Respiratory Tract Infection

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Viral Infection of Respiratory Tract

- Virus infection of the respiratory tract are the commonest of human infection and cause a large amount of morbidity and loss of time at work.

1-Influenza virus → Orthomyxoviridae

2-Rhinovirus → Picornaviridae family

3-Coronavirus → Coronaviridae family

4-Para influenza viruses → Paramyxoviridae family

5-Respiratory Synctial viruses → Paramyxoviridae

6-Adenovirus → Adenoviridae family.

Viral Infection of the Respiratory Tract

- The common respiratory viruses.

Name of the virus	Family
1 *Influenza virus*	*Orthomyxoviridae*
2 *Parainfluenza virus*	*Paramyxoviridae*
3 *Respiratory syncytial virus*	*Paramyxoviridae*
4 *Rhinovirus*	*Picornaviridae*
5 *Coronavirous* *6-Adenovius*	*Coronaviridae* *Adenoviradia*

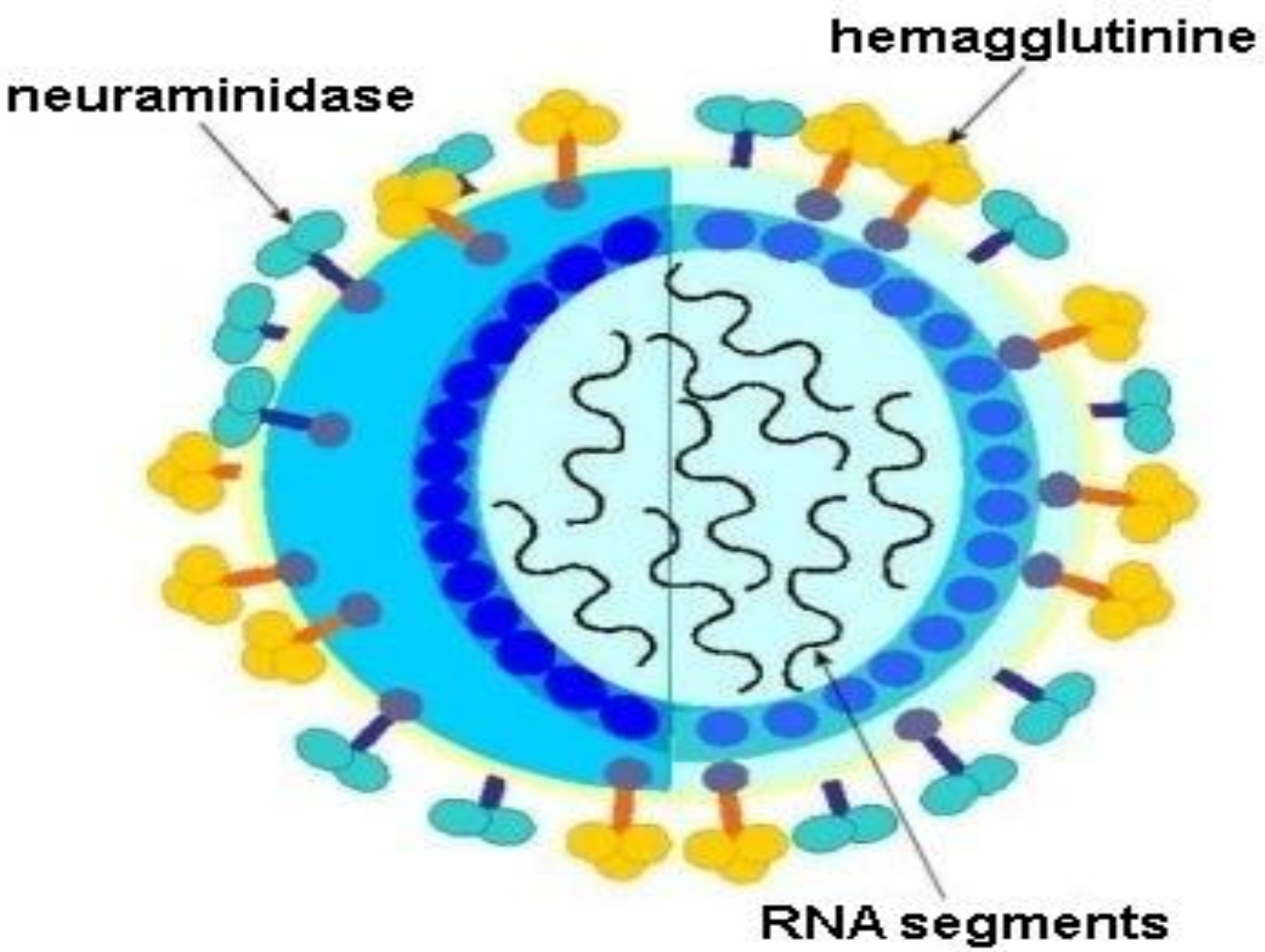
1-Orthomyxoviruses

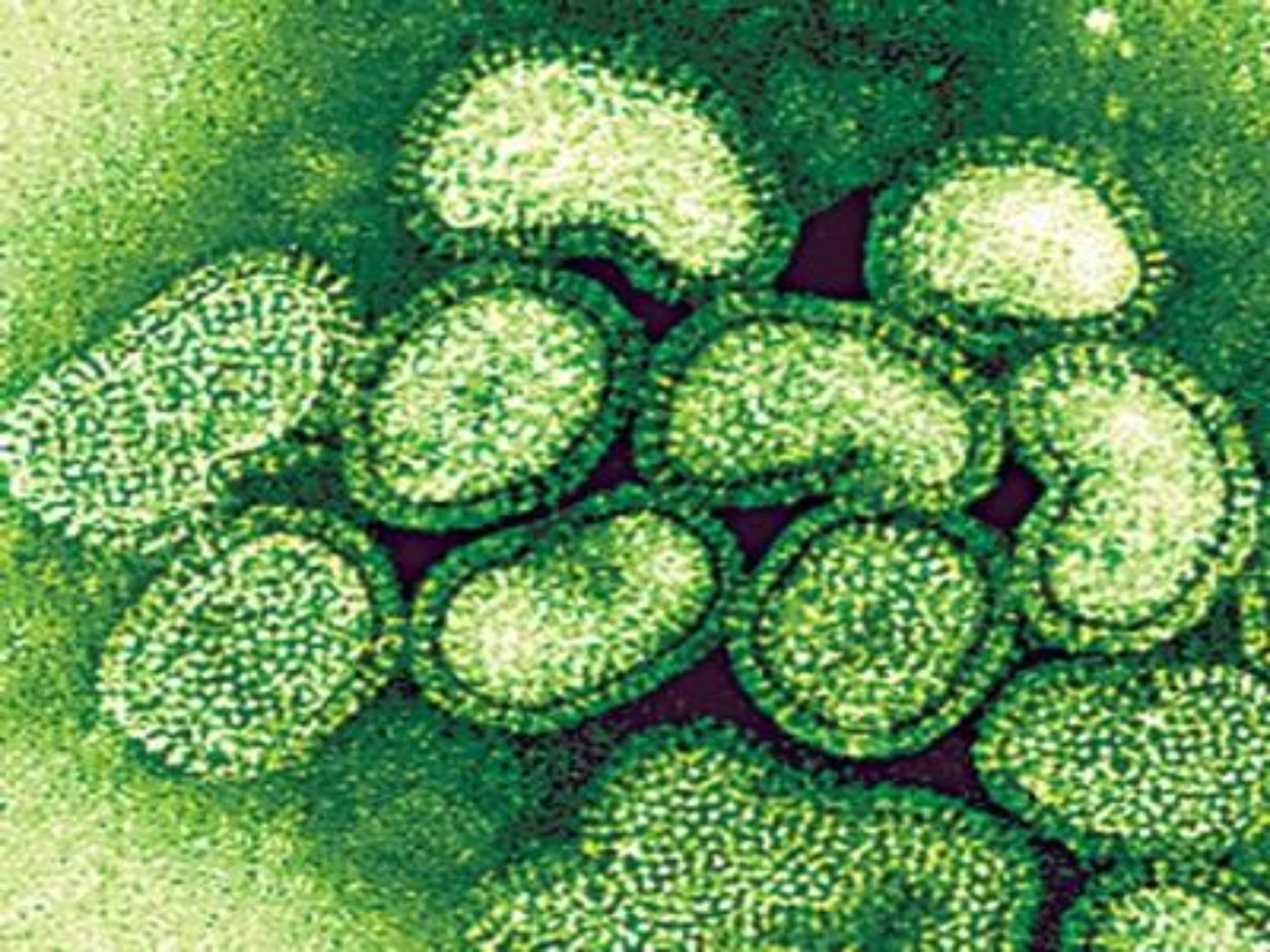
Influenza Virus

1) Single, Stranded negative **sense RNA** with **8** helical segments, This virus is highly susceptible to mutations and rearrangements within the infected host.

2) Helical capsid symmetry
3) Enveloped viruses which contains 2 projecting glycoprotein spikes.

- **Heamagglutinin HA** → attachment.
- The virus can agglutinate certain erythrocyte.
- **Neuroamindase NA** → an enzyme help in releasing progeny virus formation from infected cell.


hemagglutinine
neuraminidase
RNA segments



Influenza Virus

Epidemiology:

- Winter months mostly
- **Influenza A** can cause **epidemic** and **pandemic** which is usually associated with Antigenic shift, while **Influenza B** can cause **outbreaks & epidemic** which associated only with Antigenic drift.

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Types of Influenza Viruses

Influenza A

- Infect human & Animals and birds.
- Can cause **epidemic** and **pandemic**
- **epizootic**.
- **Antigenic drift**
- **antigenic shift**.

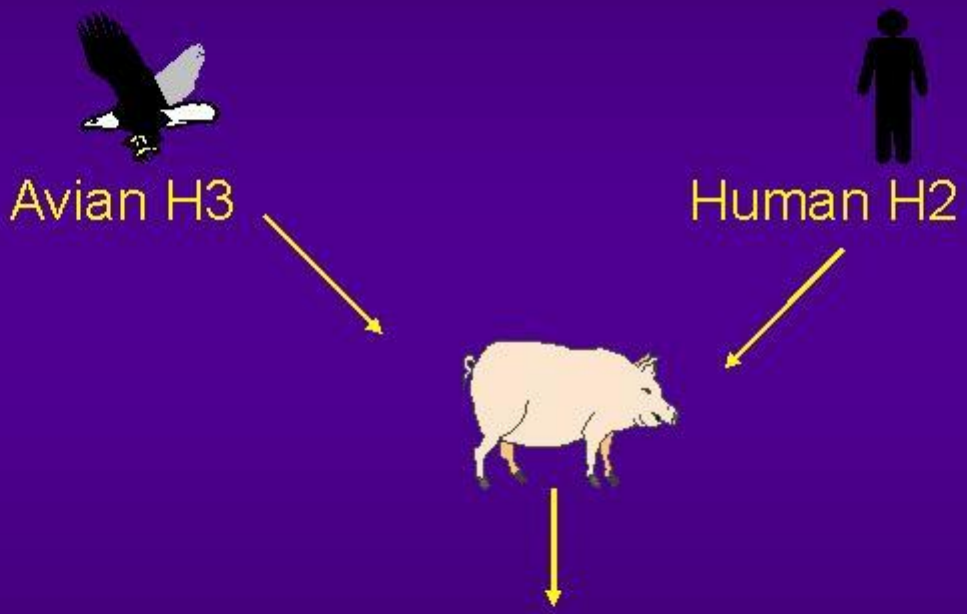
Influenza B

- Infect human only
- Cause **outbreaks &epidemic**
- **Antigenic drift only**

Influenza C

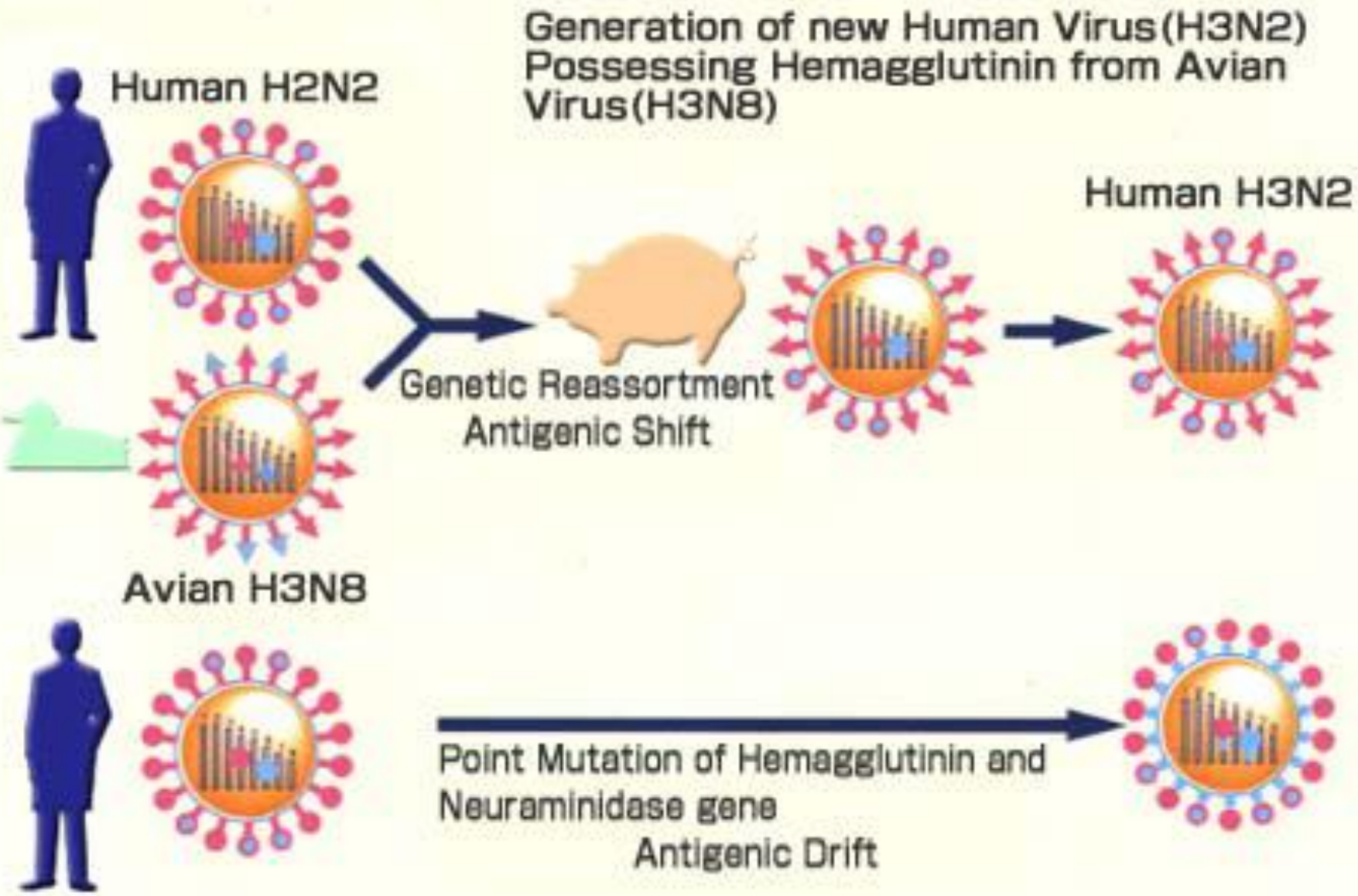
- Infect human only
- Cause mild illness

Reassortment



Variation of Influenza Viruses

GlycoWord



Past Antigenic Shifts

1918	**H1N1**	**“Spanish Influenza”**	**20-40 million deaths**
1957	**H2N2**	**“Asian Flu”**	**1-2 million deaths**
1968	**H3N2**	**“Hong Kong Flu”**	**700,000 deaths**
1977	**H1N1**	**Re-emergence**	**No pandemic**

At least 15 HA subtypes and 9 NA subtypes occur in nature. Up until 1997, only viruses of H1, H2, and H3 are known to infect and cause disease in humans.

Avian flu

Swine flu

Pathogenesis & Immunity:

- Influenza virus establish a local upper respiratory tract infection.
- According to the immunity of the host, it can cause localized infection or spread to the lower respiratory tract infection.
- Viremia usually& occurs (**fever**) .
- Influenza infection is self limiting condition in **Immunocompetent person.**

Clinical Syndrome:

- Transmission → inhalation of respiratory secretion
- Incubation period → 1 - 4 days
- Seasonal variation → usually in winter
- prognosis → **self limiting disease**

- **Symptoms:** **Sudden onset of fever**
  - Malaise – Headache
  - Sneezing – sore throat
  - Non-productive cough

Complication of Influenza:

- **Primary Influenza Pneumonia.**
- **2nd bacterial-pneuomonia**

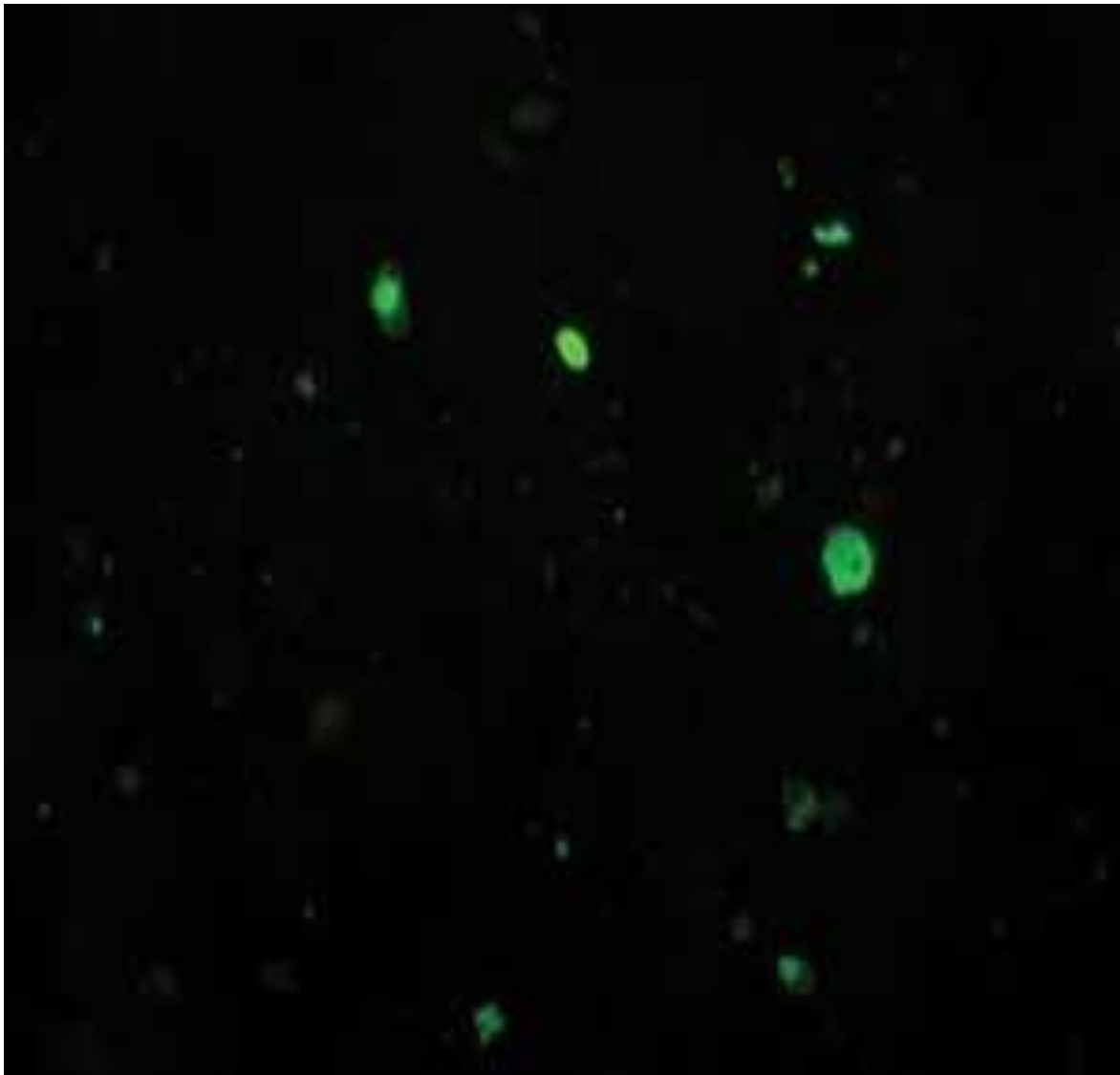
  Strep. pneumoniae, H.influenzae
- **Myositis (inflammation of the muscle).**
- **Post influenza encephalitis.**
- **Bronchial Asthma.**
- **Sinusitis.**

Laboratory Diagnosis:

- Clinical diagnosis.
- Laboratory investigation done to distinguish influenza viruses from other respiratory viruses and to identify the **type** and ***strain.***
- Specimen: Nasopharyngeal aspirate, nasal washing
- Culture: on primary Monkey Kidney cytopathic effect occur 2- 3 days.
- **Rapid and direct detection of influenza virus A or B from nasopharyngeal aspirate by immunofluorescence and ELISA. This is the most common laboratory diagnosis.**
- ***RT-PCR (Nucleic acid testing)***

Rapid antigen immunofluorescence assay

- Assay performed on cells from a nasopharyngeal aspirate, showing typical **nuclear and cytoplasmic "apple-green" fluorescence** after staining with monoclonal antibodies specific for influenza A.



Treatment:

Amantadine: Is only effective against **influenza A** virus.

inhibiting the un coating step of influenza A virus.

It has both **therapeutic** and **prophylactic** .

It significantly reduced the duration of fever and illness is given to **high risk group of patients** who are **not vaccinated because they have allergy from egg.**

Oseltamivir (Tamiflu) :

- It is **Neuraminidase inhibitor** that act by blocking the viral enzyme neuraminidase which help the **influenza** virus invade respiratory tract cells.

- It has to be given within the **first 48 hours** after the exposure of cases or appearance of symptoms.

- **Recommended dose is 75 mg twice daily for 5 days.**

INFLUANZA VACCINE

- Tow types of vaccine ,both contain the current influenza **A** & **B** .
- Vaccine should be given in October or November ,before the influenza season begins.
- Yearly booster dose recommended.

1-The Flu shot vaccine

- Inactivated (Killed vaccine),consists of virus particles which are grown in culture and then killed using a method such as heat or formaldehyde.
- Given to people older than 6 months, including healthy people as well as high risk groups (elderly, pregnant lady, patients with chronic pulmonary or cardiac diseases).
- Given annually by intramuscular injection ,vaccines includes tow influenza A virus and one influenza B virus.

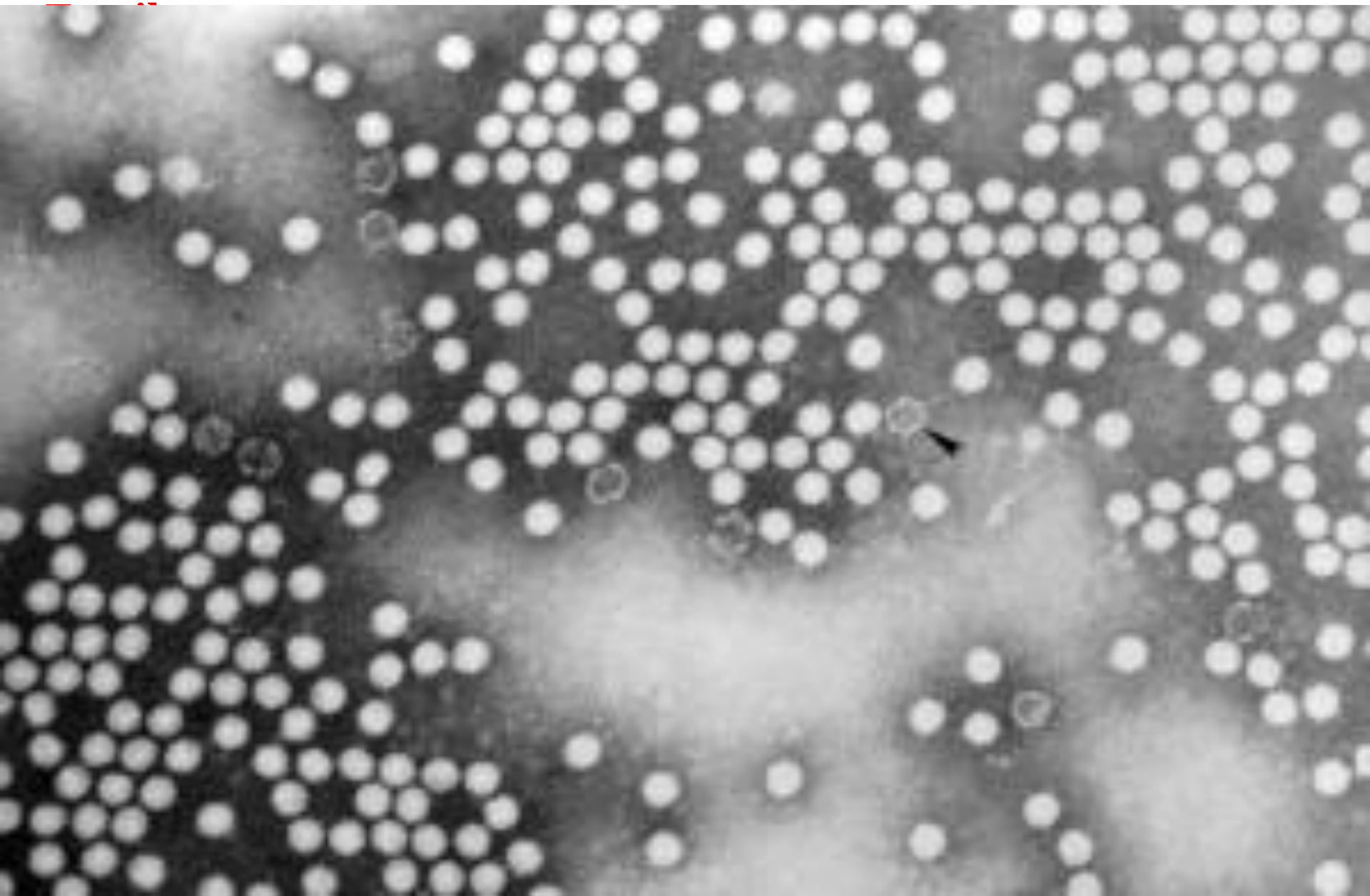
2-The Nasal spray flue vaccine (Flu mist)

- **This is a live attenuated vaccine, vaccine created by reducing the virulence of a pathogen, but still keeping it viable .**
- **Approved for use in healthy people only between 5- 49 years age.**
- **Can not be given to person at high risk ,people with asthma ,pregnant lady or immuonosuppresd persons.**
- **It must be given annually .**

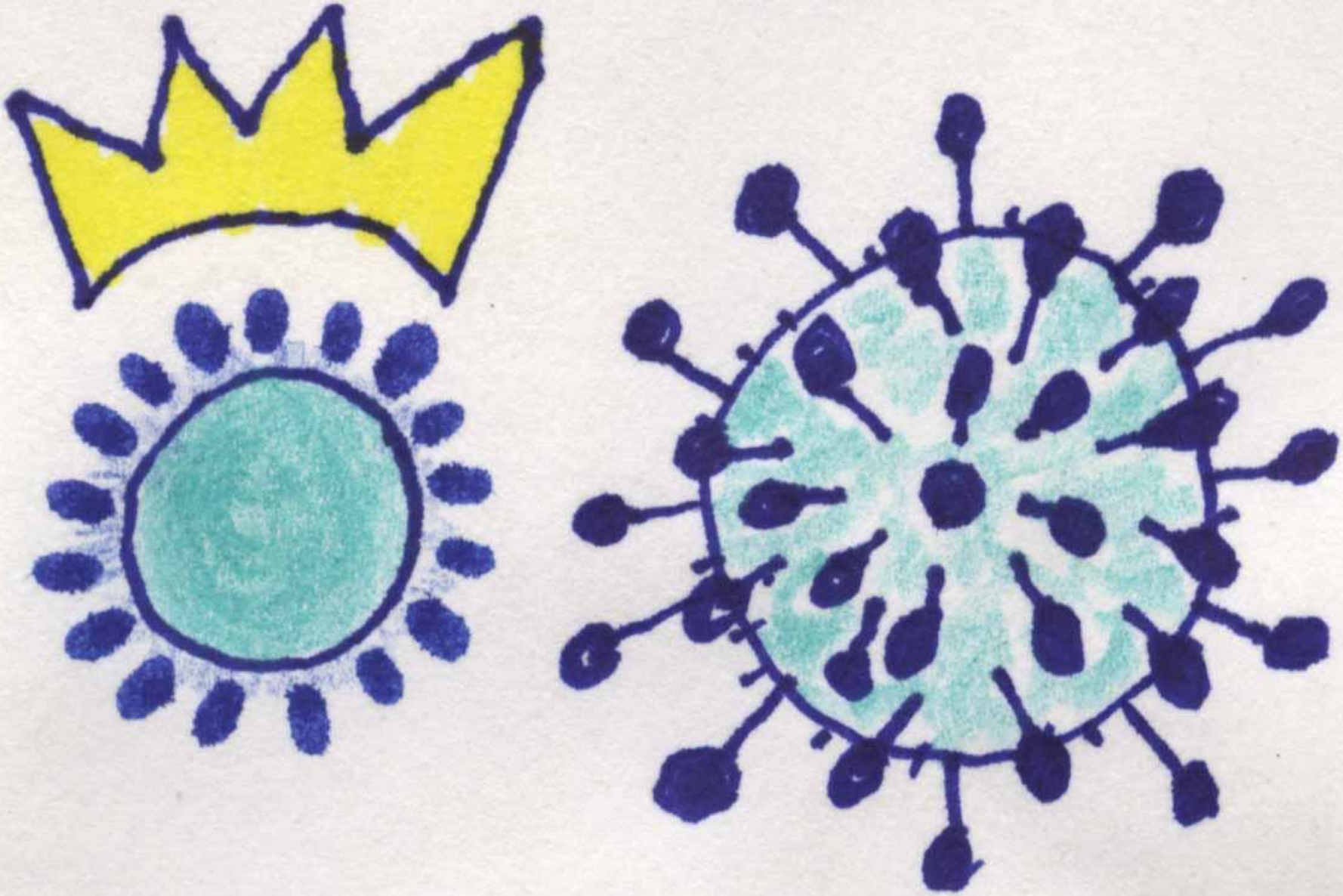
2-RHINOVIRUSES

- Common cold accounts for 1/3 to of all acute respiratory infections in humans.
- **Rhinoviruses are responsible for 60% of common colds cases,**
- ***Common cold is a self-limited illness.***
- More than 100 serologic types of rhinoviruses
  No vaccine available.
- Transmitted directly from person to person by respiratory droplet.
- **RHINOVIRUSES** is one of **PICORNAVIRUS family**,
- small non enveloped virus(20-30 nm),**SS-RNA** virus.
- RHINOVIRUS are acid labile(sensitive).

Rhinovirus



Human Coronavirus 229E



3-Coronaviruses

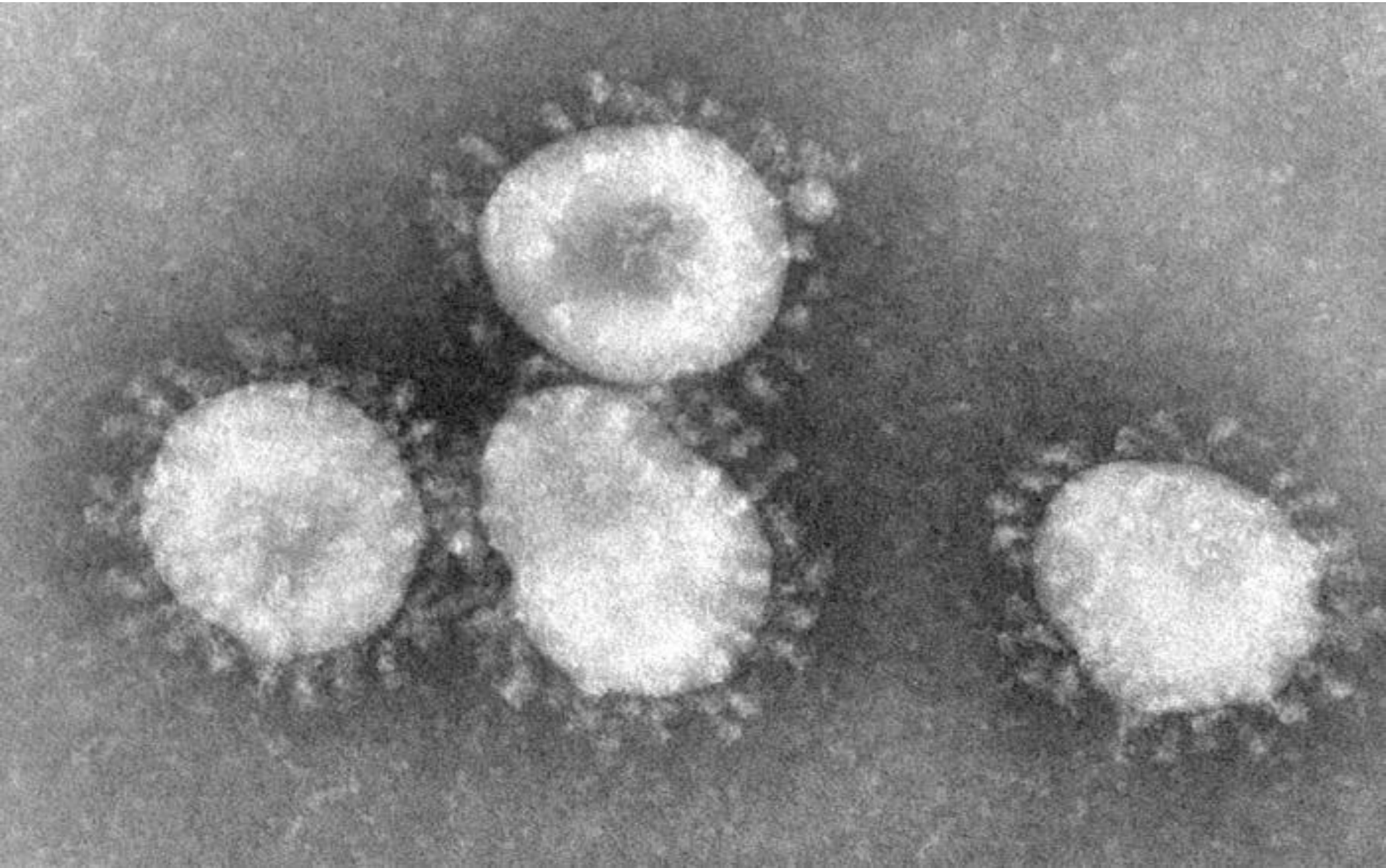
- The name Coronavirus means Crown

(when viewed with an electron microscope).

- **ssRNA enveloped with positive polarity.**

- **Coronavirus are the second cause of common cold .**

Coronavirus



Clinical presentation of common cold:

Symptoms runny nose, sneezing and nasal obstruction, mild sore throat, headache and malaise that last for one week.

Complication: Usually due to secondary bacterial infection

1. Acute sinusitis 2) Acute otitis media.

3) Exacerbation of chronic bronchitis ,bronchial asthma.

Laboratory Diagnosis:

- Usually no need.

Treatment and Prevention:

- No specific treatment.
- No vaccine available.

Severe Acute Respiratory Syndrome SARS

SARS is a viral infection, causes ***Atypical pneumonia*****,** can infect all age groups, and can lead to death especially among people with existing chronic condition.

SARS suspected to be originated in China and Hong Kong.

What we know about the causative agent of SARS?

- A new mutation of **coronavirus,** apparently a zoonosis of which the animal reservoir may be the **cat.**
- Coronavirus is difficult to isolate and not easily grown in tissue culture.
- Coronavirus is able to survive in dry air for up to 3 hours, but can be killed by exposure to ultra-violet light.

3- Coronavirus

In September 2012 ,a case of novel coronavirus infection was reported involving a man in **Saudi Arabia** who was admitted to a hospital with pneumonia and acute kidney injury.

This virus has been named as Middle East respiratory syndrome coronavirus (**MERS-CoV)** ,virus closely related to several **bat** coronaviruses.

MERS-CoV infected several human cells , including lower **but not** upper respiratory, kidney ,intestinal, and liver cells.

4-Para – Influenza Viruses

- **paramyxoviridae family**
- **Enveloped SS RNA,.**
- There are **four** para–influenza viruses: **1, 2, 3, 4**
- Para - influenza virus infection occur mainly in winter.
- Transmitted by respiratory droplets.
- Envelop surface projection presents as **Heamagglutinin HA** , **Neuroamindase NA**,
- **F-glucoprotins** **which cause** cell TO cell membrane to fuse ⟶ **syncytia**

Clinical Syndromes:

1- ***Croup or Acute Laryngotracheobronchitis:***

parainfulenza Type I,II seen in infants & young children < 5 years.

Harsh cough, inspiratory stridor with Hoarse voice and difficult inspiration which can lead to airway obstruction which need hospitalization to do tracheotomy.

2- ***Bronchiolitis and pneumonia:***

Sometime parainfluenza type 3 can cause bronchiolitis and pneumonia in young children.

3- ***Common Cold:***

Seen in older children and adult.

4- ***Immunocompromized:***

Parainfluenza type 3 very dangerous, especially in bone marrow transplant patient.

Laboratory Diagnosis:

A-Direct detection of parainfluenza virus from nasopharyngeal aspirate by **direct immunofluorescent.**

B-Culture :

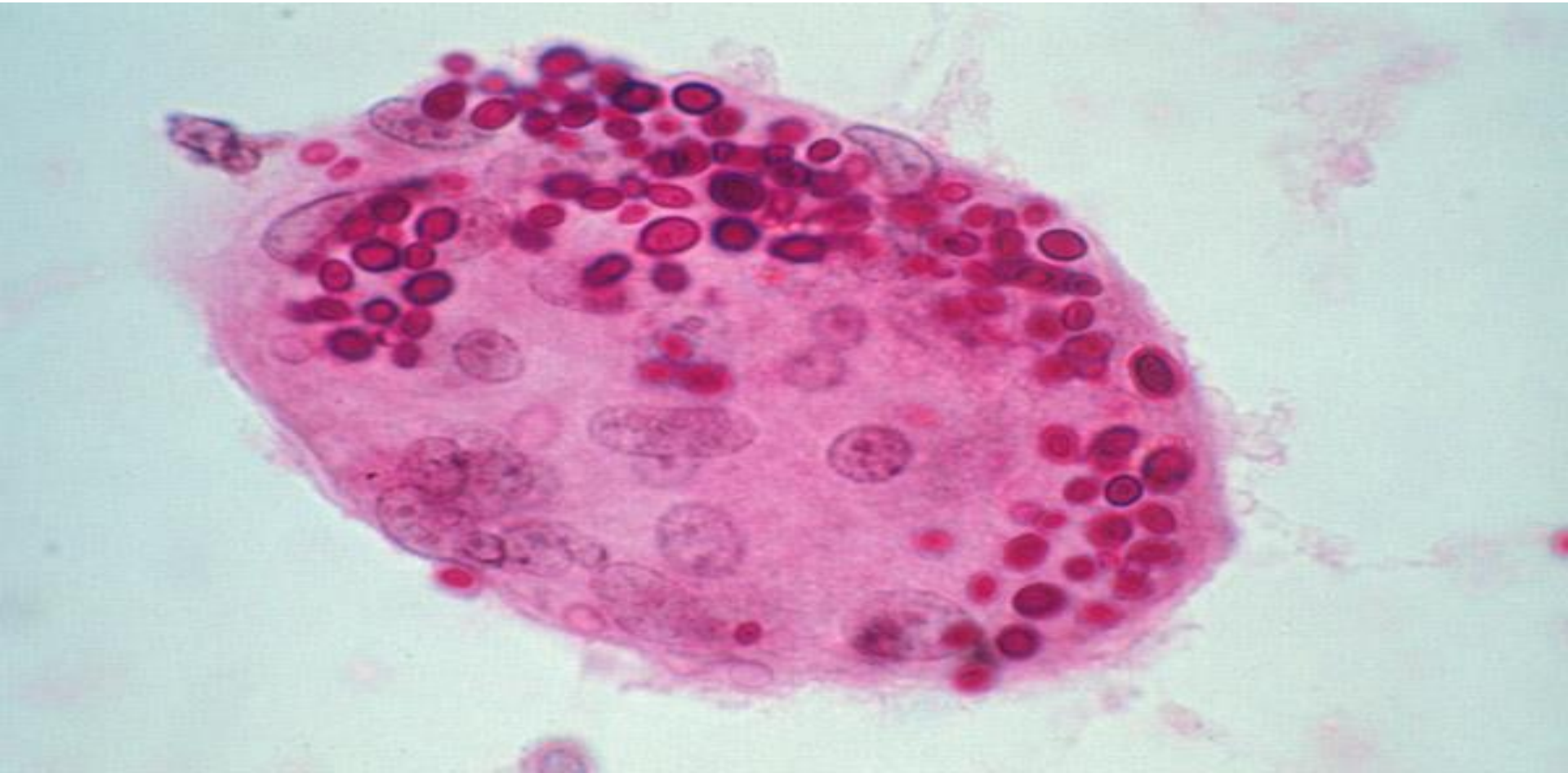
Isolation of the virus from nasopharyngeal aspirate OR mouth wash in cell culture will appear as multinucleated giant cell (syncitia).

Treatment and Prevention:

- Hospital admission for infant having **Croup** for careful monitoring of upper airway (endotracheal intubation and tracheotomy)
- No specific antiviral treatment, no vaccine available.

Viral protein that mediates fusion of an infected cell with neighboring cells leading to the formation of multi-nucleate enlarged cells called syncytia. Usually these syncytia are the result of expression of a viral fusion protein at the host cell membrane during viral replication.

Viruses such as *para-influenza virus* are known to induce the formation of syncytia.



5-Respiratory Syncytial Virus (RSV)

- **One of the paramyxoviridae family.**
- Enveloped ,**ss RNA .**
- The virus transmitted by respiratory droplets, **RSV** virus is very contagious with(I.P. 3-6 days) infection mainly in winter.
- The importance of **RSV** lies in its tendency to invade the lower respiratory tract of infant **<6** months

Bronchiolitis & pneumonia ,,

Clinical Syndromes:

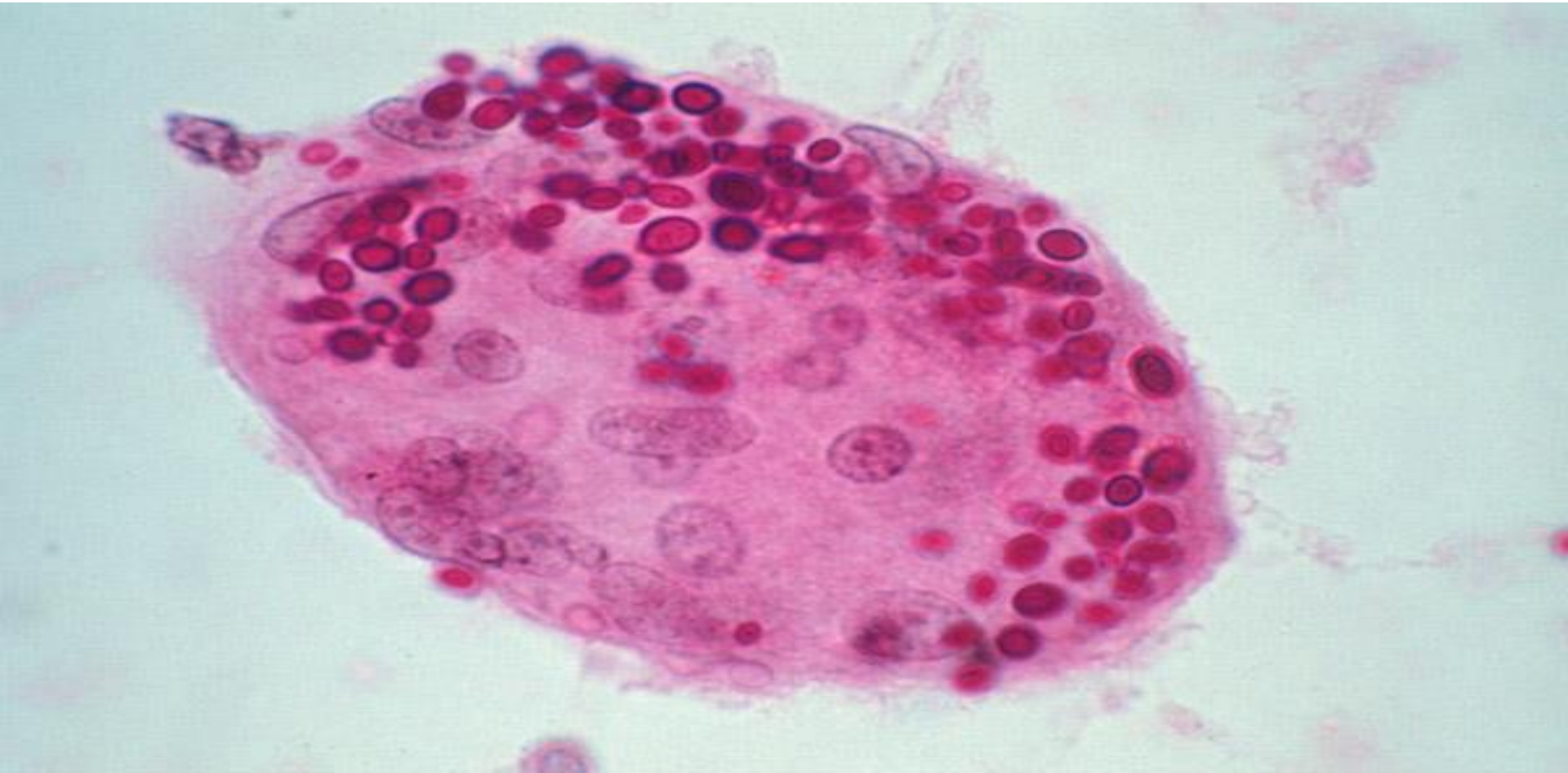
- **RSV** can cause any respiratory tract illness from **common cold** → **pneumonia**

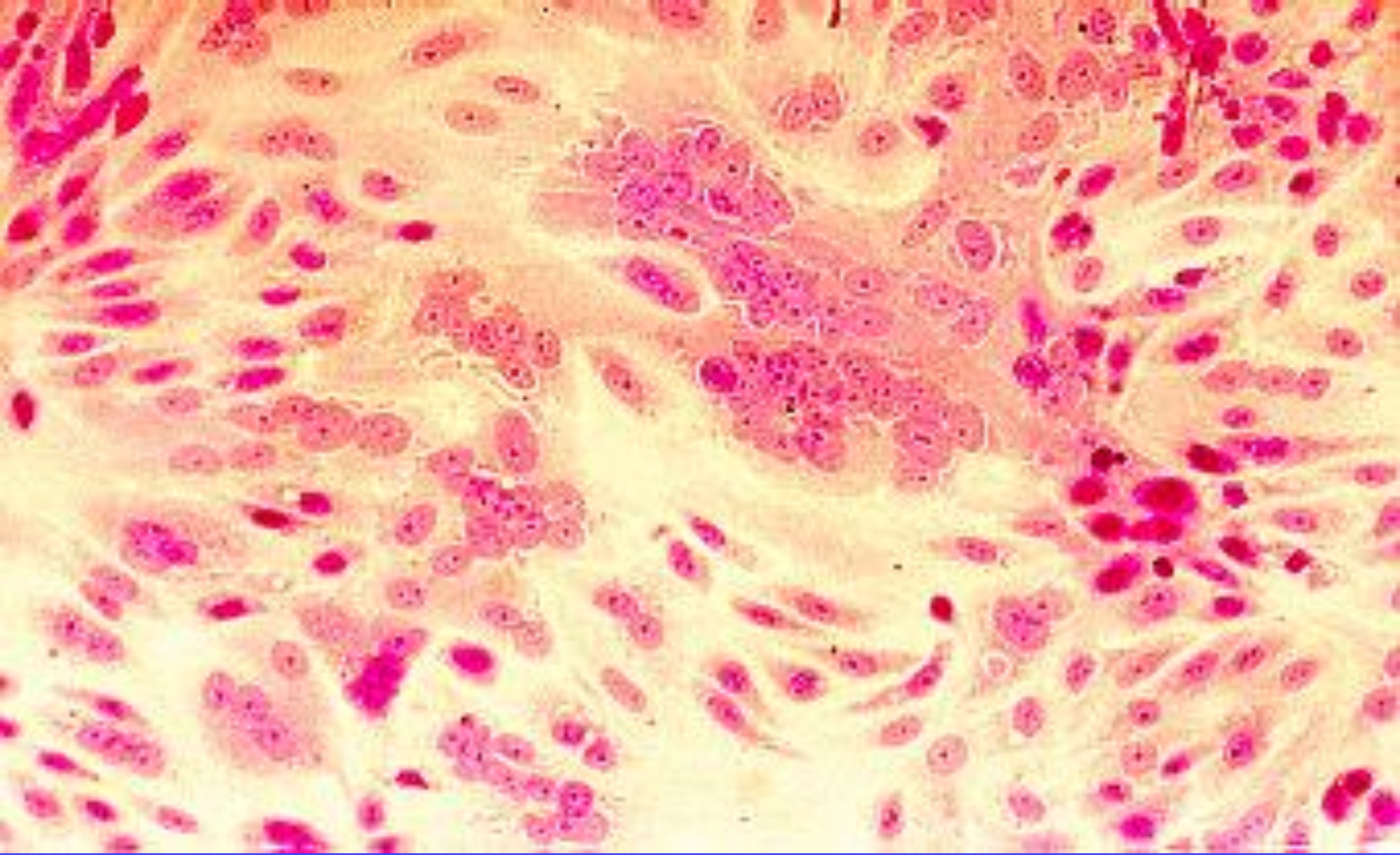
- In old children and adult can cause common cold .
- **Bronchiolitis** an important and life –threatening disease in **infant** especially under 6 months of life, started with fever, nasal discharge, rapid breathing, respiratory distress and cyanosis, it may be fatal in premature infant or infant with underlying disease or immunocompromised infant, also can lead to chronic lung disease in later life.
- **Pneumonia**: also an important and life threatening disease in infant with case fatality rate of 2-5% .

Laboratory Diagnosis:

- **Isolation of the virus from nasopharyngeal aspirate OR mouth wash in cell culture will appear as multinucleated giant cell (syncitia).**
- *ELISA and immunofluorescent for direct detection from nasopharyngeal aspirate.*

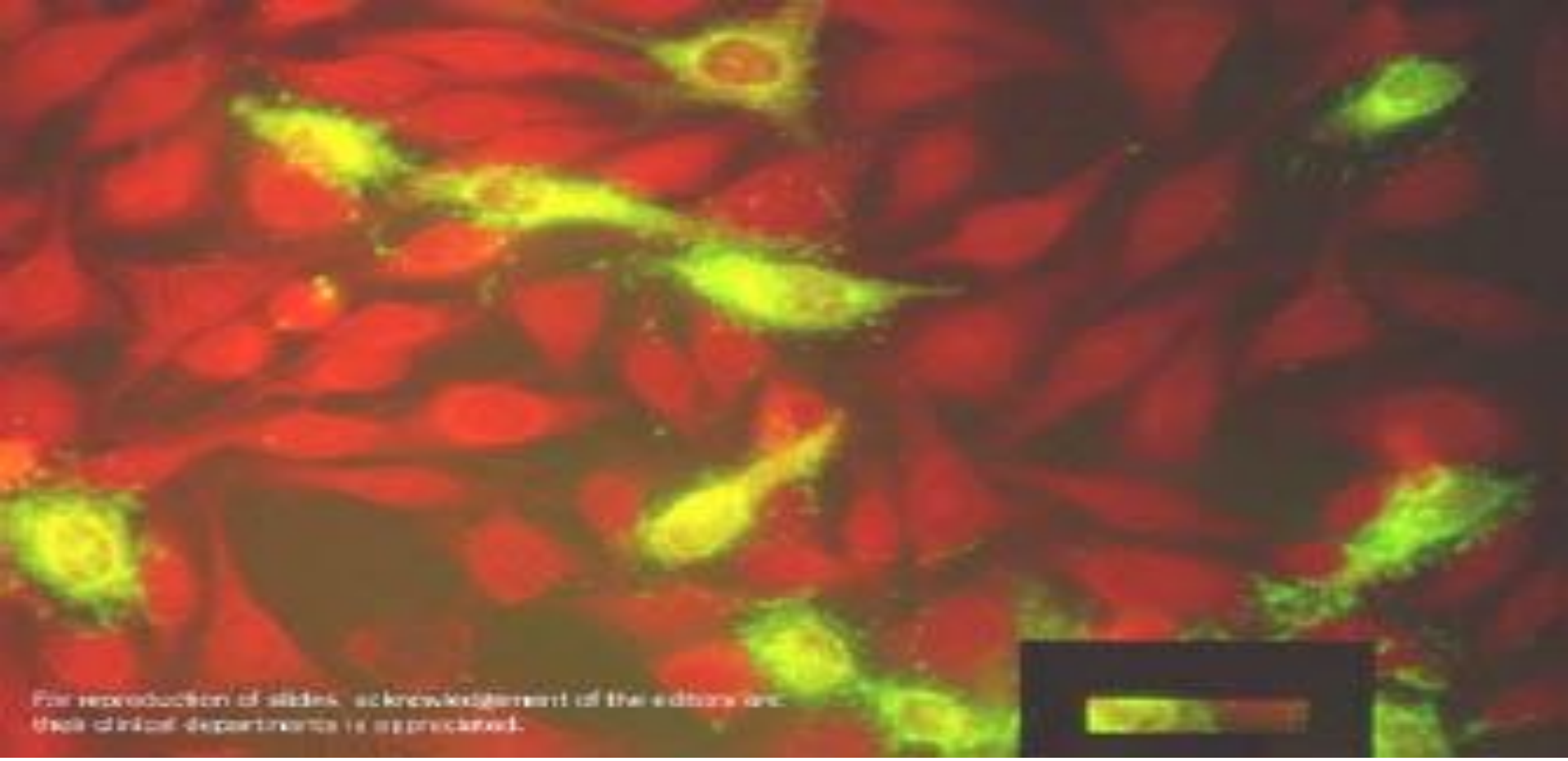
Viral protein that mediates fusion of an infected cell with neighboring cells leading to the formation of multi-nucleate enlarged cells called syncytia. Usually these syncytia are the result of expression of a viral fusion protein at the host cell membrane during viral replication. Viruses such as **RSV** are known to induce the formation of syncytia.





Isolation in cell culture

(**multinucleated giant cells or syncytia**)



- **Immunoflurescence on smears of respiratory secretions** *immunofluorescent for direct detection from*

  nasopharyngeal aspirate.

Treatment and Prevention:

Infant will be hypoxic and need hospitalization

→ **(oxygen inhalation).**

- **Ribavirin given by inhalation to treat severe Bronchiolitis and pneumonia.**
- Passive immunization with anti-RSV immunoglobulin is available for premature infant.
- Hospital staff caring for these **isolated** infants have to follow control measure as hand washing, wearing of gowns, goggles and mask.
- **No vaccine is available.**

6-Family Adenoviridae (Adenoviruses)

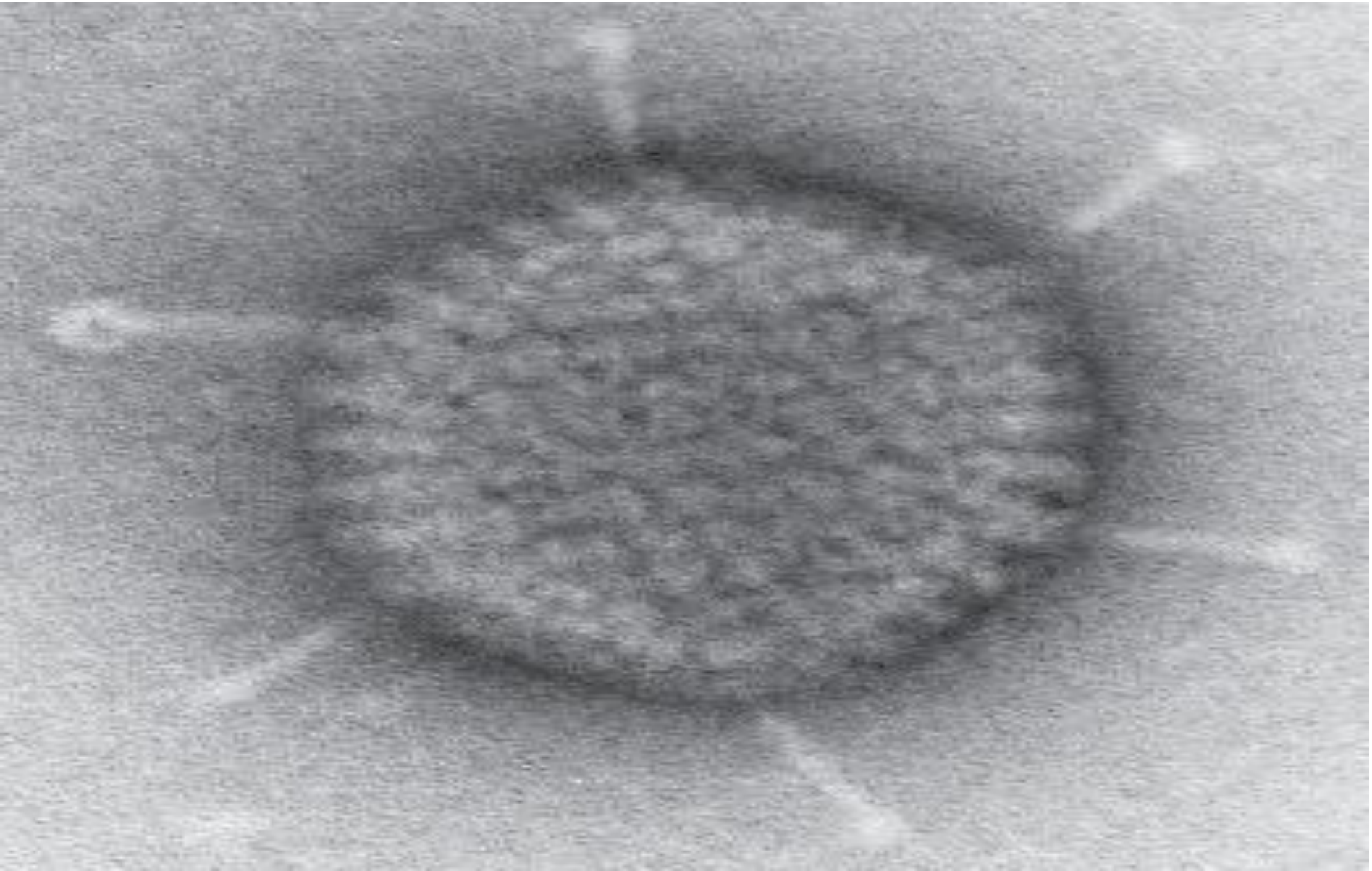
- **dsDNA, non-enveloped viruses with 47serogroup, , grouped into 6 group from A –F.**

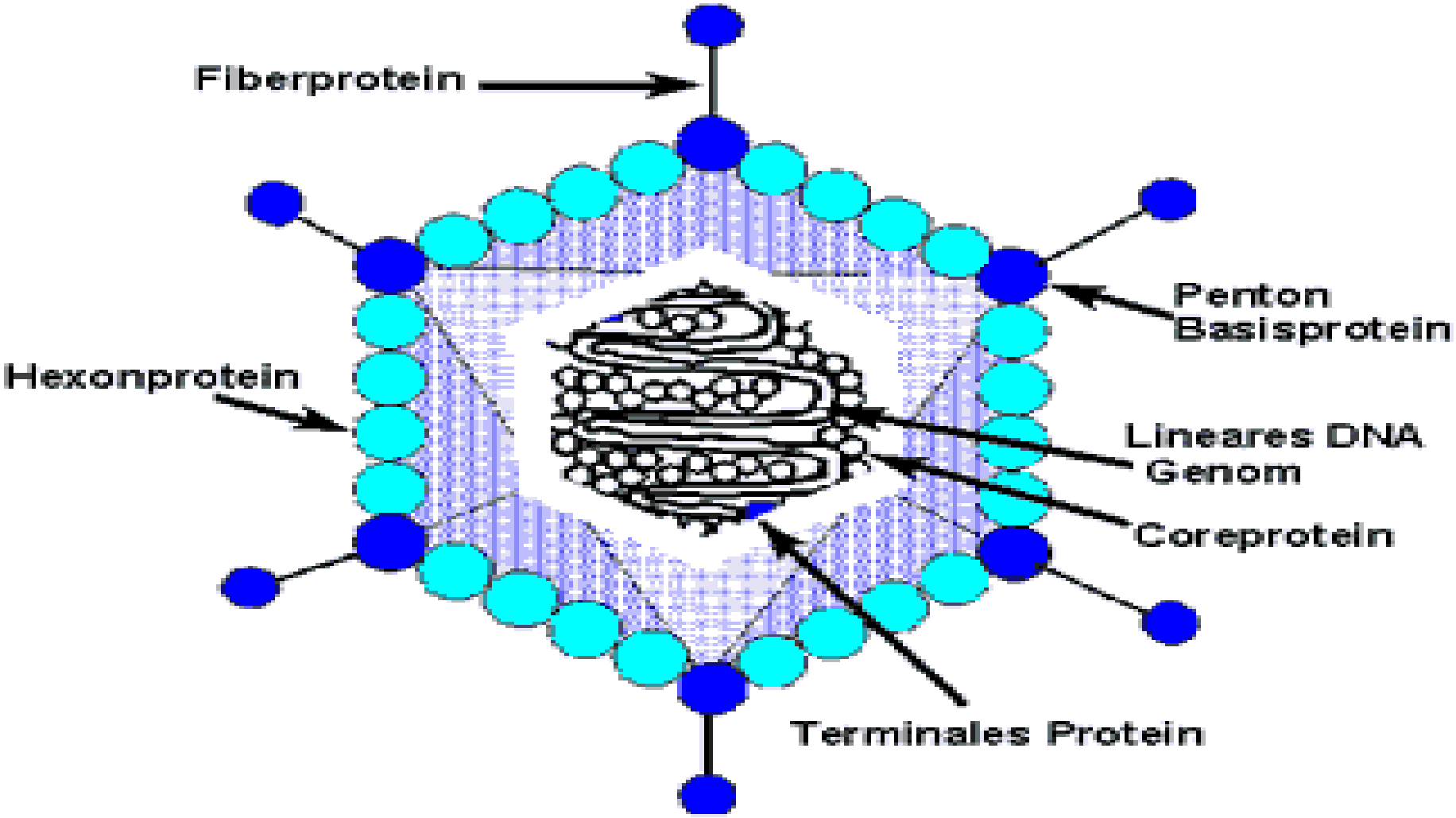
- Adenoviruses infect epithelial cells lining respiratory tract, conjunctiva, gastrointestinal tract, and genital tract

- Viremia may occur after this local replication of the viruses so virus can spread to other visceral organs… e.g. Urinary bladder

- The Adenoviruses have the tendency to become **latent** in lymphoid tissue and can be reactivated if immunity become low.

Adenovirus





The fibers possess hemagglutinating activity and mediate the attachment of the virus to cellular receptors.

Spread and Transmission:

- Fecal – oral route by fingers, fomit and poorly chlorinated swimming pool.
- Respiratory – via respiratory droplets.
- Contaminated instruments at eye – clinics.
- Adenovirus has been cultured from semen, so can be spread by sexual transmission??

Clinical Syndrome:

- Adenovirus primary infect children and less commonly infect adult.
- Reactivation occur if the patient become immunocompromised in children or adult.

- ***The main clinical syndromes:***
  1) **Acute Febrile pharyngitis:** Occur in preschool children , fever nasal congestion and cough (URTI) .
  2) **Conjunctivitis:** Follicular conjunctivitis, can occur as sporadic cases or as an outbreaks .
  3) **Pharyngo-conjunctival fever:** It occurs more often in children and presents with pharyngitis& conjunctivitis and fever

Clinical Syndrome: (Continued)

4) **Keratoconjunctivitis:** (Infection of **Cornea** and Conjunctiva) It is due to irritation of the eye by a foreign bodies, dust or debris, or contaminated instruments at eye – clinic.
5) **Acute respiratory tract disease:** Fever, cough, pharyngitis and cervical adenitis it is mainly occur in Military recruits serotype 4,7).
6) **Pneumonia:** Particularly type 3-7 are a significant cause of pneumonia in preschool children which can be followed by residual lung damage.
7) **Viral gastro-entrites** : diarrhea mainly in young children and infant (serotypes 40 and 41).
8) **Mesenteric adenitis and intussusceptions** : mainly in children.

Clinical Syndrome: (Continued)

9) Acute hemorrhagic cystitis,
dysuria and heamaturia.

10) Cervicitis and urethritis ? Sexually Transmitted.

11) Systemic infection in immunocompromised patient.

In these group of patient infection become severe as pneumonia or hepatitis it can be primary exogenous infection or reactivation.

Laboratory Diagnosis:

Specimens: nasopharyngeal aspirate (respiratory cells), Conjunctival swab and Stool.

- Mainly the diagnosis by direct detection of viral antigen by

Immunofluorescence and ELISA.

Treatment, Prevention and Control

- No specific treatment available
- Live Oral vaccine → used to prevent acute respiratory tract infection for Military recruits [adenovirus serotype 4 –7].

Good luck