BHARATHIDASAN UNIVERSITY

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Course Title : Medical Virology
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Unit-IV

Epstein – Barr Virus

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EPSTEIN-BARR VIRUS

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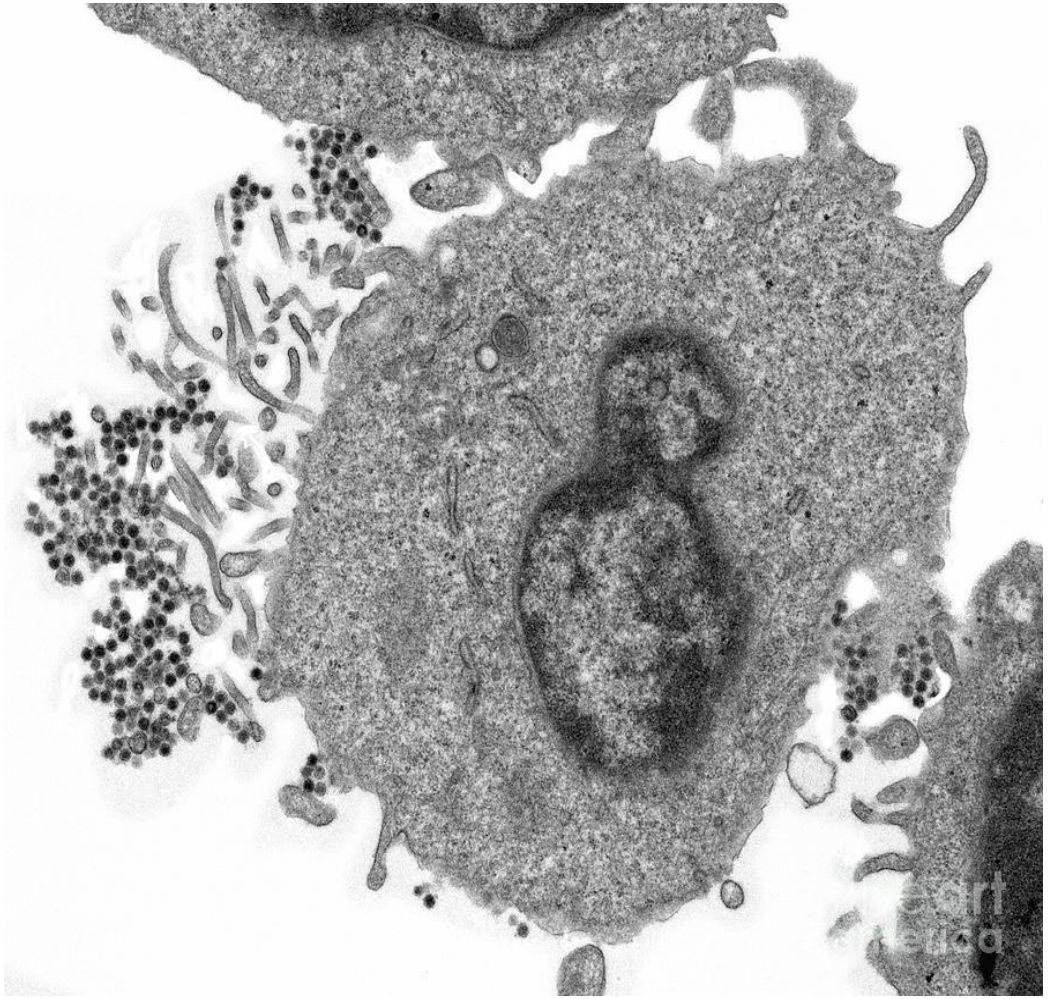
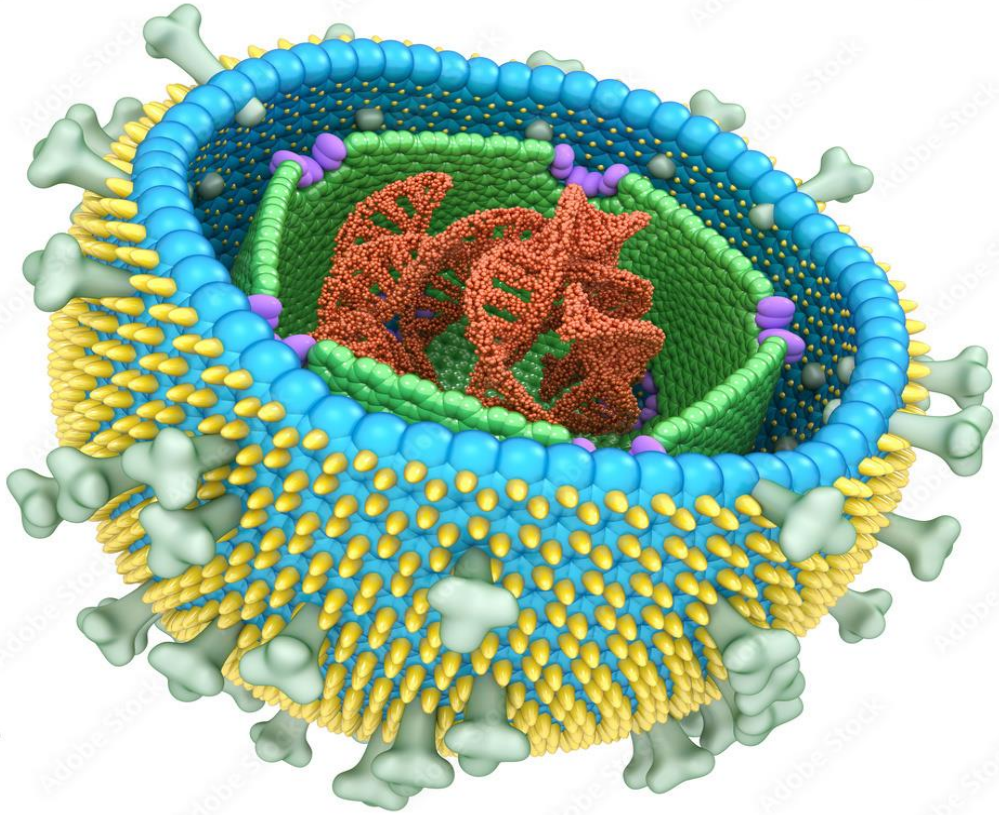
INTRODUCTION

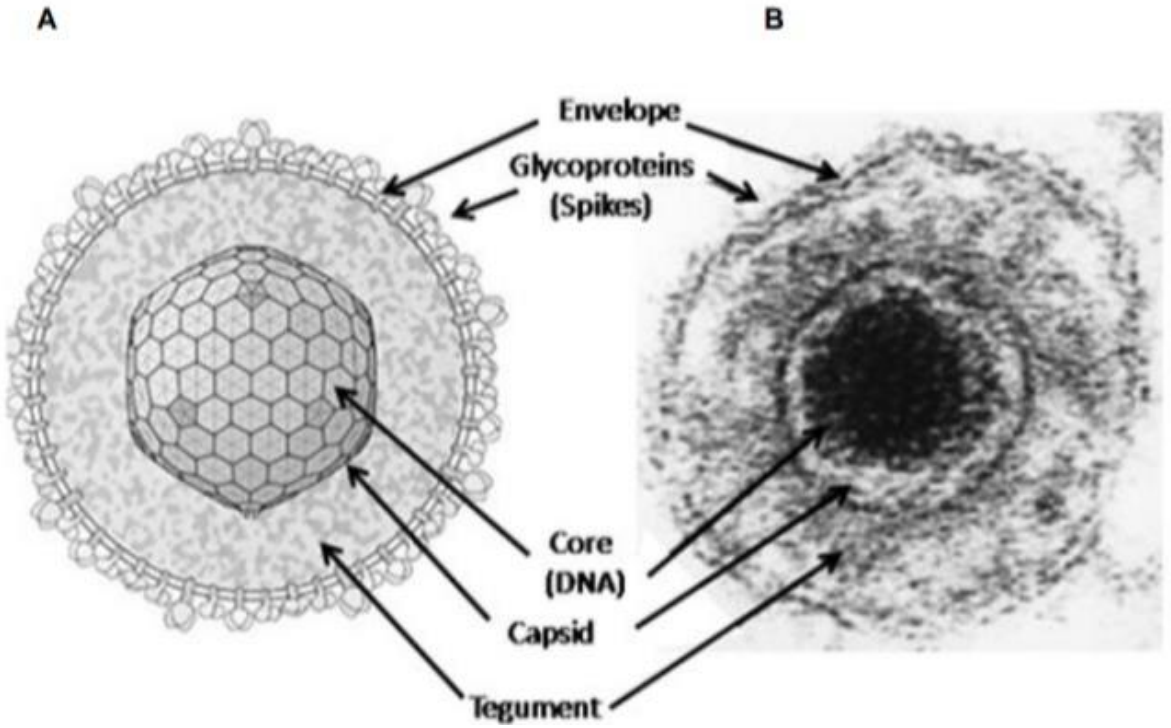
Epstein Barr virus is classified under the,

- **FAMILY** – Herpesviridae
- **SUBFAMILY** – Gamaherpesvirinae
- **GENUS** – Lymphocryptovirus
- **SPECIES** – Human herpesvirus 4



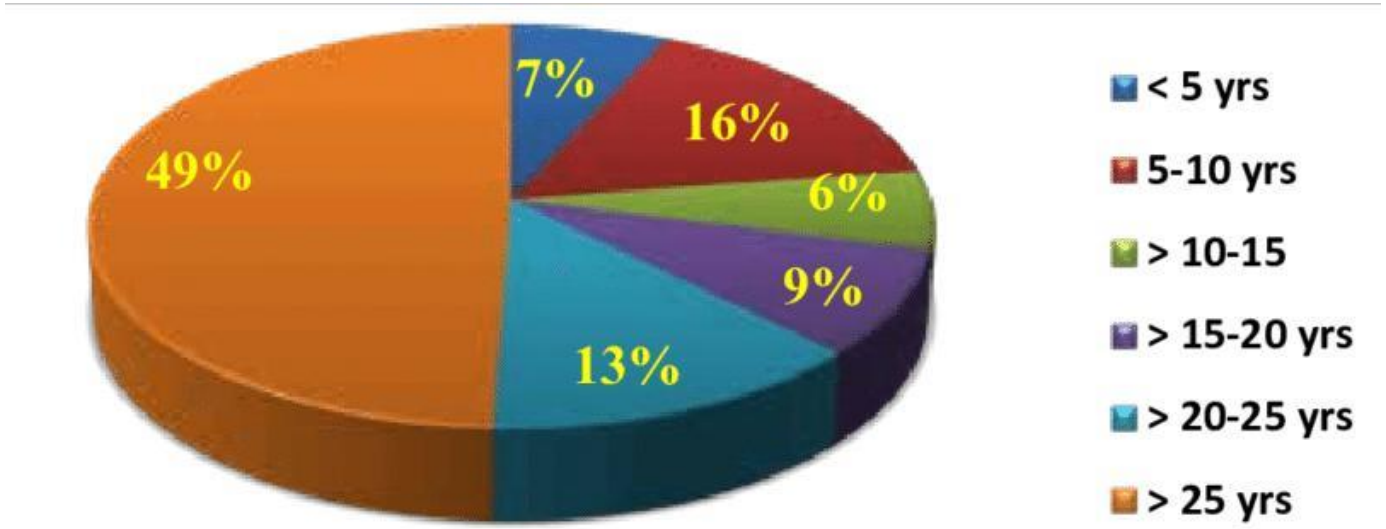
VIRAL GENOME & STRUCTURE:





EPIDEMIOLOGY

- Nearly 95% of the world's population of adults have been infected with EBV
- Adolescents (18-19 years old) had a EBV prevalence of 82.9%
- AGE DISTRIBUTION of patients with reactivation EBV infection is depicted below,



PATHOPHYSIOLOGY

1) Primary Infection and Lytic Replication

- There are three classes of viral lytic gene products, Immediate-early [IE], early[E], and late [L].

- The early products have a wide array of functions, including replication, metabolism, and blockade of antigen processing.
- The late products tend to code for structural proteins such as the viral capsid antigens (VCA)
- Gene products are also used for immune evasion

2) Latency

- Latency is the state of persistent viral infection without active viral production
- EBV persists mostly in the memory B-cell compartment and in epithelial cells
- EBV has four different programs of gene usage in latency (latency 0, I, II and

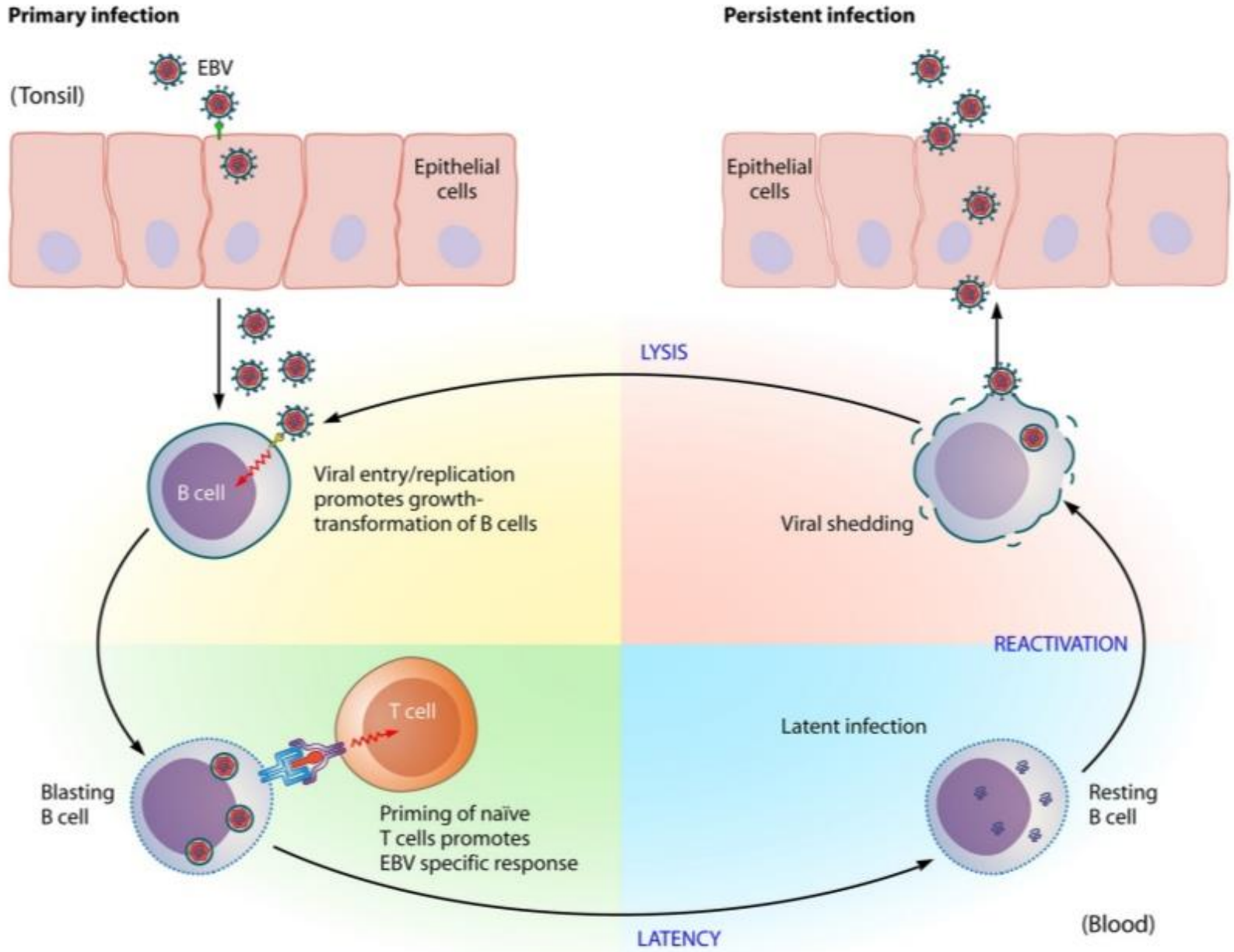
Table 1: Epstein-Barr virus latency programs and expressed transcripts
Note: all three (I-III) latency programs express EBERs

Latency Program:	EBNAs:	LMPs:	Detected in:
0	---	---	Healthy individuals
I (EBNA ONLY)	EBNA1	---	BL
II (DEFAULT)	EBNA1	LMP1,2A	NPC, GC, Hodgkin's disease
III (GROWTH)	EBNA1,2,3A,B,C and LP	LMP1,2A,2B	EBV associated diseases in immunocompromised individuals

3) Reactivation

- Latently infected B cells can occasionally be stimulated to reactivate EBV. This produces virus that can reinfect new B cells and epithelial cells, becoming a source of viral transmission.

- This likely occurs *in vivo* when the EBV infected memory B cells are triggered to differentiate.


Primary infection
Persistent infection
EBV
(Tonsil)
Epithelial cells
Epithelial cells
LYSIS
B cell
Viral entry/replication promotes growth-transformation of B cells
Viral shedding
REACTIVATION
T cell
Latent infection
Blasting B cell
Priming of naïve T cells promotes EBV specific response
Resting B cell
(Blood)
LATENCY

CLINICAL MANIFESTATIONS OF EBV INFECTION

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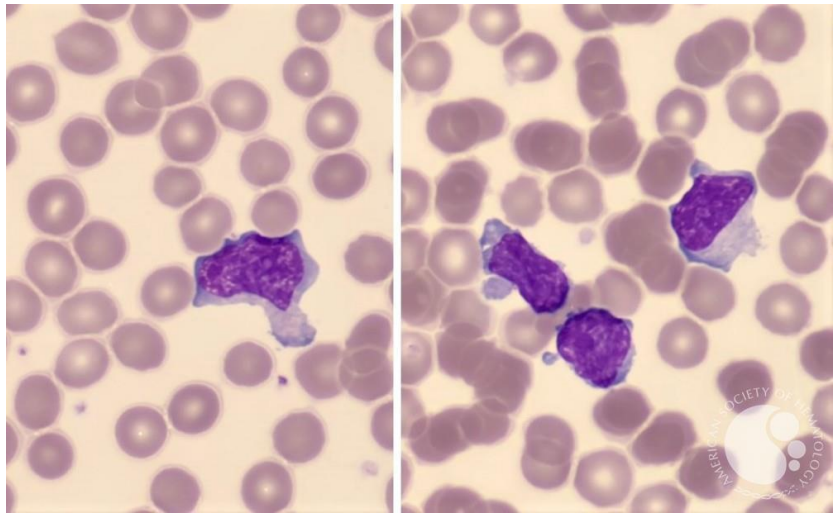
- Infectious mononucleosis resembles an Acute infectious disease accompanied by atypical large peripheral blood lymphocytes, called DOWNEY CELLS, which are activated CD8 T Lymphocyte, most of which are probably responding to EBV-infected B cells.

- The peripheral blood flim in IM by EBV is depicted below,



Prevalence of Signs and Symptoms in Infectious mononucleosis

Finding	Prevalence (%)	Comment
Signs		
Pharyngitis	100	Occasionally seen without sore throat
Cervical lymphadenopathy	95	Especially posterior cervical and postauricular
Fever	50	Often masked by antipyretics
Hepatomegaly	25	
Splenomegaly	33	
Eyelid edema	10	Unusual in other acute illnesses
Rash	5	Virtually all patients given penicillin derivatives develop a rash
Symptoms		
Sore throat	95	Many patients describe this as the "worst" they have ever had
Fatigue	90	Usually the last symptom to resolve
Headache	75	Common but underappreciated
Fever	70	
Body aches	50	Patients describe this as "like the flu"
Decreased appetite	50	
Abdominal discomfort	40	Due to mesenteric adenitis or hepatosplenomegaly

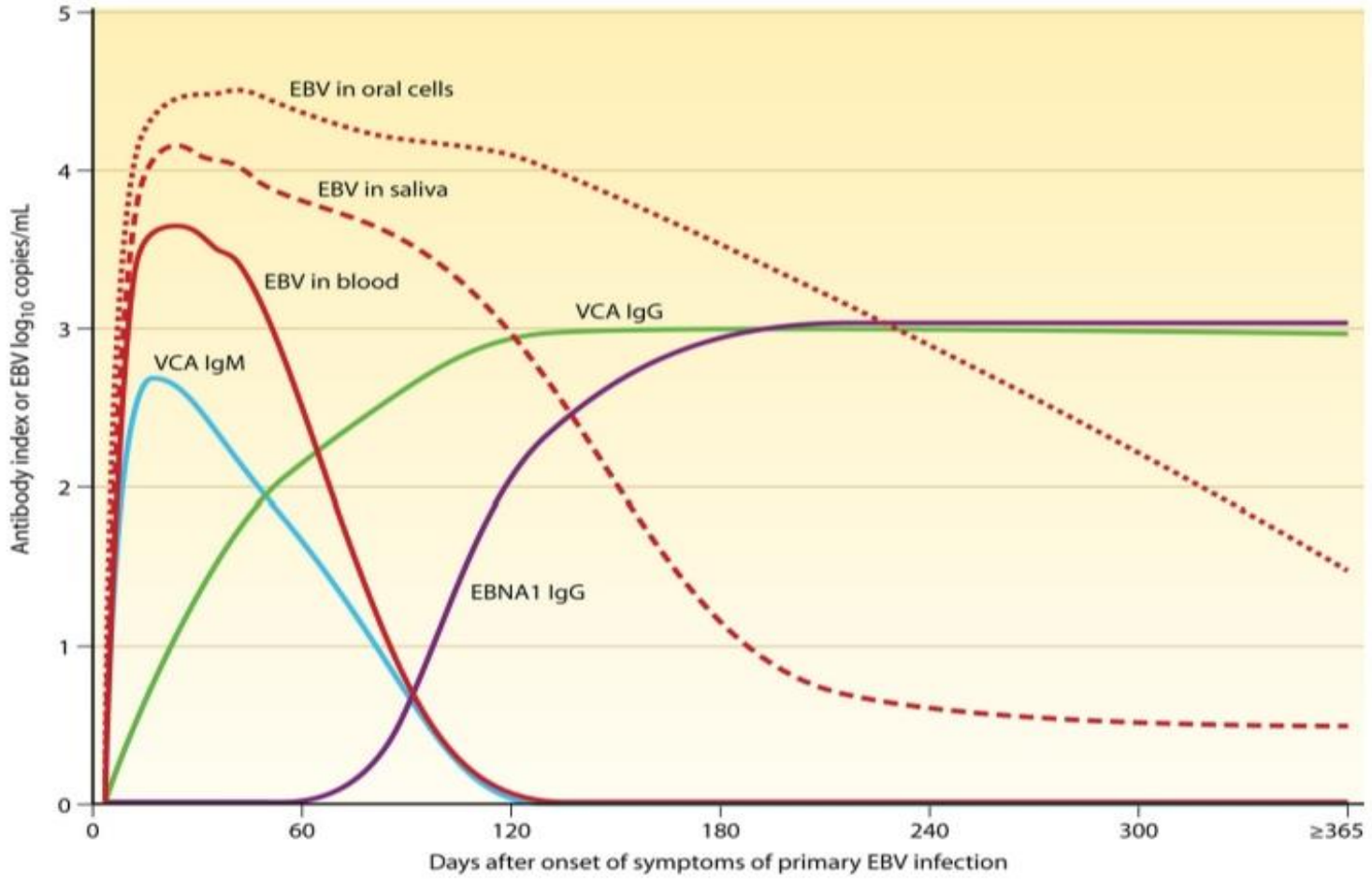
Complications reported in ≥1% of cases of infectious mononucleosis

Complication	Comment
Airway obstruction	Due to oropharyngeal swelling and edema
Meningoencephalitis	Other neurologic complications have been reported but are rare
Hemolytic anemia	Thought to be autoimmune
Thrombocytopenia	Thought to be autoimmune
Rash	Rash due to EBV is uncommon, but maculopapular rashes occur in the majority of patients inadvertently given penicillin derivatives

PRIMARY RESPONSE TO EBV INFECTION

1) Virological events

Kinetics of EBV-specific antibodies and viral load in infectious mononucleosis is depicted below,



2) Immune response to EBV

→ INNATE IMMUNE RESPONSE

- During primary EBV infection, both type I and type II Interferon-regulated genes were strongly unregulated.
- The inflammatory cytokines, TNF α, IL-6 are increased in tonsillar tissue from patients with IM.

→ ADAPTIVE IMMUNE RESPONSE

- The first Humoral response detected is an IgM class antibody against the VCA.
- Anti-gp350 antibodies may be detected after natural exposure to EBV or in response to gp350 subunit vaccines

DIAGNOSIS

1) **Peripheral blood smear** - Downey cells

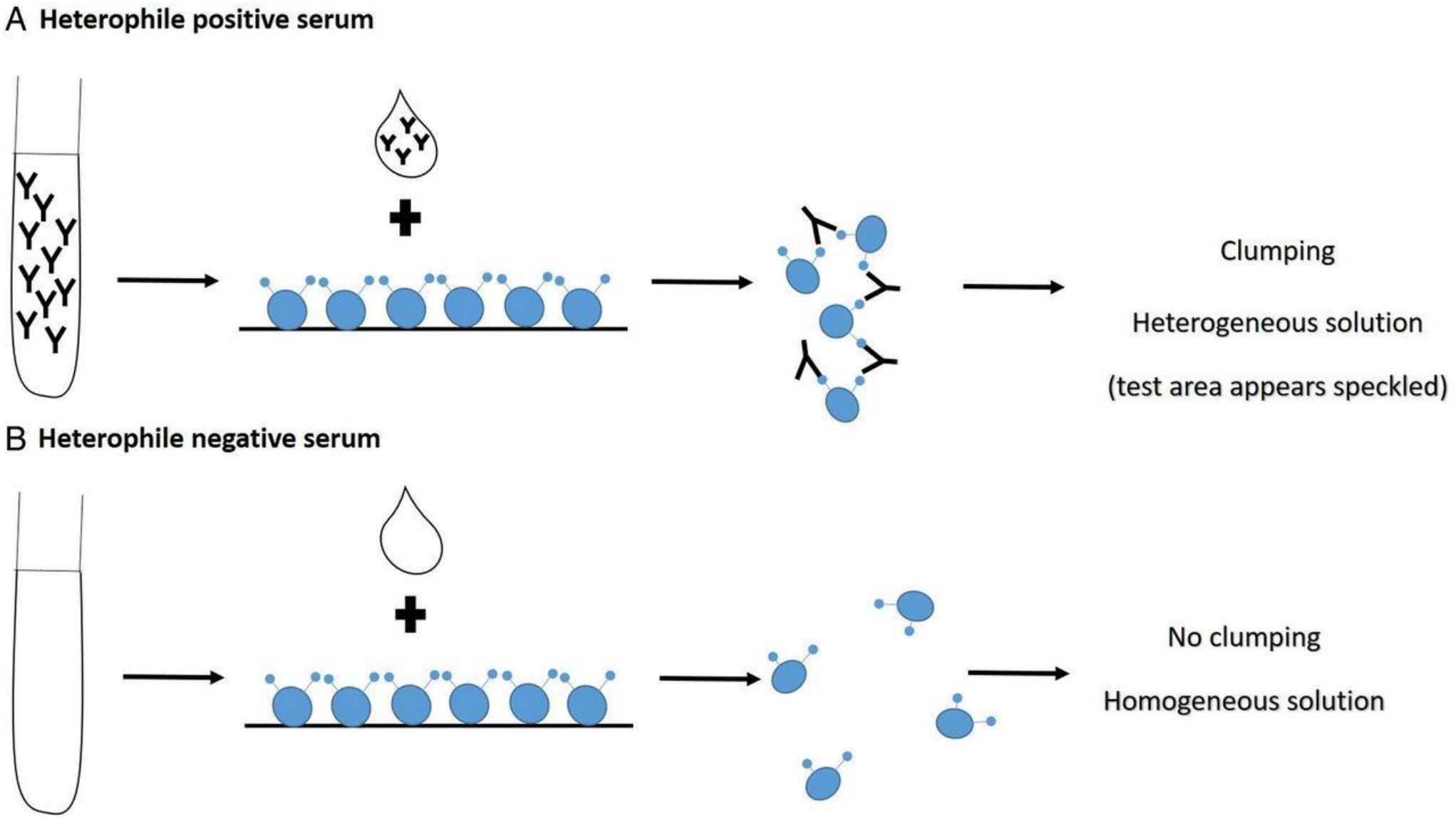
2) **CBC & WBC count** – High lymphocyte count is an indicator of EBV infection

3) **EBV antibody test** – Elevated level of VCA IgM indicates acute infection and elevated level of VCA IgG indicates chronic infection.

4) **Liver function test** – Elevated Alanine aminotransferase strengthen the clinical impression of IM

5) **Viral detection and quantification** – PCR technique detects and quantities EBV in body fluids.

6) Monospot test / Heterophile test -



TREATMENT

1. **Antipyretics** – Acetaminophen, Aspirin can be used to control fever.

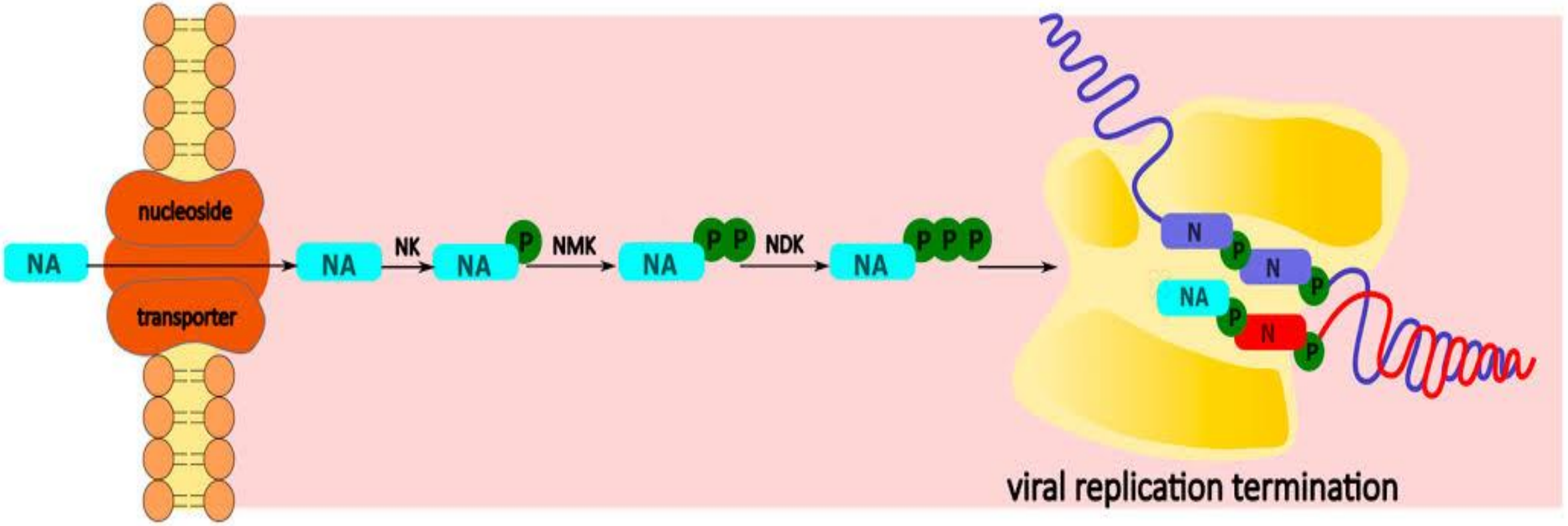
2. **Analgesics** – NSAIDs, Anesthetic throat lozenges, Viscous lidocaine hydrochloride are used to relieve pain.

3. **Fluids and Nutrition**

4. **Corticosteroid** – used to manage complications such as airway obstruction, autoimmune anemia and thrombocytopenia

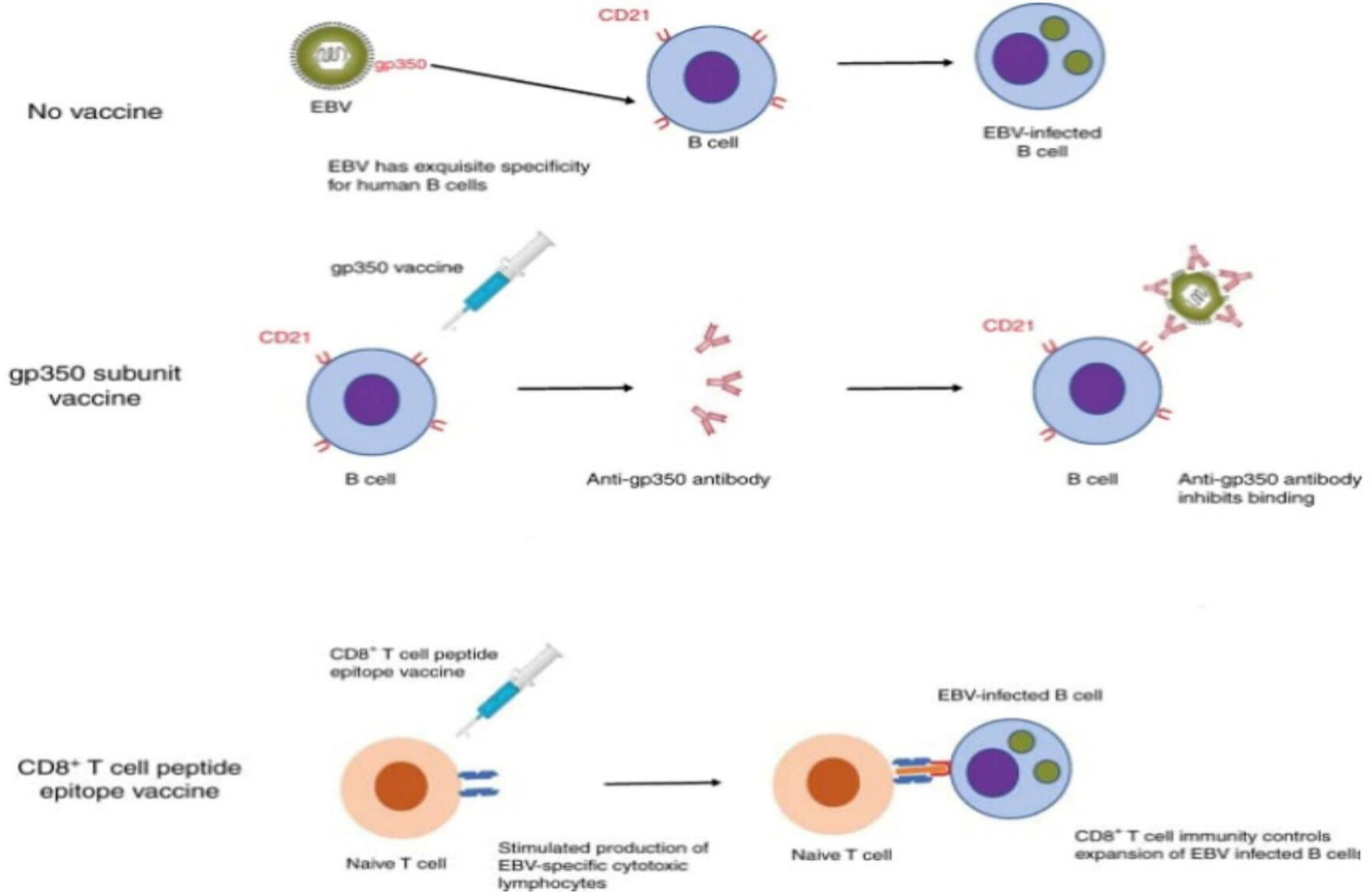
5. **Antiviral drugs** – Nucleoside analogues (Acyclovir, Valacyclovir)

→ Nucleoside Analogues (**DNA polymerase inhibitors**) – act as a faulty substrates for viral DNA polymerase, terminating synthesis of DNA chain



PREVENTION

1. **Antiviral prophylaxis**
2. **Vaccines**



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Thank You