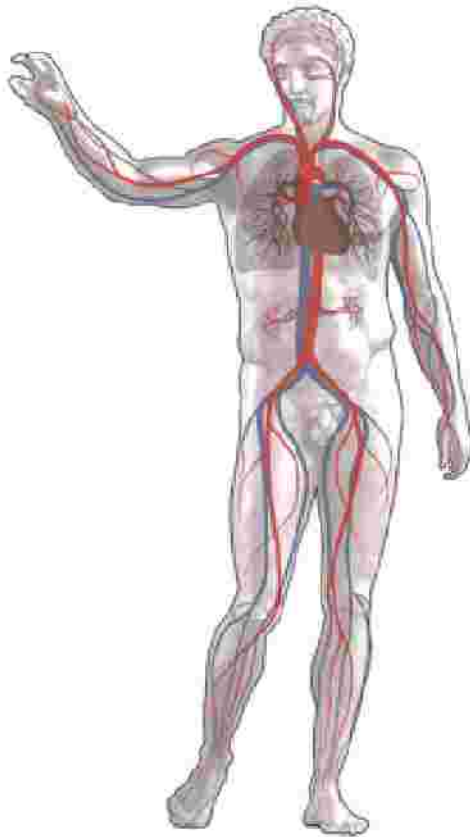


Encephalitis and Meningitis: Pathogens, Pathogenesis or
Symptoms

Microorganisms that can be spread via the bloodstream.
Pathogenesis & Prevention



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Encephalitis

- Encephalitis is an acute inflammation of the brain.
- 7.4 cases per 100,000 population in Western countries, 6.34 per 100,000 population and tropical countries per year.
- Common symptoms include headache, fever, confusion, drowsiness, and fatigue with more serious symptoms ranging from seizures/convulsions, tremors, hallucinations, and memory problems.
- Several common causes of encephalitis are the Japanese encephalitis virus, the West Nile Virus, and Cryptococcus neoformans.

Meningitis

- Meningitis is inflammation of the protective membranes covering the brain and the spinal cord (meninges)
- Bacterial infections occur in 3 people per 100,000 and 10.9 per 100,000 for viral infections in Western countries.
- More common in places where people live together for the first time.
- Typical symptoms consist of nuchal rigidity, sudden high fever, and altered mental status.
- Streptococcus pneumoniae, Neisseria meningitidis, and LCMV are common microbes that lead to meningitis.

Japanese Encephalitis Virus

- Mosquito-borne, incubation period of 5 to 15 days, but only 1 in 250 infections develop into encephalitis
- Signs which develop during the acute encephalitic stage include neck rigidity, cachexia, hemiparesis, convulsions and a raised body temperature between 38 and 41 degrees Celsius
- Generally much higher in children. Transplacental spread has been noted. Lifelong neurological defects such as deafness, emotional ability and hemiparesis may occur in those who have had central nervous system involvement
- Increased microglial (immune cells of the CNS) activation follows JEV infection, Activated microglia secrete cytokines, such as interleukin-1 (IL-1) and tumor necrosis factor alpha (TNF- α), which can cause toxic effects in the brain, as well as neurotoxins, excitatory neurotransmitters, prostaglandin, reactive oxygen, and nitrogen species
- In a nonregenerating organ such as brain, a dysregulated innate immune response would be deleterious.

West Nile Virus

- Incubation period is usually between 2 to 15 days
- Mosquitoes which are the prime vector, with birds being the most commonly infected animal and serving as the prime reservoir host. Also found in various species of ticks, mammals, reptiles, and amphibians
- Not all susceptible hosts develop sufficient levels to transmit the disease to uninfected mosquitoes
- 80% of West Nile virus infections in humans are subclinical, causing no symptoms
- Most common symptom is the west nile fever, but 1% of the cases result in neurological disease, such as west nile encephalitis
- Similar symptoms to other viral encephalitis with fever, headaches, and altered mental status, however, there is also muscular weakness (30-50%), with lower motor neuron symptoms, flaccid

Lymphocytic Choriomeningitis Virus

- Spread by the common mouse, as mice can become chronically infected by maintaining the virus in their blood, as well as vertical transmission.
- Humans can be infected through inhalation, ingestion, and exposure to open cuts and wounds
- Onset typically occurs 1 to 2 weeks after exposure, and the initial phase's common symptoms include fever, lack of appetite, headache, muscle aches, malaise, nausea, and/or vomiting.
- Meningitis or encephalitis occurs in the second phase, several days after the recovery of the initial phase.
- Pathological findings during the first stage consist of leukopenia and thrombocytopenia. During the second phase, typical findings include elevated protein levels, increased leukocyte count, or a decrease in glucose levels of the cerebrospinal fluid.

Streptococcus pneumoniae

- Gram-positive, alpha-hemolytic, aerotolerant anaerobic member of the [genus Streptococcus](#)
- Normally found in the [nasopharynx](#) of 5-10% of healthy adults, and 20-40% of healthy children
- The organism causes many types of pneumococcal infections other than pneumonia. These include acute sinusitis, otitis media, meningitis, bacteremia, sepsis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, and brain abscess
- *S. pneumoniae* is one of the most common causes of bacterial meningitis in adults and young adults, along with [Neisseria meningitidis](#), and is the leading cause of bacterial meningitis in adults in the USA
- Attaches to nasopharyngeal cells through interaction of bacterial surface [adhesins](#). This normal colonization can become infectious if the organisms are carried into areas such as the Eustachian tube or nasal sinuses where it can cause otitis media and sinusitis.
- The organism's [polysaccharide](#) capsule makes it resistant to phagocytosis, and if there is no pre-existing anticapsular antibody, alveolar macrophages cannot adequately kill the pneumococci. The organism spreads to the blood stream and is carried to the meninges, joint spaces, bones, and peritoneal cavity, and may result in meningitis, brain abscess, septic arthritis, or osteomyelitis.
- Has several virulence factors: the polysaccharide capsule, that help it evade a host's immune system, a pneumococcal surface proteins that inhibit complement-mediated opsonization, and secretion of IgA1 protease that will destroy secretory IgA produced by the body and mediates its attachment to respiratory mucosa.

Neisseria meningitidis

- referred to as meningococcus, appears as a Gram-negative [diplococcus](#) and test positive for cytochrome c oxidase
- exists as normal flora in the [nasopharynx](#) of up to 5-15% of adults, infects the host cell by sticking to it using [Trimeric Autotransporter Adhesins](#)
- Meningococci only infect humans, and is the only form of bacterial meningitis known to occur epidemically
- N. meningitidis exploits host cell signaling pathways to promote its uptake by host cells, induced by the [type IV pili](#), which are the main means of meningococcal adhesion onto host cells. Formation of [microvilli](#)-like structures at the site of the bacterial-cell interaction then occurs, which trigger the internalization of the bacteria into host cells.
- A major consequence of these signaling events is a reorganization of the [actin cytoskeleton](#), which leads to the formation of membrane protrusions, engulfing bacterial pathogens into intracellular [vacuoles](#). Efficient internalization of N. meningitidis also requires the activation of an alternative signaling pathway coupled with the activation of the [tyrosine kinase](#) receptor [ErbB2](#). Beside Type IV pili, other outer membrane proteins may be involved in other mechanisms of bacterial internalization into cells
- Initially produces general symptoms like fatigue, it can rapidly progress from fever, headache and neck stiffness to coma and death, along with a notable non-blanching purpuric rash

Brief Introduction of Bacteria found in Bloodstream.

- Several types of bacteria live on the surface of the skin or colonize the moist linings of the urinary tract, lower digestive tract, and other internal surfaces. These bacteria are normally harmless as long as they are kept in check by the body's natural barriers and the immune system.
- People in good health with strong immune systems rarely develop bacteremia. However, when bacteria are introduced directly into the circulatory system, especially in a person who is ill or undergoing aggressive medical treatment, the immune system may not be able to cope with the invasion, and symptoms of bacteremia may develop.
- ↳ Common immediate causes of bacteremia include:
 - drainage of an abscess, including an abscessed tooth
 - urinary tract infection, especially in the presence of a bladder catheter
 - decubitus ulcers (pressure sores)
 - intravenous procedures using unsterilized needles, including IV drug use
 - prolonged IV needle placement

General Pathogenesis and Prevention

- Bacteremia is diagnosed by culturing the blood for bacteria. Samples may need to be tested several times over several hours. Blood analysis may also reveal an elevated number of white blood cells. Blood pressure is monitored closely; a decline in blood pressure may indicate the onset of septic shock.
- Bacteremia may cause no symptoms, but may be discovered through a blood test for another condition. In this situation, it may not need to be treated, except in patients especially at risk for infection, such as those with heart valve defects or whose immune systems are suppressed

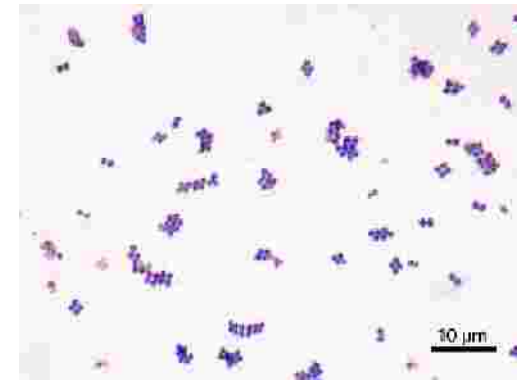
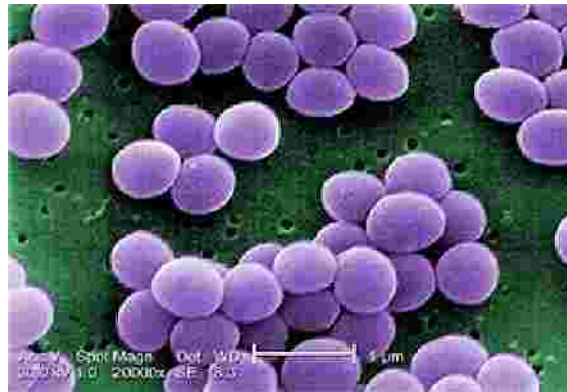
- Prognosis

Prompt antibiotic therapy usually succeeds in clearing bacteria from the bloodstream. Recurrence may indicate an undiscovered site of infection. Untreated bacteria in the blood may spread, causing infection of the heart (endocarditis or pericarditis) or infection of the covering of the central nervous system (meningitis).

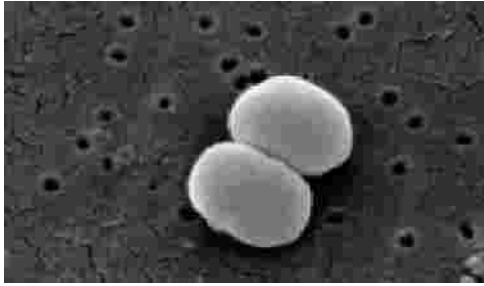
- Prevention

Bacteremia can be prevented by preventing the infections which often precede it. Good personal hygiene, especially during viral illness, may reduce the risk of developing bacterial infection. Treating bacterial infections quickly and thoroughly can minimize the risk of spreading infection. During medical procedures, the burden falls on medical professionals to minimize the number and duration of invasive procedures, to reduce patients' exposure to sources of bacteria when being treated, and to use scrupulous technique.

S. aureus



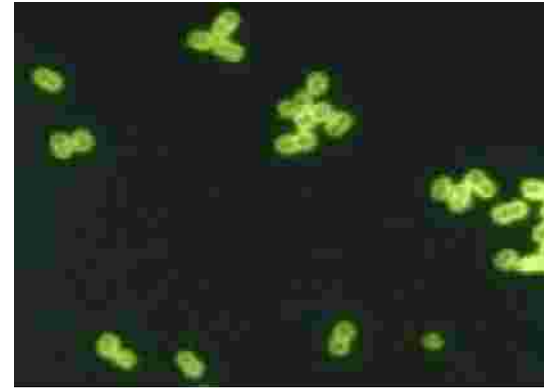
- *S. aureus* is the most common species of staphylococcus to cause Staph infections and is a successful pathogen due to a combination of nasal carriage and bacterial immuno-evasive strategies.
- *S. aureus* can cause a range of illnesses, from minor skin infections, such as pimples, impetigo, boils (furuncles), cellulitis folliculitis, carbuncles, scalded skin syndrome, and abscesses, to life-threatening diseases such as pneumonia, meningitis, osteomyelitis, endocarditis, toxic shock syndrome (TSS), bacteremia, and sepsis.
- *S. aureus* infections can spread through contact with pus from an infected wound, skin-to-skin contact with an infected person by producing hyaluronidase that destroys tissues, and contact with objects such as towels, sheets, clothing, or athletic equipment used by an infected person. Deeply penetrating *S. aureus* infections can be severe. Prosthetic joints put a person at particular risk of septic arthritis, and staphylococcal endocarditis (infection of the heart valves) and pneumonia. *S. aureus* can host phages, such as Panton-Valentine leukocidin, that increase its virulence.
- The treatment of choice for *S. aureus* infection is penicillin



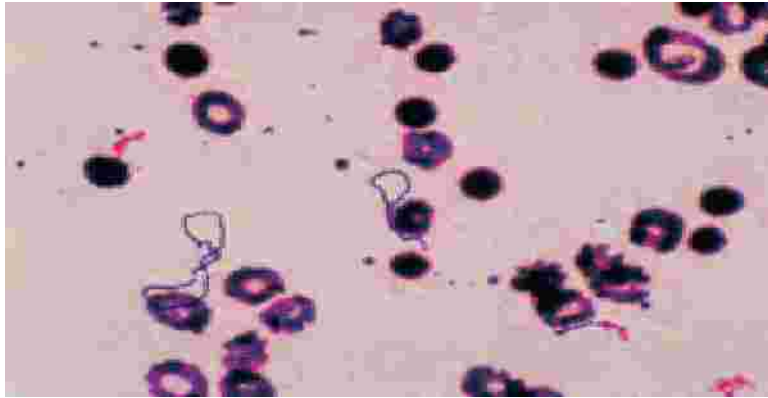
S. epidermidis

- S. epidermidis causes biofilms to grow on plastic devices placed within the body. This occurs most commonly on intravenous catheters and on medical prostheses.
- Infection can also occur in dialysis patients or anyone with an implanted plastic device that may have been contaminated.
- Another disease it causes is endocarditis. This occurs most often in patients with defective heart valves. In some other cases, sepsis can occur in hospital patients.
- Antibiotics are largely ineffective in clearing biofilms. The most common treatment for these infections is to remove or replace the infected implant, though in all cases, prevention is ideal. The drug of choice is often vancomycin, to which rifampin or aminoglycoside can be added. Hand washing has been shown to reduce the spread of infection.

S. pneumoniae

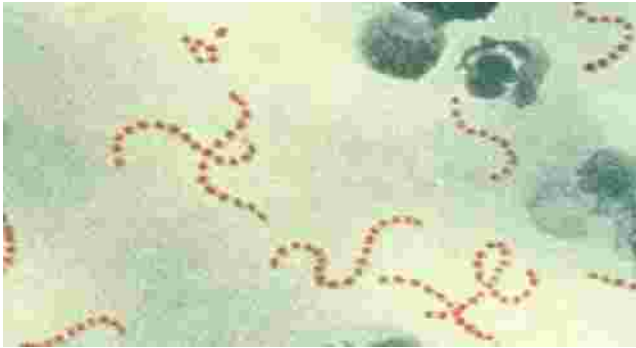


- The organism causes many types of pneumococcal infections other than pneumonia. These invasive pneumococcal diseases include acute sinusitis, otitis media, meningitis, bacteremia, sepsis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, and brain abscess.
- S. pneumoniae is one of the most common causes of bacterial meningitis in adults and young adults, along with Neisseria meningitidis, and is the leading cause of bacterial meningitis in adults in the USA. It is also one of the top two isolates found in ear infection, otitis media
- Diagnosis is generally made based on clinical suspicion along with a positive culture from a sample from virtually any place in the body. S. pneumoniae is, in general, optochin sensitive, although optochin resistance has been observed.
- Penicillin-resistant strains are more likely to be resistant to other antibiotics. Atromentin and leucomelone possess antibacterial activity.



S. viridans

- The organisms are most abundant in the mouth, and one member of the group, *S. mutans*, is the etiologic agent of dental caries. Others may be involved in other mouth or gingival infections.
- If they are introduced into the bloodstream, they have the potential of causing endocarditis, particularly in individuals with damaged heart valves. They are the most common causes of subacute bacterial endocarditis.
- Viridans streptococci have the unique ability to synthesize dextrans from glucose, which allows them to adhere to fibrin-platelet aggregates at damaged heart valves. This mechanism underlies their ability to cause subacute valvular heart disease following their introduction into the bloodstream (e.g., following tooth extraction).



S. pyogenes

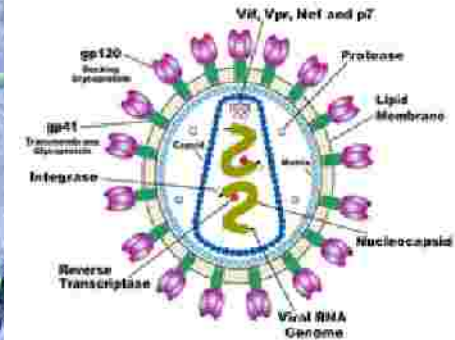
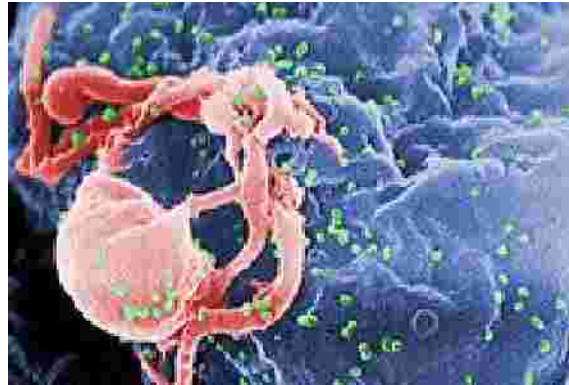
- S. pyogenes is the cause of many important human diseases, ranging from mild superficial skin infections to life-threatening systemic diseases. Infections typically begin in the throat or skin. Examples of mild S. pyogenes infections include pharyngitis ("strep throat") and localized skin infection ("impetigo"). Erysipelas and cellulitis are characterized by multiplication and lateral spread of S. pyogenes in deep layers of the skin. S. pyogenes invasion and multiplication in the fascia can lead to necrotizing fasciitis, a potentially life-threatening condition requiring surgical treatment.
- Infections due to certain strains of S. pyogenes can be associated with the release of bacterial toxins. Throat infections associated with release of certain toxins lead to scarlet fever. Other toxigenic S. pyogenes infections may lead to streptococcal toxic shock syndrome, which can be life-threatening.
- S. pyogenes can also cause disease in the form of postinfectious "nonpyogenic" (not associated with local bacterial multiplication and pus formation) syndromes. These autoimmune-mediated complications follow a small percentage of infections and include rheumatic fever and acute postinfectious glomerulonephritis. Both conditions appear several weeks following the initial streptococcal infection. Rheumatic fever is characterised by inflammation of the joints and/or heart following an episode of streptococcal pharyngitis. (Acute glomerulonephritis, inflammation of the renal glomerulus, can follow streptococcal pharyngitis or skin infection.)
- the treatment of choice is penicillin and the duration of treatment is well established as being 10 days minimum. No vaccines are currently available to protect against S. pyogenes infection for prevention.

Viruses spread via the Bloodstream

Cell type Associated	DNA Viruses	RNA Viruses
Lymphocytes	Epstein-Barr Virus, cytomegalovirus, hepatitis B virus, JC virus, BK virus	Mumps, measles, rubella, HIV
Monocytes- macrophages	Cytomegalovirus	Poliovirus, HIV, measles virus
Neutrophils		Influenza virus
RBC	Parvovirus B19	Colorado tick fever virus
None (free in plasma)		Togavirus, picornavirus

HIV

(Human immunodeficiency syndrome)

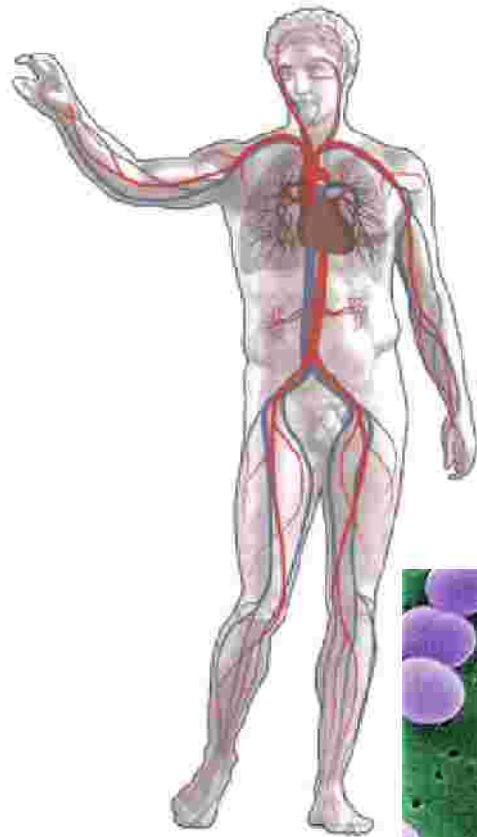
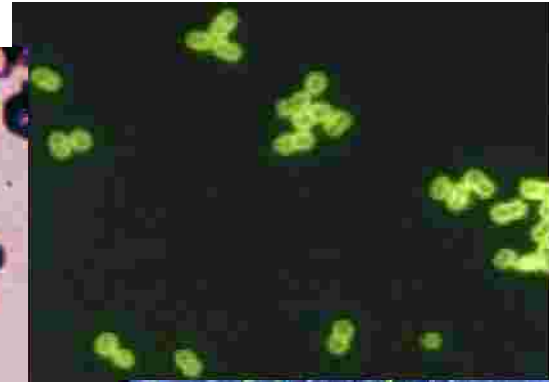
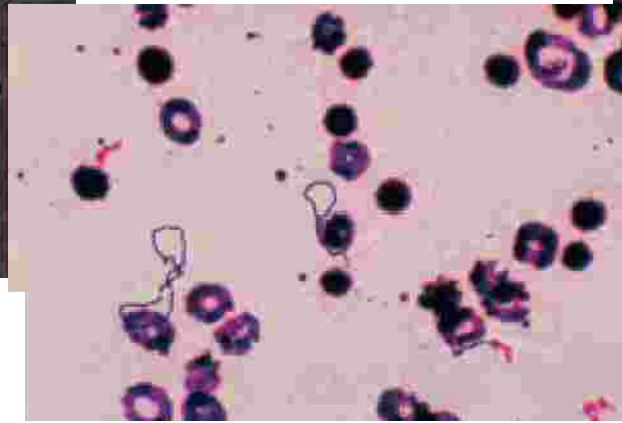
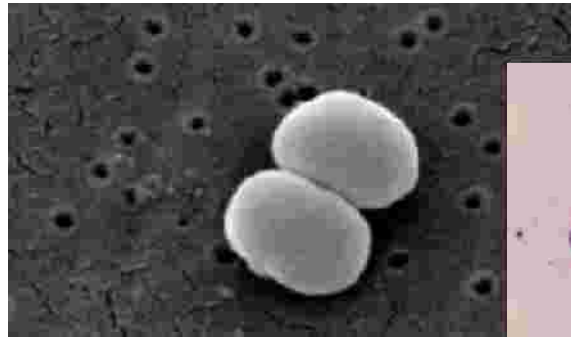


- a lentivirus (a member of the retrovirus family) that causes acquired immunodeficiency syndrome (AIDS), a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive.
- HIV infects vital cells in the human immune system such as helper T cells (specifically CD4+ T cells), macrophages, and dendritic cells.
- HIV infection leads to low levels of CD4+ T cells through three main mechanisms: First, direct viral killing of infected cells; second, increased rates of apoptosis in infected cells; and third, killing of infected CD4+ T cells by CD8 cytotoxic lymphocytes that recognize infected cells. When CD4+ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections.
- Many HIV-positive people are unaware that they are infected with the virus. For example, in 2001 less than 1% of the sexually active urban population in Africa have been tested and this proportion is even lower in rural populations. Furthermore, in 2001 only 0.5% of pregnant women attending urban health facilities are counselled, tested or receive their test results. Again, this proportion is even lower in rural health facilities [

EBV (Epstein–Barr virus)



- The Epstein–Barr virus (EBV), also called human herpesvirus 4 (HHV-4), is a virus of the herpes family, and is one of the most common viruses in humans.
- It is best known as the cause of infectious mononucleosis (glandular fever). It is also associated with particular forms of cancer, such as Hodgkin's lymphoma, Burkitt's lymphoma, nasopharyngeal carcinoma, and central nervous system lymphomas associated with HIV.
- There is evidence that infection with the virus is associated with a higher risk of certain autoimmune diseases, especially dermatomyositis, systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, and multiple sclerosis. EBV infects B cells of the immune system and epithelial cells. Infection with EBV occurs by the oral transfer of saliva and genital secretions.
- Once the virus's initial lytic infection is brought under control, EBV latently persists in the individual's B cells for the rest of the individual's life.



Thank you!

