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Rhinoviruses

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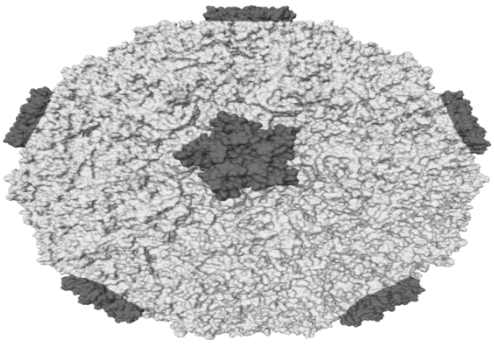
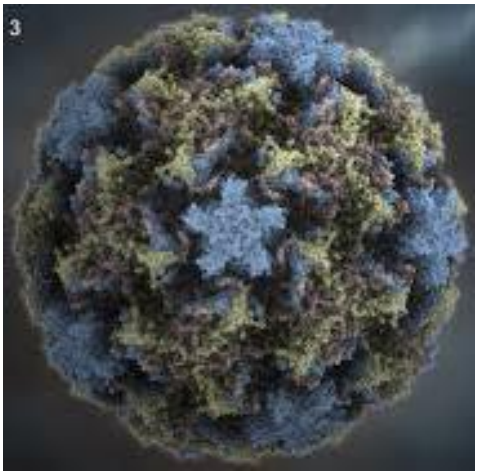
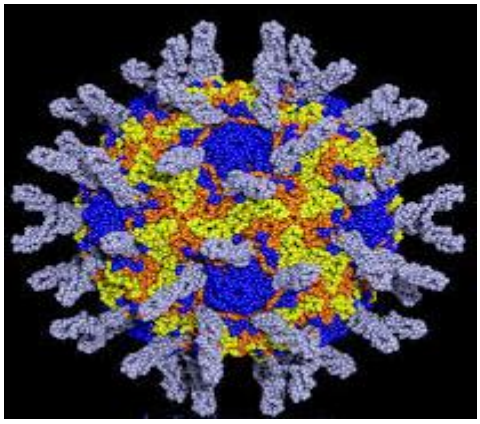
Introduction :-



Human rhinoviruses (HRVs) are icosahedral (30 nm in diameter) and nonenveloped with a (+) ssRNA genome of ~7100 bases. Belonging to the family Picornaviridae, genus Enterovirus, they are composed of 60 copies each of four capsid proteins, VP1 to VP4. In 1987, HRVs from clinical samples were serotyped into 100 strains . Recently, complete genome sequences of all known HRVs were determined. Phy3logenetic analyses grouped them into 3 species; 74 HRV-A, 25 HRV-B, and 6 HRV-C. Since then, many more rhinoviruses (mostly of type C) were identified in clinical specimens . Independent from this classification, HRV-A and HRV-B are divided into two groups based upon the receptors exploited for host cell attachment .





Virus Structure :-

- Simple single-stranded RNA viruses that are a cause of the common cold.
- Rhinovirus enters a cell after attaching to the Icam receptor. (IcAm)
- The positive-sense RNA is directly translated into a polyprotein, which is processed by a viral protease, resulting in the release of the functional proteins of the virus.
- A protein encoded by the virus copes the single-stranded RNA.
- The virus is released by lysing the host cell.

Genome characterization :-

- simple single-stranded RNA viruses that are a cause of the common cold.
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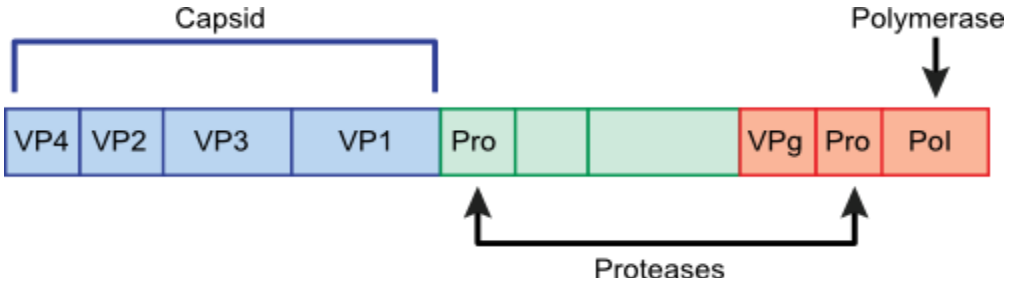
- The virus is released by lysing the host cell.
- Rhinovirus is part of the Picornaviridae family ("Pico" meaning small and "RNA" signifying that these are RNA viruses) The rhinoviral genome is composed of a single strand of positive-sense RNA (meaning it can be translated directly by the ribosome) enclosed in a small tetrahedral capsid . The single-stranded RNA is translated into a large polyprotein that is subsequently digested into about 10 proteins .



- This figure shows the genome of the virus .

Replication cycle :-

1. virus attach to host cell surface ICAM receptor then enter the endosome at low PH of endosome make uncoating virus and movement of single RNA into the cytoplsm.

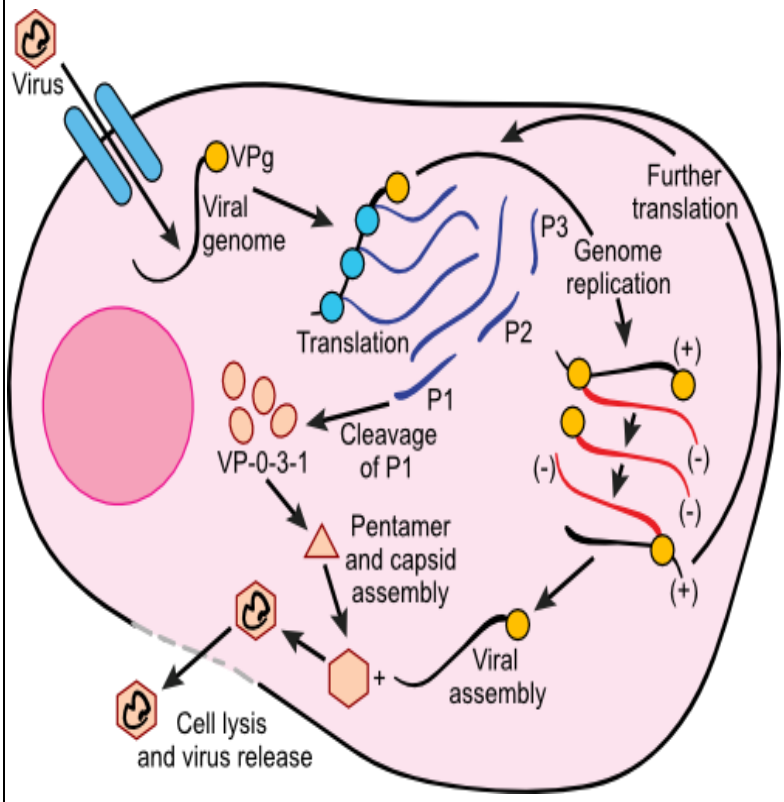
   * intercellular adhesion molecule (ICAM) , It's a protein that in humans is encoded by gene, ICAM-1 has been characterized as a site for the cellular entry of human rhinovirus .

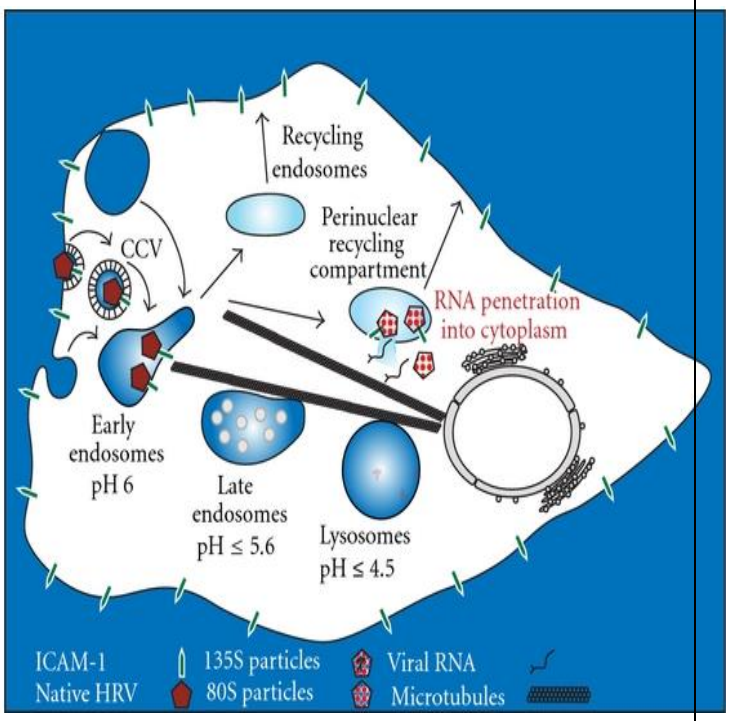
2. The cellular receptor triggers conformational changes when the virus capsid, eventually leading to a release of viral RNA into the cytoplasm.

3. Viral RNA forward by channel from capsid to the cytoplasm , then mRNA fool the ribosome to translate it into polyprotein .

4. The polyprotein breakdown for producing the protease and RNA polymerase .

5. Capsid protein assemble to make an intact particle then they will exits by cell lysis .





- The two figures show the replication cycle of rhinovirus.

Disease and pathogenicity :-

Rhinoviruses (Rhinos - nose "Greek") that can cause the common cold can infect the upper respiratory tract lasting for hours on fomites, but are sensitive to temperature and to low pH. Thus, they do not spread to the lower respiratory tract since they replicate best at a few degrees below normal body temperature. Although the most common route of infection is the nose, virus can also enter via the mouth and the eyes. There is usually no gastrointestinal involvement because of the acid lability of the virus. The virus is therefore not spread from the intestinal tract.

- Rhinovirus infections usually occur at times of increased human contact, that is in the colder months of the year.
- Many different serotypes circulate simultaneously. Frequently children become infected and then pass the virus to adults after an incubation time of about two or three days.
- They can also be spread by fomites such as hands and other forms of direct contact. Rhinoviruses are spread easily through person-to-person contact.
- When a child with a rhinovirus infection has a runny nose, nasal secretions get onto her hands and from there onto tables, toys, and other surfaces. Your child might touch the hands or skin of another youngster or toys that have been contaminated by the virus and then touch her own eyes or nose, infecting herself. She might breathe in airborne viruses spread by a sneeze or cough.

clinical features :-

Symptoms of a common cold usually appear about one to three days after exposure to a cold-causing virus. Signs and symptoms of a common cold may include:

- Runny or stuffy nose
- Itchy or sore throat
- Cough
- Congestion
- Slight body aches or a mild headache
- Sneezing
- Watery eyes
- Low-grade fever (101°F–102°F or 38.3°C–38.9°C)
- Mild fatigue

The incubation period for a rhinovirus infection is usually 2 to 3 days. Symptoms generally persist for 10 to 14 days, sometimes less.

The discharge from your nose may become thicker and yellow or green in color as a common cold runs its course. What makes a cold different from other viral infections is that you generally won't have a high fever. You're also unlikely to experience significant fatigue from a common cold.

If you have these seek medical attention , you should go to hospital

For adults :

- Fever of 103 F (39.4 C) or higher
- Fever accompanied by sweating, chills and a cough with colored phlegm
- Significantly swollen glands
- Severe sinus pain

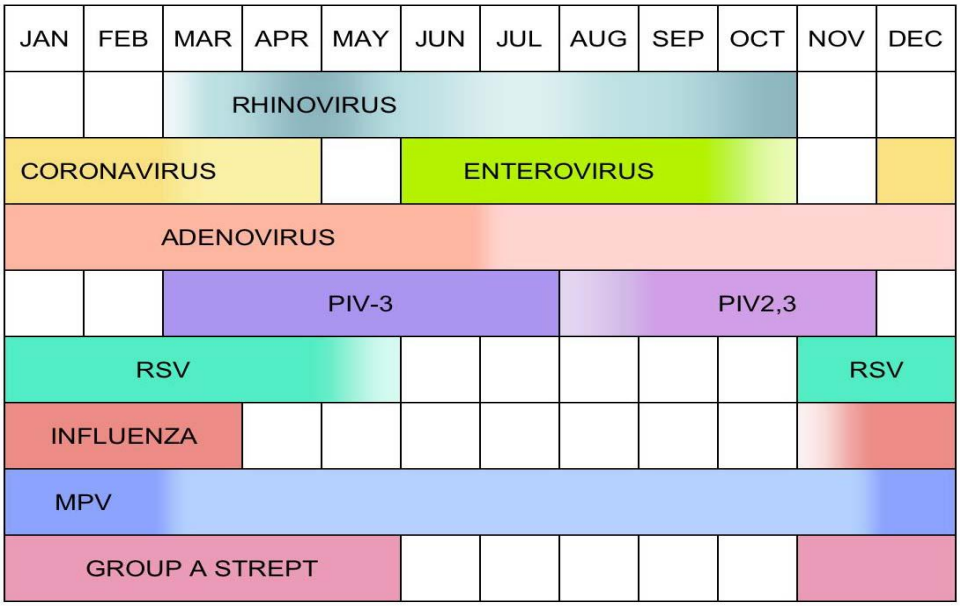
For children : in general, children are sicker with a common cold than adults are and often develop complications, such as ear infections. Your child doesn't need to see the doctor for a routine common cold. But seek medical attention right away if your child has any of the following signs or symptoms:

- Fever of 100.4 F (38 C) in newborns up to 12 weeks
- Fever that rises repeatedly above 104 F (40 C) in a child of any age
- Signs of dehydration, such as urinating less often than usual
- Not drinking adequate fluids
- Fever that lasts more than 24 hours in a child younger than 2
- Fever that lasts more than three days in a child older than 2
- Vomiting or abdominal pain
- Unusual sleepiness
- Severe headache
- Stiff neck
- Difficulty breathing
- Persistent crying
- Ear pain
- Persistent cough

When your child has a cold, make sure she gets enough rest. She should drink extra fluid if she has fever. If she is uncomfortable, talk to your pediatrician about giving her acetaminophen to reduce her fever. Don’t give her over-the-counter cold remedies or cough medicines without first checking with your doctor. These over-the-counter medicines do not kill the virus and, in most circumstances, do not help with the symptoms .

Epidemiology :-

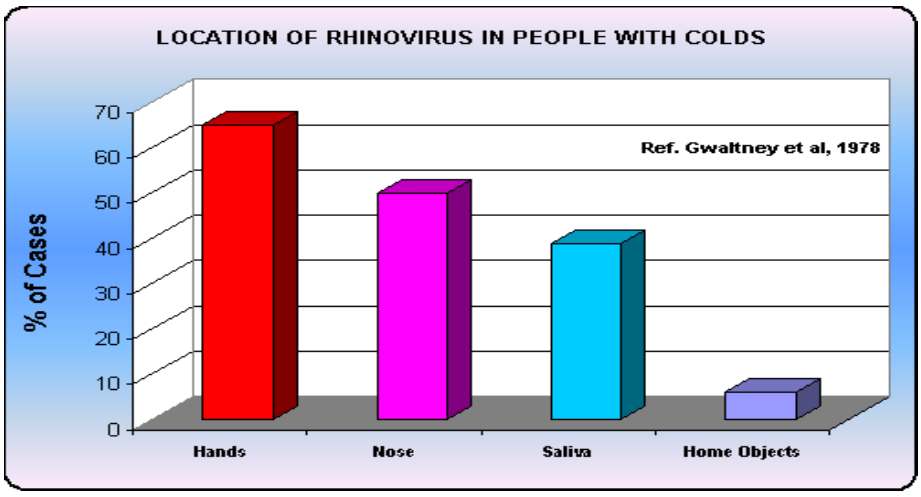
Rhinovirus cause 70% of common cold , the virus has been found one of the most common illnesses to man 35 to 50% from the number of the common cold , it become more active in low temperatures (32°C) . the figure shows the



T

- This figure shows the common viruses prevalent.

A. via aerosols of respiratory droplets and from contaminated surfaces .
B. direct person-to-person contact .



- This figure shows the location of the virust.

Laboratory Diagnosis of Rhinoviruses Infection :-

Usually, a common does not require laboratory investigation. If required, the diagnosis is generally made by the isolation of the virus in a sensitive cell culture. Nasal washings are the best specimens and should be collected early in the disease when maximal titres of virus is excreted .

1-Virus Isolation :

Rhinoviruses are best isolated in human embryo lung fibroblasts eg. MRC-5, or a sensitive continuous cell line such as Ohio HeLa. Samples should be inoculated into triplicates and rolled at 33oC. The virus CPE, which consists of the rounding of cells similar to that induced by enteroviruses should appear within 8 days of inoculation. The identity can be confirmed by acid lability tests. (pH3)

2-Antigen Detection :

For a investgating the precens of rhinovirus one of different ways can be used such as immunofluorescence or immunoperoxidase, these methods are serotype specific.

A highly conserved way among different serotypes, is to use An immunoassay by using antibody directed against the 3C protease of rhinovirus.

3-Nucleic Acid Detection :

RT-PCR is the standard process to detect rhinoviruse at the Laboratory because it is more sensitive, faster, and easier to do than the old methods. The 5′-NTR of the rhinoviral genomic RNA has several short stretches of sequence that are almost completely conserved among all 100 serotypes.

Recently, a molecular typing assay was developed for rapid identification of individual rhinovirus serotypes or strains in original clinical samples. This assay uses sensitive pan-HRV primers and seminested PCR to amplify a 260-bp variable region in the 5′-NTR of the rhinoviral genome for sequence determination. The serotype or strain is then determined by phylogenetic comparisons of the resulting sequence to homologous reference sequences of 100 known serotypes. In situ hybridization using rhinovirus-specific probes has been used to locate the anatomic

sites and cell types that support viral replication in the airways of infected subjects, making it useful to study pathogenesis.

4-Serologic Assays

The only way a serological assay is done on Rhinovirus is if the serotype for the infiction virus in known, Rhinovirus neutralizing antibody in human serum and nasal washes is measured by mixing the test material with a small inoculum (3 to 30 TCID50) of virus to detect the relatively low concentration of antibody in these specimens.

Treatment :-

- There are some medicines which decrease the activity of Rhinovirus include :

1- Antihistamines .

2- Anticholinergics .

3- α -Adrenergic agonists .

4- Steam inhalation .

5- Mast cell stabilizers .

6-Non-steroidal anti-inflammatory drugs .

7- Vitamin C .

8- Zinc .

9- Specific antiviral drugs .

❖ Antihistamines:

First generation antihistamines have achieved the most favourable results in both naturally occurring and experimentally induced common colds. Oral doxylamine succinate, clemastine fumarate, and chlorpheniramine maleate significantly reduced rhinorrhoea, sneezing, and weight of nasal secretions but had minimal effects on other cold symptoms. The effective dose varied depending on the compound studied.

❖ Anticholinergics :

Intranasal ipratropium bromide spray significantly reduced nasal drainage and sneezing in studies of naturally occurring colds. The optimum dose used in these studies was 84 μg (two sprays of a 0.06% solution in buffered saline solution) in each nostril three to four times daily. The main side effects included nasal dryness, occasional epistaxis, and headache. The duration of relief of rhinorrhoea was not well defined but thought to be over three hours. These data suggest that inhaled anticholinergics could be useful for the average cold.

❖ α Adrenergic agonists:

These substances are potent decongestants and have been long used for treating the common cold. Both oral and nasal forms proved effective in natural and experimental cold models. These drugs are not without hazards, however, and prolonged use can lead to a rebound effect (rhinitis medicamentosa). Care needs to be taken in patients with hypertension because of the sympathomimetic effect of these drugs.

❖ Steam inhalation:

Breathing in steam from a bowl or jug is widely believed to ease the soreness and discomfort of a cold. Nasal hyperthermia (420-440C) administered for natural or experimental common colds resulted in subjective improvement of symptoms and objective increased nasal patency in two studies from Israel and the United Kingdom. Attempts to reproduce these findings in the United States were unsuccessful. Possible explanations given for this discrepancy included variations in the technique of administering steam and different strains of viruses involved.

It is a cheap and safe treatment for patients who find it helpful Steam inhalation is a method of introducing warm, moist air into the lungs via the nose and throat for therapeutic benefit. Essential oils are often added to provide additional relief.

Ancient Egyptians recognized the good therapeutic effects of inhalation therapy through the use of public baths.

Steam inhalation has since become a simple and effective home remedy for various health issues.

❖ Mast cell stabilizers :

Nedocromil and sodium cromoglycate administered intranasally or by inhalation have been shown to reduce the severity of naturally and experimentally induced rhinovirus upper respiratory tract infections. These drugs prevent the release of chemical mediators in response to infection and down regulate the intracellular adhesion molecule type 1 (the receptor for rhinovirus) in the inflamed airway epithelium. However, they have no effect on the frequency of viral shedding or the

serological response to infection. Even though the safety profile of these drugs is excellent, they have not yet been evaluated in large epidemiological studies .

- ❖ Non-steroidal anti-inflammatory drugs:

Aspirin as well as other non-steroidal anti-inflammatory drugs has been suggested to increase nasal symptoms and virus shedding and decrease serum neutralising antibody response in volunteers infected with rhinovirus. More recently, the cyclo-oxygenase inhibitor naproxen was found to reduce headache, malaise, and cough without altering virus shedding or antibody responses in experimentally induced rhinovirus colds.

- ❖ Vitamin C:

During the past three decades numerous studies have assessed the potential role of vitamin C in the treatment or prevention of common cold. In 1975 Chalmers reviewed the available literature and published a meta-analysis concluding that "the minor benefits of questionable validity are not worth the potential risk, no matter how small that might be." A more recent analysis of the same review by Hemila pointed out several errors and suggested that vitamin C significantly decreases the duration of episodes and the severity of symptoms of the common cold by an average of 23%. The best dose of vitamin C for the treatment of the common cold was not determined, but the maximal benefit was not thought to be obtained with 1 g/day of the vitamin .

- ❖ Zinc:

The exact mechanism through which zinc affects the common cold remains to be determined. One hypothesis is that zinc prevents rhinovirus from binding to the respiratory intracellular adhesion molecule type 1 on the epithelium, thus blocking viral entry into the cells. Other hypotheses include inhibition of viral capsid protein synthesis, a membrane stabilising effect, inhibiting prostaglandin metabolites, and increasing production of interferon .

- ❖ Specific antiviral drugs:

Influenza virus infections have been successfully treated with drugs such as amantadine, rimantadine, and zanamivir. On the other hand, several studies using

antiviral drugs against rhinovirus colds showed no appreciable clinical benefit, even though in vitro studies gave promising results. These drugs share a common mechanism of action, binding to specific hydrophobic pockets in the virion capsid and inhibiting virion attachment or uncoating. The main obstacles for the development of effective antiviral drugs for the common cold include the wide variety of causative agents, mutant strains, and development of resistance. As with interferon, capsid binding drugs have no effect when given after symptoms have developed, and the local adverse effects of intranasal formulations may mask some of their beneficial effects.

Prevention :-

Rhinovirus infections are associated with substantial morbidity and economic cost.

The available common cold remedies are of limited utility and specific antiviral approaches have been unsuccessful.

Viral contamination of the hands appears to play an important role in the transmission of rhinovirus from person-to-person.

Interruption of this step in transmission presents a potential target for intervention. Initial studies demonstrated that the common cold could be prevented by treatment of hands with iodine.

Inactivation of the rhinoviruses by acid is well known and a survey of organic acids considered safe for consumer use revealed that salicylic acid and pyroglutamic acid have potent virucidal activity for the rhinoviruses that persists for several hours after application to the hands.

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