

# **Viral Lymphadenitis**

**Microbiology & Immunology department**

# Objectives

**By the end of this lecture, the student will be able to:**

- List the major viruses causing lymphadenitis.
- Describe the taxonomy and the structure of some important viruses causing lymphadenitis.
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- Mention the mode of transmission of some important viruses causing lymphadenitis.

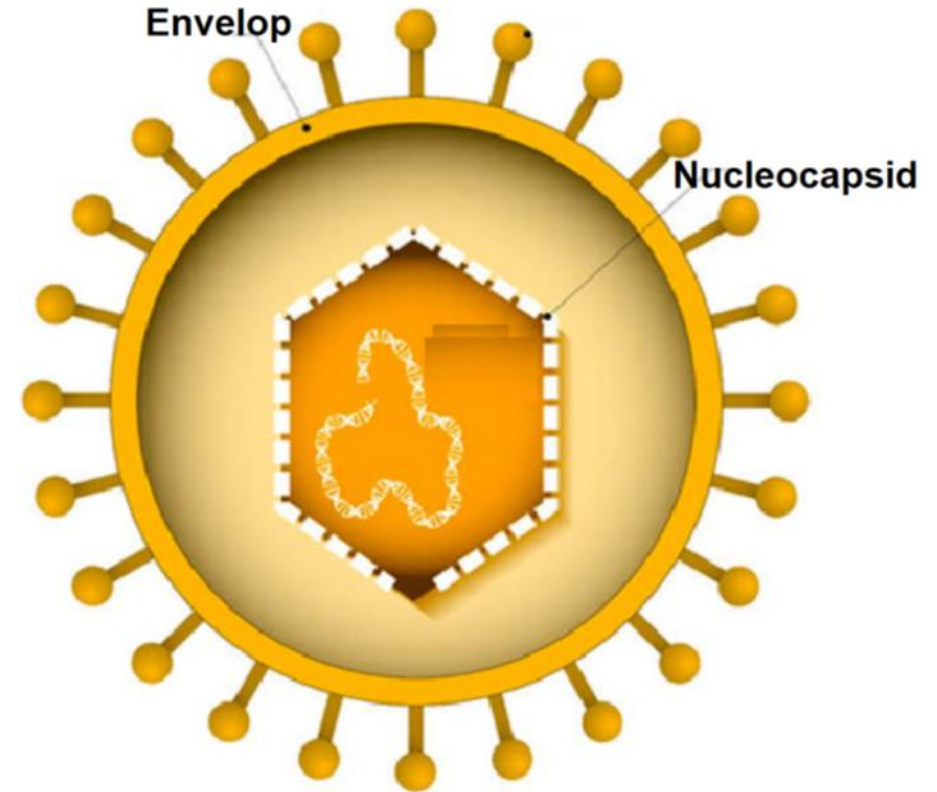
# Epstein Barr Virus

**Family:** Herpesviridae (Icosahedral, enveloped, double-stranded DNA)

**Causes** painful localized bilateral cervical or generalized lymphadenitis

## **Transmission:**

- ❑ Body secretions especially infected saliva “kissing disease”.
- ❑ Others: blood transfusion or after bone marrow transplantation.



## Pathogenesis:

I. EBV → **CD21 receptor** on B lymphocytes and epithelial cells of oropharynx.

II. Infected B lymphocytes cause:

### **Humoral (B-cell) immune response:**

Heterophile antibodies: non-specific antibodies that recognizes the Paul-Bunnell antigen on sheep, horse, and bovine erythrocytes.

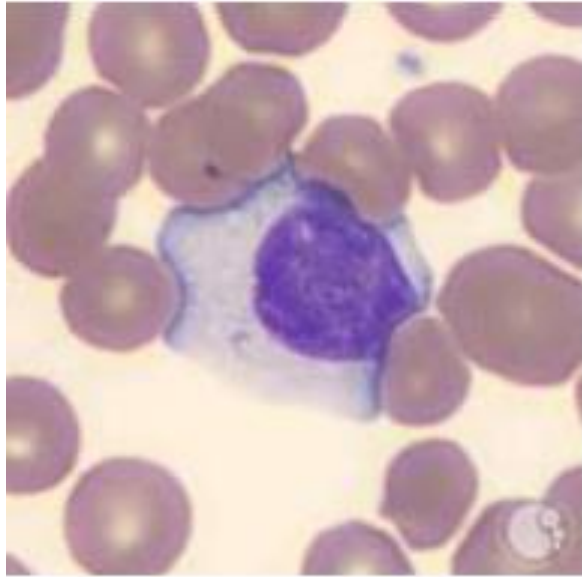
### **Cellular (T-cell) immune response:**

high concentration of atypical CD8+ (cytotoxic) T lymphocytes in the bloodstream that fight infected B lymphocytes (**Downey cells**).

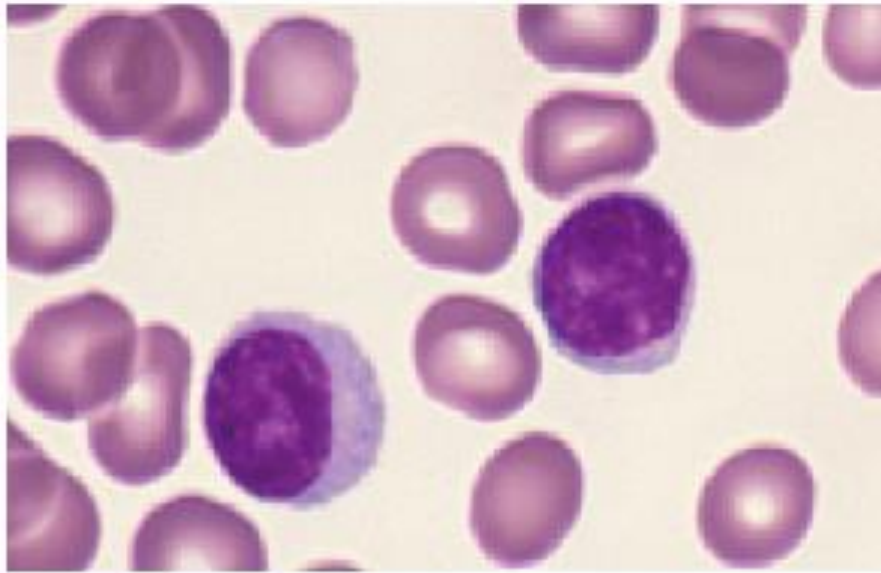
### **Malignant transformation**

Arises from immortal B cells

III. EBV can cause **latent infection** of B cells in presence of competent T cells.



**Downey cell**



**Normal lymphocyte**

## Diseases:

### **A. Infectious mononucleosis (Heterophile-positive):**

- ❑ It results from a “civil war” between EBV-infected B cells and the protective T cells causing the classic lymphocytosis (increase in mononuclear cells).
- ❑ Patients present with fever, and a triad of sore throat, enlarged lymph nodes and splenomegaly.

### **B. Lymphoproliferative disease:**

- ❑ Occurs in immunocompromised patients.
- ❑ T cells can't control the B-cell growth causing life-threatening polyclonal leukemia-like B cell proliferation.

### C. Hairy oral leukoplakia :

- ❑ Occurs in AIDS patients
- ❑ White plaques are present on the tongue due to hyperproliferation of lingual epithelial cells infected with EBV.

### D. Malignancies:

- ❑ African or Burkitt's lymphoma.
- ❑ Nasopharyngeal carcinoma.
- ❑ B cell lymphoma: Hodgkin and non-Hodgkin lymphoma.



## Laboratory Diagnosis of EBV:

Sample: blood.

Hematologic examination: Lymphocytosis with atypical lymphocytes (Downey cells).

### Serology:

#### 1. Monospot/Paul bunnell test:

- ☐ Not specific and used for screening.
- ☐ Detects heterophile antibodies (IgM antibodies that recognize Paul-Bunnell antigen on sheep, horse, and bovine erythrocytes).



## 2. EBV specific serologic tests:

Detect antibodies to viral capsid antigen (VCA) and EBV nuclear antigen (EBNA).

Antibodies	acute infection	Past infection	No infection/susceptible
VCA-IgM	+	—	—
VCA-IgG	+	+ lifelong	—
EBNA-IgG	—	+ lifelong	—

(remember EBNA=Never Acute)

# Cytomegalovirus

Family: Herpesviridae (Icosahedral, enveloped, double-stranded DNA).

Causes painful generalized lymphadenitis.

Transmission: blood transfusion, sexual, transplacental, perinatal, body fluids as saliva and transplant-transmitted infection.

Pathogenesis: CMV infects epithelial cells and becomes latent in mononuclear cells

## **Diseases:**

### **1. In immunocompetent patients:**

90%: asymptomatic course

< 10%: CMV mononucleosis → heterophile antibodies-negative mononucleosis (EBV infection is heterophile-positive mononucleosis).

### **2. In immunocompromised patients:** may be present as:

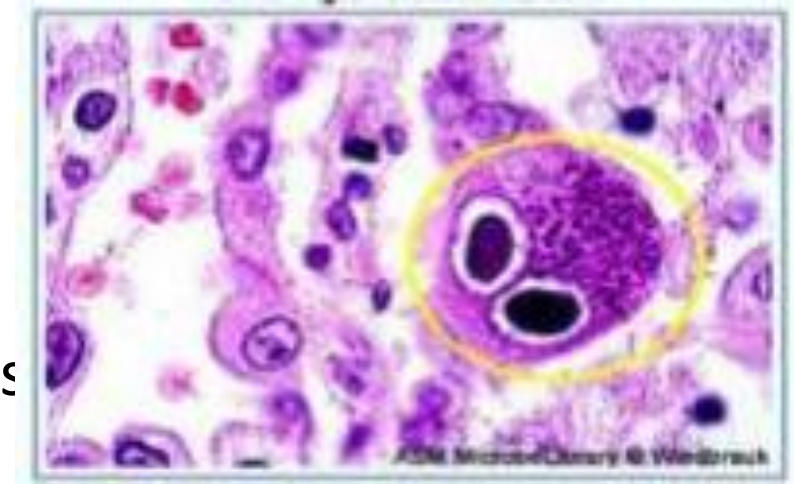
- \* CMV mononucleosis
- \* CMV pneumonia
- \* CMV retinitis
- \* CMV esophagitis and/or CMV colitis
- \* CMV encephalitis.

### **3. Cytomegalic inclusion disease:** in-utero (congenital) CMV infection.

## Diagnosis:

**1. Owl-eye inclusion** in biopsy material and urine

(cytomegalic cell that contains basophilic intranuclear inclusion)



**2. PCR:** diagnosis is primarily based on PCR.

**3. Serology:**

Detection of CMV specific antibodies: -IgM=current infection -IgG=past infection.

**4. Cell culture:**

- Too slow to guide treatment.
- Characteristic cytopathic effect include cytomegalic cell that contains basophilic intranuclear inclusion.

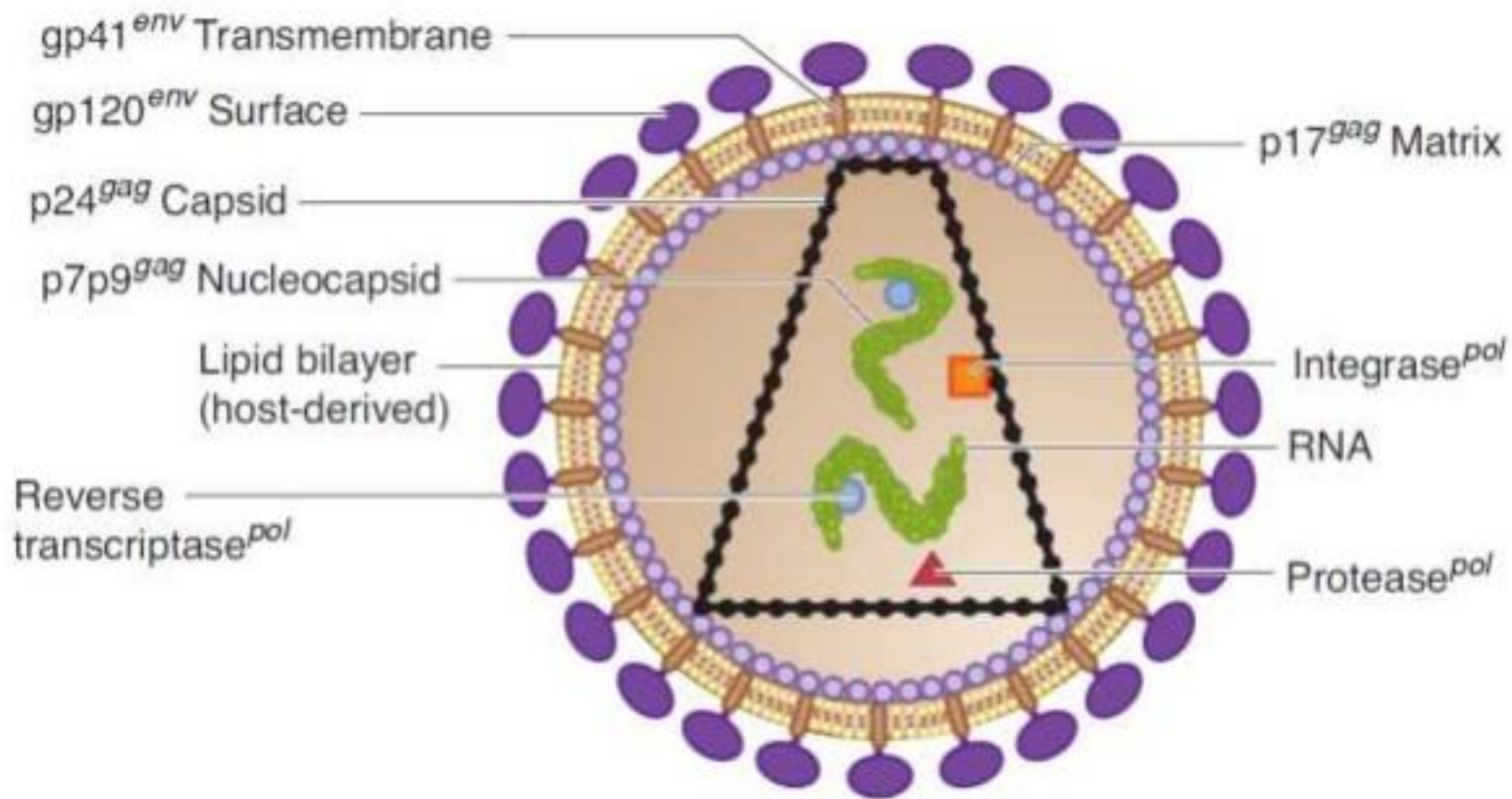
# Human Immune deficiency virus (HIV)

Family: Retroviridae (Icosahedral).

Types of HIV: HIV-1 and HIV-2

The HIV virion contains:

- 1– Envelope
- 2– Two copies of the ss (+) RNA
- 3– RNA-dependent DNA polymerase (reverse transcriptase)
- 4– Integrase (for integration of viral DNA into the host genome)
- 5– Protease (breaks down proteins)



## **Transmission:**

1-Sexual contact

2-Bloodborne (transfusions, dirty needles and infectious blood on mucous membranes)

3-Vertical

## **Pathogenesis:**

❑ Surface glycoprotein (gp120) of HIV binds to CD4 of T-helper cells and macrophages.

❑ The virus attacks and destructs CD4+ T cells ending in loss of immunity manifested by repeated infections or cancers.

## **Clinical course:**

**Incubation period:** The duration between primary infection and progression to clinical disease. Averages about 10 years.

### **Stage 1- Acute HIV infection**

- The earliest stage
- Develops within 2–4 weeks after infection
- People have mononucleosis-like symptoms (fever, fatigue, generalized lymphadenopathy, etc.)
- The level of HIV in the blood is very high, with great risk of HIV transmission



## **Stage 2- Chronic HIV infection:**

- Also called asymptomatic HIV infection or clinical latency
- HIV continues to multiply but at low levels
- People may not have any HIV-related symptoms
- Without treatment, it usually advances to AIDS in 10 years or longer

### Stage 3- AIDS (Acquired immunodeficiency syndrome):

- It is the final, most severe stage of HIV infection.
- Because HIV has severely damaged the immune system, the body can't fight opportunistic infections and malignancies
- Wasting syndrome (progressive weight loss and weakness) is a common complication.
- Patients usually have a high viral load and are able to transmit HIV to others very easily.
- Without treatment, people with AIDS typically survive about 3 years.

## Opportunistic infections associated with AIDS

- 1) Fungal infections: e.g., Pneumocystis jirovecii, **candida** and Cryptococcus.
- 2) Viral infections: e.g., – Cytomegalovirus retinitis – Herpes simplex 8
- 3) Bacterial infections: e.g.,
  - Mycobacterium tuberculosis, any site (pulmonary or extrapulmonary).
  - Mycobacterium avium complex
  - Salmonella: septicemia, recurrent Parasitic infection

## Malignancies associated with AIDS

- Invasive cervical carcinoma
- Kaposi sarcoma: a cancer develops from the cells that line lymph or blood vessels.



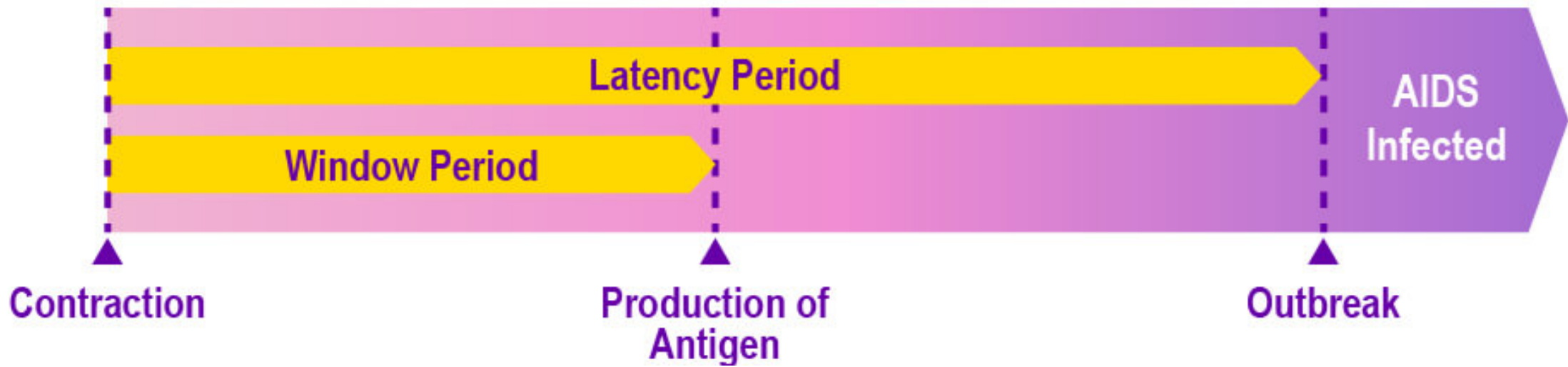
- Burkitt lymphoma, immunoblastic lymphoma, or primary CNS lymphoma

## Laboratory diagnosis of HIV:

<b>Initial screening</b>	<b>Detection of:</b> <ul style="list-style-type: none"><li>▪ HIV p24 capsid antigen (an early marker of infection).</li><li>▪ IgM &amp; IgG antibodies to HIV</li></ul>
<b>Confirmation</b>	<ul style="list-style-type: none"><li>- HIV1/HIV2 differentiation immunoassay</li><li>- Nucleic acid testing (NAT) e.g. PCR</li><li>- Western blot (in Egypt)</li></ul>
<b>Evaluate progression of disease</b>	CD4 count CD4:CD8 T-cell ratio

## Window period

- Time from initial infection with HIV until antibodies are detected by a single test
- Usually about 3–8 weeks before antibodies are detected
- Laboratory tests are false-negative for HIV during this time period
- Can still pass the virus to others during this period



# Questions



## Case 1

A 19-year-old college student presents to the clinic with a 5-day history of fever, severe sore throat, and swollen neck glands. He reports feeling extremely fatigued and has lost his appetite. On examination, he has bilateral tender cervical lymphadenopathy, pharyngitis, and mild splenomegaly.

### **Questions:**

- A. What is the most possible diagnosis?
- B. Which virus is most likely responsible for this presentation?
- C. What is the virus receptor on B lymphocytes?
- D. Mention 2 diagnostic tests for this disease?



## Case 2

A 35-year-old male with a known history of HIV infection (diagnosed 8 years ago, poorly adherent to antiretroviral therapy) presents with progressive weight loss, chronic diarrhea, and persistent generalized lymphadenopathy. He also reports blurry vision and floaters in his right eye. On fundoscopic examination, you notice retinal hemorrhages and exudates.

### **Questions:**

- A. Which opportunistic viral infection could explain his visual symptoms?
- B. What is the diagnostic histological finding associated with this virus in infected tissues?
- C. Besides the visual symptoms, name two other clinical manifestations this virus can cause in AIDS patients.

THANK  
YOU

A vibrant, comic-style illustration of the words "THANK YOU" in large, 3D block letters. The word "THANK" is pink with yellow and blue sides, and "YOU" is yellow with pink and blue sides. The letters are surrounded by a black outline with motion lines, and several yellow and pink stars are scattered around the text.