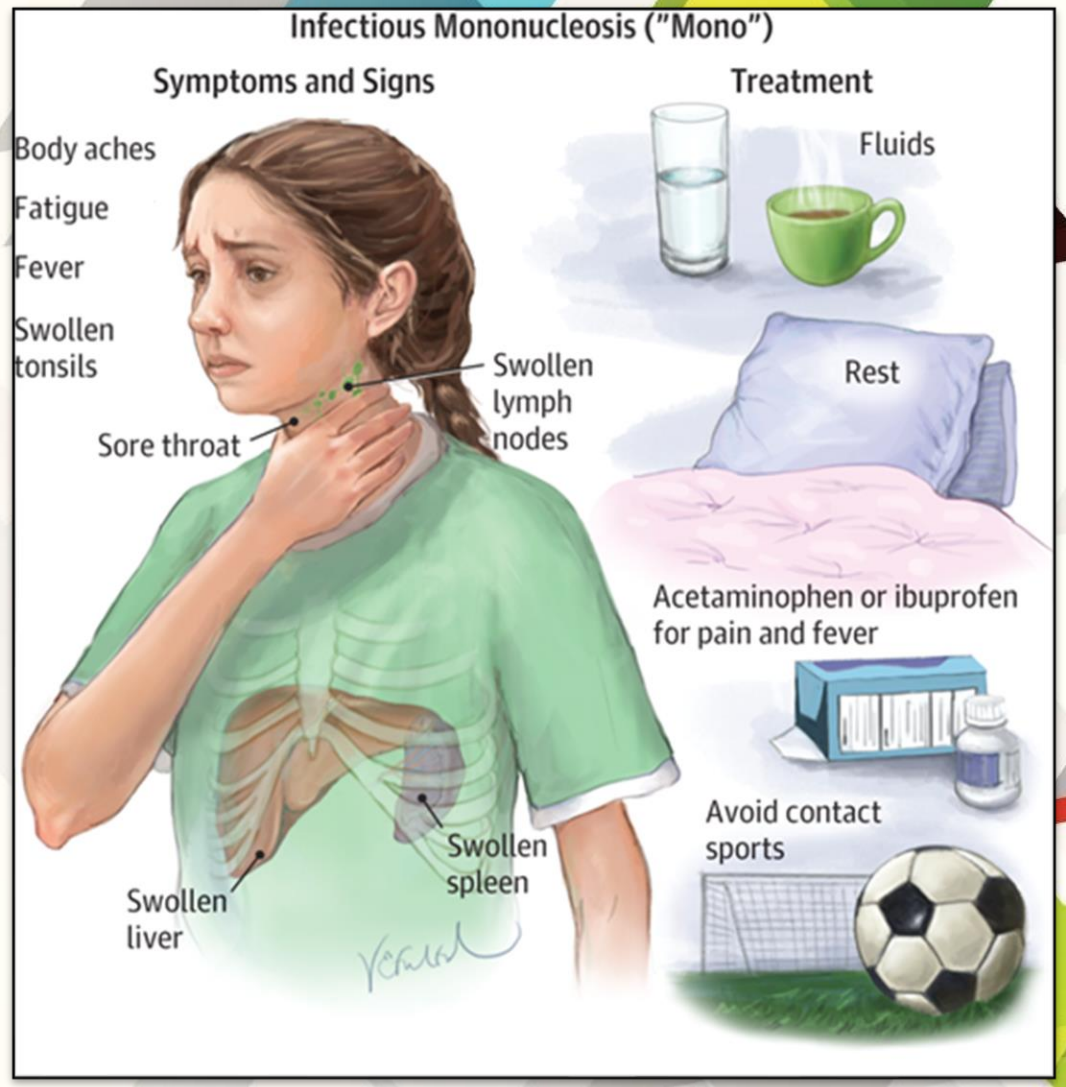
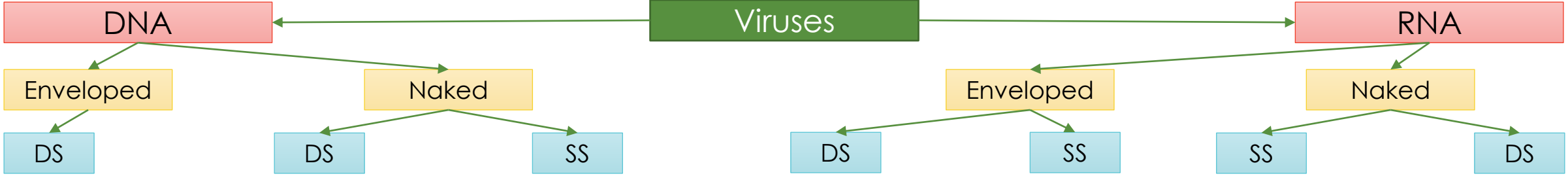
→ Causes infectious mononucleosis (kissing disease)



→ Considered as an onco-virus

Epstein-barr virus

Done by: Abdelhadi Okasha



Herpesviridae (Ic)

-Herpes simplex virus 1&2

-Varicella-zoster

-Epstein-Barr virus

-Cytomegalovirus

Adenoviridae (Ic)

Adenovirus

Parvoviridae (Ic)

Parvovirus B19

Bocaviruses

Guidelines:
SS: single stranded
DS: Double stranded
Ic: Ichosahedral capsid
He: Helical capsid
Co: Complex capsid

0- Introduction

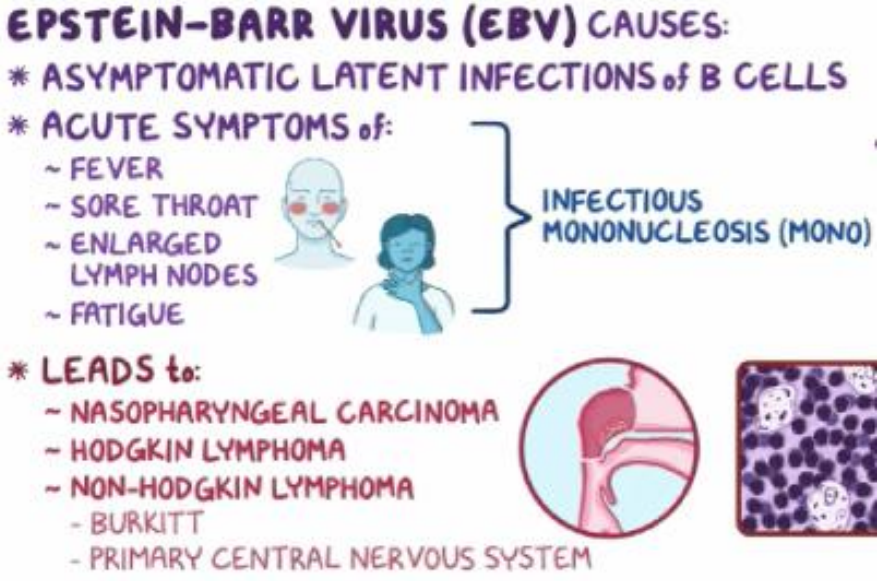
	Biologic Properties			Examples	
Subfamily ("-herpesvirinae")	Growth Cycle and Cytopathology	Latent Infections	Genus ("-*virus*")	Official Name ("Human Herpesvirus")	Common Name
Alpha	Short, cytolytic	Neurons	*Simplex*	1	Herpes simplex virus type 1
				2	Herpes simplex virus type 2
			Varicello	3	Varicella-zoster virus
Beta	Long, cytomegalic	Glands, kidneys	*Cytomegalo*	5	Cytomegalovirus
	Long, lymphoproliferative	Lymphoid tissue	*Roseolo*	6	Human herpesvirus 6
				7	Human herpesvirus 7
Gamma	Variable, lymphoproliferative	Lymphoid tissue	*Lymphocrypto*	4	Epstein-Barr virus
			Rhadino	8	Kaposi sarcoma-associated herpesvirus

Epstein-Barr virus

1- Structure

* The EBV DNA genome contains about 172 kbp, and encodes about 100 genes.

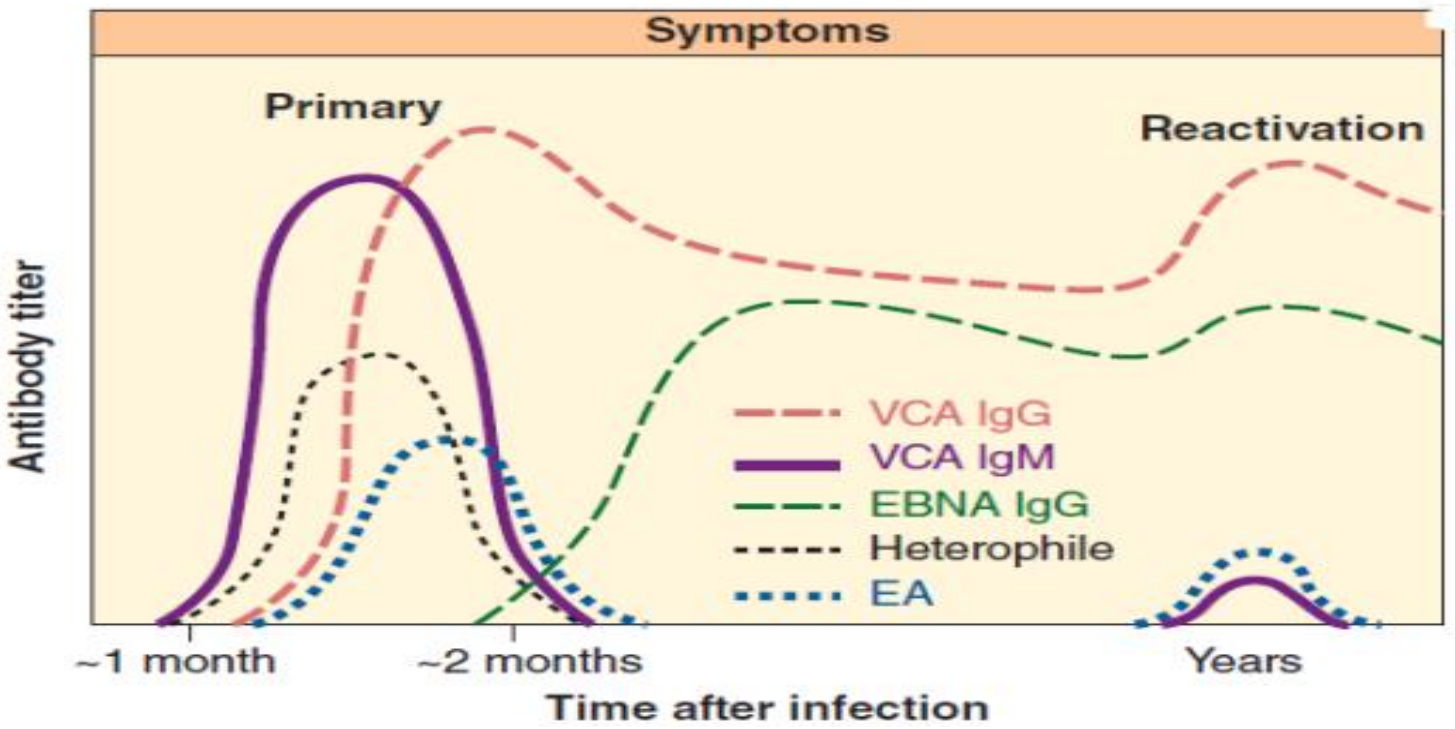
2- Pathogenesis & clinical manifestations



3- Immunity

→ EBV infections elicit an intense immune response consisting of antibodies against many virus-specific proteins, several cell mediated responses, and secretion of lymphokines.
→ Cell-mediated immunity and cytotoxic T cells are important in limiting primary infections and controlling chronic infections.

4- Diagnosis



5- Epidemiology

In developing areas, infections occur early in life; more than 90% of children are infected by age 6 years. These infections in early childhood usually occur without any recognizable disease. The inapparent infections result in permanent immunity to infectious mononucleosis.
In industrialized nations, more than 50% of EBV infections are delayed until late adolescence and young adulthood. In almost half of cases, the infection is manifested by infectious mononucleosis.

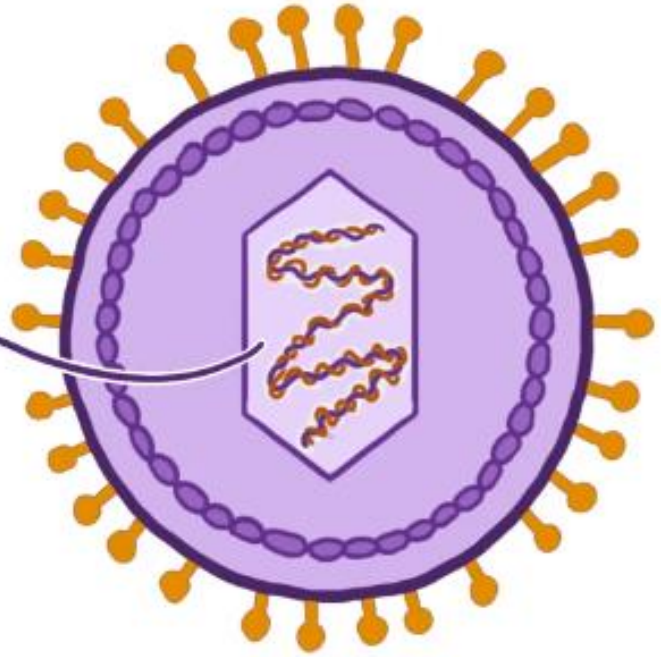
6- Treatment

→ No vaccine available
→ Acyclovir can decrease shedding but doesn't affect symptoms

1- Structure

EPSTEIN-BARR VIRUS (EBV)

* HUMAN HERPESVIRUS-4 (HHV-4)
* ENVELOPED
* HERPESVIRIDAE FAMILY
* LINEAR, DOUBLE-STRANDED DNA
* MOST COMMON CAUSE of INFECTIOUS MONONUCLEOSIS (MONO)



* The EBV DNA genome contains about 172 kbp, and encodes about 100 genes.

2- Pathogenesis & Clinical manifestations

- EBV is transmitted by infected saliva and initiates infection in the epithelial cells in the oropharynx (that's why it's said to cause kissing disease)
- The virus is transferred to lymph nodes were it infects B cell (major target) by binding to the viral receptor, which is the receptor for the C3d component of complement (CR2 or CD21).
- When human B lymphocytes are infected with EBV, continuous cell lines can be established, indicating that cells have been immortalized by the virus. Very few of the immortalized cells produce infectious virus.
- EBV directly enters a latent state in the lymphocyte without undergoing a period of complete viral replication.
- Several patterns of latent viral gene expression are recognized based on the spectrum of proteins and transcripts expressed. These include EBV nuclear antigens (EBNA1, 2, 3A-3C, LP), latent membrane proteins (LMP1, 2), and small untranslated RNAs (EBERs)

2- Pathogenesis & Clinical manifestations

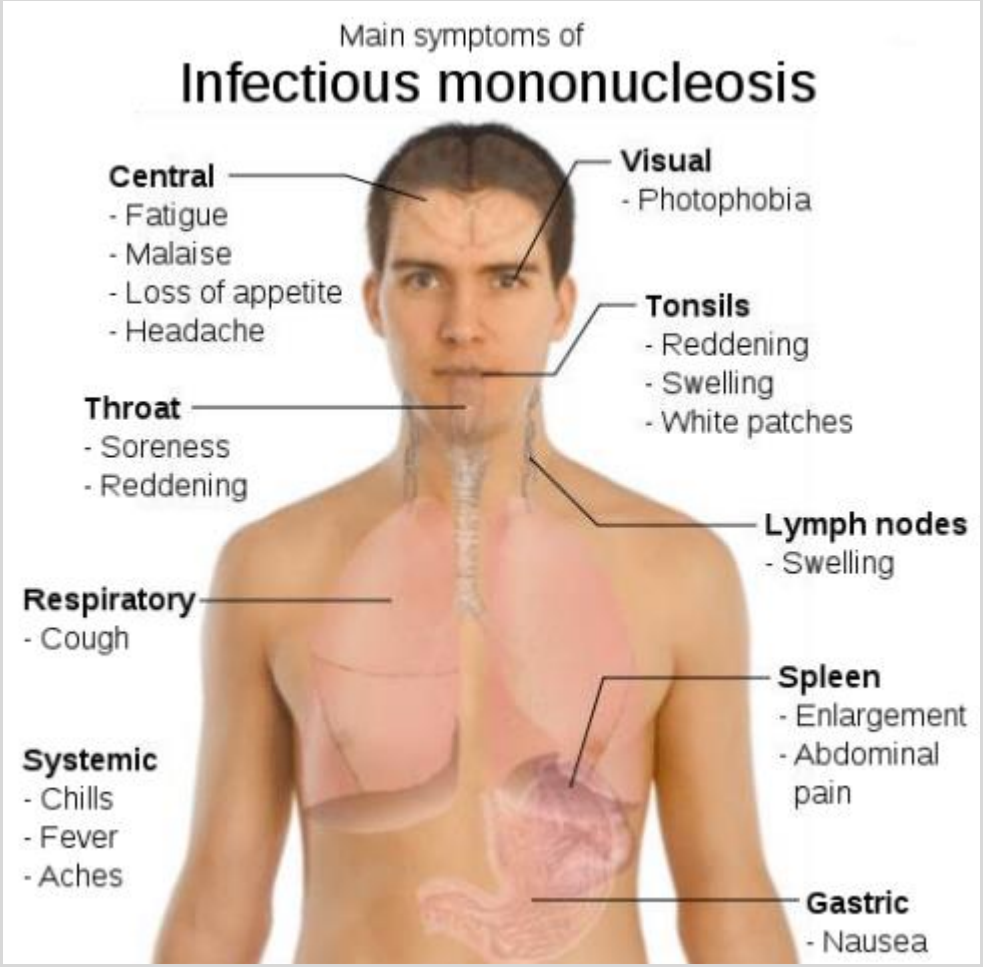
- The hallmarks of latency are viral persistence, restricted virus expression, and the potential for reactivation and lytic replication
- EBV-immortalized B lymphocytes express differentiated functions, such as secretion of Ig.
- B-cell activation products (e.g., CD23) are also expressed.
- At any given time, very few cells (<10%) in an immortalized population release virus particles.
- Infected B cells spread infection throughout the body.
- Immune response is established against EBV, T & B cells kick in, they increase in the blood and eliminate most of the infected b cells, but small numbers of latently infected lymphocytes persist for the lifetime of the host (one in $10^5 - 10^6$ B cells)
- Note: Many of T cells will form large atypical form when activated

2- Pathogenesis & Clinical manifestations

- The infection can lead to four pathways:
  1) Asymptomatic (Mostly effect young children)
  2) Acute infectious mononucleosis (if they occur in young adults)
  3) Cancer
  4) oral hairy leukoplakia and other manifestations in immunodeficient people

2- Pathogenesis & Clinical manifestations

- 2) Acute infectious mononucleosis (if they occur in young adults)
- After an incubation period of 30–50 days, symptoms of headache, fever, malaise, fatigue, and sore throat occur. Enlarged lymph nodes and spleen are characteristic. Some patients develop signs of hepatitis.
- The typical illness is self-limited and lasts for 2–4 weeks.
- During the disease, there is an increase in the number of circulating white blood cells, with a predominance of lymphocytes.
- Many of these are large, atypical T lymphocytes.
- Low-grade fever and malaise may persist for weeks to months after acute illness. Complications are rare in normal hosts.

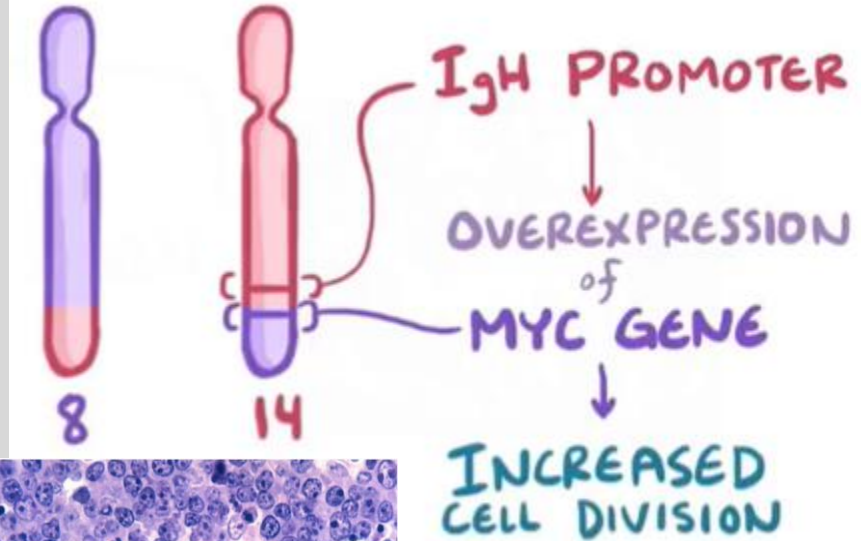


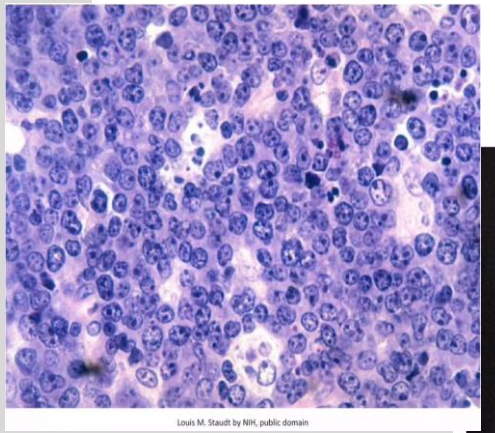
2- Pathogenesis & Clinical manifestations

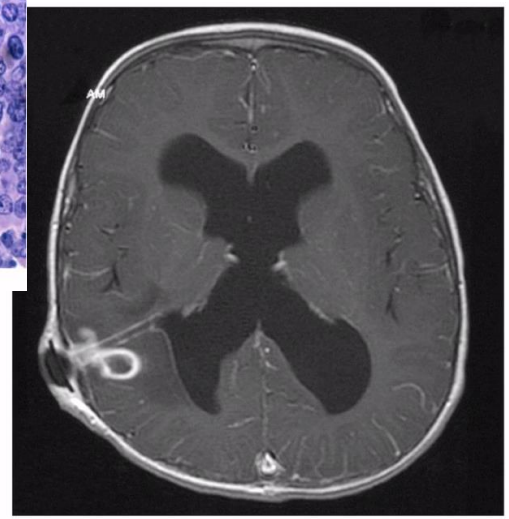
- 3) Cancer: EBV is associated with:
  a- nasopharyngeal carcinoma
  b- gastric carcinoma
  c- Hodgkin lymphoma
  d- Non-Hodgkin lymphoma (especially Burkitt lymphoma)
- a- Nasopharyngeal carcinoma is a cancer of epithelial cells and is common in males of Chinese origin.
  EBV DNA is regularly found in nasopharyngeal carcinoma cells, and patients have high levels of antibody to EBV.
  Genetic and environmental factors are believed to be important in the development of nasopharyngeal carcinoma.

2- Pathogenesis & Clinical manifestations

- C- EBV is associated with classic Hodgkin disease, with the viral genome detected in the malignant Reed-Sternberg cells in up to 50% of cases
- D- Virtually all CNS non-Hodgkin lymphomas are associated with EBV (Usually in immunocompromised people) , but fewer than 50% of systemic lymphomas are EBV positive. Burkitt lymphoma is a tumor of the jaw in African children and young adults. Most African tumors (>90%) contain EBV DNA.
  In other regions, only about 20% of Burkitt lymphomas contain EBV DNA.
  Malaria, may foster enlargement of the pool of EBV infected cells. Finally, there are characteristic chromosome translocations that involve immunoglobulin genes and result in deregulation of expression of the c-myc proto-oncogene.

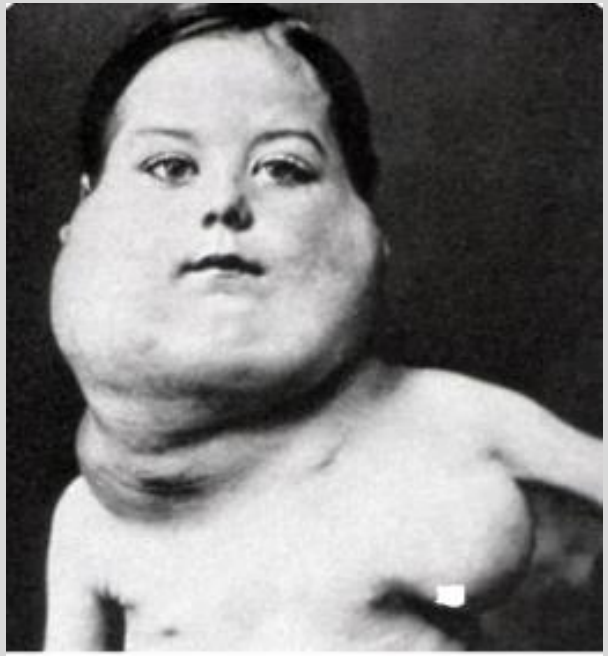


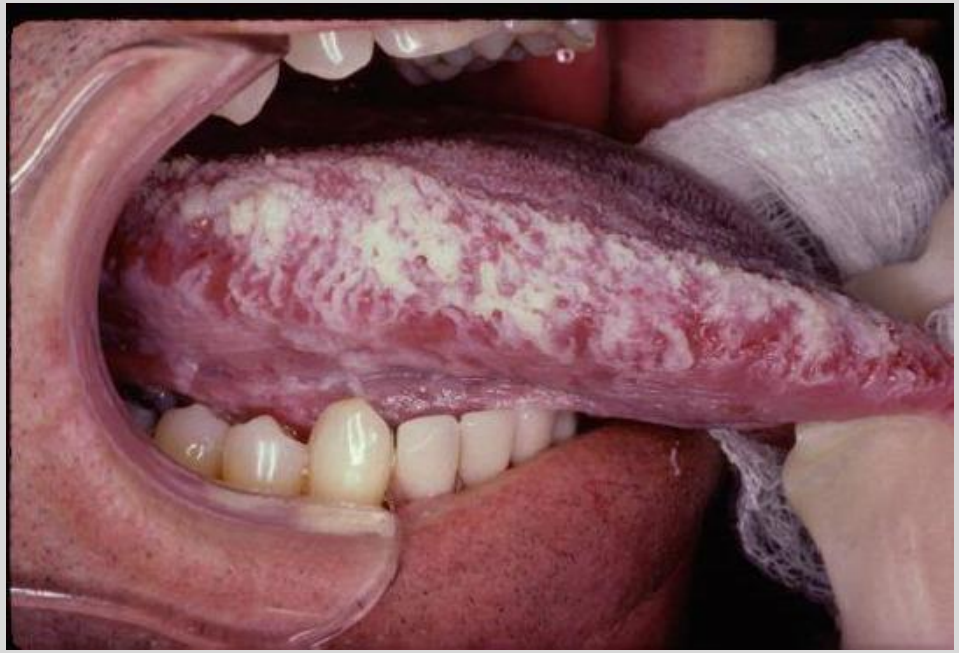




2- Pathogenesis & Clinical manifestations

- 4) AIDS patients are susceptible to EBV associated lymphomas and oral hairy leukoplakia, a wart-like growth that develops on the tongue; it is an epithelial focus of EBV replication.





3- Immunity

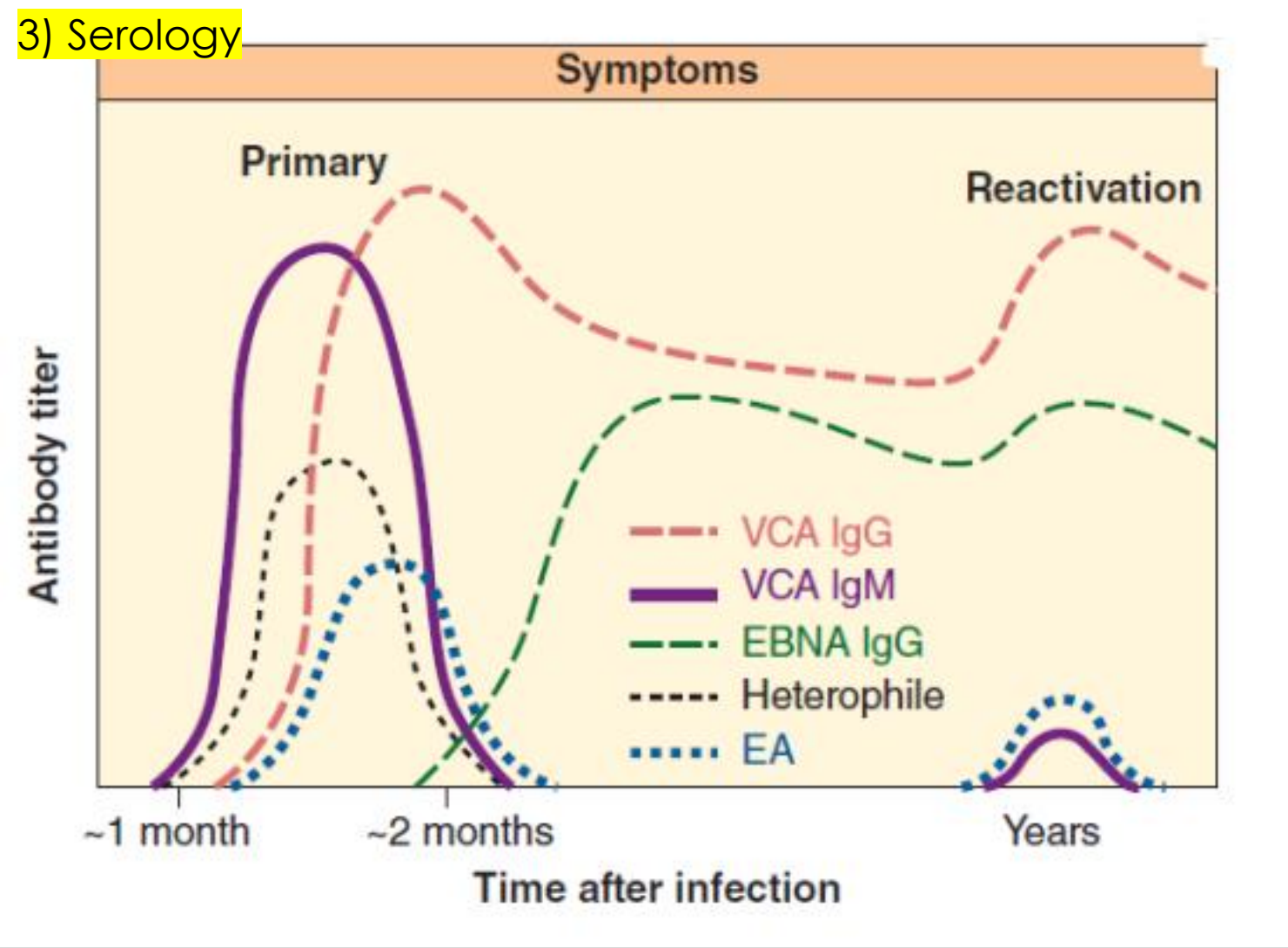
- EBV infections elicit an intense immune response consisting of antibodies against many virus-specific proteins, several cell mediated responses, and secretion of lymphokines.
- Cell-mediated immunity and cytotoxic T cells are important in limiting primary infections and controlling chronic infections.
- Serologic testing to determine the pattern of specific antibodies to different classes of EBV antigens is the usual means of ascertaining a patient's status regarding EBV infection.

4- Laboratory diagnosis

- 1) Nucleic acid hybridization is the most sensitive means of detecting EBV in patient materials. EBER RNAs are abundantly expressed in both latently infected and lytically infected cells and provide a useful diagnostic target for detection of EBV infected cells by hybridization.
- 2) Viral antigens can be demonstrated directly in lymphoid tissues and in nasopharyngeal carcinomas.
  Note: During the acute phase of infection, about 1% of circulating lymphocytes will contain EBV markers; after recovery from infection, about one in 1 million B lymphocytes will carry the virus.

4- Laboratory diagnosis

3) Serology



4- Laboratory diagnosis

- The less-specific heterophil agglutination test may be used to diagnose EBV infections. In the course of infectious mononucleosis, most patients develop transient heterophil antibodies that agglutinate sheep cells.
- Serologic tests for EBV antibodies require some interpretation. The presence of antibody of the IgM type to the viral capsid antigen is indicative of current infection.
- Antibody of the IgG type to VCA is a marker of past infection and indicates immunity.
- EA antibodies are generally evidence of current viral infection, although such antibodies are often found in patients with Burkitt lymphoma or nasopharyngeal carcinoma.
- Antibodies to the EBNA antigens reveal past infection with EBV, although detection of a rise in anti-EBNA antibody suggests a primary infection. Not all persons develop antibody to EBNA.

5- Epidemiology

- EBV is common with more than 90% of adults being sero-positive
- It is transmitted primarily by contact with oropharyngeal secretions.
- In developing areas, infections occur early in life; more than 90% of children are infected by age 6 years. These infections in early childhood usually occur without any recognizable disease. The inapparent infections result in permanent immunity to infectious mononucleosis.
- In industrialized nations, more than 50% of EBV infections are delayed until late adolescence and young adulthood. In almost half of cases, the infection is manifested by infectious mononucleosis.

6- Treatment and Prevention

- There is no EBV vaccine available.
- Acyclovir reduces EBV shedding from the oropharynx during the period of drug administration, but it does not affect the number of EBV-immortalized B cells.
- Acyclovir has no effect on the symptoms of mononucleosis and is of no proved benefit in the treatment of EBV-associated lymphomas in immunocompromised patients