Respiratory Viruses

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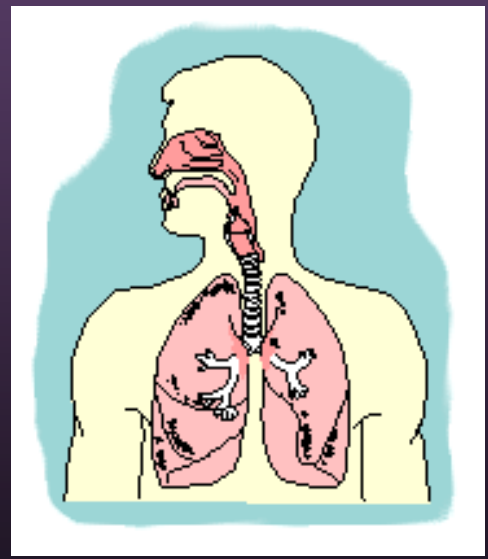


Viral Respiratory Infections

- Respiratory infections are common, eg. colds in both adults and children.
- Most are fairly mild, self- limiting and confined to the upper respiratory tract (URT).
- Most are probably viral induced - at least initially.
- However, in infants and children, URT infections may spread downwards and cause more severe infections and even death.

Upper Respiratory Tract

1. Colds- Main feature: watery to mucoid, sometimes purulent nasal discharge "coryza". Often preceded by a sore throat, sometimes accompanied by fever and often followed by transient opportunist bacterial infection.

2. Pharyngitis "sore throat"- Generalized erythema of pharynx, not localized to the tonsils and not associated with coryza. Some fever present.

3. Tonsillitis- Local infection of tonsils = red, swollen with exudates on the surface. (Bacterial tonsillitis is quite common).

Upper Respiratory Tract – Cont.

4. Sinusitis & Otitis Media- Painful inflammatory conditions of sinuses and middle ear. Drainage of these spaces may be impaired and lead to bacterial infection. (Bacterial infections are usually secondary to viral infection of the nose and pharynx).

5. Influenza- Fever, myalgia, sore throat, headache, prostration - usually NOT much nasal discharge compared to a cold. Maybe some cough.

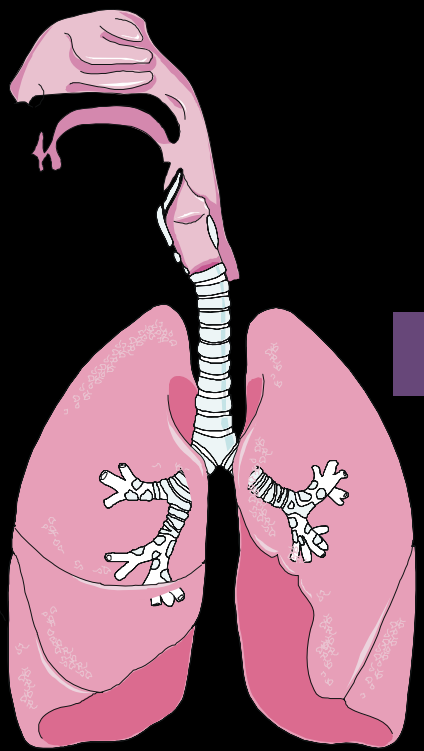
Lower Respiratory Tract

1. Laryngo-Tracheo Bronchitis (Croup)- An acute viral inflammation of larynx and trachea in small children. Often preceded by a "cold". Accompanied by pyrexia, hoarseness, croaking cough, restlessness (respiratory insufficiency). Can be fatal - i.e.. life-threatening disease.
2. Acute Bronchitis- Inflammation of bronchi, accompanied by fever, cough, wheezing and "noisy chest".
3. Pneumonia & Bronchopneumonia- Acute respiratory disease accompanied by fever, restlessness and cyanosis. Often not much clinical "consolidation". Again, can be life-threatening.

Lower Respiratory Tract – Cont.

4. Acute Bronchiolitis- Inflammation of terminal bronchioles in small children. Bronchiole diameter is larger during inspiration than during expiration and this leads to hyperinflation of air sacs distal to bronchiole. These changes cause respiratory embarrassment and can be life-threatening. Usually preceded by coryza symptoms which later develops into the major pulmonary illness. Clinically there is fever, rapid respiration, exhausting cough and wheezing.

RESPIRATORY TRACT VIRUSES



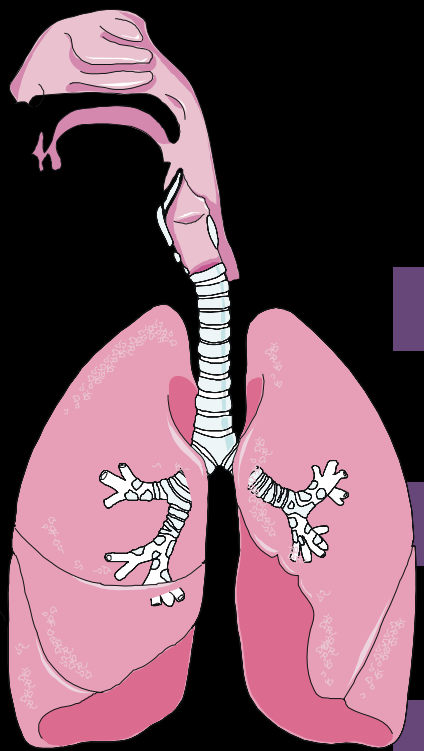
LOCALIZED

- Adenoviruses
- Coronaviruses
- Influenza ‘A’, ‘B’
- Epstein-Barr virus
- Parainfluenza 1, 3
- Respiratory syncytial
- Rhinoviruses

DISSEMINATED

- Coxsackie
- Mumps virus
- Measles virus
- Smallpox virus
- Herpes simplex 1
- Varicella
- Rubellavirus

RESPIRATORY TRACT VIRUSES



Upper Respiratory Infection

- Rhinovirus
- Coronaviruses
- Echovirus
- Influenza ‘A’, ‘B’
- Parainfluenza 1-7, 14, 21
- Herpes simplex 1
- Adenovirus
- Respiratory syncytial
- Epstein-Barr virus

Croup (laryngotracheobronchitis)

- Pneumonitis

Bronchiolitis

- Measles

Varicella

- Influenza ‘A’

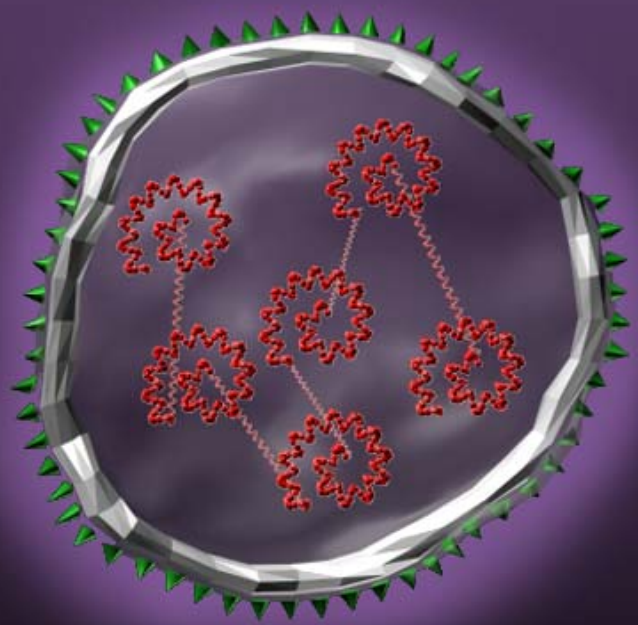
Viruses Associated with Respiratory Infections

Syndrome	Commonly Associated Viruses	Less Commonly Associated Viruses
Corza	Rhinoviruses, Coronaviruses	Influenza and parainfluenza viruses, enteroviruses, adenoviruses
Influenza	Influenza viruses	Parainfluenza viruses, adenoviruses
Croup	Parainfluenza viruses	Influenza virus, RSV, adenoviruses
Bronchiolitis	RSV	Influenza and parainfluenza viruses, adenoviruses
Bronchopneumonia	Influenza virus, RSV, Adenoviruses	Parainfluenza viruses, measles, VZV, CMV

ORTHOMYXOVIRIDAE

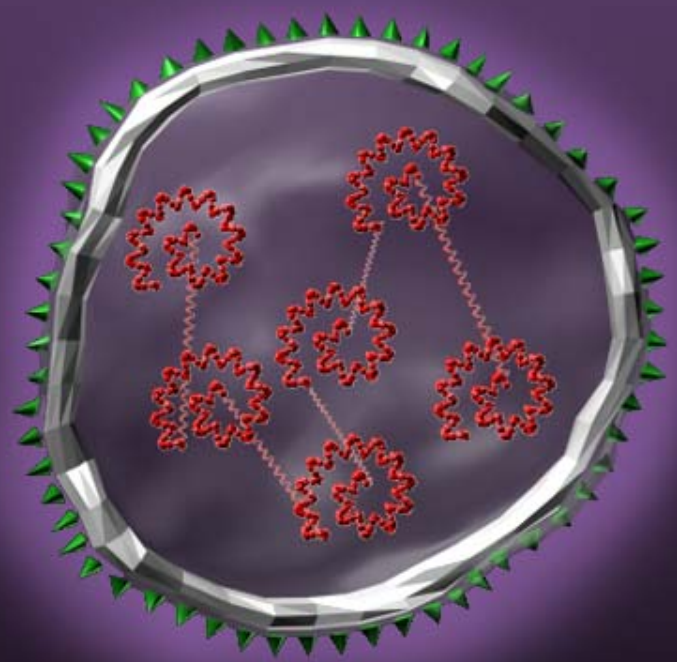
IMPORTANT ASPECTS

1. Enveloped, minus strand, segmented RNA
2. Segmentation allows random assortment in mixed infections
3. Pandemics approximately every 15 years due to antigenic shift
4. Yearly epidemics due to antigenic drift
5. Multiplication sensitive to Amantadine



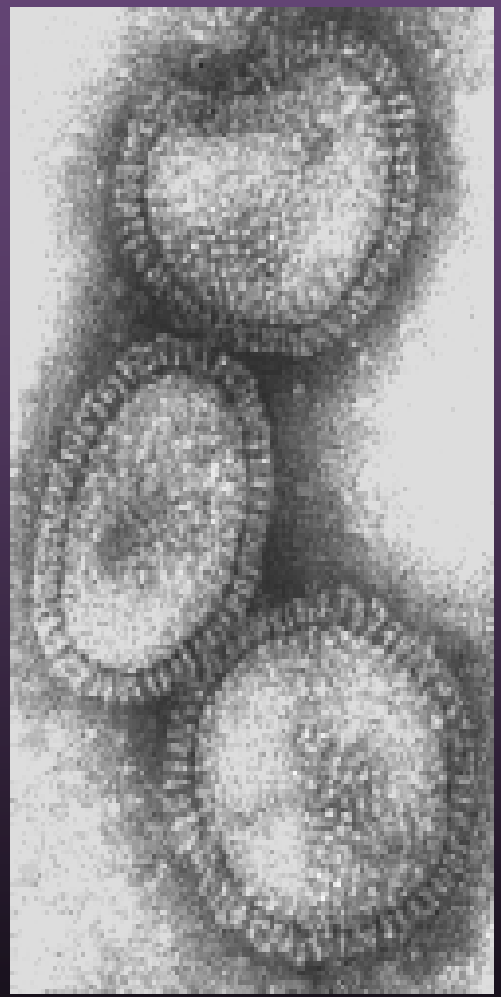
ORTHOMYXOVIRIDAE

SIZE (nm): 100
ENVELOPED: Yes
CAPSID SYMM: Helix
NUCLEIC ACID: RNA
CLASS: V
FORM: ss-
SEG: 8
GENES: 10
KB: 13.6

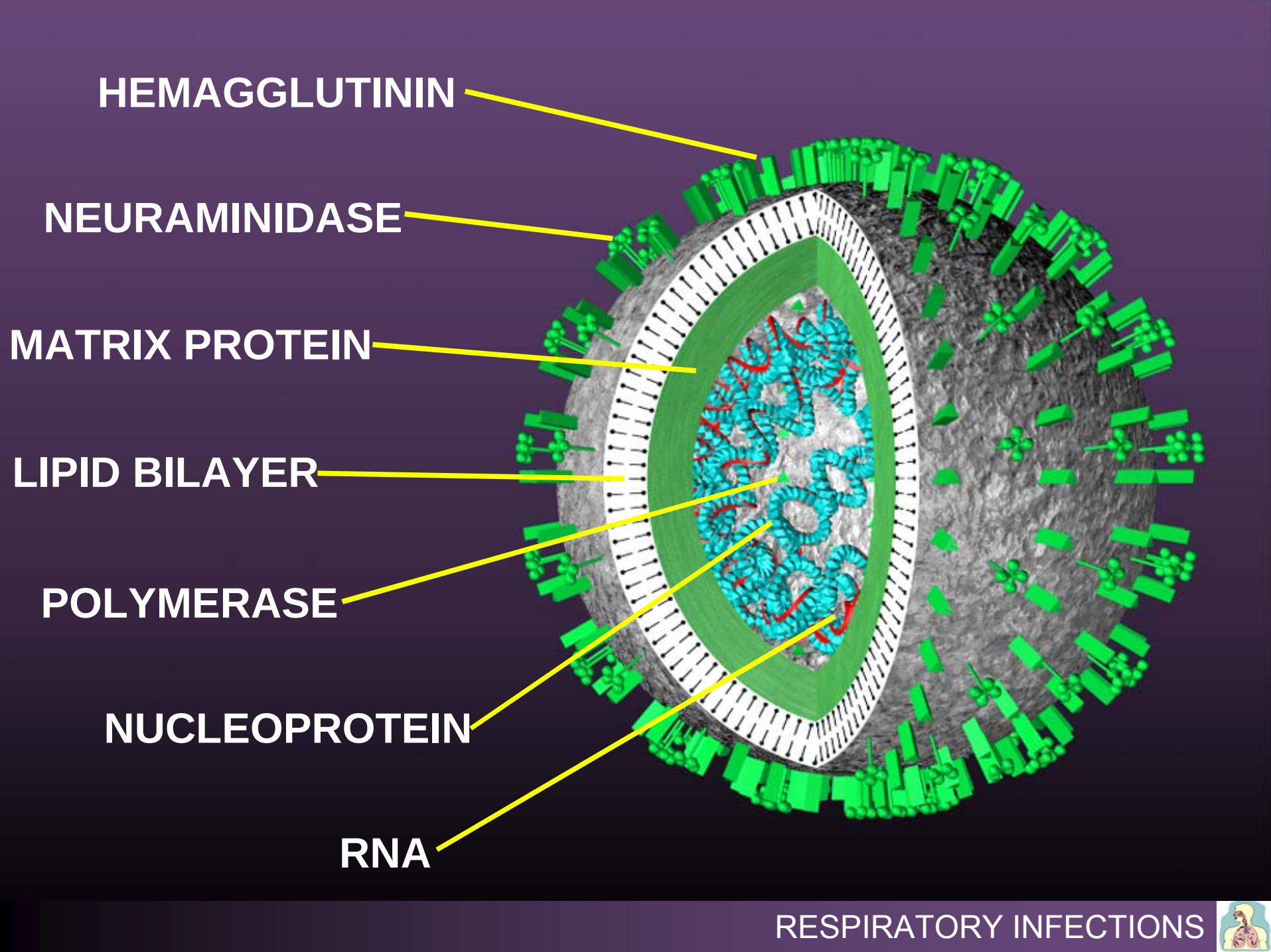


MEMBERS
INFLUENZA

Influenza Virus

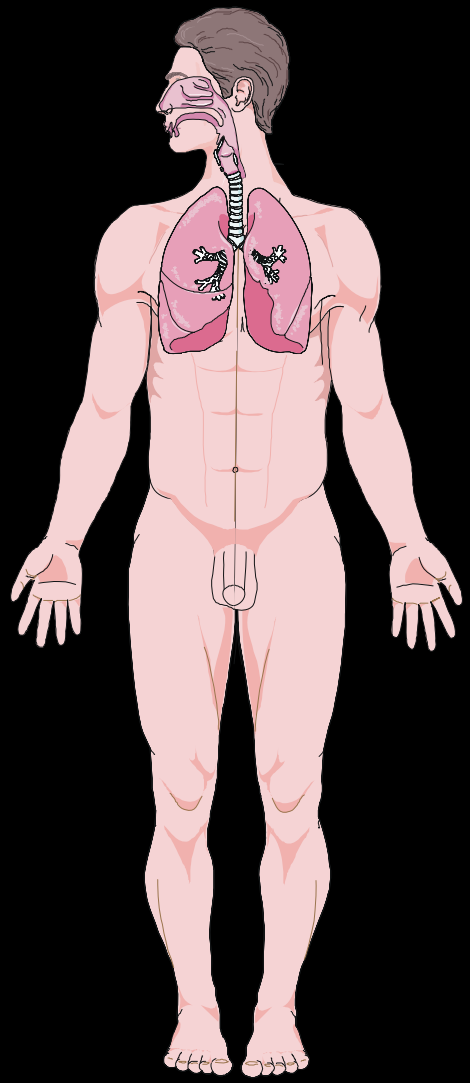


- RNA virus, genome consists of 8 segments
- enveloped virus, with haemagglutinin and neuraminidase spikes
- 3 types: A, B, and C
- Type A undergoes antigenic shift and drift.
- Type B undergoes antigenic drift only and type C is relatively stable


HEMAGGLUTININ
NEURAMINIDASE
MATRIX PROTEIN
LIPID BILAYER
POLYMERASE
NUCLEOPROTEIN
RNA

ORTHOMYXOVIRIDAE

DISEASE Influenza



SYMPTOMS

Fever, chills, aches, nausea, sore throat, cough, general malaise

COMPLICATIONS

Secondary bacterial infections

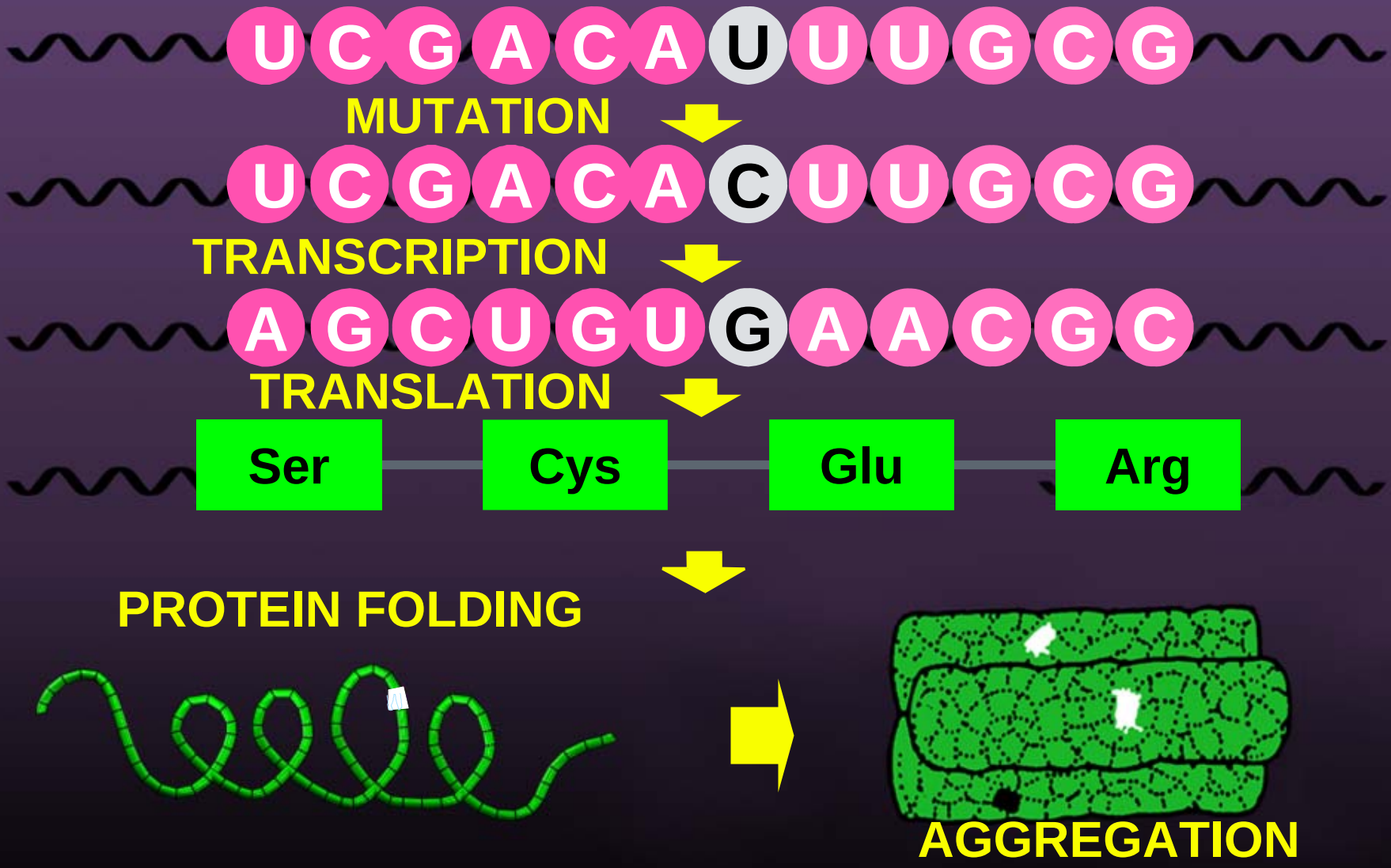
Pneumonia

Reyes Syndrome (follows Type B)

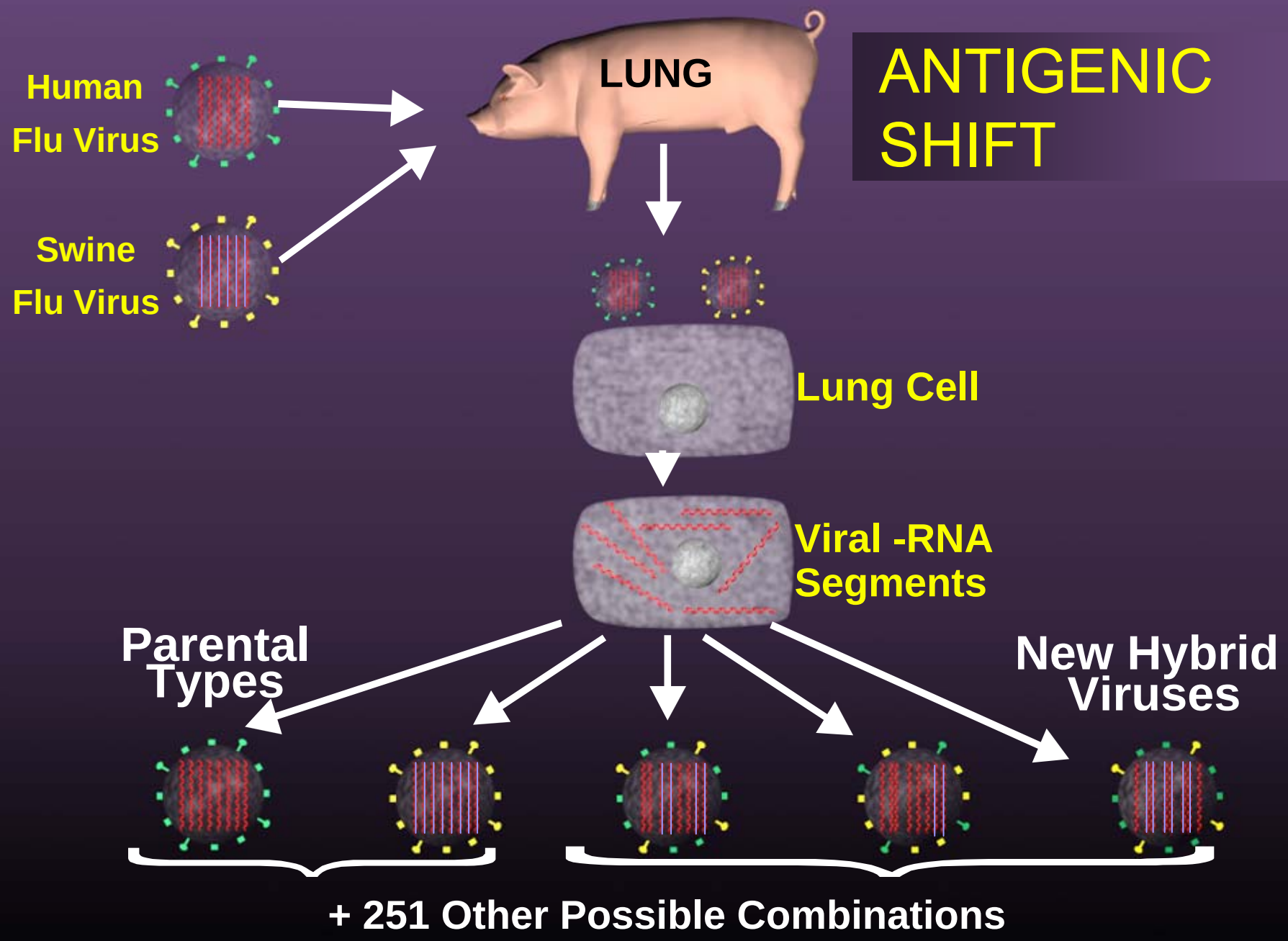
Influenza A Virus

- Undergoes antigenic shifts and antigenic drifts with the haemagglutinin and neuraminidase proteins.
- Antigenic shifts of the haemagglutinin results in pandemics. Antigenic drifts in the H and N proteins result in epidemics.
- Usually causes a mild febrile illness
- Death may result from complications such as viral/bacterial pneumonia

ANTIGENIC DRIFT



ANTIGENIC SHIFT



Classification of Virus Strains

On the basis of antigenicity of NP and MP into three main groups:

1. **Influenza A -HA undergoes minor and occasional major changes - very important.**

   - NA some variation.

2. **Influenza B Undergoes relatively slow change in HA with time. Known only in man.**
3. **Influenza C Uncommon strain, known only in man.**

A	SINGAPORE	6	86	(H1N1)
TYPE of influenza	**TOWN** where first isolated	**No.** of isolates	**YEAR** of isolation	MAJOR **TYPE of HA and NA**

Past Antigenic Shifts

1918	H1N1	“Spanish Flu”	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
1997	?H5N1		6 deaths to date

At least 16 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.

Epidemiology

- Pandemics - influenza A pandemics arise when a virus with a new haemagglutinin subtype emerges as a result of antigenic shift. As a result, the population has no immunity against the new strain. Antigenic shifts had occurred 3 times in the 20th century.

- Epidemics - epidemics of influenza A and B arise through more minor antigenic drifts as a result of mutation.

Laboratory Diagnosis

- Detection of Antigen - a rapid diagnosis can be made by the detection of influenza antigen from nasopharyngeal aspirates and throat washings by IFT.

- Virus Isolation - virus may be readily isolated from nasopharyngeal aspirates and throat swabs.

- Serology - a retrospective diagnosis may be made by serology. CFT most widely used. HAI and EIA may be used to give a type-specific diagnosis

Management

- **Amantidine** is effective against influenza A if given early in the illness. However, resistance to amantidine emerges rapidly
- **Rimantidine** is similar to amantidine but but fewer neurological side effects.
- **Ribavirin** is thought to be effective against both influenza A and B.
- **Neuraminidase inhibitors** are becoming available. They are highly effective and have fewer side effects than amantidine. Moreover, resistance to these agents emerge slowly

Types of Influenza Vaccine

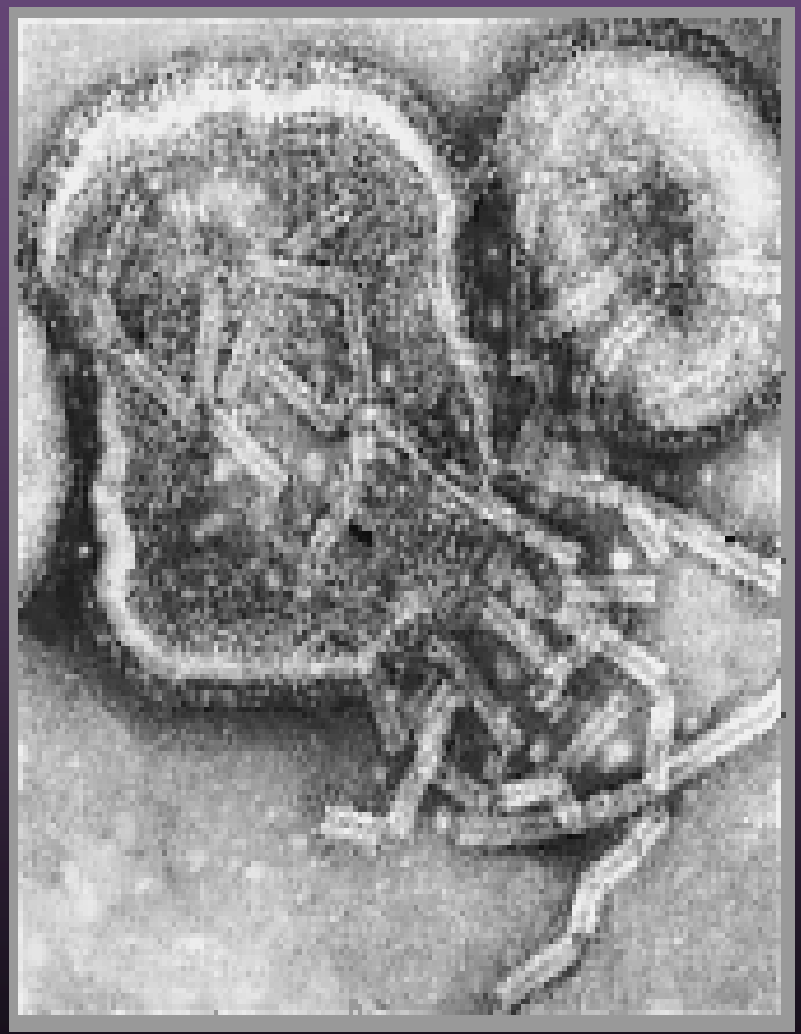
- **Killed Whole Virus**
  Not used today.
- **Live Virus**
  Attenuated strains were widely used in Russia but not elsewhere.
- **Virus Subunit**
  HA extracted from recombinant virus forms the basis of today's vaccines.
  For example, the WHO Recommendation for Influenza Vaccine, 1995-1996, contains two A strains and one B strain:-

A / Singapore / 6 / 86 (H1N1)
A / Johannesburg / 33 / 94 (H3N2)
B / Beijing / 84 / 93

Prevention

- Inactivated split/subunit vaccines are available against influenza A and B.
- The vaccine is normally trivalent, consisting of one A H3N2 strain, one A H1N1 strain, and one B strain.
- The strains used are reviewed by the WHO each year.
- The vaccine should be given to debilitated and elderly individuals who are at risk of severe influenza infection.
- Amantidine can be used as an prophylaxis for those who are allergic to the vaccine or during the period before the vaccine takes effect.

Parainfluenza Virus



- ssRNA virus
- enveloped,
- 5 serotypes: 1, 2, 3, 4a and 4b
- No common group antigen
- Closely related to Mumps virus

Clinical Manifestations

- **Croup (laryngotraheobroncitis) - most common manifestation of Parainfluenza virus infection. However other viruses may induce croup e.g. influenza and RSV.**

- **Other conditions that may be caused by Parainfluenza viruses include Bronchiolitis, Pneumonia, tracheobronchitis, Flu-like and Corza-like illnesses**

Laboratory Diagnosis

- Detection of Antigen - a rapid diagnosis can be made by the detection of Parainfluenza antigen from nasopharyngeal aspirates and throat washings

- Virus Isolation - virus may be readily isolated from nasopharyngeal aspirates and throat swabs.

- Serology - a retrospective diagnosis may be made by serology. CFT most widely used.

Management

- No specific antiviral chemotherapy available.
- Severe cases of croup should be admitted to hospital and placed in oxygen tents
- No vaccine is available

Respiratory Syncytial Virus (RSV)

- ssRNA enveloped virus
- belong to the genus Pneumovirus of the Paramyxovirus family
- Considerable strain variation exists, may be classified into subgroups A and B by monoclonal sera
- Both subgroups circulate in the community at any one time.

Clinical Manifestations

- Most common cause of severe lower respiratory tract disease in infants, responsible for 50-90% of Bronchiolitis and 5-40% of Bronchopneumonia.
- Other manifestations include croup (10% of all cases).
- In older children and adults, the symptoms are much milder: it may cause a corza-like illness or bronchitis.

Infants at Risk of Severe Infection

1. Infants with congenital heart disease - infants who were hospitalized within the first few days of life with congenital disease are particularly at risk.

2. Infants with underlying pulmonary disease - infants with underlying pulmonary disease, especially bronchopulmonary dysplasia, are at risk of developing prolonged infection with RSV.

3. Immunocompromized infants - children who are immunosuppressed or have a congenital immunodeficiency disease may develop lower respiratory tract disease at any age.

Laboratory Diagnosis

- Detection of Antigen - a rapid diagnosis can be made by the detection of RSV antigen from nasopharyngeal aspirates. A rapid diagnosis is important because of the availability of therapy

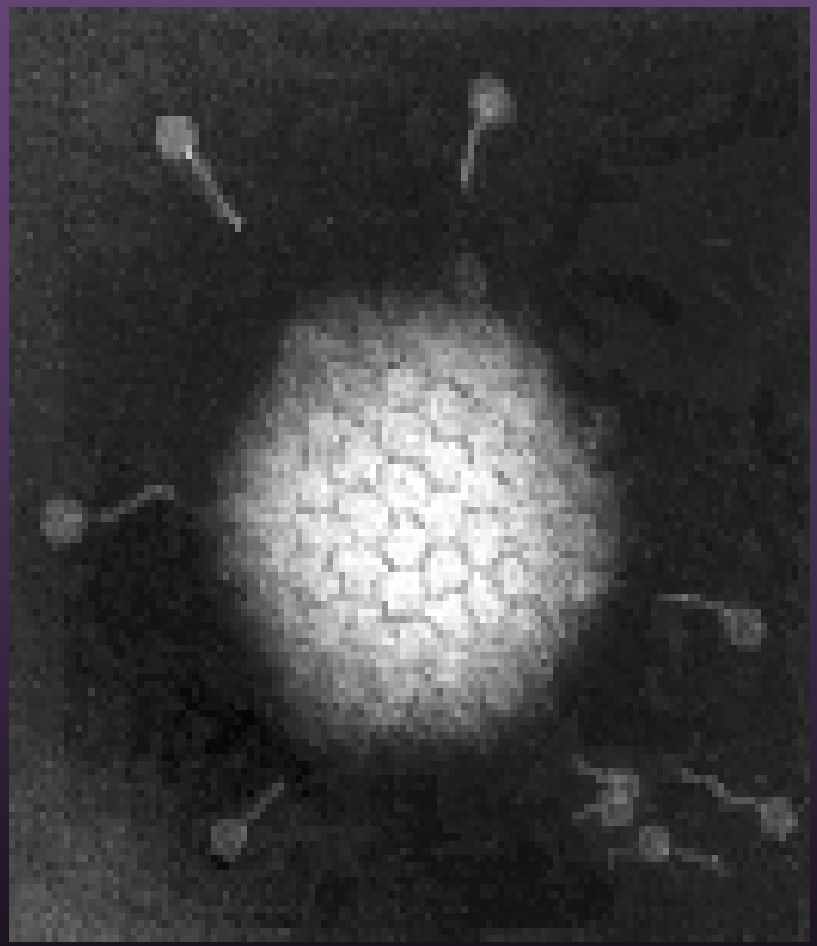
- Virus Isolation - virus may be readily isolated from nasopharyngeal aspirates. However, this will take several days.

- Serology - a retrospective diagnosis may be made by serology. CFT most widely used.

Treatment and Prevention

- Aerosolized ribavirin can be used for infants with severe infection, and for those at risk of severe disease.
- There is no vaccine available.
- RSV immunoglobulin can be used to protect infants at risk of severe RSV disease.

Adenovirus



- ds DNA virus
- non-enveloped
- At least 47 serotypes are known
- classified into 6 subgenera: A to F

Clinical Syndromes

1. **Pharyngitis 1, 2, 3, 5, 7**
2. **Pharyngoconjunctival fever 3, 7**
3. **Acute respiratory disease of recruits 4, 7, 14, 21**
4. **Pneumonia 1, 2, 3, 7**
5. **Follicular conjunctivitis 3, 4, 11**
6. **Epidemic keratoconjunctivitis 8, 19, 37**
7. **Petussis-like syndrome 5**
8. **Acute haemorrhaghic cystitis 11, 21**
9. **Acute infantile gastroenteritis 40, 41**
10. **Severe disease in AIDS and other immunocompromized patients 5, 34, 35**
11. **Meningitis 3, 7**

Laboratory Diagnosis

- Detection of Antigen - a rapid diagnosis can be made by the detection of adenovirus antigen from nasopharyngeal aspirates and throat washings.

- Virus Isolation - virus may be readily isolated from nasopharyngeal aspirates, throat swabs, and faeces.

- Serology - a retrospective diagnosis may be made by serology. CFT most widely used.

Treatment and Prevention

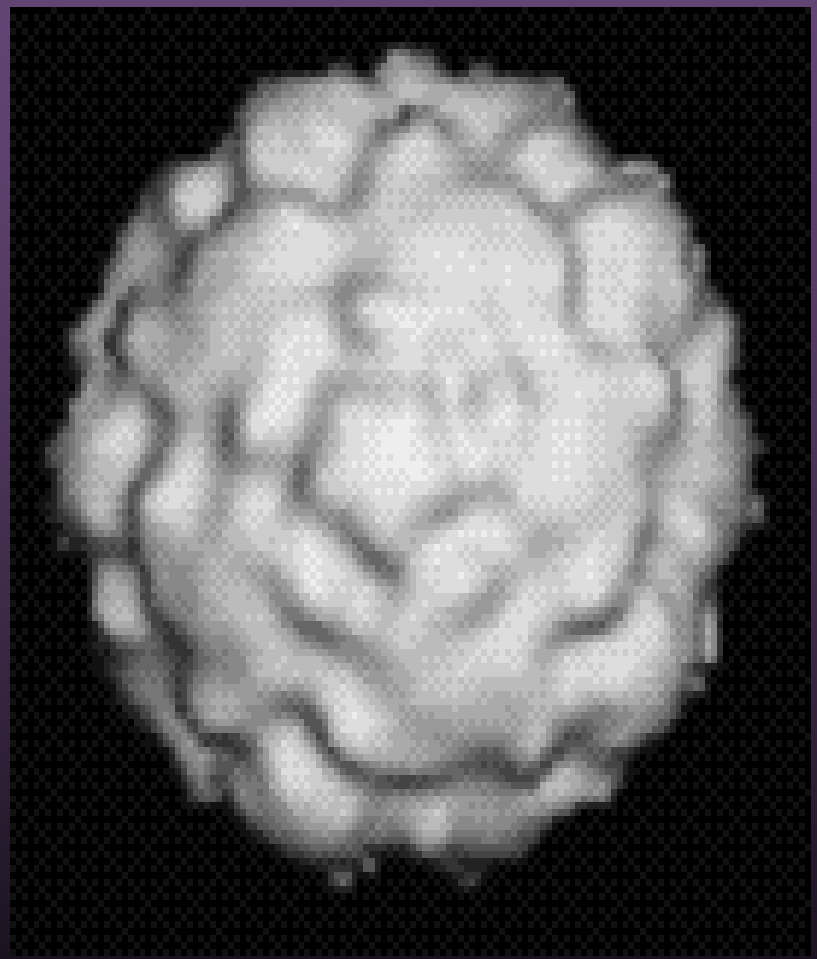
- There is no specific antiviral therapy

- A vaccine is available against Adult Respiratory Distress Syndrome. It consists live adenovirus 4, 7, and 21 in enterically coated capsules. It is given to new recruits into various arm forces around the world.

Common Cold Viruses

- Common colds account for one-third to one-half of all acute respiratory infections in humans
- Rhinoviruses are responsible for 30-50% of common colds, Coronaviruses 10-30%
- The rest are due to adenoviruses, enteroviruses, RSV, influenza, and Parainfluenza viruses, which may cause symptoms indistinguishable to those of rhinoviruses and coronaviruses

Rhinovirus



- ssRNA virus
- Belong to the Picornaviruses family
- ssRNA virus
- acid-labile
- at least 100 serotypes are known

Rhinovirus

- Clinical
  An inhalational infection of the URT. Incubation period is short: 1 to 3 days followed by headache, sore throat, fullness in the nose. The infection resolves in about a week.

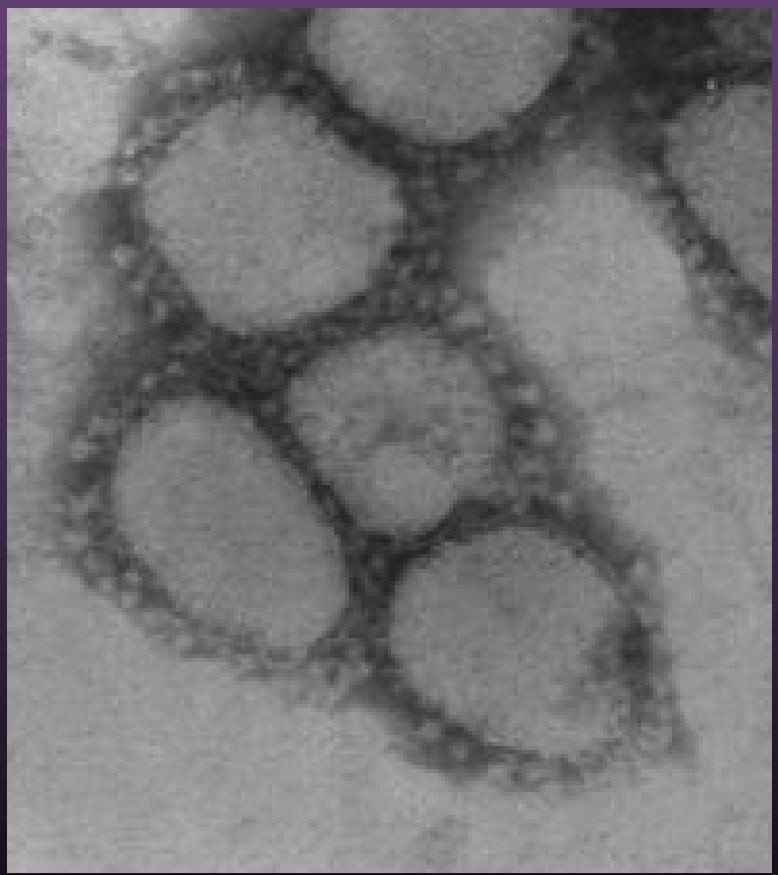
- Complications
  A cold may temporarily upset the mucosal cilia and predisposes to secondary invaders especially bacterial infections, eg. sinusitis (pneumococcus, haemophilus, etc) and bronchitis and possibly pneumonia. These may require antibiotic treatment.

Rhinovirus

- Epidemiology
  An infected person is infectious in the first two days of coryza. Colds are readily acquired from breathing room air from a room crowded with people. Wet cold weather does not cause colds, but may predispose to infection from other persons.

- Treatment
  No specific treatment but numerous symptomatic treatments are available.

Coronavirus



- ssRNA Virus
- Helical capsid with enveloped
- 2 serogroups: OC43 and 229E