

1- Epstein-Barr Virus and Parvoviruses B19

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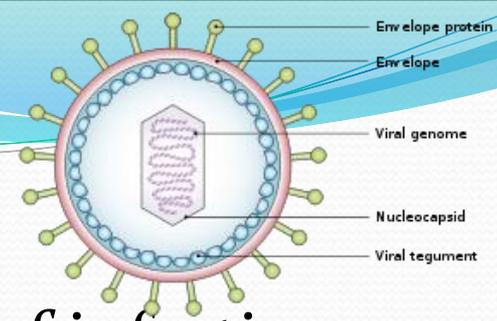
Objectives

- Describe the virology, epidemiology, pathogenesis, clinical presentation and management of Epstein-Barr Virus
- Describe the virology, epidemiology, pathogenesis, clinical presentation and management of Parvovirus B19



Epstein-Barr Virus (EBV)

Virology



- Epstein-Barr virus is the etiologic agent of infectious mononucleosis and African Burkitt's lymphoma
- Its complete nucleotide sequence of 172 kbp is smaller than other herpes viruses
- The virus is approximately 120 nm to 180 nm in diameter and is composed of a double helix of DNA wrapped in a protein capsid. The capsid is surrounded by a tegument made of protein, which in turn is surrounded by an envelope made from lipids. The viral envelope contains glycoproteins, which are essential to infection of the host cell
- In vivo, EBV is tropic for both human B lymphocytes and epithelial cells

History



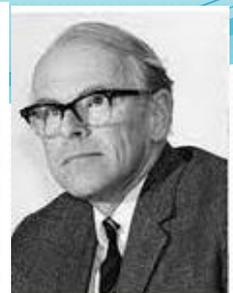
Tony Epstein



Bert Achong



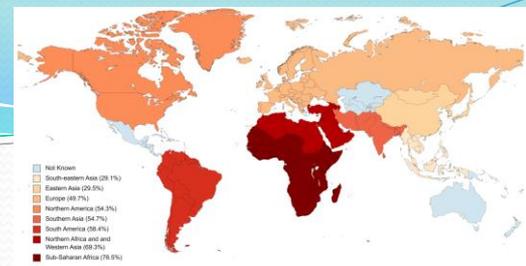
Yvonne Barr



Denis Burkitt

- The Epstein–Barr virus is named after Epstein, a professor emeritus at the University of Bristol, and Barr a PhD graduate from the University of London
- Epstein attended a lecture on Children's Cancer in Tropical Africa by Burkitt, a surgeon practicing in Uganda
- Specimen was sent from Uganda to be cultured and virus particles were identified
- Later on, a technician in their laboratory developed mononucleosis and they were able to compare a stored serum sample, showing that antibodies to the virus developed and the virus was linked to mononucleosis

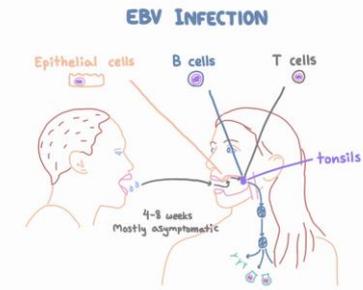
Epidemiology



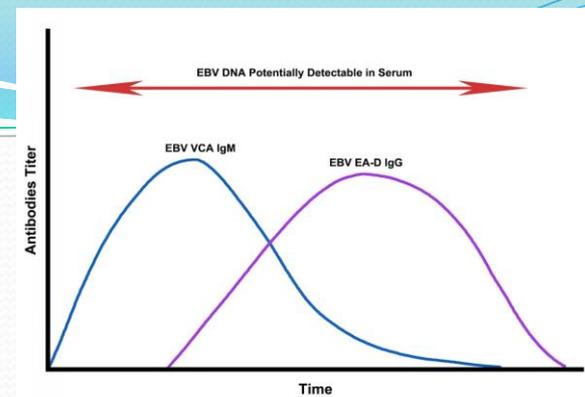
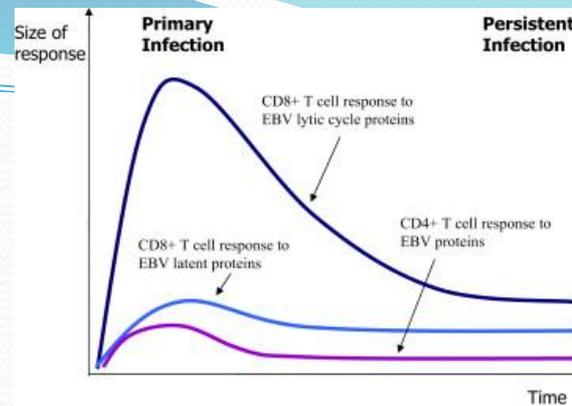
- EBV is one of the most common viral infections to human
- EBV can be cultured from saliva of 10 to 20% of healthy adults and is intermittently recovered from most seropositive individuals
- It is of low contagiousness, and most cases are contracted after repeated contact between susceptible persons and those asymptotically shedding the virus (by respiratory droplets)
- Secondary attack rates of infectious mononucleosis are low (<10%), because most family or household contacts already have antibody to the agent
- Worldwide 90-95% of adults are seropositive
- Infectious mononucleosis has also been transmitted by blood transfusions

Pathogenesis

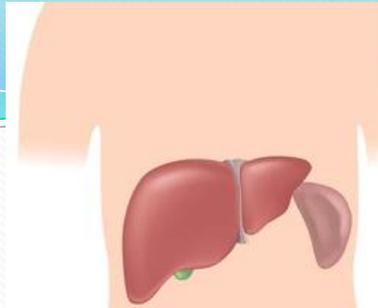
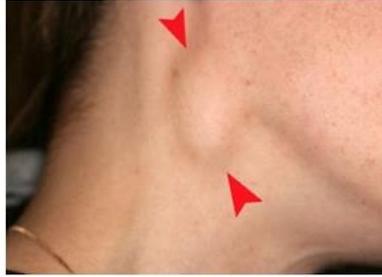
- EBV initially infects epithelial cells
- The virus enters B lymphocytes by envelope glycoprotein binding to a surface receptor CD21, which is the receptor for the C3b component of complement
- 18 to 24 hours later, EBV nuclear antigens are detectable within the nucleus of infected cells
- EBV has been associated with several lymphoproliferative diseases, including African Burkitt's lymphoma, nasopharyngeal carcinoma, and lymphomas in immunocompromised patients
- The distribution of EBV infections in Africa has suggested an infectious cofactor, such as malaria, which may cause immunosuppression



Immunity



- Virus-induced infectious mononucleosis is associated with circulating antibodies against specific viral antigens
- The “atypical” lymphocytosis associated with infectious mononucleosis is caused by an increase in the number of circulating T cells, which appear to be activated cells developed in response to the virus-infected B lymphocytes
- With recovery from illness, the atypical lymphocytosis gradually resolves, and cell-mediated immune functions return to preinfection levels, although memory T cells maintain the capacity to limit proliferation of EBV-infected B cells



Clinical Manifestations

1. Infectious Mononucleosis (Glandular fever)

- Most primary EBV infections are asymptomatic
- Clinically apparent infectious mononucleosis is characterized by fever, malaise, pharyngitis, tender lymphadenitis, and splenomegaly
- These symptoms persist for days to weeks; they slowly resolve
- Complications such as laryngeal obstruction, meningitis, encephalitis, hemolytic anemia, thrombocytopenia, or splenic rupture may occur in 1 to 5% of patients

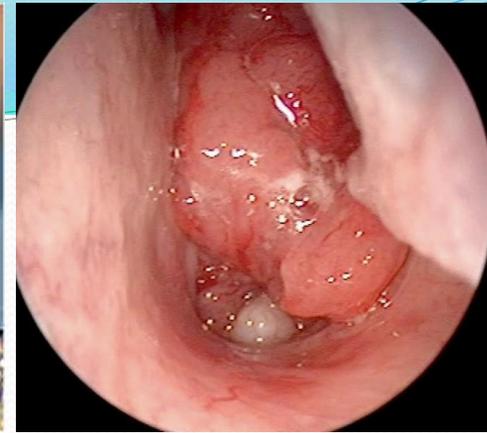
2. Lymphoproliferative Syndrome

- Patients with primary or secondary immunodeficiency are susceptible to EBV-induced lymphoproliferative disease
- The risk is greatest in patients experiencing primary EBV infection rather than reactivation
- Most characteristic is persistent fever, lymphadenopathy, and hepatosplenopathy

3. Burkitt's lymphoma

- In sub-Saharan Africa, Burkitt's lymphoma is the most common malignancy in young children
- The risk is greatest in equatorial Africa, where there is a high incidence of malaria
- Burkitt's lymphoma is thought to result from an early EBV infection that produces a large pool of infected B lymphocytes
- Malarial infection may further increase the size of this pool and provide a constant antigenic challenge
- Serologic screening for increased IgA antibody levels can be used for early diagnostic purposes

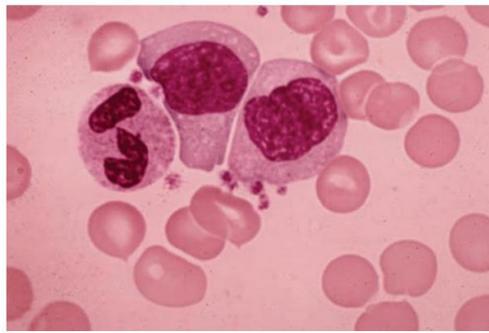




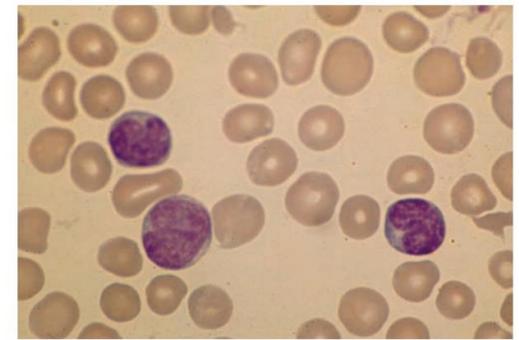
4. Nasopharyngeal Carcinoma

- Nasopharyngeal carcinoma (NPC) is endemic in southern China, where it is responsible for approximately 25% of the mortality from cancer
- The high incidence of NPC among the southern Chinese people suggests that genetic or environmental factors in addition to EBV may also be important in the pathogenesis of the disease

Diagnosis



A



B

FIGURE 14-9. A. Atypical lymphocytes (Downey cells) in blood smear from a patient with infectious mononucleosis. Note indented cell membranes. Polymorphonuclear leukocyte is adjacent to the two affected cells. B. Normal lymphocytes contrast sharply with those in A.

- Positive EBV- specific serologic findings
- PCR studies is confirmatory
- Hematologic examination reveals a markedly raised lymphocyte and monocyte count with more than 10% atypical lymphocytes
- Atypical lymphocytes, although not specific for EBV, are present with the onset of symptoms and disappear with resolution of disease
- Alterations in liver function tests may also occur, and hepatosplenomegally is a frequent finding

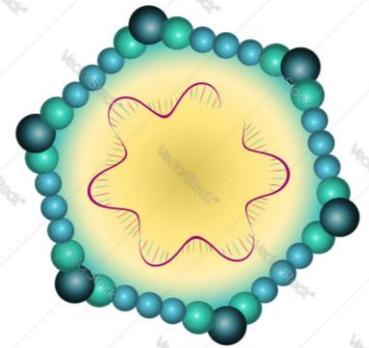
Treatment and Prevention

- Treatment of infectious mononucleosis is largely supportive. More than 95% of patients recover uneventfully
- In a small percentage of patients, splenic rupture may occur; restriction of contact sports or heavy lifting during the acute illness is recommended
- Systemic acyclovir makes little or no impact on the clinical illness
- Laryngeal obstruction should be treated with corticosteroids
- Immunization with virus specific antigen have shown to be effective against Burkitt's lymphoma and nasopharyngeal carcinoma in animal model and the vaccine is under development



Parvovirus B19 Infections

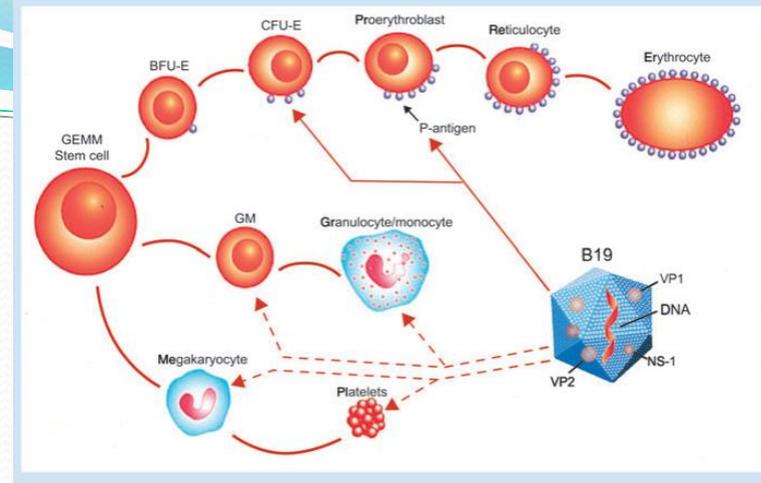
Virology



ParvoVirus B19

- Parvoviruses are very small (18 to 26 nm), naked virions that contain a linear single-stranded DNA molecule
- The major cellular receptor for the virus is globoside (also known as blood group P antigen, which is commonly found on erythroid progenitors, erythroblasts, megakaryocytes, and endothelial cells)
- A primary site of replication appears to be the nucleus of an immature cell in the erythrocyte lineage. Such infected cells then cease to proliferate, resulting in an impairment of normal erythrocyte development

Pathogenesis



- The clinical consequences of the viral effect on erythrocytes are generally trivial, unless patients are already compromised by a chronic hemolytic process, such as sickle cell disease or thalassemia
- Primary infection in such individuals often produces an acute, severe, sometimes fatal anemia manifested as a rapid fall in RBC counts and hemoglobin
- Patients may present initially with no clinical symptoms other than fever, and is commonly referred to as aplastic crisis

Epidemiology

- The viral infection is common among children 5-15 years old
- Epidemiologic evidence suggests that spread of the virus is primarily by the respiratory route, and high transmission rates occur in households
- Once skin rash appears the virus is no more contagious
- Outbreaks tend to be small and localized, particularly during the spring months, with the highest rates among children and young adults
- Seroepidemiologic studies have demonstrated evidence of past infection in 30 to 60% of adults

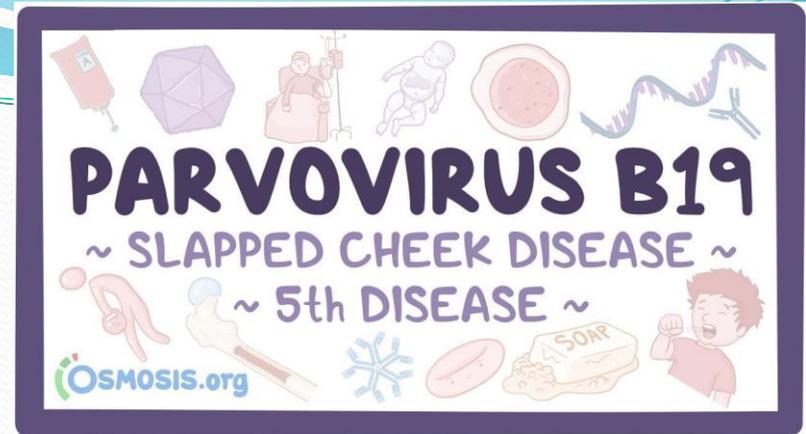
Clinical Manifestations

- Erythema infectiosum (also referred to as fifth disease, slapped cheek, apple face, or academy rash) is attributable to parvovirus B19
- After an incubation period of 4 to 12 days, a mild illness appears, characterized by fever, malaise, headache, myalgia, and itching in varying degrees
- A confluent, indurated rash appears on the face, giving a “slapped-cheek” appearance. The rash spreads in a day or two to other areas, particularly exposed surfaces such as the arms and legs, where it is usually macular and reticular
- During the acute phase, generalized lymphadenopathy or splenomegaly may be seen, along with a mild leukopenia and anemia

- The illness lasts 1 to 2 weeks, but rash may recur for periods of 2 to 4 weeks thereafter, exacerbated by heat, sunlight, exercise, or emotional stress
- Arthralgia sometimes persists or recurs for weeks to months, particularly in adolescent or adult females
- Serious complications, such as hepatitis, thrombocytopenia, nephritis or encephalitis are rare
- like rubella, active transplacental transmission of parvovirus B19 can occur during primary infections in the first 20 weeks of pregnancy, sometimes resulting in stillbirth of fetuses that are profoundly anemic



Diagnosis



- Viremia usually lasts 7 to 12 days but can persist for months in some individuals
- CBC (low Hb)
- It can be detected by specific DNA probe or polymerase chain reaction (PCR) methods
- Alternatively, the presence of IgM-specific antibody late in the acute phase or during convalescence strongly supports the diagnosis