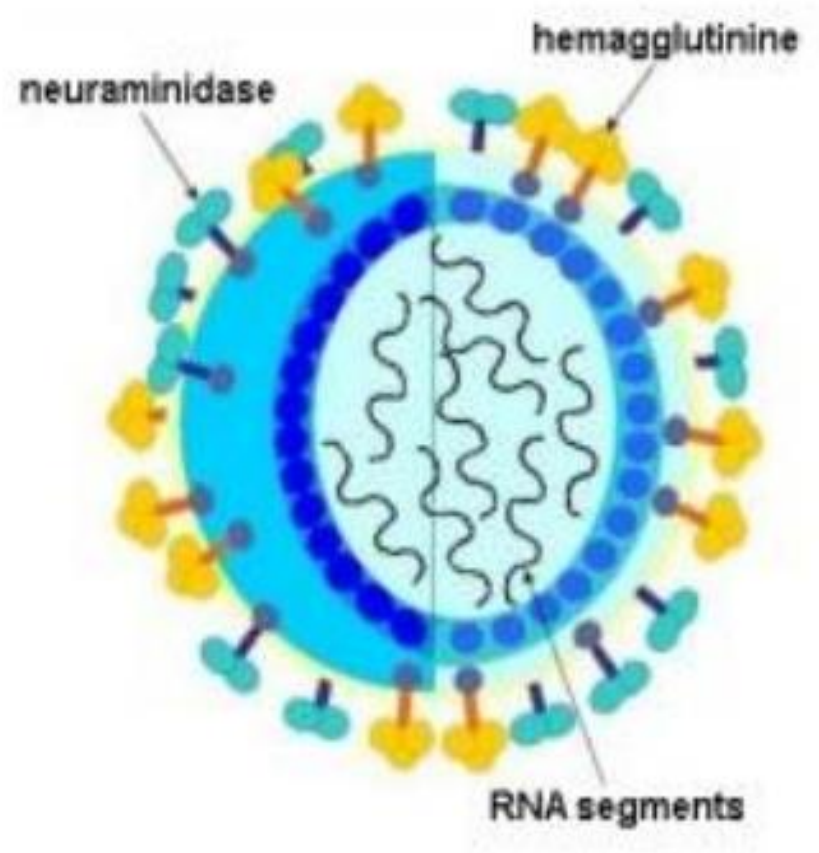


Structure of Virion



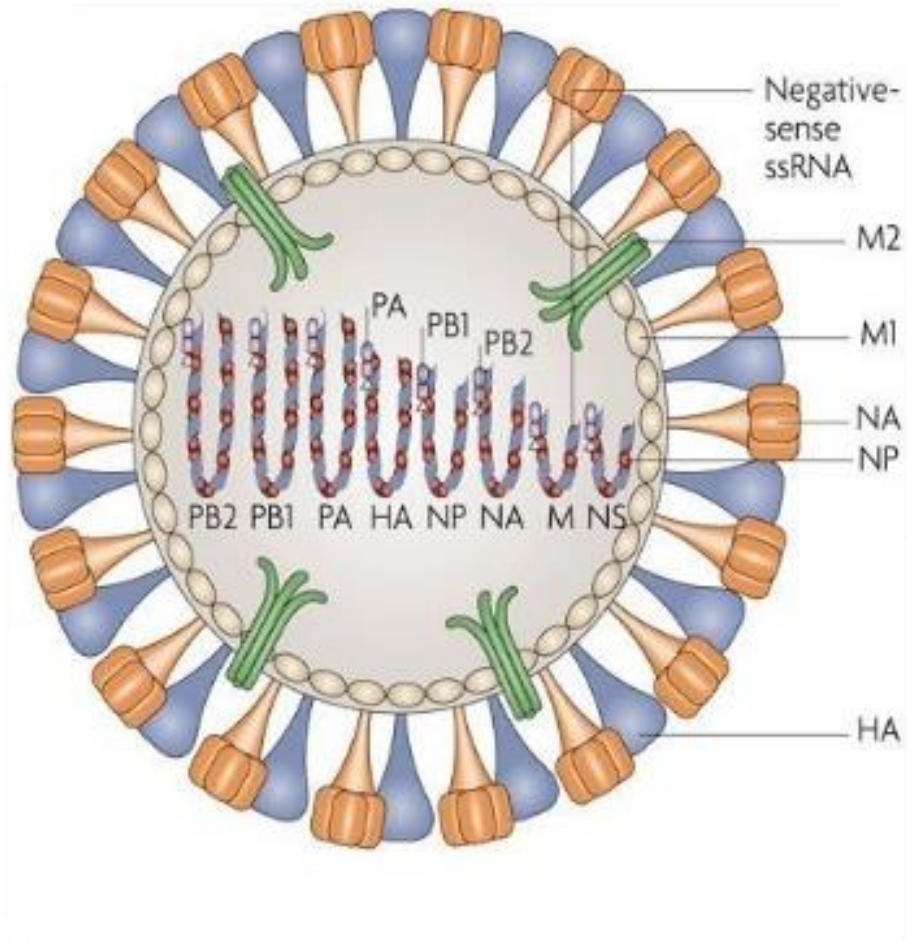
Viral structure

- The nucelocapsid is surrounded by an envelope with inner membrane protein layer and outer lipid
- From the envelop there are projections of two types
- 1 **Hem agglutinins**
- **2 Neuraminidase**



Types of Haemagglutinnins

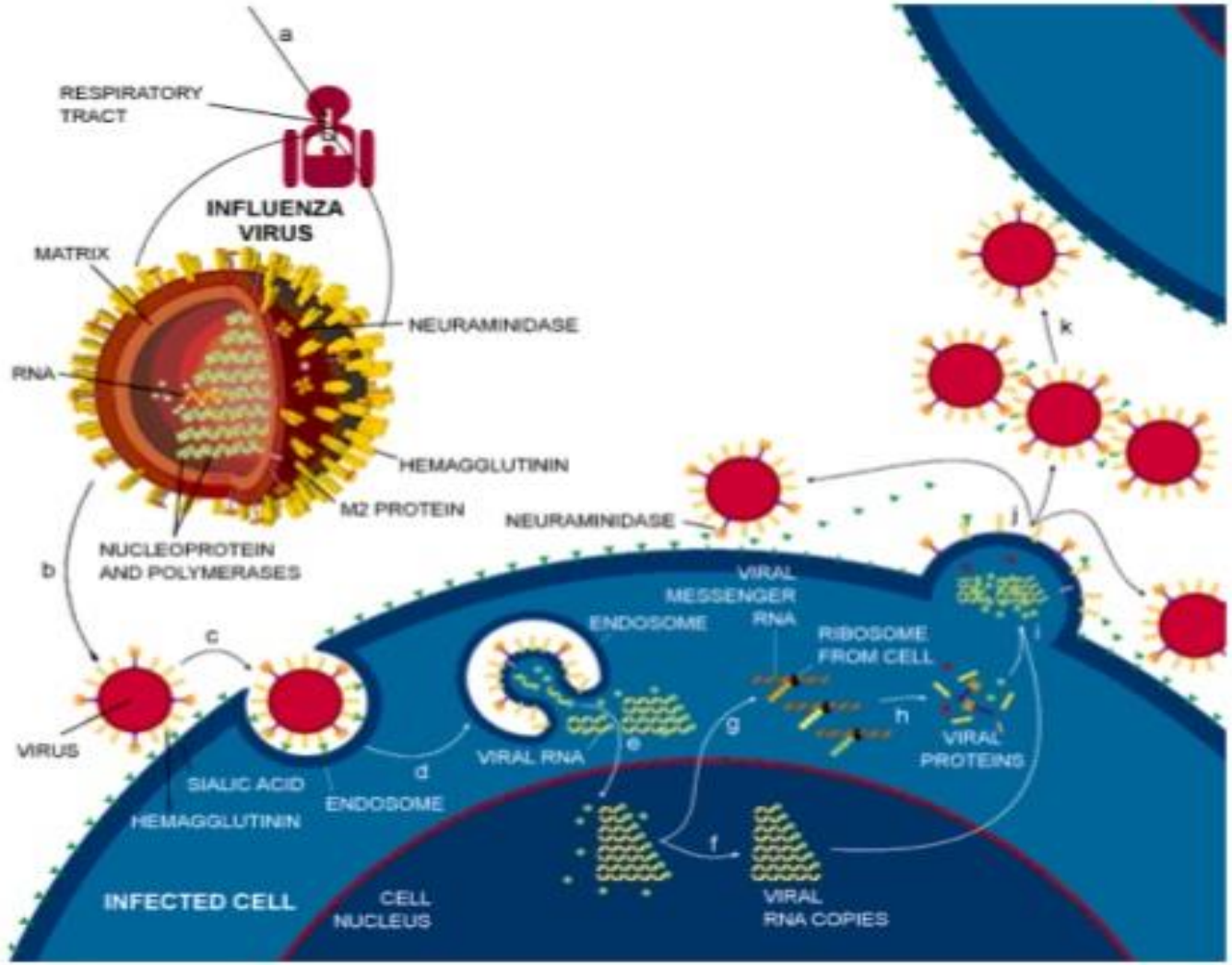
- Haemagglutination is strain specific
- Great variation
- H A there are 15 subtypes H 1 to H15 in avian influenza
- But only 4 variants in humans



Neuraminidases

- Neuraminidase are glycoprotein's
- Destroys cell receptors by hydrolysis cleavage
- Anti neuraminidase antibodies are produced following infection and immunization
- Not protective as Antihemagglutinin antibodies
- Helps to inhibit the release and spread of progeny
- Strain specific exhibit variation, There are nine different subtypes N 1 – N9.

Life cycle of the ‘flu virus



Antigenic Variation

- Unique feature of this virus lies with antigenic variation.
- High in type A virus
- Less in type B virus
- Not in type C virus
- RNP and Matrix proteins are stable
- Haemagglutination and Neuraminidase are independent of the variations.

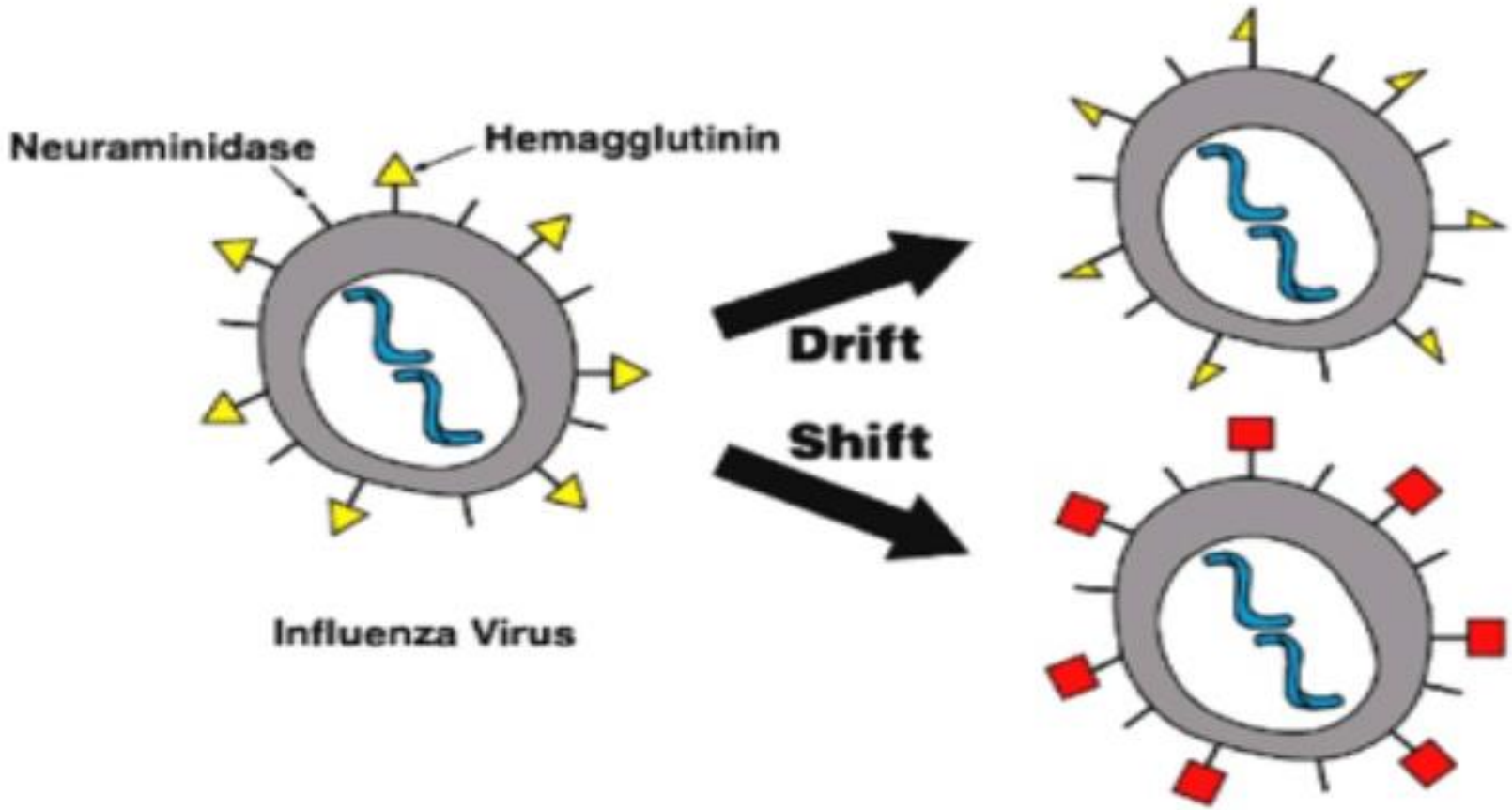
Influenza prominent Antigenic Changes

- Antigenic Shift
  - major change, new subtype
  - caused by exchange of gene segments
  - may result in pandemic
- Example of antigenic shift
  - H2N2 virus circulated in 1957-1967
  - H3N2 virus appeared in 1968 and completely replaced H2N2 virus

Influenza Antigenic Changes

- Antigenic Drift
  - minor change, same subtype
  - caused by point mutations in gene
  - may result in epidemic
- Example of antigenic drift
  - in 2002-2003, A/Panama/2007/99 (H3N2) virus was dominant
  - A/Fujian/411/2002 (H3N2) appeared in late 2003 and caused widespread illness in 2003-2004

Antigenic Variations



Resistance of Virus

- Inactivated by heating at 50^0c for 30 mt
- Survive for 1 week at 0 – 4^0c for 1 week
- Virus preserved at – 70^0c
- **Survive in the blankets for 2 weeks**
- Ether, formaldehyde, Phenol destroy the virus

INFLUENZA

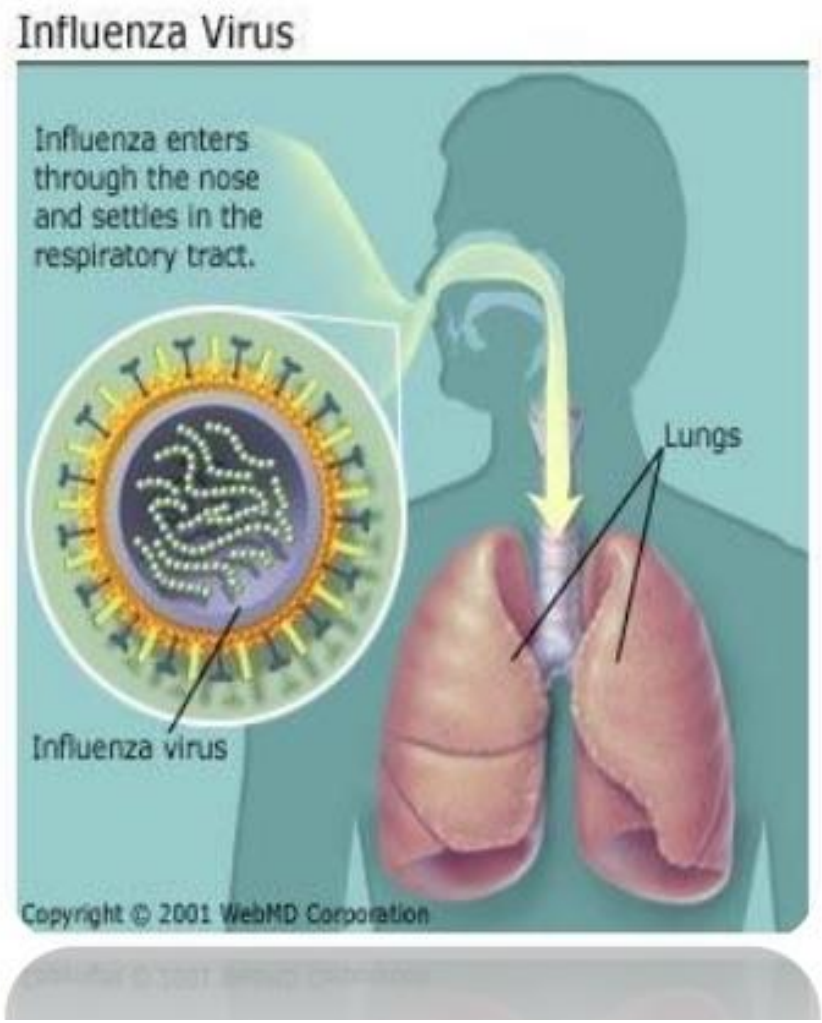
- Cause of the infection of the Respiratory tract.
- Occurs as

  Sporadic

  Epidemic

  Pandemic

Major pandemic in 1918 – 1919



Epidemiology

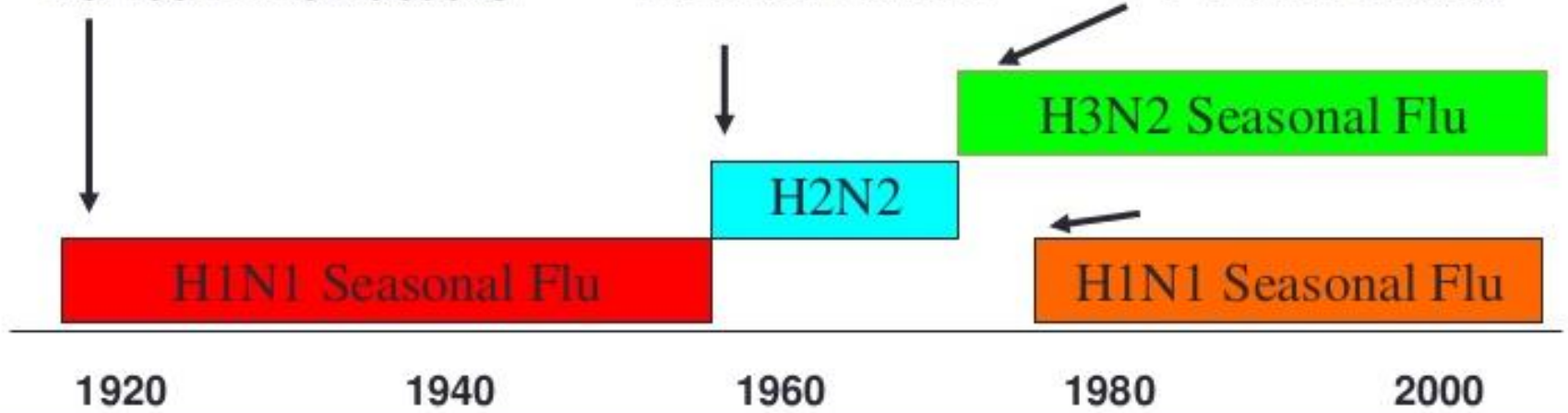
- Virus enters through respiratory route
- In 3 – 4 days majority manifest
- Many are subclinical infections
- Type A produce pandemics
- Type B sporadic cases, epidemics
- Dangerous in the Temperate regions
- Higher mortality in aged and patients with existing cardiopulmonary involvement

Circulating Seasonal Influenza A Sub-Types from Pandemics of the 20th Century

1918/19
40-100 million deaths

1957/58
~2 million deaths

1968/69
~1 million deaths



4 pandemics since 1889, with 11 to 39 years (average ~30 years) between each = ~3.3% annual risk of pandemic onset (but likely higher now)

TRANSMISSION

- AEROSOL
  - 100,000 TO 1,000,000 VIRIONS PER DROPLET
- 18-72 HR INCUBATION
- SHEDDING

Spread of Influenza

- The virus is transmitted easily from person to person via droplets and small particles produced when infected people cough or sneeze.

Pathogenesis

- Infects the respiratory tract
- Even 3 or few viral particles can infect
- Neuraminidase facilitates infection reducing the viscosity of Mucous
- Ciliated cells are infected in the Respiratory tract - site of viral infection
- When superficial layers are damaged exposes the basal layers
- And exposure of the basal layer causes the bacterial infections.

Pathogenesis – Viral Pneumonia

- Thickening of the Alveolar cells
- Intestinal infiltration with leucocytes with capillary thrombosis of Leucocytic exudates
- Hyaline membrane is formed occupying alveolar ducts and alveoli
- In late stages infiltration with Macrophages

Clinical features

- Incubation 1 to 3 days
- Present with mild cold lead to fulminating rapidly fatal Pneumonia
- Can abruptly present with head ache malign
- Can also present with abdominal pain with type B in children
- Bacteria superinfect

SYMPTOMS

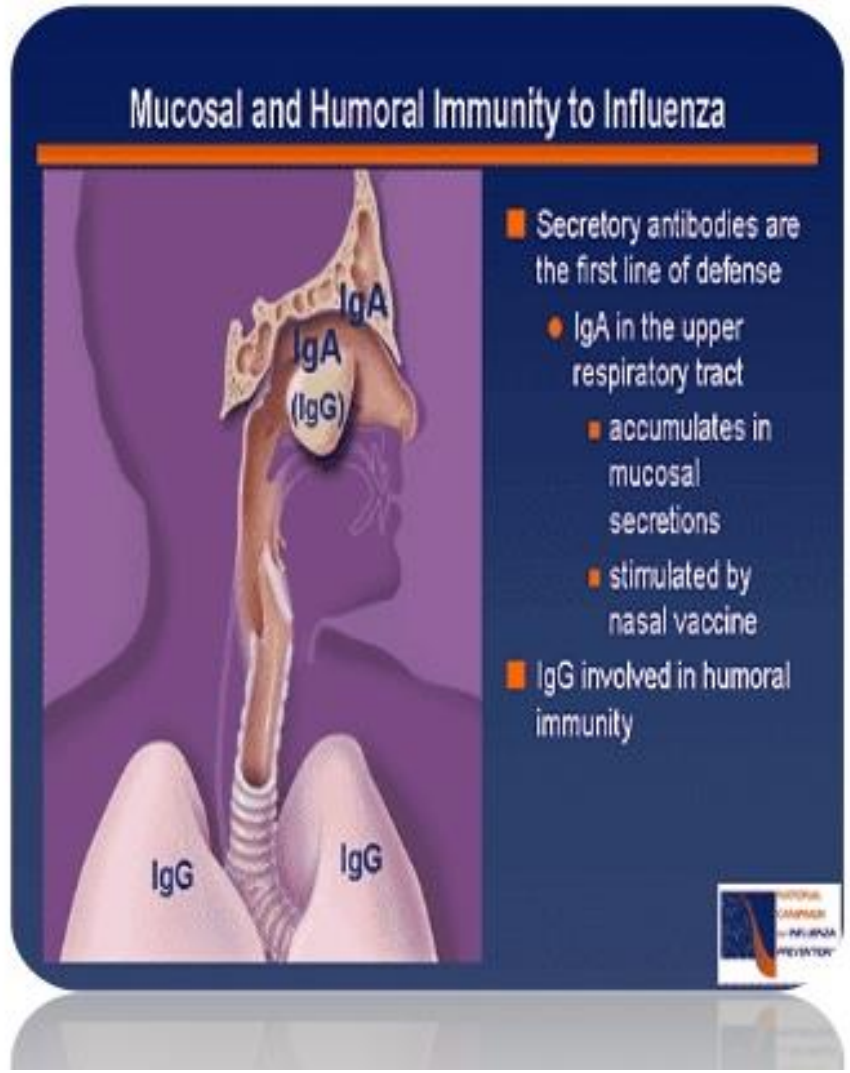
- FEVER
- HEADACHE
- MYALGIA
- COUGH
- RHINITIS
- OCULAR SYMPTOMS

Complications of Influenza

- Bacterial super infections
- Cardiac complications
- Congestive heart failure
- Myocarditis
- Neurological involvement
- Encephalitis
- Type B virus can produce Reye's syndrome
- Degenerative changes in the Brain and Liver
- Gastric flu with type B virus

Immunity in Influenza

- After infection immunity lasts 1 to 2 years
- Immunity lasts short duration due antigenic variants infecting at intervals.
- Antibodies produced locally are effective IgA immunoglobulin.
- Anti Hemagglutinins and Antinerumanidase are effective in prevention of infection.



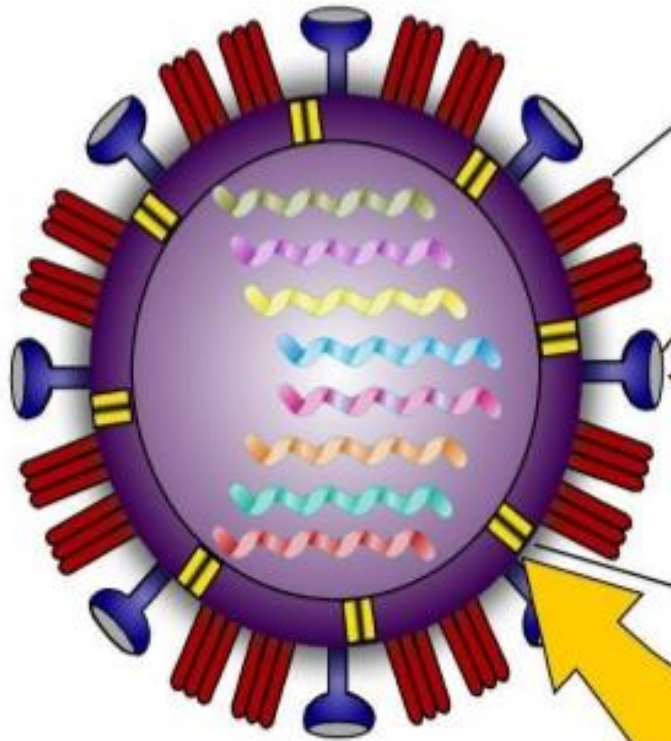
Influenza Diagnosis

- Clinical and epidemiological characteristics
- Isolation of influenza virus from clinical specimen (e.g., nasopharynx, throat, sputum)
- Significant rise in influenza IgG by serologic assay
- Direct antigen testing for type A virus

Serology

- Compliment fixation test
- Haemagglutination Inhibition testing
- *Testing on paired sera*
- Detection of Haemagglutination Inhibition testing
- Radial Immunodiffusion

Antiviral Therapies for Influenza



Hemagglutinin (H)

Neuraminidase (N)

M2 Protein

(Injectable **Peramivir** has completed phase-1 trials)

Tamiflu! (oral)

Oseltamivir
Zanamivir

Ralenza (inhaled)

Amantadine
Rimantadine (Older drugs)

(Viral resistance to these is more common)

New strain Hon Kong

H5 N1 strain

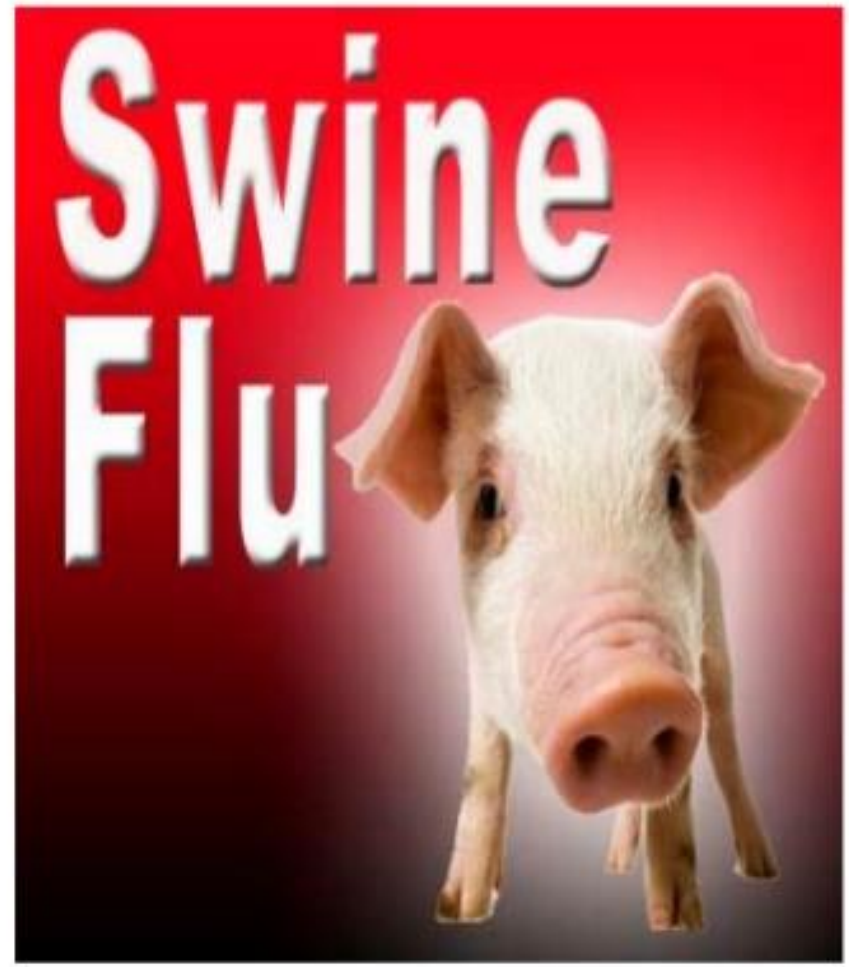
- Originated in Hong Kong
- 18 confirmed 6 dead
- Can spread from Chicken to Humans
- Wild aquatic birds spread.

What is Bird Flu

- Avian Influenza in Animals
- Only birds get infected
- Less common Pigs
- Avian influenza is species specific
- Less common in Humans
- Can spread from poultry to Humans can produce sever disease

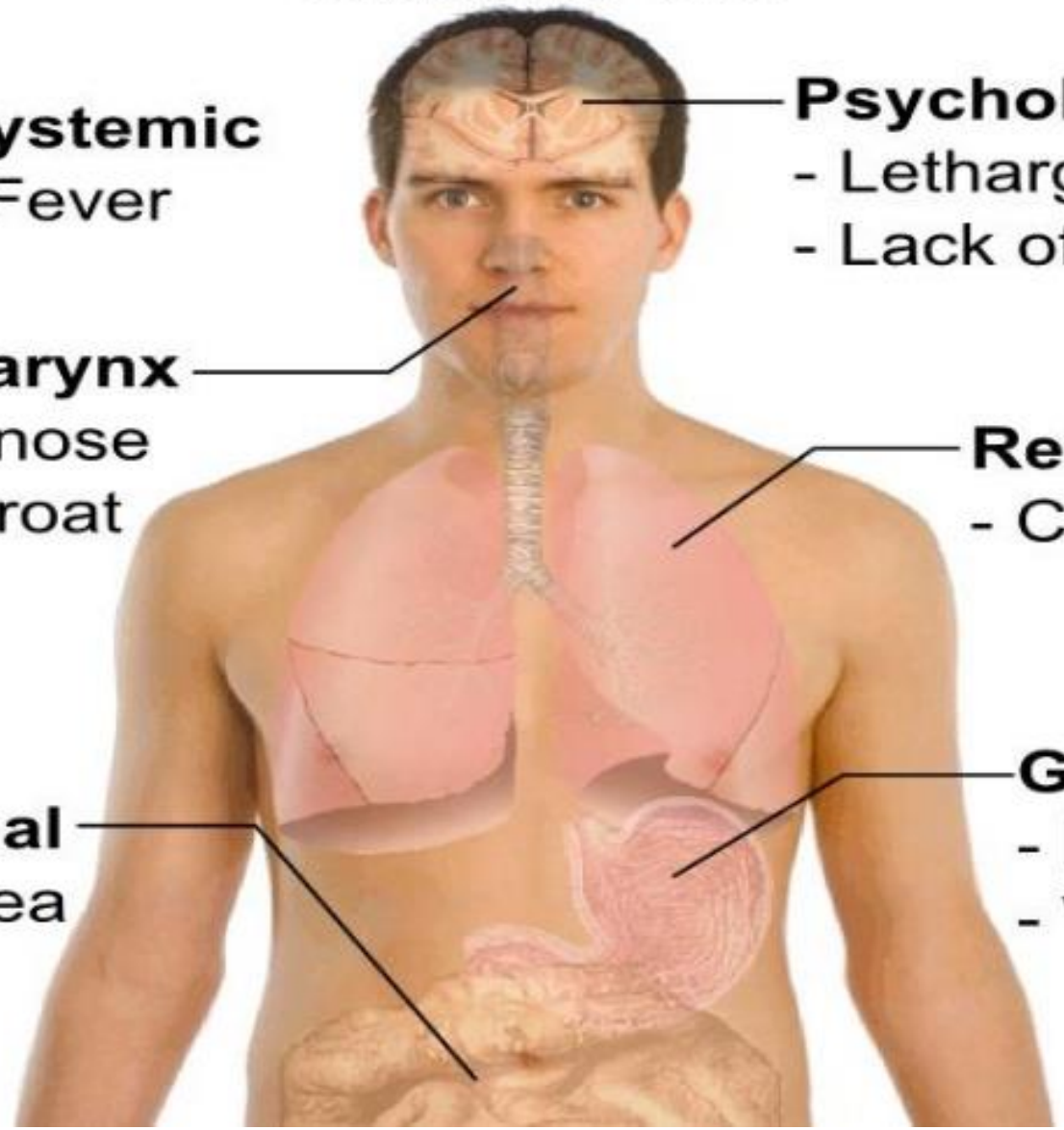
SWINE FLU 2009

- **Swine influenza** (also called **H1N1 flu**, **swine flu**, **hog flu**, and **pig flu**) is an infection by any one of several types of swine influenza virus. **Swine influenza virus** (**SIV**) is any strain of the influenza family of viruses that is endemic in pigs



Symptoms of

Swine flu



Systemic
- Fever

Psychological
- Lethargy
- Lack of appetite

Nasopharynx
- Runny nose
- Sore throat

Respiratory
- Coughing

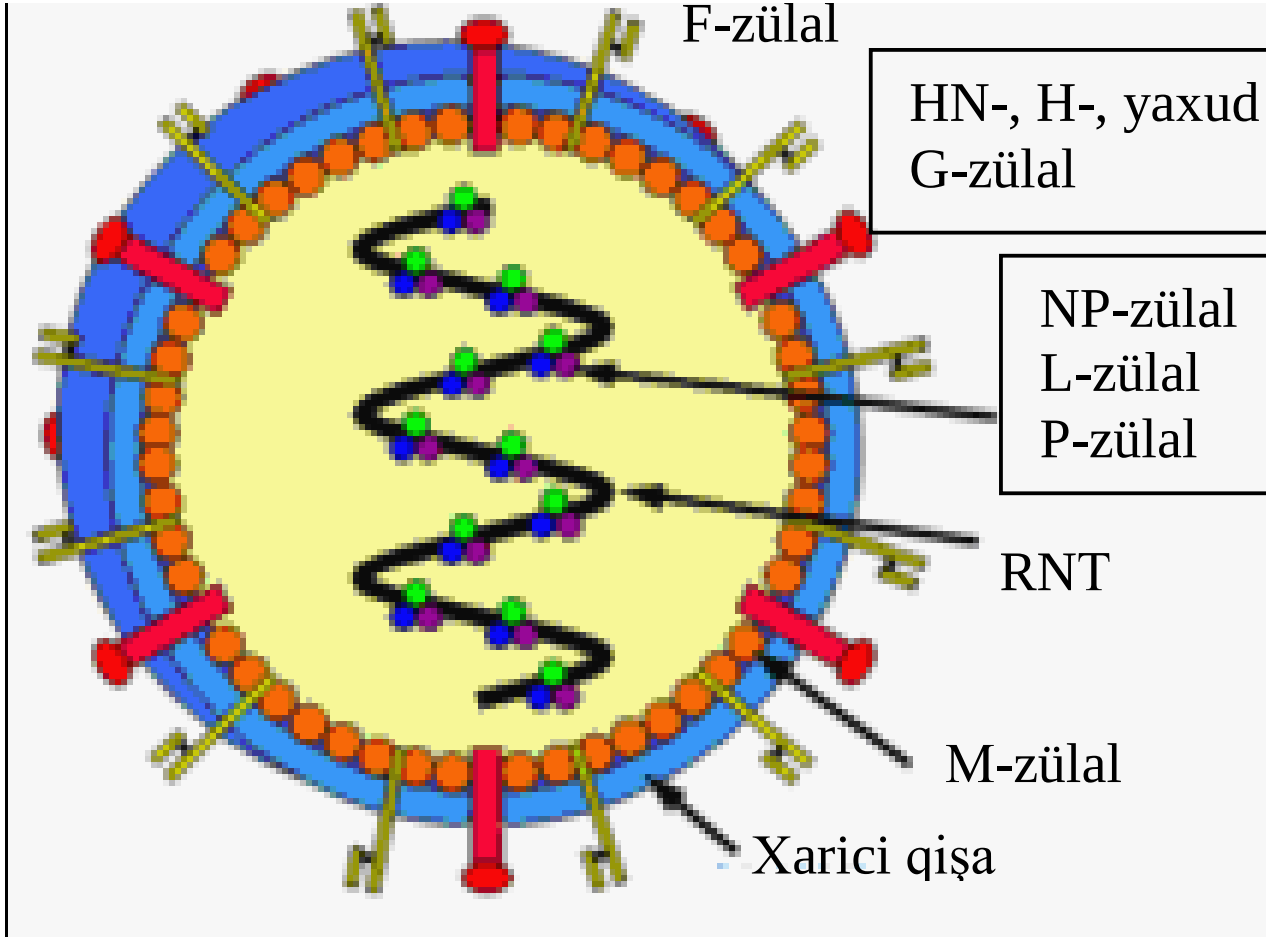
Intestinal
- Diarrhea

Gastric
- Nausea
- Vomiting

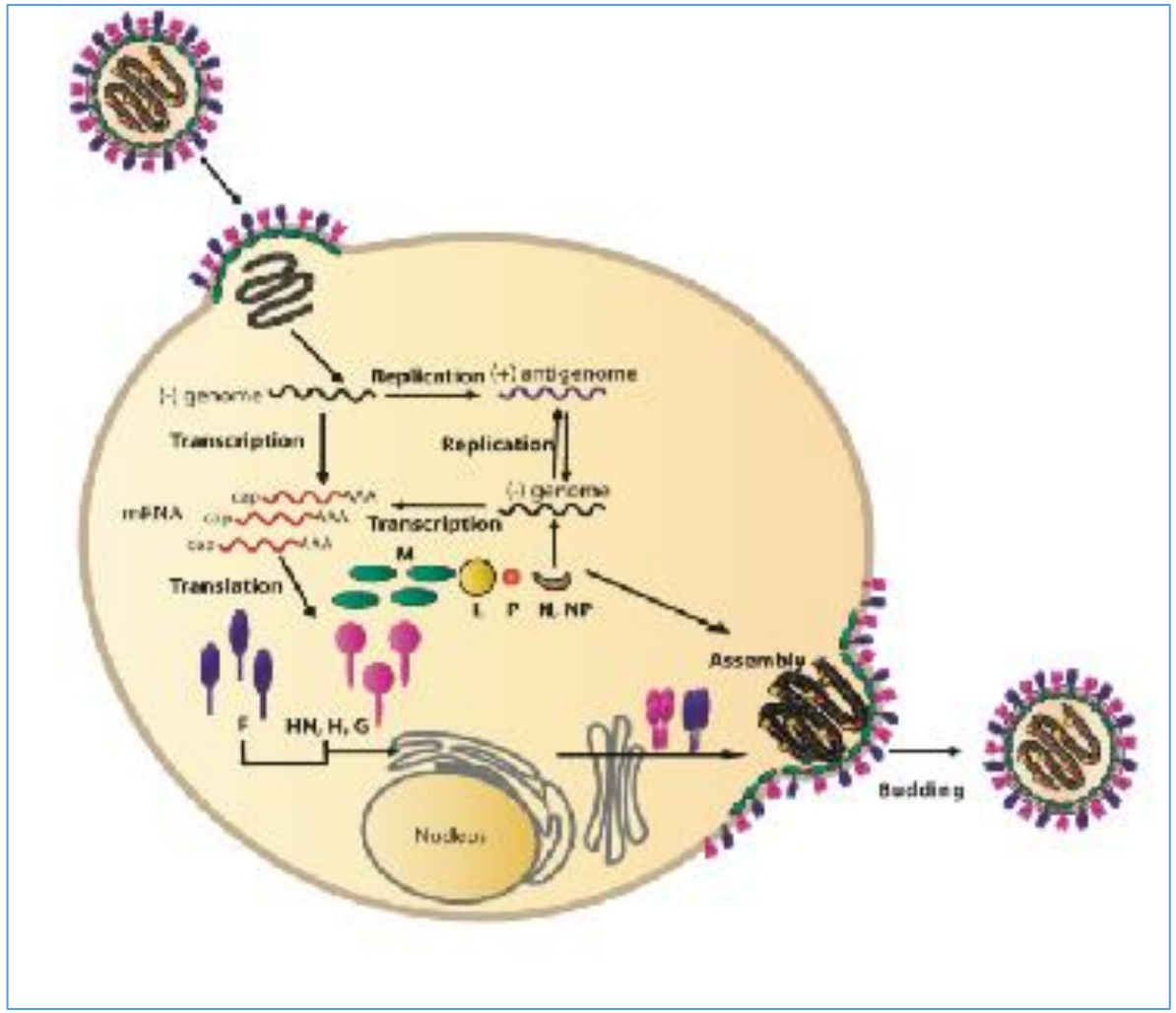
Paramyxoviridae family

- *Paramyxoviridae* consist of 2 subfamily - *Paramyxovirinae and Pnevmovirinae*
- *Paramyxovirinae* include: *Morbillivirus*, *Respirovirus*, *Rubulavirus, Avulovirus* and *Henipavirus*
- *Pnevmovirinae* include: *Pnevmovirus* and *Metapneumovirus*

Paramyxoviridae structure

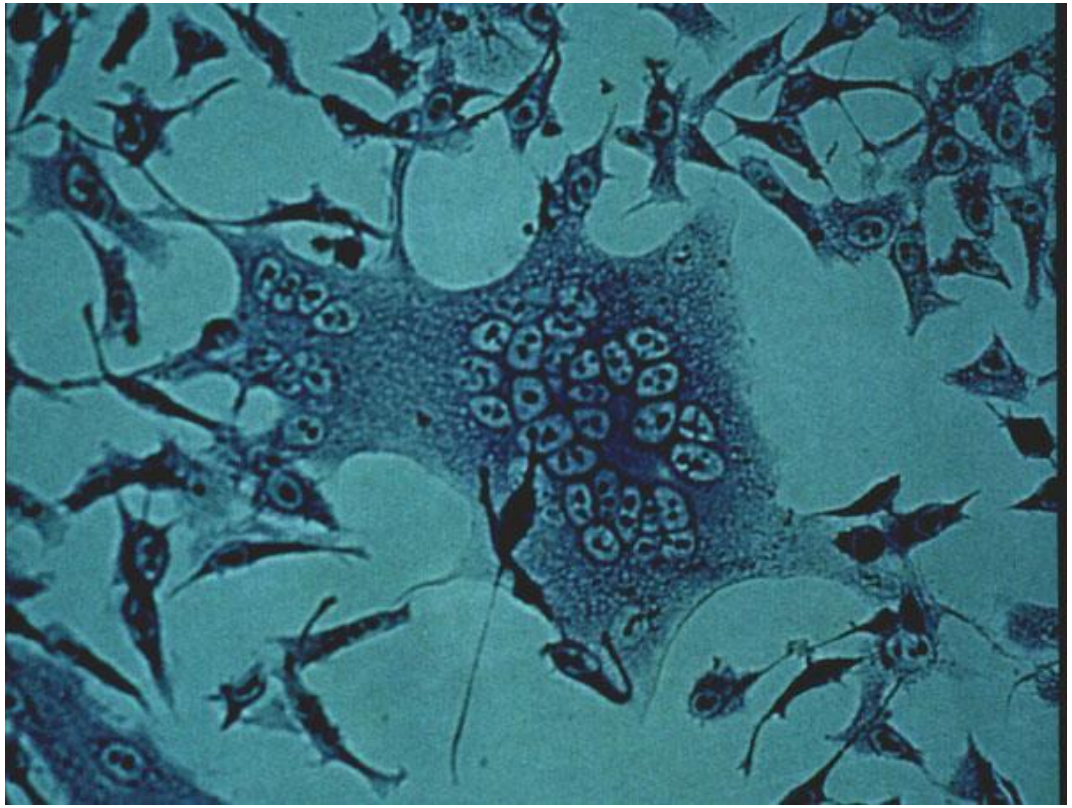


Paramyxoviridae replication

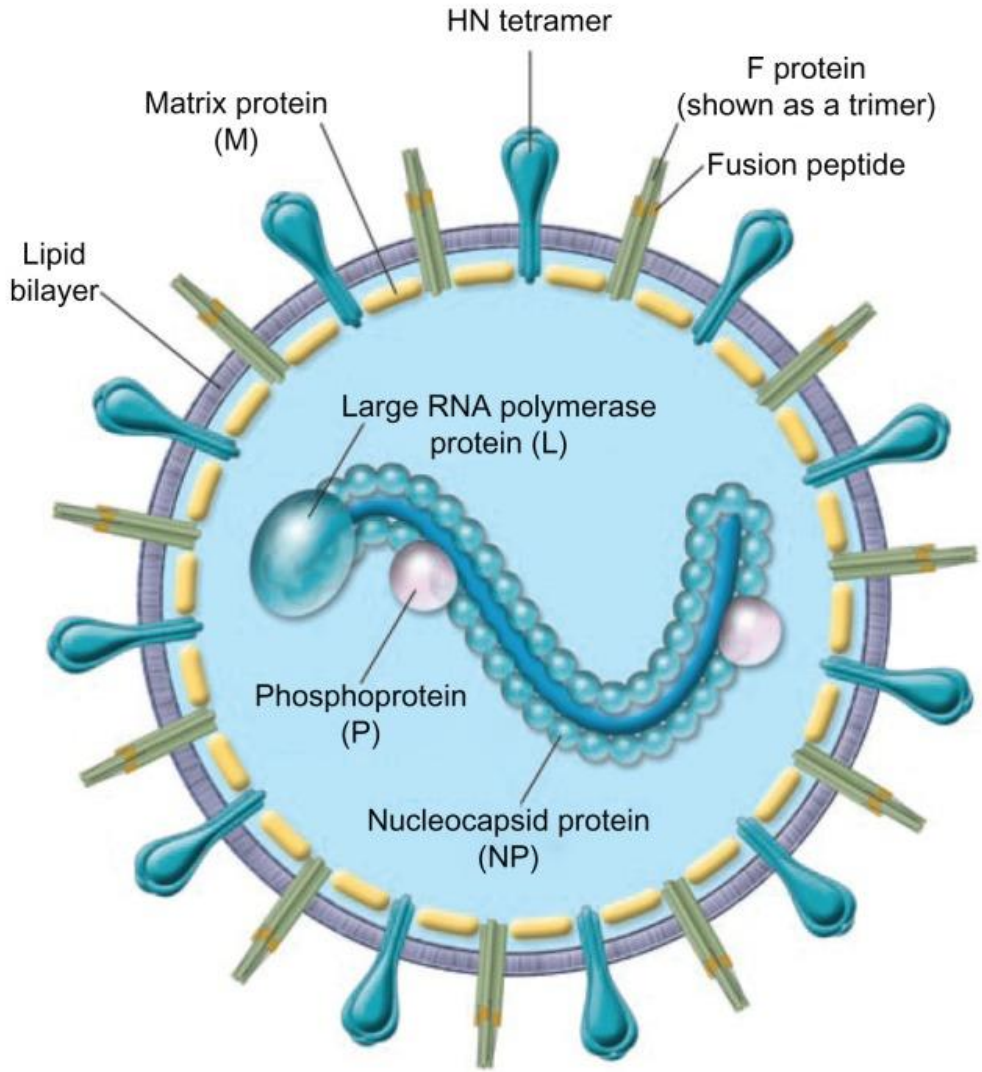


Paramyxoviridae cultivation

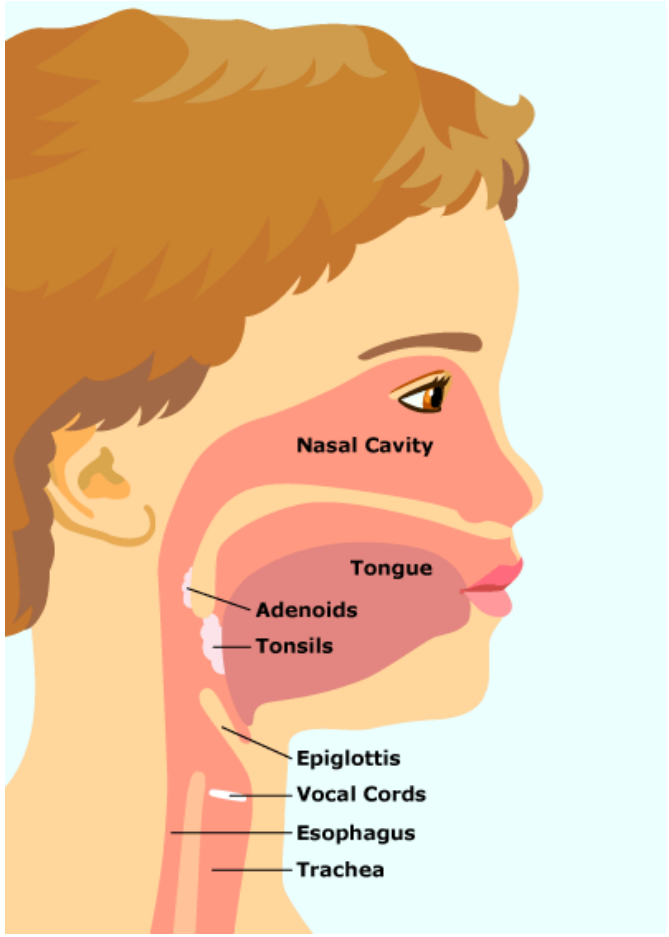
- Forms the cytopathic effect on cell culture as **inclusions** and **polikarions**

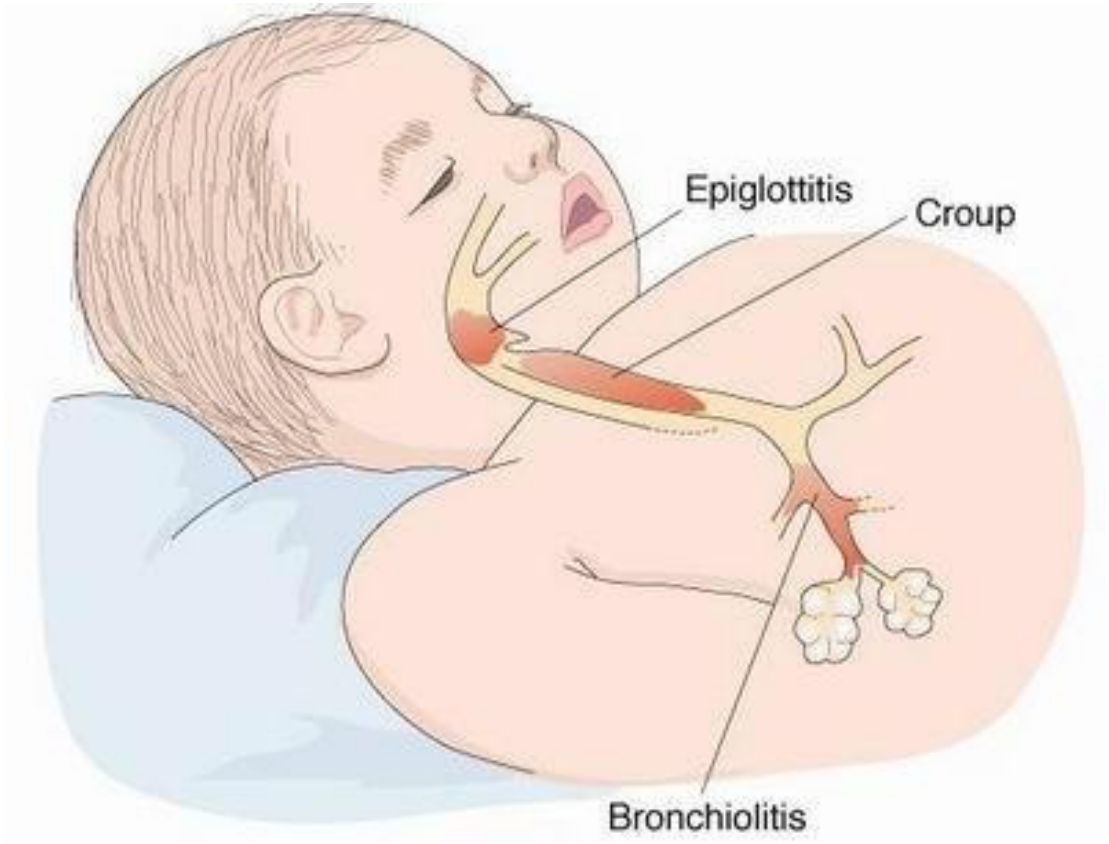


Parainfluenza virus

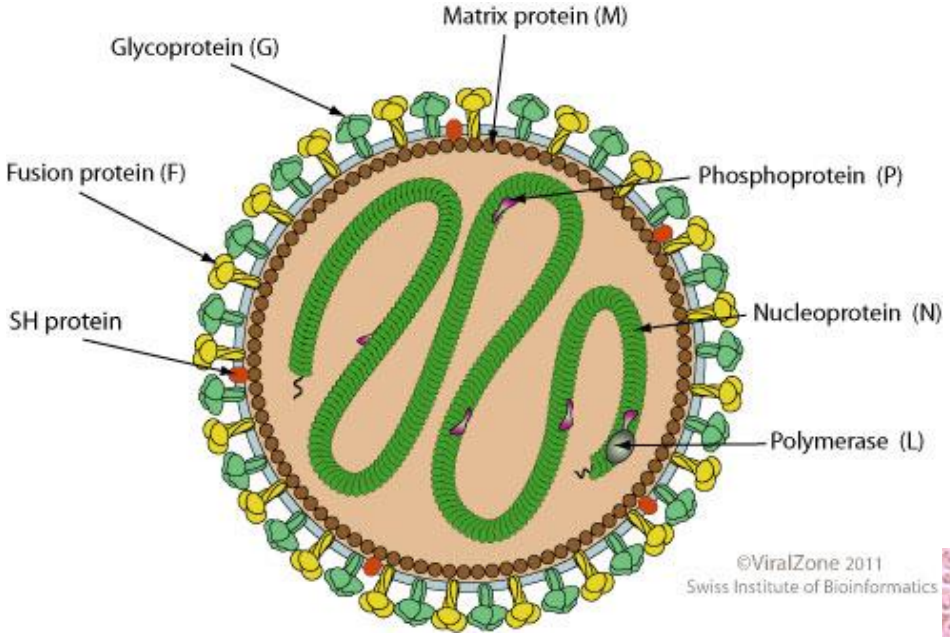


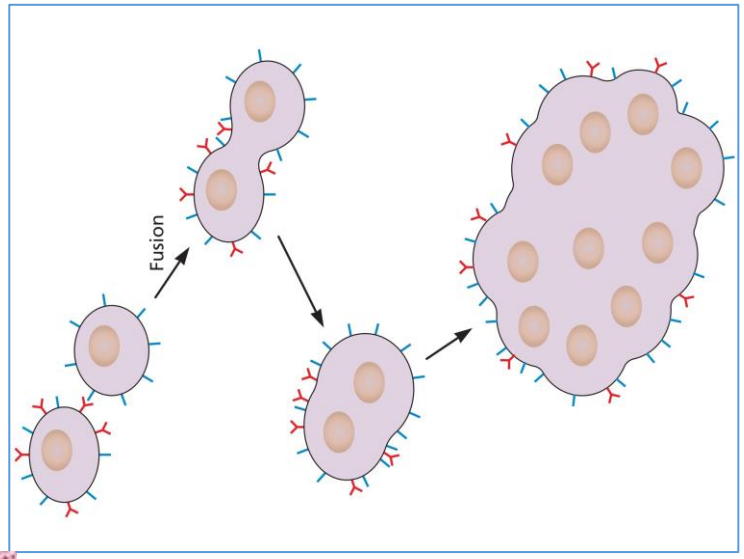
Parainfluenza: clinical manifestations

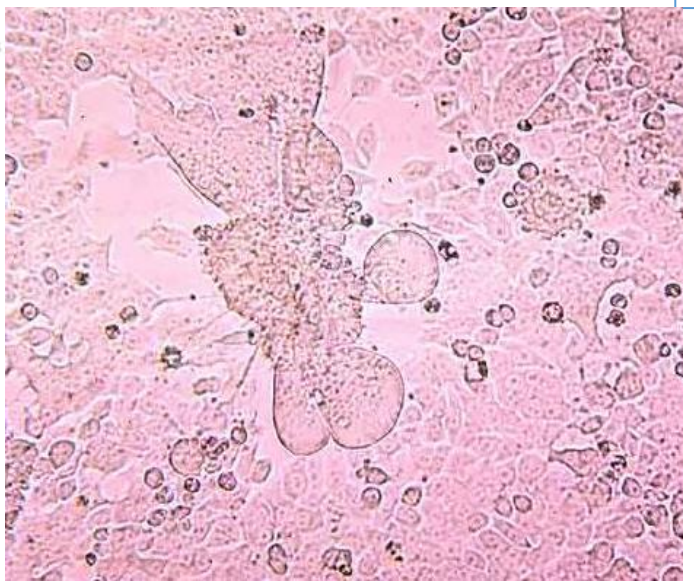




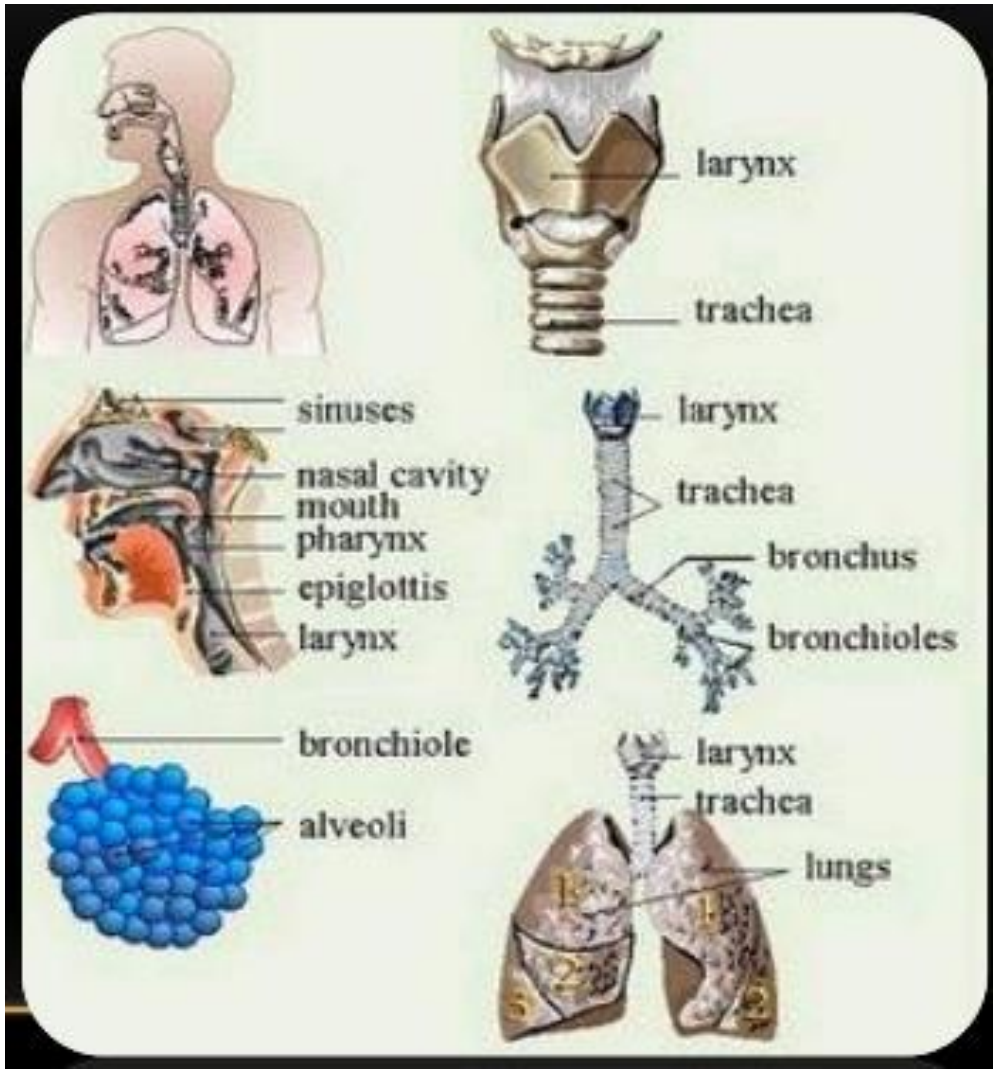
Respiratory syncytial virus (RS-virus)





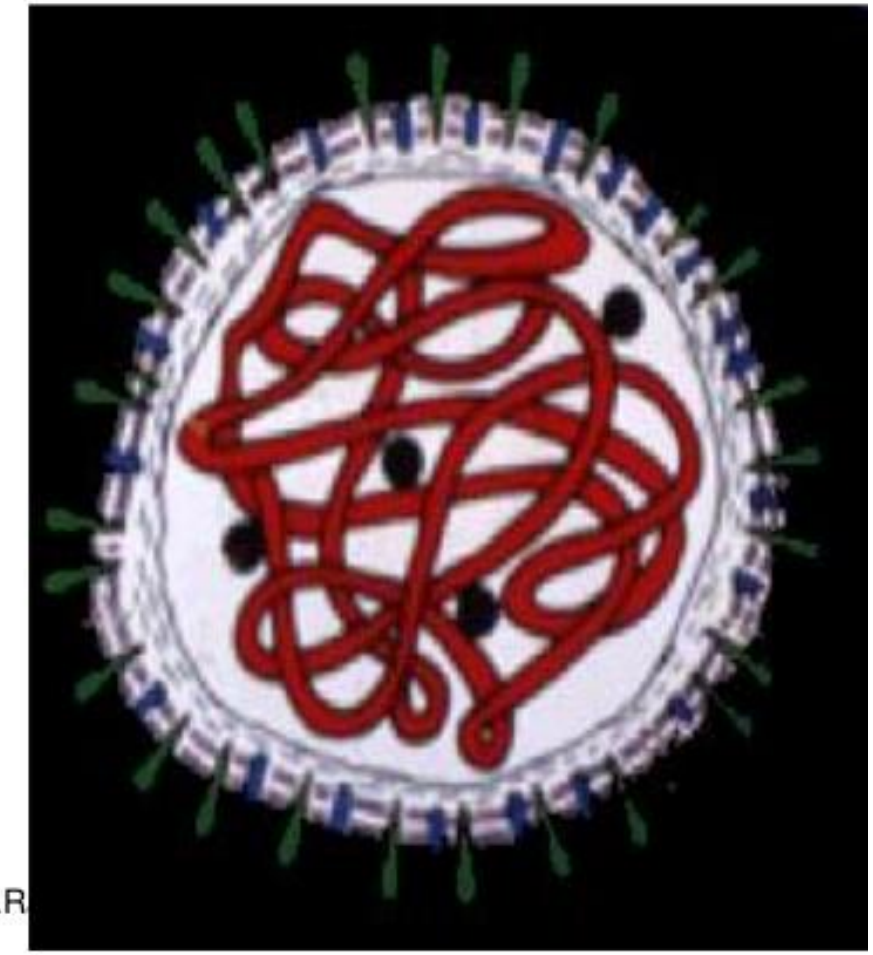


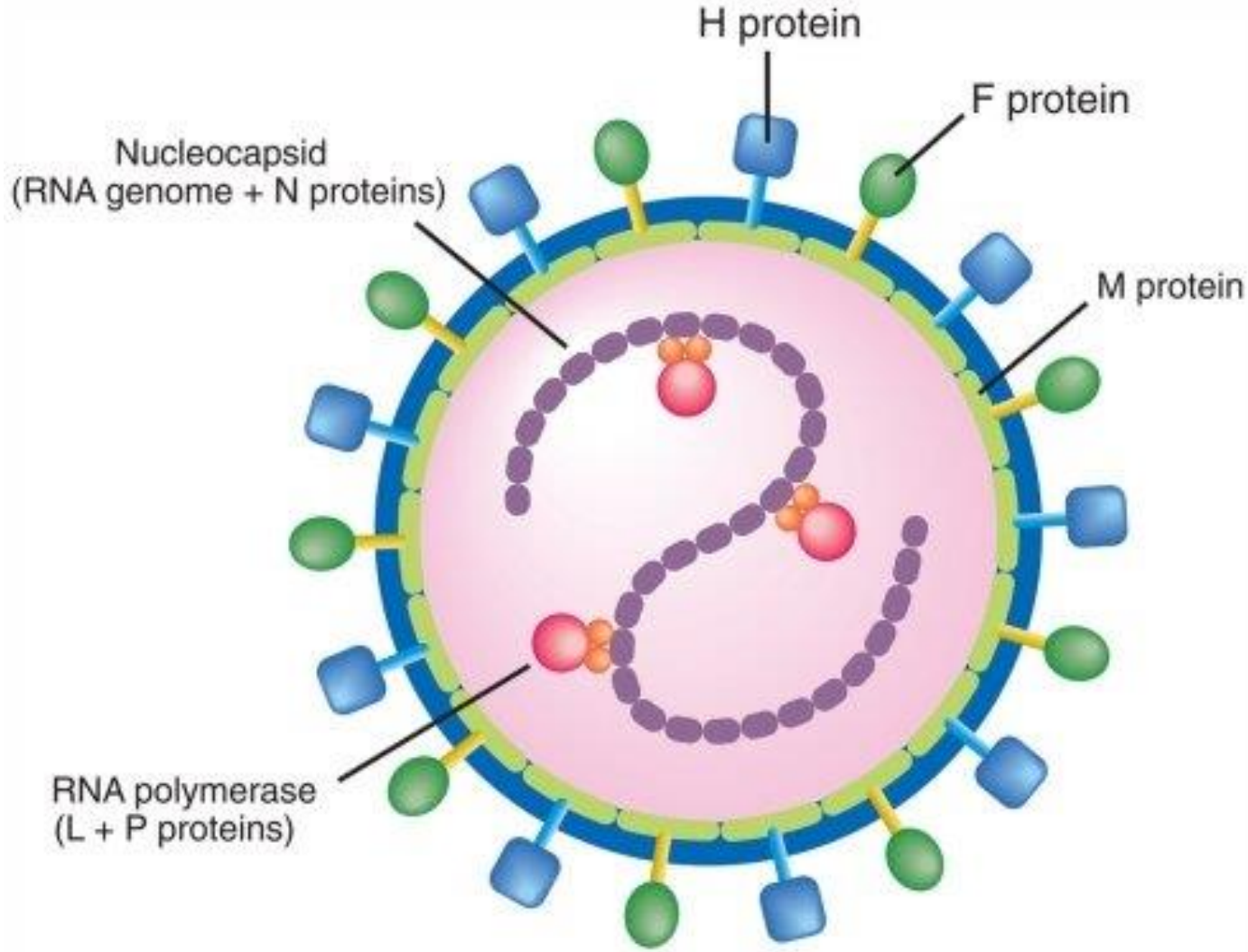
Pathogenesis of RS-virus infection



Measles - Paramyxoviridae

- **Measles** is an infection of the respiratory system caused by a virus, specifically a Paramyxovirus of the genus *Morbillivirus* Morbilliviruses, like other paramyxovirus, are enveloped, single-stranded, negative-sense RNA viruses.





Morbillivirus

Measles a Childhood Infection

- Age-specific attack rates may be highest in susceptible infants younger than 12 months, school-aged children, or young adults, depending on local immunization practices and incidence of the disease.

EPIDEMIOLOGY

- Infection sources
  - Patients of acute stage and viral carriers of atypical measles
- Transmission
  - Highly contagious, approximately 90% of susceptible contacts acquire the disease.
  - Respiratory secretions: maximal dissemination of virus occurs by droplet spray during the prodromal period (catarrhal stage).
  - Contagious from 5 days *before symptoms*, 5 days *after onset of rash*
  - Seasons: in the spring, peak in Feb-May

PATHOGENESIS AND PATHOLOGY

- Portal of entry
  - Respiratory tract and regional lymph nodes
  - Enters bloodstream (primary viraemia) → monocyte – phagocyte system → target organs (secondary viraemia)
- Target organs
  - The skin; the mucous membranes of the nasopharynx, bronchi, and intestinal tract; and in the conjunctivae, ect

Resulting In-----

1) Koplik spots and skin rash: serous exudation and proliferation of endothelial cells around the capillaries
2) Conjunctivis

PATHOGENESIS AND PATHOLOGY

3) Laryngitis, croup, bronchitis :general inflammatory reaction

4) Hyperplasia of lymphoid tissue: multinucleated giant cells (Warthin-Finkeldey giant cells) may be found

5) Interstitial pneumonitis: Hecht giant cell pneumonia.

6) Bronchopneumonia: due to secondary bacterial infections

7) Encephalomyelitis: perivascular demyelinization occurs in areas of the brain and spinal cord.

8) Subacute sclerosing panencephalitis(SSPE):

degeneration of the cortex and white matter with intranuclear and intracytoplasmic inclusion bodies

CLINICAL MANIFESTATION

Typical Manifestation:

patients havn't had measles immunization, or vaccine failure with normal immunity or those havn't used immune globulin

1. Incubation period (infection to symptoms) :

6-18days (average 10 days)

2. Prodromal period:

- 3-4 days
- Non-specific symptoms: fever, malaise, anorexia, headache
- Classical triad: cough, coryza, conjunctivitis (with photophobia, lacrimation)

CLINICAL MANIFESTATION

Enanthem (Koplik spots):

- ***Pathognomonic for measles***
- 24-48 hr before rash appears
- 1mm, grayish white dots with slight, reddish areolae
- Buccal mucosa, opposite the lower 2nd molars
- increase within 1day and spread
- fade soon after rash onset

CLINICAL MANIFESTATION

3. Rash period

3-4days

Exanthem:

Erythematous, non-pruritic, maculopapular

- Upper lateral of the neck, behind ears, hairline, face → trunk → arms and legs →feet

- The severity of the disease is directly related to the extent and confluence of the rash

,

CLINICAL MANIFESTATION

Temperature:

- Rises abruptly as the rash appears
- Reaches 40°C or higher
- Settles after 4-5 days – if persists, suspect secondary infection

Coryza, fever, and cough:

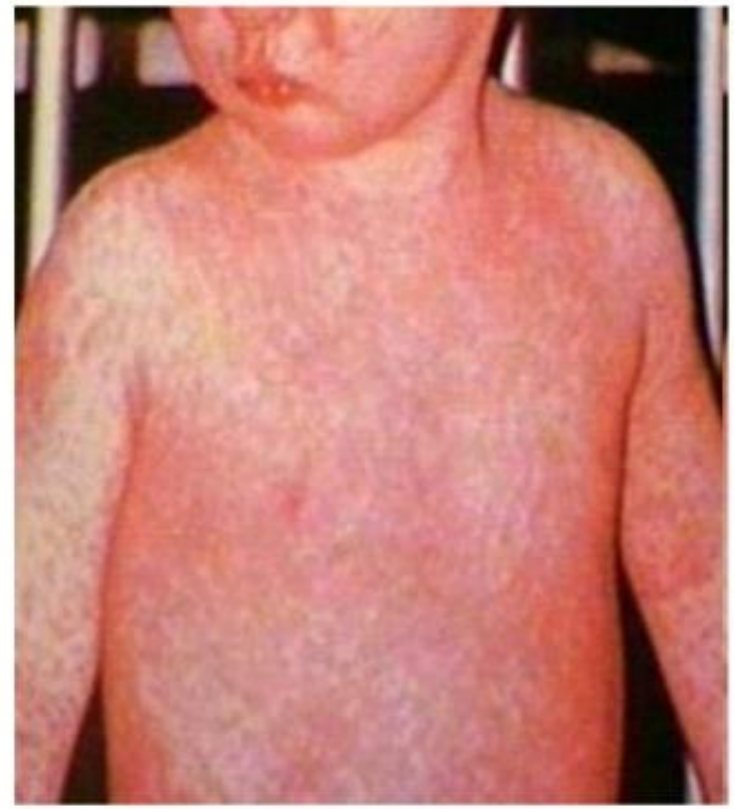
- Increasingly severe up to the time the rash has covered the body

Lymphadenopathy (posterior cervical region, mesenteric) splenomegaly, diarrhoea, vomiting

Chest X ray:

- May be abnormal, even in uncomplicated cases

Rash is a Prominent Feature



CLINICAL MANIFESTATION

4. Recovery period

3-4days

Exanthem:

- Fades in order of appearance
- Branny desquamation and brownish discoloration

Entire illness – 10 days

LABORATORY EXAMINATION

- Isolation of measles virus from a clinical specimen (e.g., nasopharynx, urine)
- Significant rise in measles IgG by any standard serologic assay
- Positive serologic test for measles IgM antibody
- Immunofluorescence detects Measles antigens
- Multinucleated giant cells in smears of nasal mucosa

- Low white blood cell count and a relative lymphocytosis in PB
- Measles encephalitis – raised protein, lymphocytes in CSF

DIAGNOSIS

characteristic clinical picture:

- Measles contact
- Koplik spot
- Features of the skin rash
- The relation between the eruption and fever

Laboratory confirmation is rarely needed

TREATMENT

- Supportive, symptom-directed
  - Antipyretics for fever
  - Bed rest
  - Adequate fluid intake
  - Be protected from exposure to strong light
- Antibiotics for otitis media, pneumonia
- High doses Vitamin A in severe/ potentially severe measles/ patients less than 2 years
  - 100,000IU—200,000IU

PREVENTION

- 1. Quarantine period

  5 days after rash appears, longer for complicated measles

- 2. Vaccine

  The initial measles immunization is recommended at 8mo of age

  A second immunization is recommended routinely at 7yr of age

- 3. Postexposure Prophylaxis

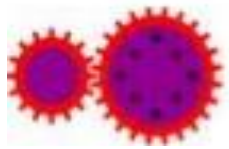
  Passive immunization with immune globulin (0.25mL/kg) is effective for prevention and attenuation of measles within 5 days of exposure.

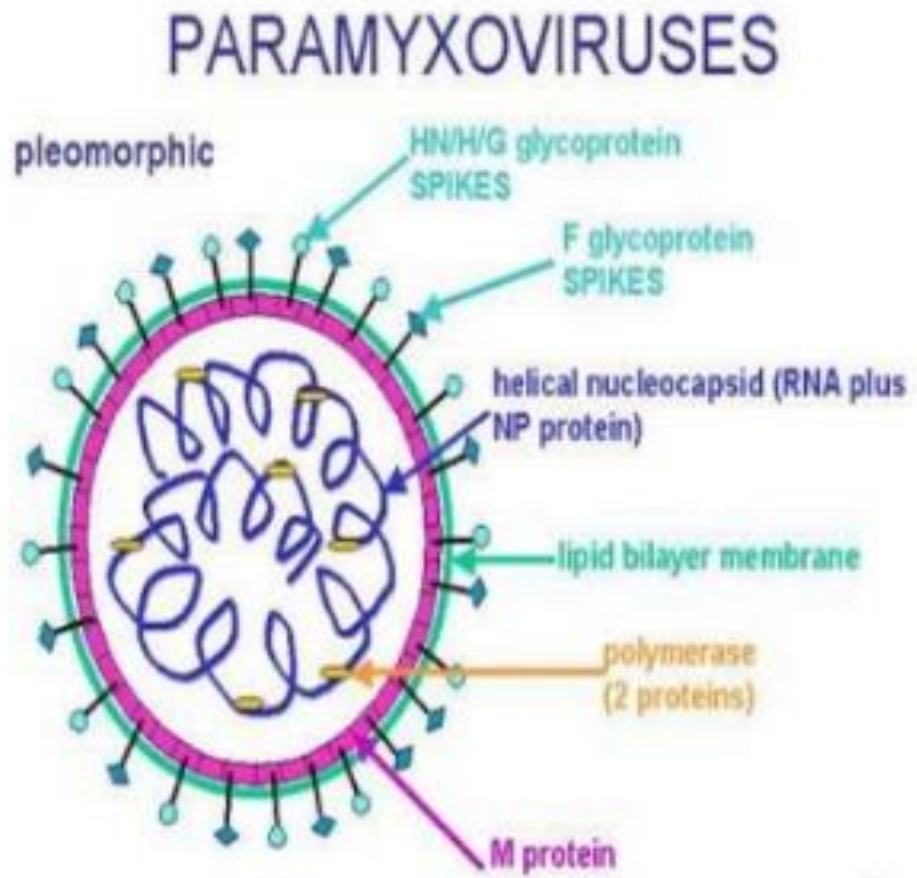
MUMPS

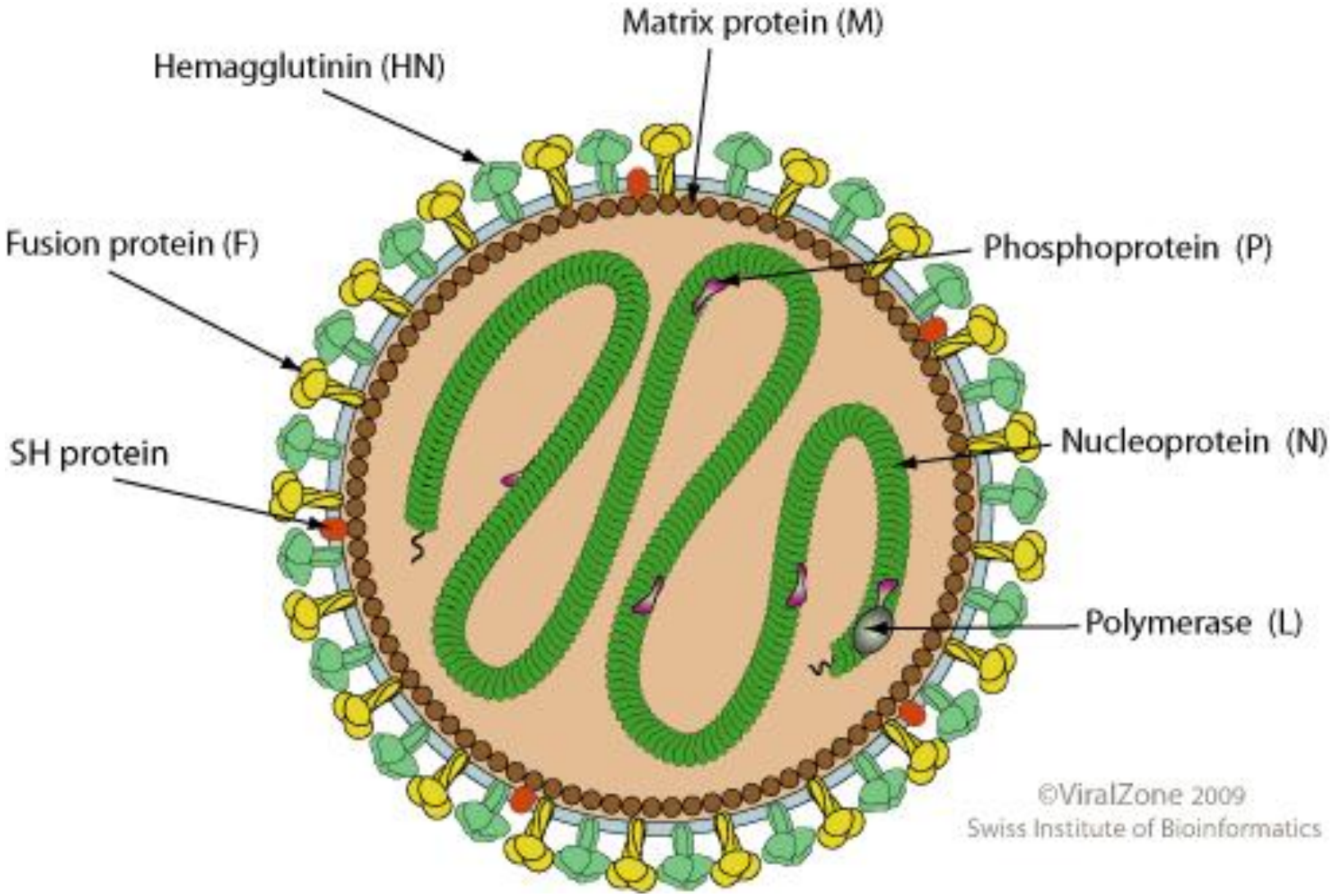
1

Properties of MUMPS virus.

- Posses HN and F properties.
- Growth in Chick Embryos, in the Amniotic cavity, Adopts in allantoic cavity,
- Cell cultures – Primary Monkey kidney,
- Typical Paramyxoviruses, produce cytopathic effects.






Matrix protein (M)
Hemagglutinin (HN)
Fusion protein (F)
Phosphoprotein (P)
SH protein
Nucleoprotein (N)
Polymerase (L)
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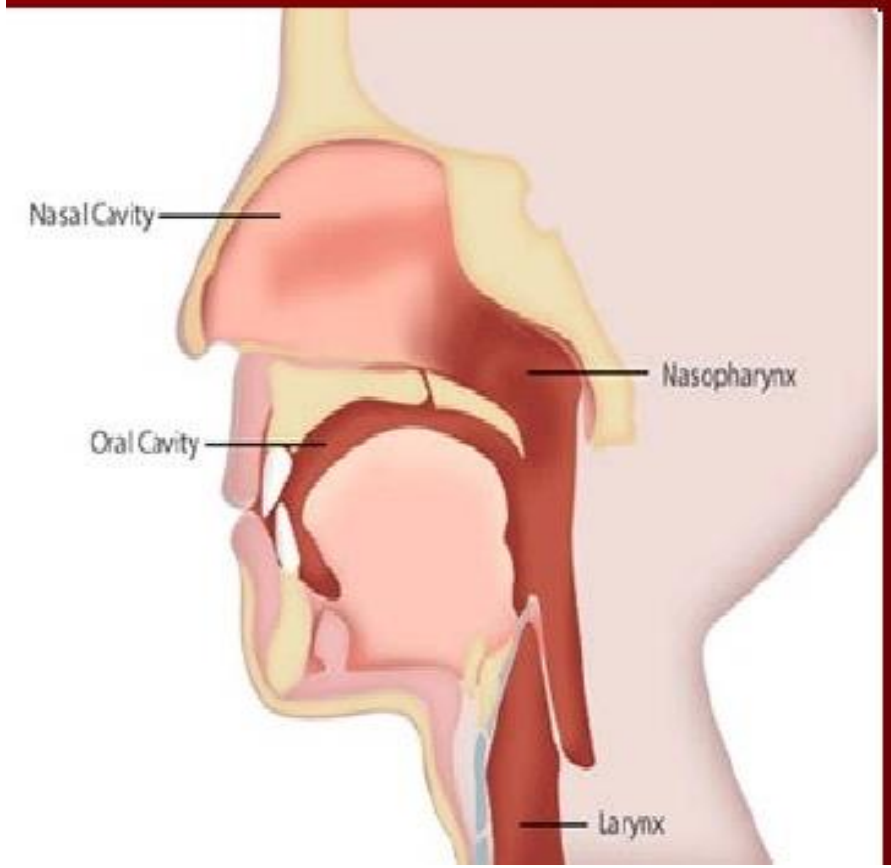
Pathogenesis - Mumps



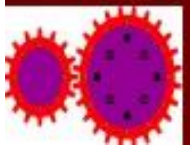
- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes
- Viremia 12-25 days after exposure with spread to tissues
- Multiple tissues infected during viremia

Mumps Clinical Features

- Incubation period 14-18 days
- Nonspecific prodrome of myalgia, malaise, headache, low-grade fever
- Parotitis in 30%-40%
- Up to 20% of infections asymptomatic

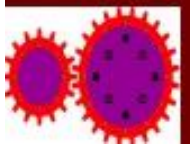
Complication with MUMPS.

- Epididymo orchids.
- May lead to atrophy, sterility, Low sperm counts.
- CNS involvement in 60% cases
- May manifest with Aseptic meningitis,
- Deafness,
- Arthritis,Oopharitis,Nephritis and Myocarditis,



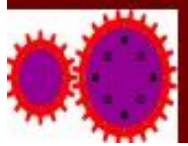
Complication with MUMPS.

- **Orchitis.** This inflammatory condition causes swelling of one or both testicles. Orchitis is painful.
- **Pancreatitis..**
- **Encephalitis.** A viral infection, such as mumps, can lead to inflammation of the brain (encephalitis). Although it's serious, encephalitis is a rare complication of mumps.



Complication with MUMPS.

- **Meningitis.** Meningitis is infection and inflammation of the membranes and fluid surrounding your brain and spinal cord.
- **Inflammation of the ovaries.** Pain in the lower abdomen in women may be a symptom of this problem. Fertility doesn't seem to be affected.
- **Hearing loss.**
- **Miscarriages.**



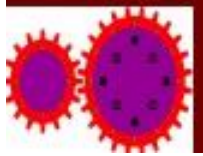
Laboratory Diagnosis

- **No Laboratory confirmation needed.**
- Atypical infection needs laboratory Diagnosis.
- Virus isolated from

  Saliva
  Urine
  CSF.

Culturing in **Human amnion, He la cells.**
Immunoflorecence Methods. Isolation in Chick Embryos
ELISA, Complement fixation tests,

Doctortvrao's 'e' learning



MEASLES, MUMPS & RUBELLA (MMR) VACCINE:

2 D

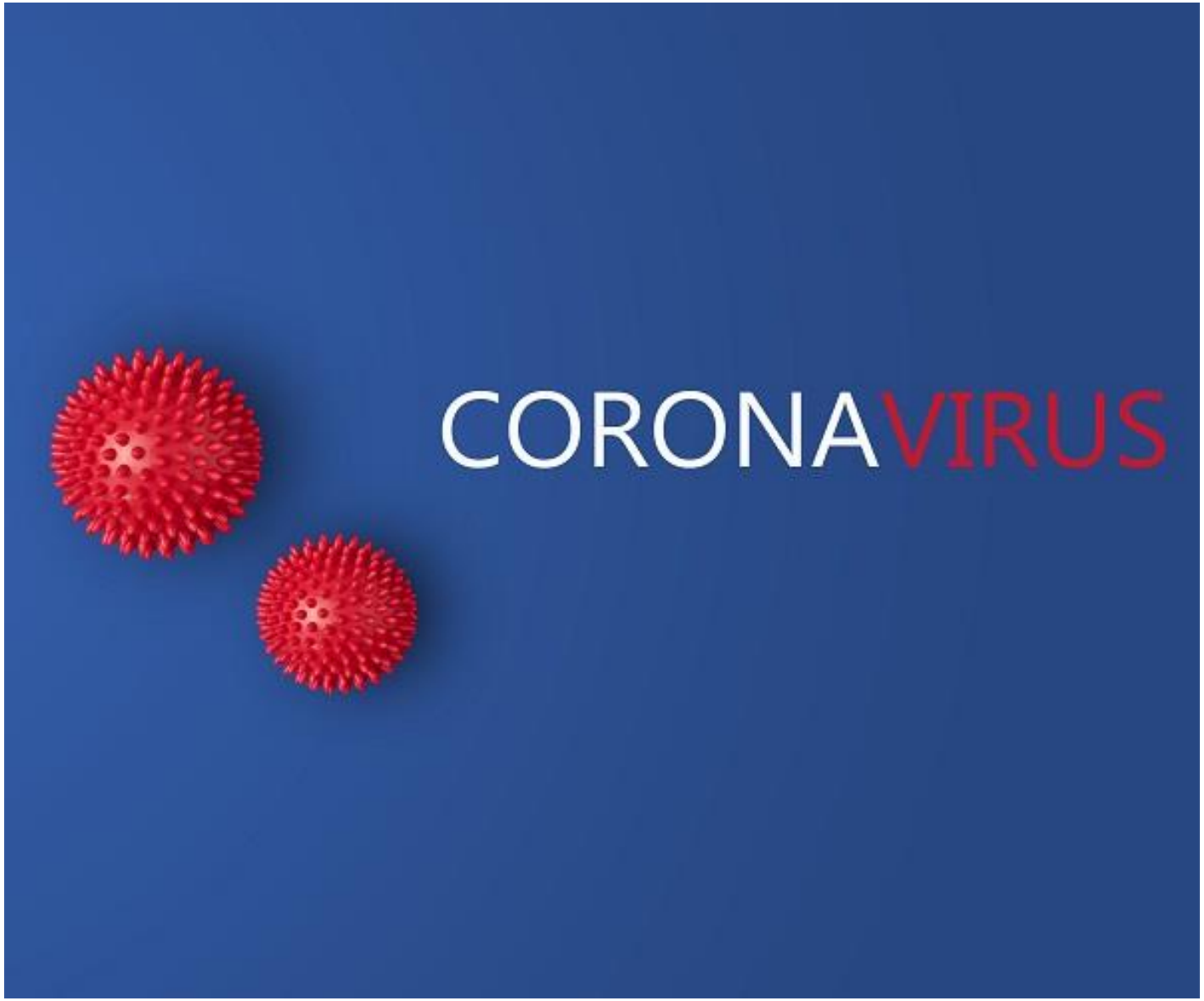
Measles vaccine is available as a monovalent preparation or combined as measles-mumps-rubella (MMR) vaccine.

MMR:

- Minimum age 12 mo.
- The current recommendations include a first dose at **12-15 mo** followed by a second dose at **4-6 yr** of age. **Seroconversion** is slightly lower in children who receive the first dose before or at 12 mo of age because of persisting maternal antibody.
- MMR may be administered **before** age 4-6 yr, provided **≥ 4wk** have elapsed since the 1st dose.
- For children who have ***not*** received 2 doses by 11-12 yr of age, a second dose should be provided.
- Infants who ***receive a dose before 12 mo*** of age should be given 2 additional doses at 12-15 mo and 4-6 yr of age.

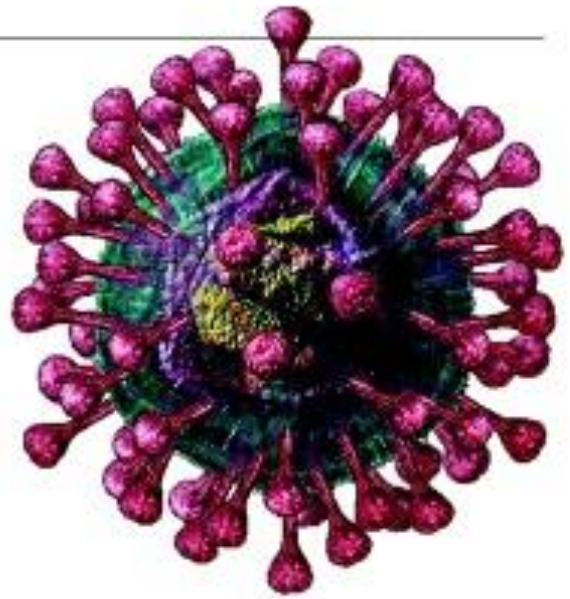
Measles vaccine:

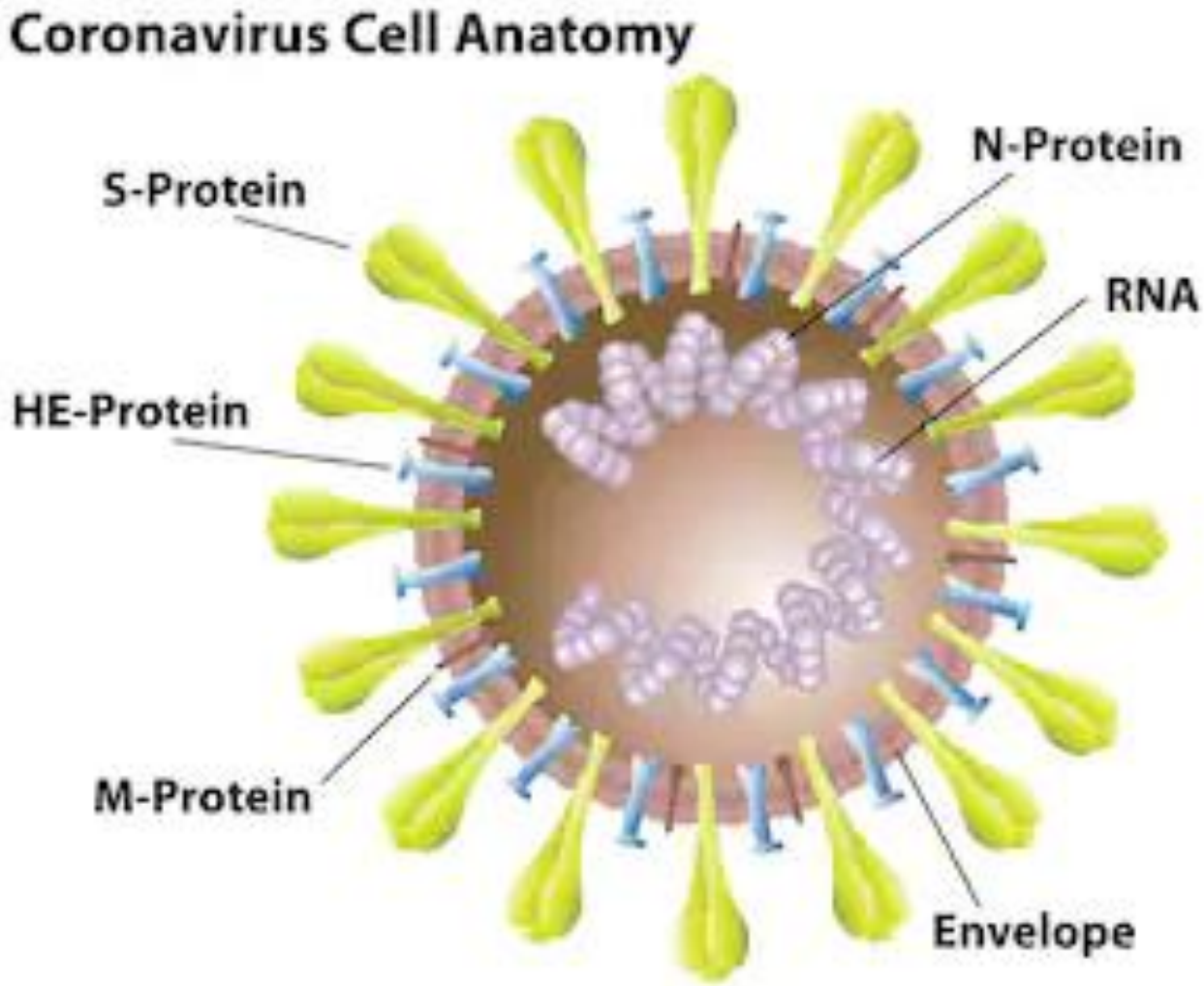
- For children 6-11 mo of age in epidemic situations or prior to international travel.


CORONAVIRUS

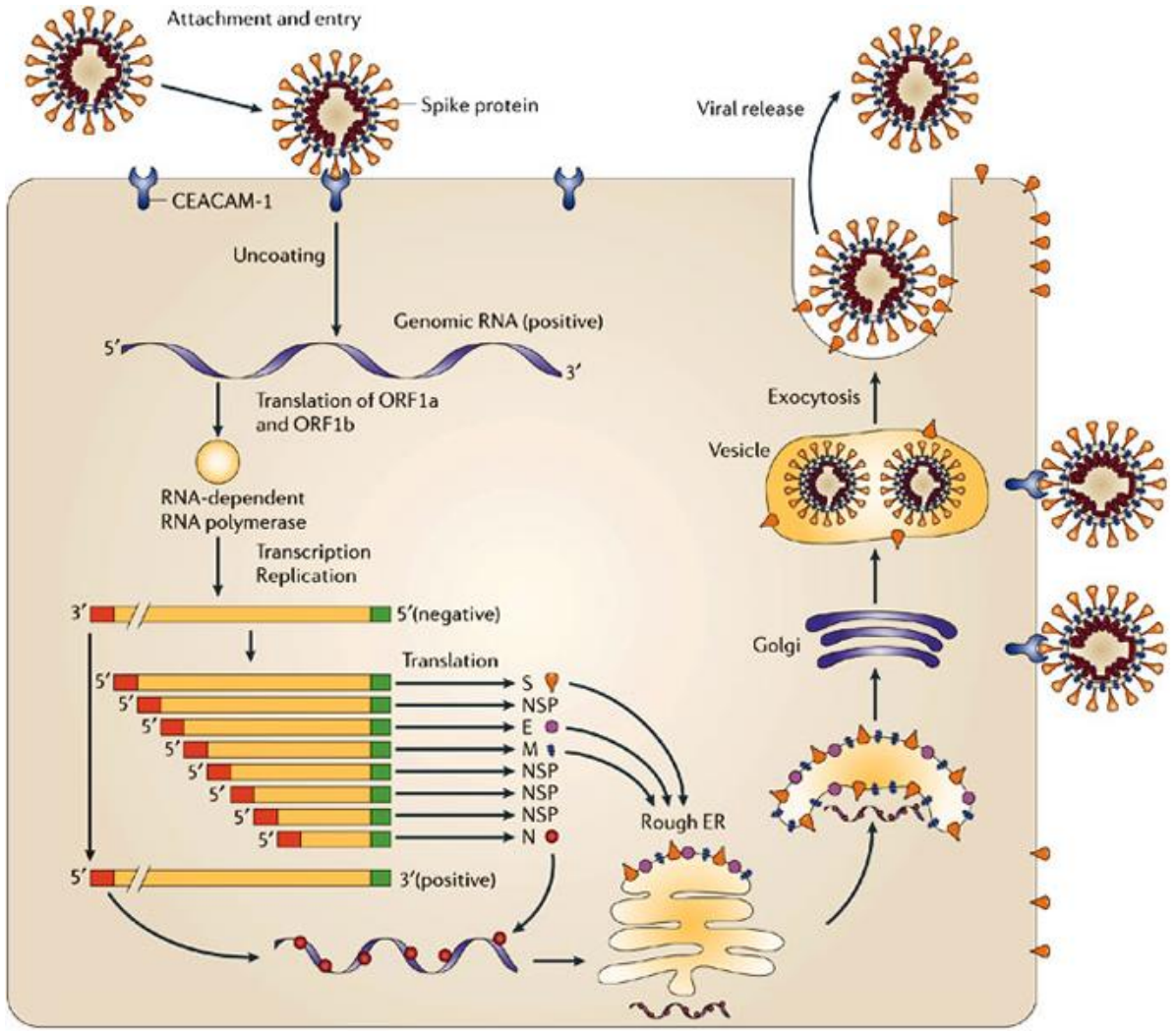
Classification :

- Family: Coronaviridae
- Gender: Coronavirus
- Genome: linear single-stranded RNA +
- pleomorphic, Wrapped
- 80 to 220 nm
- 30 serotypes

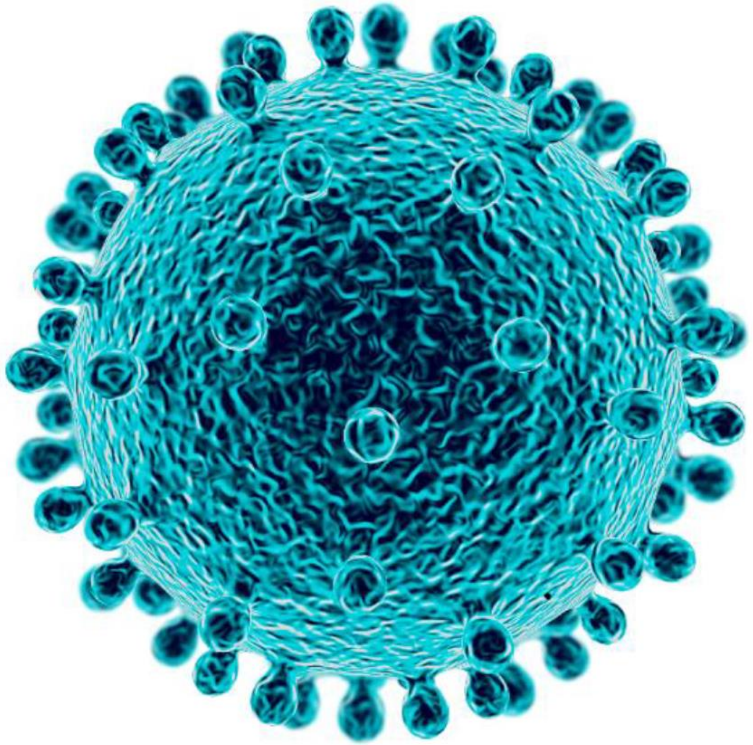



Coronavirus Cell Anatomy
S-Protein
N-Protein
RNA
HE-Protein
M-Protein
Envelope

Reproductive scheme of coronaviruses



What Do We Know About Coronaviruses?



Coronaviruses have a crown-like appearance under the microscope

Coronaviruses are a large family of viruses - some cause illness in people, and others only infect animals.

Some coronaviruses infect animals then spread to people, and then spread person to person such as:

- Middle East Respiratory Syndrome (MERS)
- Severe Acute Respiratory Syndrome (SARS)
- **Coronavirus Disease 2019 (COVID-19)**

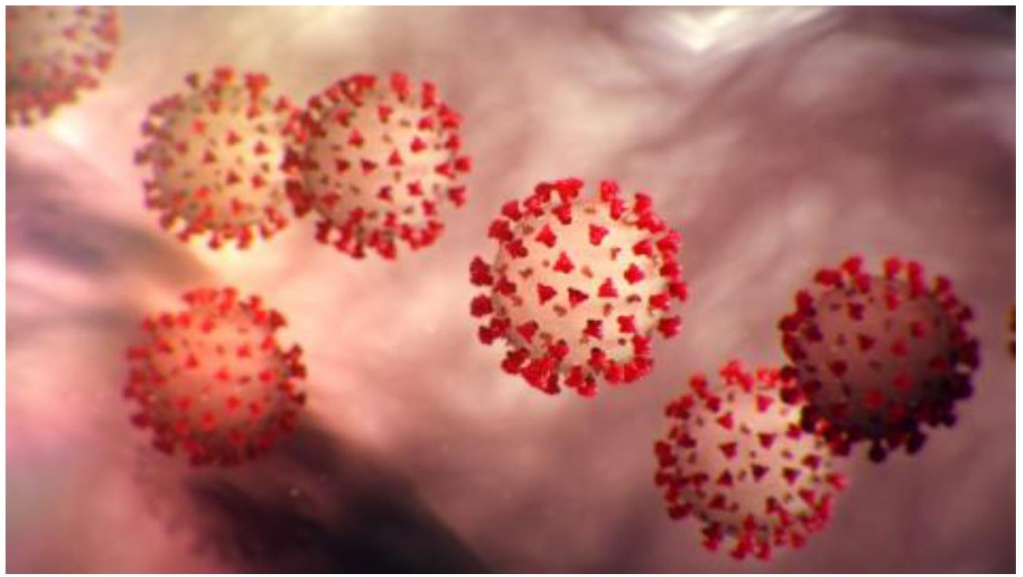
Common coronaviruses include some that cause mild upper-respiratory illnesses, like the common cold.

What is COVID-19?

Coronavirus disease 2019 or COVID-19 is a respiratory illness that can spread from person to person.

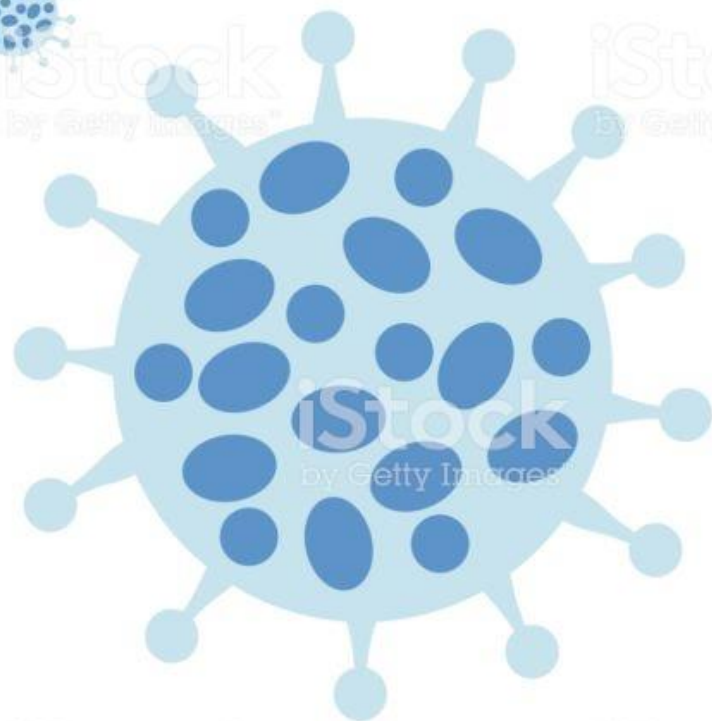
The virus that causes COVID-19 is a **new** coronavirus first identified during an investigation into an outbreak in Wuhan, Hubei Province, China.

Initial case-patients reported visiting a large seafood and live animal market in Wuhan.



Symptoms

- Corona viruses primarily infect the upper respiratory and gastrointestinal tract of humans.
- Most people who got infected with the novel corona virus developed severe acute respiratory illness with symptoms of **fever**, **cough**, and **shortness of breath**. Some people were reported as having a mild respiratory illness



2019-nCoV Coronavirus

Symptoms

- fever
- headache
- cough, sore throat
- runny noise
- difficulty breathing

2-14 days incubation period

Microbiological diagnosis of coranovirus infections

- Viruses can be detected in respiratory secretions by ELISA, IFR and PCR.
- RNA for SARS and Covid-19 virus can also be found in the blood.
- Since the virus is difficult to obtain in cell cultures, the main diagnostic method is PCR.
- An increase in the antibody titer in the double serum studied by ELISA confirms coronavirus infection.

Testing, testing

Promising drugs to treat covid-19

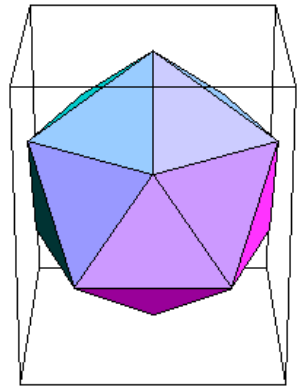
Drug	Current use	Original mode of action	Being tested?
Chloroquine	Antimalarial	Heme polymerase inhibitor	Yes
Kaletra (ritonavir + lopinavir)	HIV	Protease inhibitor	Yes
Interferon alfa-2b	Hepatitis-C	Immune modulator	Yes
Remdesivir	Experimental	Nucleotide analogue	Yes
Favipiravir	Influenza	RNA polymerase inhibitor	Yes
Actemra (tocilizumab)	Rheumatoid arthritis; covid-19	Anti-inflammatory	Approved*
Kevzara (sarilumab)	Rheumatoid arthritis	Anti-inflammatory	Trials expected

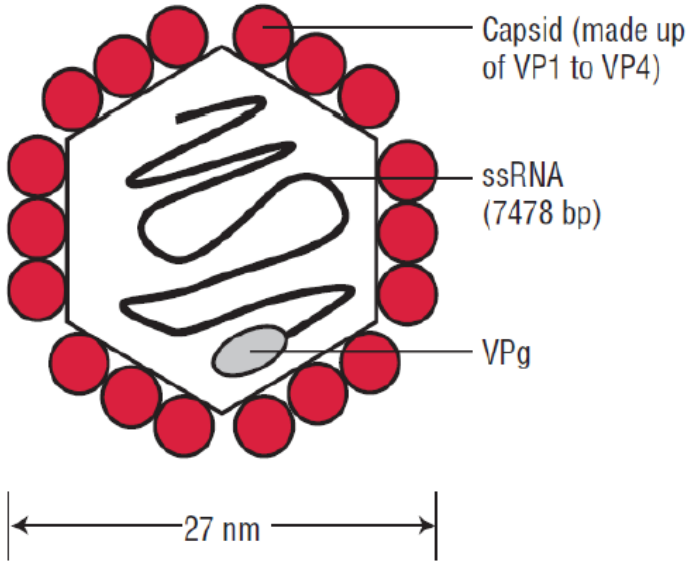
Source: WHO, adapted from landscape analysis, 17th February 2020

*For use on covid-19 in China, March 2020

Picornaviridae family

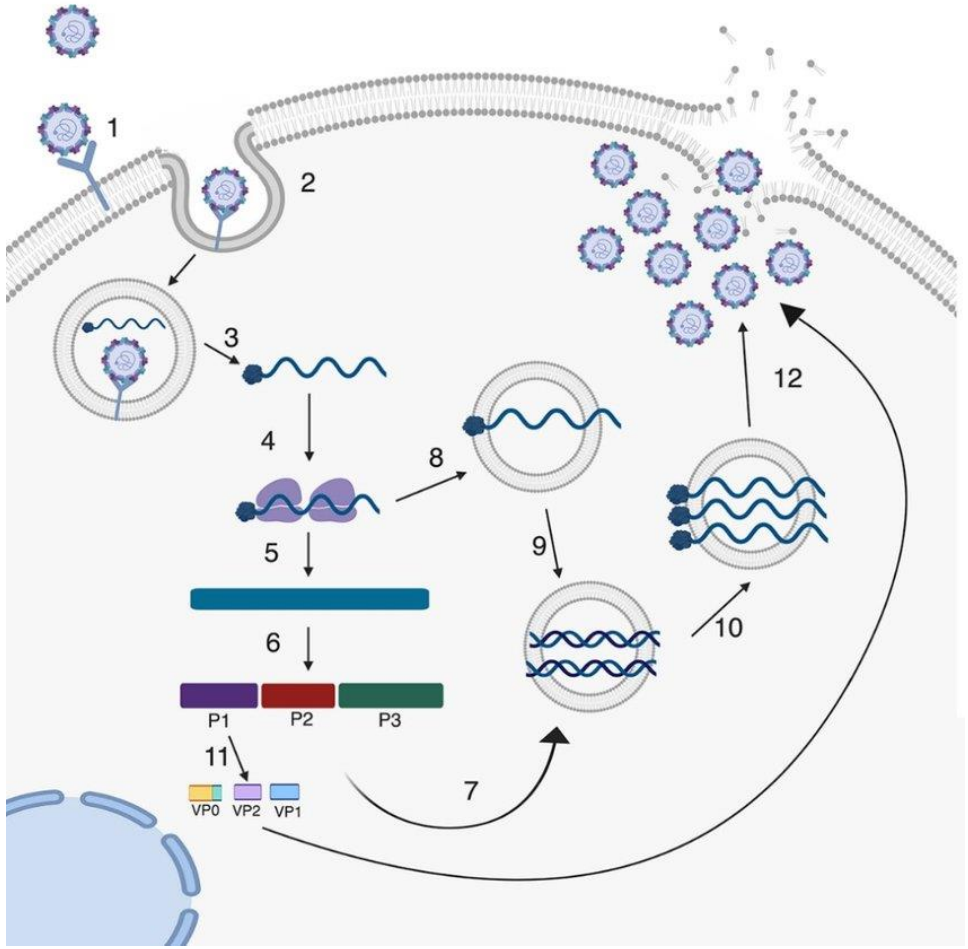
- Members of the Picornaviridae family are non-enveloped viruses with single-stranded RNA. The name of the section is related to the very small size of these viruses (pico-small, rna-RNA).
- They are viruses with a simple structure (without a membrane), 28-30 nm in size.
- The capsid has 12 pentomers with icosahedral symmetry. On the surface of each pentomer there are special grooves ("canyons") that ensure the connection of the virus with the host cell, as well as with the Fab-fragments of antibodies.
- The genome of viruses consists of positive RNA of infectious nature and VPg-protein combined with it.





Reproduction of picornaviruses

- Reproduction occurs in the cytoplasm of host cells.
- The virus enters the host cell by endocytosis.
- Genome RNA plays the role of information-RNA and participates in the synthesis of viral proteins, including RNA-dependent RNA-polymerase.
- This enzyme synthesizes negative-RNA over positive-RNA, and again positive-RNA (genomic RNA) over it.
- The genome-RNA is surrounded by a capsid made of structural proteins and forms the mature virion.
- As a result of cell lysis, virions are released.



Classification of picornaviruses:

- The Picornaviridae family consists of 9 genera: *Enterovirus* (enteroviruses), *Hepatovirus* (hepatitis A virus), *Rhinovirus* (rhinoviruses), *Aphtovirus* (skin virus), *Parechovirus* (parechoviruses), *Cardiovirus*, etc. consists of. The first 5 genera are more important in human pathology.

ENTEROVIRUSES

- Enteroviruses are a genus of the picornavirus family which replicate mainly in the gut.
- Single stranded naked RNA virus with icosahedral symmetry.
- Unlike rhinoviruses, they are stable in acid pH.
- Capsid has 60 copies each of 4 proteins, VP1, VP2, VP3 and VP4 arranged with icosahedral symmetry around a positive sense genome.

ENTEROVIRUSES

- At least 71 serotypes are known: divided into 5 groups
  - Polioviruses
  - Coxsackie A viruses
  - Coxsackie B viruses
  - Echoviruses
  - Enteroviruses (more recently, new enteroviruses subtype have been allocated sequential numbers (68-71))

CATAGORIES OF ENTEROVIRUSES

VIRUS	SEROTYPES	CLINICAL DISEASES
Polioviruses	3 types	Asymptomatic infection, viral meningitis, paralytic disease, poliomyelitis
Coxsackie A viruses	23 types (A1-A22, A24)	Viral meningitis plus, rash, ARD, myocarditis, orchitis
Coxsackie B viruses	6 types (B1-B6)	Viral meningitis, but no orchitis
Echoviruses	32 types	Viral meningitis, with orchitis
Other Enteroviruses	4 types(68-71)	Viral meningitis

PROPERTIES OF ENTEROVIRUSES

PROPERTY	ENTEROVIRUSES
Size (nm)	22 – 30
Capsid Form	Icosahedral
Polypeptide	VP1, VP2, VP3, VP4
RNA Type	SS – PS
RNA Molecular Weight	2000,000 – 2600,000
Acid	Stable
Optimal Temp.for growth (^{0} C)	37^0 C
Density in Cesium chloride (g / m)	1 . 34

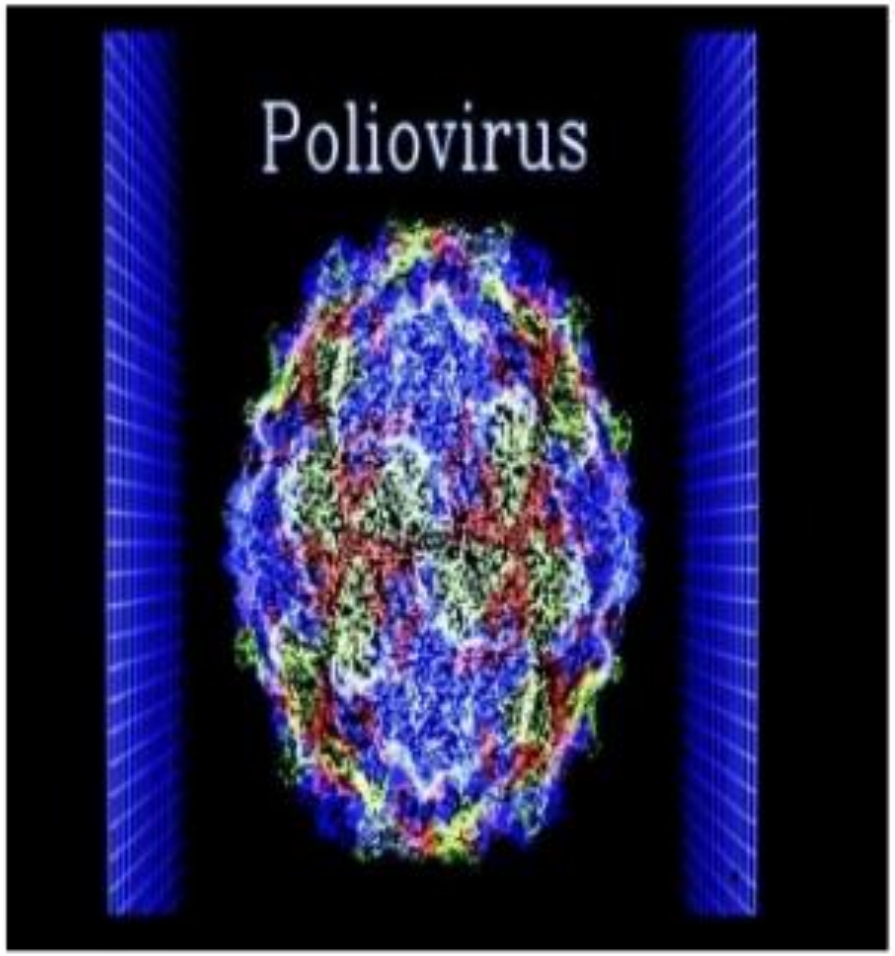
TRANSMISSION OF ENTEROVIRUSES

- Fecal – oral route: poor hygiene, dirty diapers(especially in day-care settings)
- Ingestion via contaminated food and water
- Contact with infected hands
- Inhalation of infectious aerosols

POLIO – AN ENTEROVIRUS

- Poliovirus, the causative agent of poliomyelitis, is a human enterovirus and member of the family of Picornaviridae. Poliovirus is composed of a RNA genome and a protein capsid. The genome is single-stranded positive-sense RNA genome that is about 7500 nucleotides long. The viral particle is about 300 Angstrom in diameter with icosahedral symmetry.

CLASSIFICATION OF POLIOVIRUS



- Size is 27 nm
- Contains 4 viral protein VP1 to VP 4
- VP1 Carries the major antigenic site, and combines with type specific neutralizing antibodies

PROPERTIES OF POLIOVIRUS

- Typical Entero virus.
- Inactivated at 55^0 c for 30 mt.
- Chlorine at 0.1 ppm
- Ether is not effective.
- Animal susceptibility.

  Monkey brain

  Requires Primate specific membranes.

  Contains 3 Antigenic types 1,2,3

Can be differentiated by ELISA and CF methods.

POLIOMYELITIS

- Poliomyelitis (polio) is a highly infectious viral disease, which mainly affects young children. The virus is transmitted through contaminated food and water, and multiplies in the intestine, from where it can invade the nervous system.

DWD

POLIOMYELITIS

- Polio = gray matter, Myelitis = Inflammation of the spinal cord.
- Involves CNS, produces serious Illness.
- Causes Destruction of Motor Neurons in Spinal cord.
- Produces FLACID PARALYSIS.
- India has still has many cases of Poliomyelitis.

EPIDEMIOLOGY

- Endemic
- Epidemic
- Hygiene plays in spread of diseases.
- Children < 5 in Developing countries.

POLIO INFECTION

- Incubation 3 – 21 days
- On average 14 days
- Predisposing factors.

  Severe muscular activity can lead to paralysis, as it increases the blood flow

  May produce paralysis in the limb or bulbar region

  Injecting vaccines with adjuvant can predispose to paralysis

  Patients who underwent tonsillectomy have higher incidence as Ig G secretion is reduced

  Rarely oral Polio vaccine produces poliomyelitis.

PATHOLOGY & PATHOGENESIS

- Destroy the Anterior horn cells of the Spinal Cord
- Do not Multiply in Muscles only muscles manifest with weakness and flaccid paralysis result is secondary.
- Occasionally produce
  - Myocarditis,
  - Lymphatic hyperplasia.

PATHOLOGY & PATHOGENESIS

- Enter through Mouth,
- Multiplies in Oropharynx tonsils and Intestines,
- Excreted in Stool.
- Enters the CNS from Blood.
- Spread along the Axons of peripheral nerves to CNS.
- Progress along the fibers of the lower motor neurons spinal cord or brain.

VIRUS INFECTION PROCESS

- The polio virus infects human cells by binding to an immunoglobulin-like receptor called CD155 (poliovirus receptor).
- The exact mechanism that poliovirus uses for entering the cell is unknown. However, the interaction of poliovirus and CD155 causes a change in the shape of the viral particle that is needed to enter the cell
- There are two thesis' for the way the viral nucleic acid to enters the cell. The first thesis is that the RNA of poliovirus is injected into the host cell through a pore in the membrane of the host cell. The second, and the one that is most likely and has the most support through research, is that the poliovirus is taken in by the host cell through endocytosis.
- Poliovirus has ssRNA. Also known as single-strand RNA.

CLINICAL MANIFESTATIONS

- In apparent, Only 1% manifest with clinical features.
- Can lead to permanent paralysis.
- Incubation 7-14 days, (3-35)
- May be abortive Poliomyelitis,

Only Fever, Malaise, Drowsiness,

Non paralytic Poliomyelitis,

Aseptic Meningitis.

PARALYTIC POLIOMYELITIS

- Manifest as Flaccid Paralysis.
  (Caused due to damage to Lower Motor Neurons.)
- Partial recovery within 6 months.
- Patient may continue with life time disability
- Can involve Spinal cord, and Bulbo spinal region
- Bulb spinal involvement can paralyze respiratory muscle and lead to Respiratory failure

ASEPTIC MENINGITIS

- Present with Non paralytic form with stiffness and pain in the back and neck region
- Lasts for 2 -10 days
- Recovery rapid and complete
- On rare occasions advance to paralysis

LABORATORY DIAGNOSIS

- Viral isolation from
  - Throat swabs,
  - Rectal swabs.
  - Stool specimens,
- Transported in frozen containers.
- Produce cytopathic effect on
  - Human and Monkey cells
- Produce cytopathic effects.

VIRAL ISOLATION

- From feces - present in 80% of cases in 1st week
- In 50 % till 3rd week
- In 25 % till several weeks
- Collect the fecal sample at the earliest.
- Primary monkey kidney is the ideal cell line for isolation of virus
- Viral isolation must be interpreted with caution and clinical presentation

LABORATORY DIAGNOSIS (SEROLOGY)

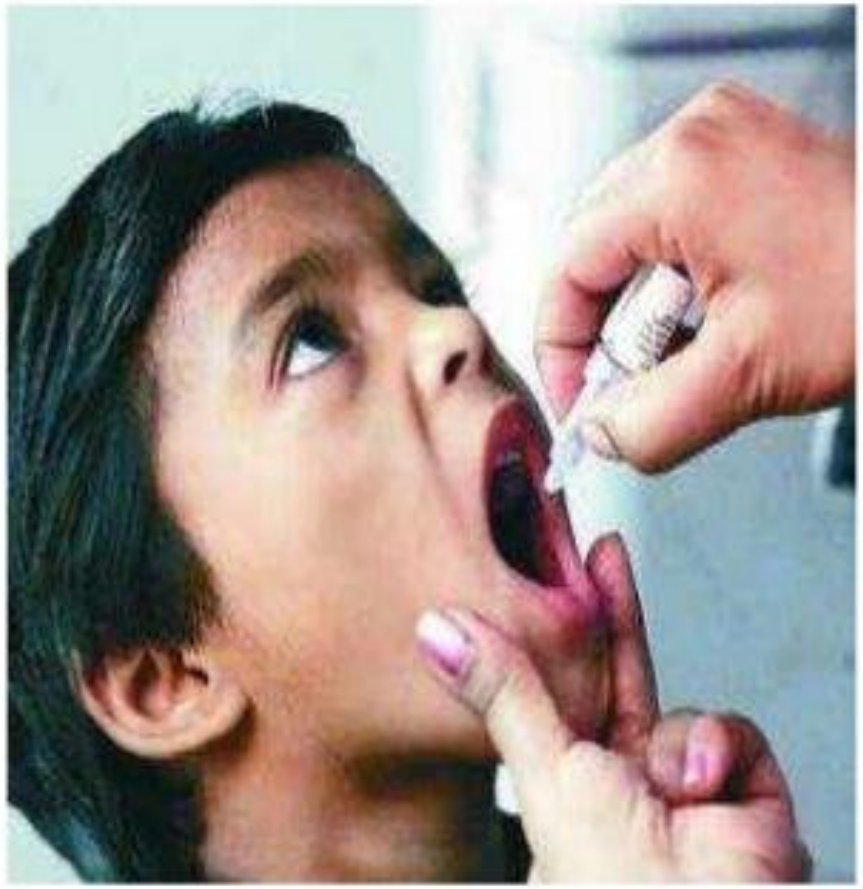
- Estimation of Antibodies IgM
- A paired sample is essential.
- ELISA
- CFT
- Neutralisation.

PREVENTION & CONTROL

- Sabin's Live attenuated vaccine
- Grown in Monkey kidney cells, Human Diploid cells. Preserved at 4^0 C
- Multiple doses are given
- Given as oral Drops
- At present only vaccine given in our National Programme of Immunization
- Boosts Immunity with Production IgG ,IgM
- And also IgA Participate as participant in Prevention.

ORAL POLIO VACCINE (SABIN'S)

- Highly effective in producing immunity to poliovirus
- 50% immune after 1 dose
- >95% immune after 3 doses
- Immunity probably lifelong



ADVANTAGES OF LIVE VACCINE

- Induces long lasting immunity.
- Induces local immunity in the form of IgA production (gut immunity).
- Administered orally, without the need of sterile syringes.

DISADVANTAGES OF LIVE VACCINE

- The only disadvantage of this vaccine is the vaccine strain particular type 3 strain can reverts to virulerence and cause paralysis in those who just been vaccinated.

- It is estimated that vaccine induced poliomyelitis is seen in rate of 1 in 3000,000 vaccinations.

INJECTABLE KILLED SALK VACCINE

- Salk Vaccine - A Killed Vaccine. (INACTIVATED)
- Four Injections are administered in a period of two years,
- Administration of periodic booster recommended.
- Most of the Western Nations do use it.

DISEASES ASSOCIATED WITH COXASKIE A VIRUS

- Febrile illness with maculopapular rash.
- Upper respiratory tract infection.
- Paralytic disease.
- Meningitis & encephalitis.
- Peri and myocarditis.
- Herpangina.
- Hand, foot & mouth disease.
- Acute hemorrhagic conjunctivitis.

DISEASES ASSOCIATED WITH COXASKIE A VIRUS

- Caused by group A Coxsackieviruses.
- Characterized by fever, sore throat, pain on swallowing .
- Small vesicles appear on the pharynx, Palate, uvula and tonsils .
- Recovery is usual .

HAND FOOT & MOUTH DISEASE

- Caused by group A coxsackie viruses .
- Small papules &vesicles develop on the buccal mucosa, hands and feet .
- Recovery is usual .

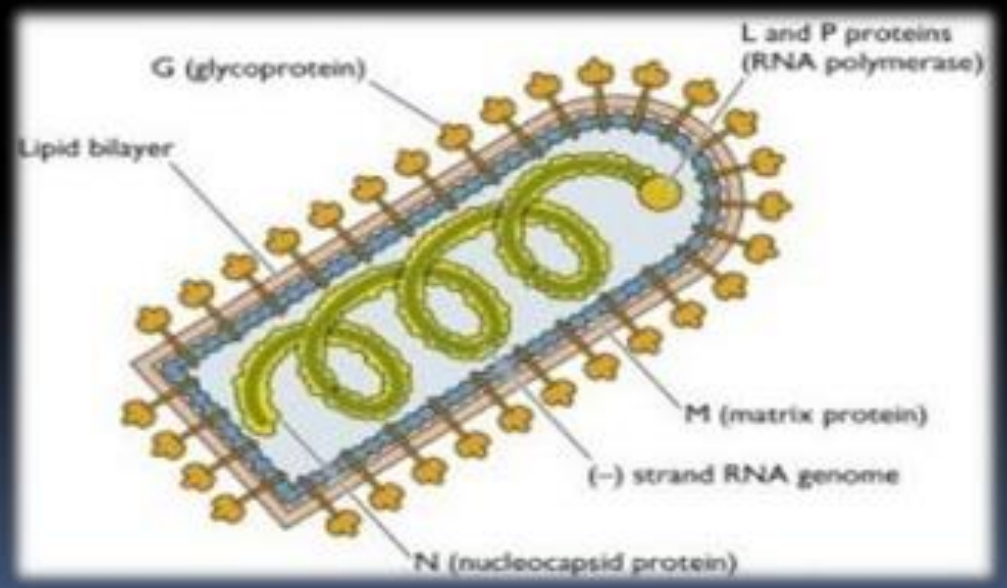
DISEASES ASSOCIATED WITH COXASKIE B VIRUS

- Febrile illness with maculopapular rash.
- Upper respiratory tract infection.
- Paralytic disease.
- Meningitis & encephalitis.
- Peri & myocarditis.
- Pleurodynia.
- Juvenile diabetes/ pancreatitis .

DISEASES ASSOCIATED WITH ECHO VIRUS

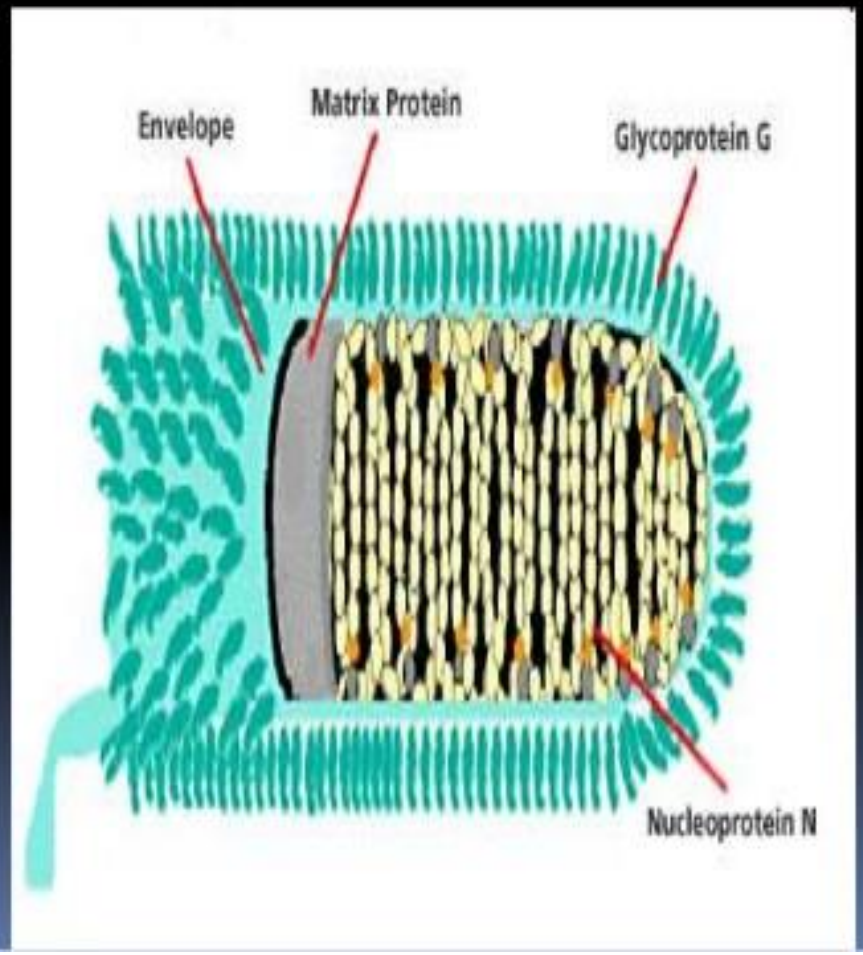
- Febrile illness with maculopapular rash.
- Upper respiratory tract infection.
- Paralytic disease.
- Meningitis & encephalitis.
- Peri & myocarditis.

RHABDO VIRUS

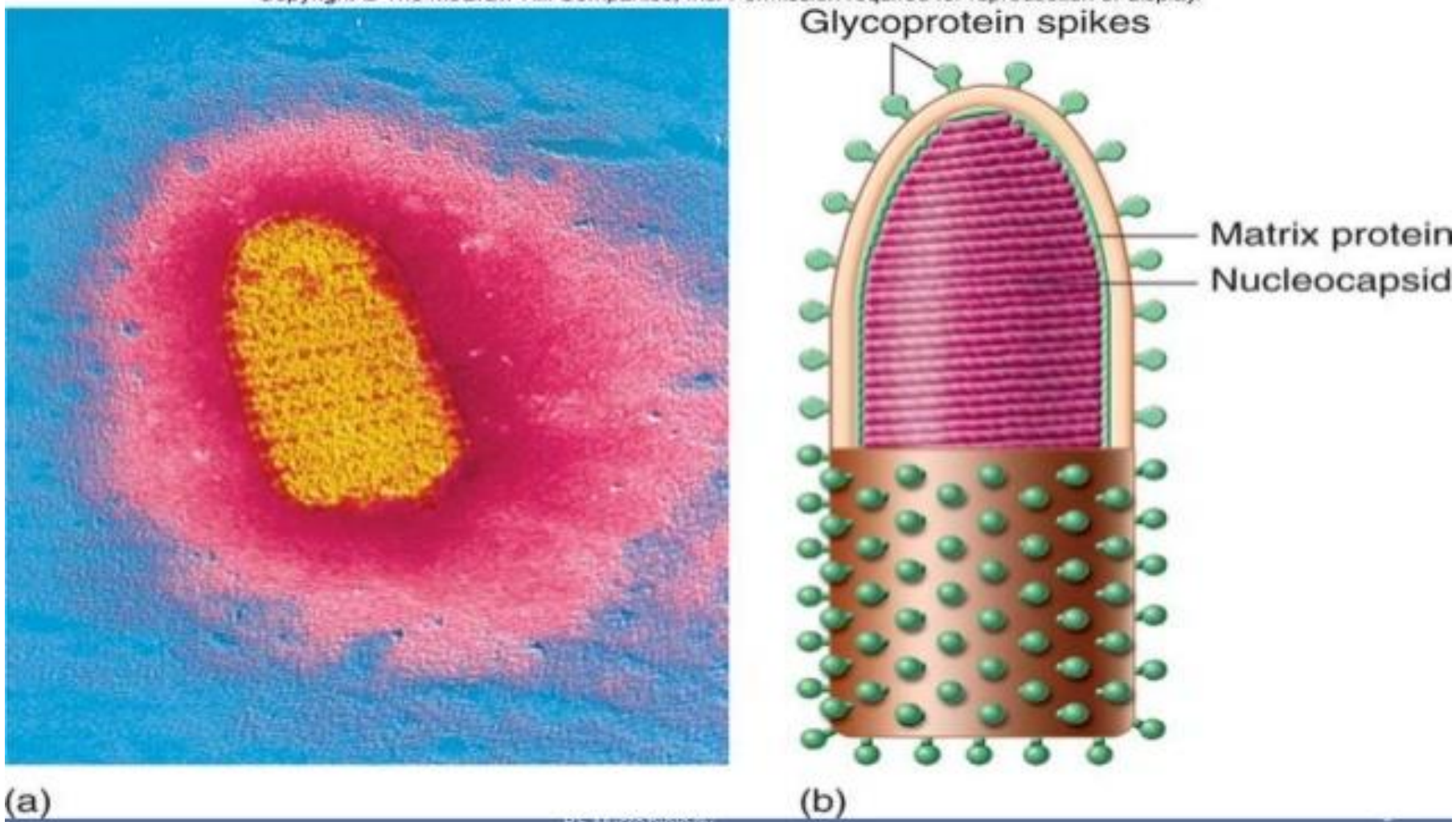


RhabdoVirus

- Single stranded ,linear ,negative sense ,non segmented RNA
- These are enveloped
- Bullet shaped virus
- Multiply in cytoplasm

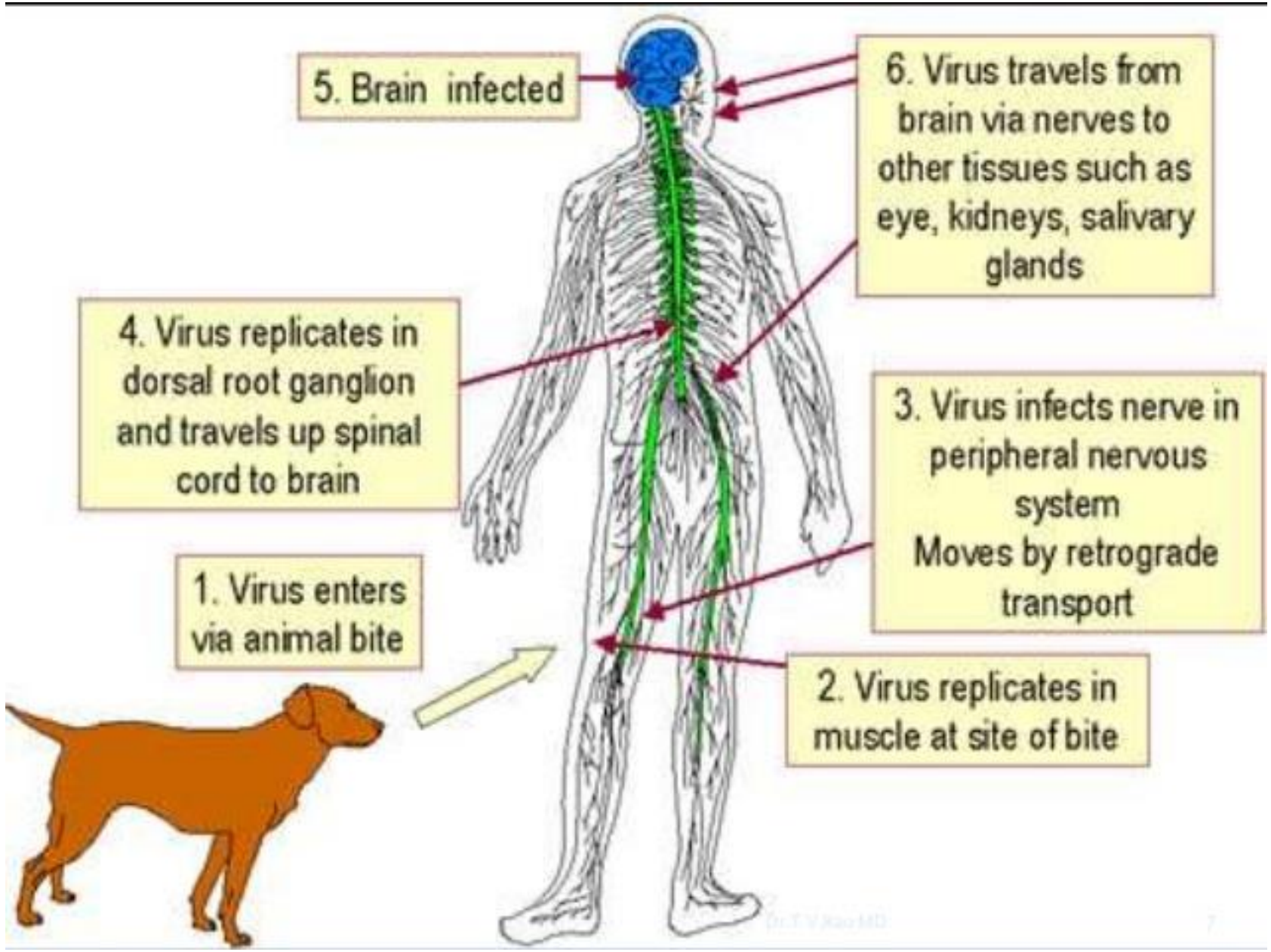


Structure of the rabies virus



Pathogenesis of Rabies

- Bite by Rabid dog or other animals
- Virus are carried in saliva virus deposited on the wound site.
- If untreated 50% will Develop rabies.
- Rabies can be produced by licks and corneal transplantation.
- Virus multiply in the muscle ,connective tissue, nerves after 48 – 72 hours.
- Penetrated nerve endings.


5. Brain infected
6. Virus travels from brain via nerves to other tissues such as eye, kidneys, salivary glands
4. Virus replicates in dorsal root ganglion and travels up spinal cord to brain
3. Virus infects nerve in peripheral nervous system
Moves by retrograde transport
1. Virus enters via animal bite
2. Virus replicates in muscle at site of bite

Symptoms

- Headache, fever, sore throat
- Nervousness, confusion
- Pain or tingling at the site of the bite
- **Hallucinations**
  - Seeing things that are not really there
- **Hydrophobia**
  - "Fear of water" due to spasms in the throat
- **Paralysis**
  - Unable to move parts of the body
- Coma and death

Clinical Findings

- Bizarre behavior.
- Agitation
- Seizures.
- Difficulty in drinking.
- Patients will be able to eat solids
- Afraid of water - Hydrophobia.
- Even sight of sound disturbs the patient.
- But suffer with intense thirst.
- Death in 1 -6 days.
- Respiratory arrest / Death / Some may survive.

Diagnosis

- Based on the history
- Signs and symptoms
- Clinical examination
- Detection of antigen by taking skin biopsy using immunofluorescence.
- Virus isolation from saliva & other secretions.
- CSF analysis, MRI and CT scan.
- ELISA
- RT-PCR
- direct Fluorescent Antibody (DFA) testing
- Negri bodies

Prevention

- Vaccination of susceptible animal species, particularly dogs and cats, will control this zoonotic disease.

Rabies PEP — Vaccination

- Previously unvaccinated persons get 4 doses
  - Days 0, 3, 7, and 14
  - 5th dose dropped from vaccine schedule last year
  - Intramuscular injections