Herpes viruses

The main general characters of this family

- Slow replication time
- The ability to establish latent infections
- Susceptibility to antiviral agents
- Some members are oncogenic

Herpes viruses that infect humans:

- Herpes simplex viruses (HSV) type 1 and 2
- Varicella-zoster virus
- Cytomegalovirus (CMV)
- Epstein-Barr virus (EBV)
- Human herpes virus 6,7,8: (HHV 6), (HHV 7), (HHV 8).

HERPES SIMPLEX VIRUSES

- There are two herpes simplex virusus, that cross-react serologically but some unique epitopes exist for each type.
- Mood of transmission:

HSV-1 spread by contact with infected saliva.

HSV-2 transimitted sexually or to newborns through transvaginal delivery.

The infections that occurs by these routes are primary infections.

Primary infection

- Commonly occur in children 2-4 years of ages in case of herpes simplex 1 after droplet infection, and in case of HSV 2 Primary infection occur after sexual contact In adults or after vaginl delivery in newborns.

PATHOGENESIS

- HSV multiply locally in the mucous membranes or abraded skin causing cytolysis, necrosis, ballooning, and multinucleated giant cell formation with intranuclear inclusion bodies.
- Giant cell formation occurs due cell fusion that provide cell-to-cell spread even in the presence of neutralizing antibodies.

Clinical manifestations

HSV-1:

Primary infection is either asymptomatic or in the form of tonsillopharyngitis.

Reactivation:

After disappearance of the primary lesions the virus persist in a latent focus (trigeminal ganglia), where the persists life long.

- Reactivation takes the form of vesicular eruption that changes to shallow ulcers and scab forms that heals without scarring.
- In HSV-1 reactivation may take one of the following forms:

1- herpes labialis: crops of vesicles at the mucocutaneous junctions of the lips or the nose that recurred at the same site.

2- keratoconjunctivitis: corneal ulcers that may leave opacities after healing and leads to blindness.

3- encephalitis: that has a fatal outcome.

4- disseminated infections: such as pneumoniae in immunocompromized patients e.g. AIDS or transplant patients

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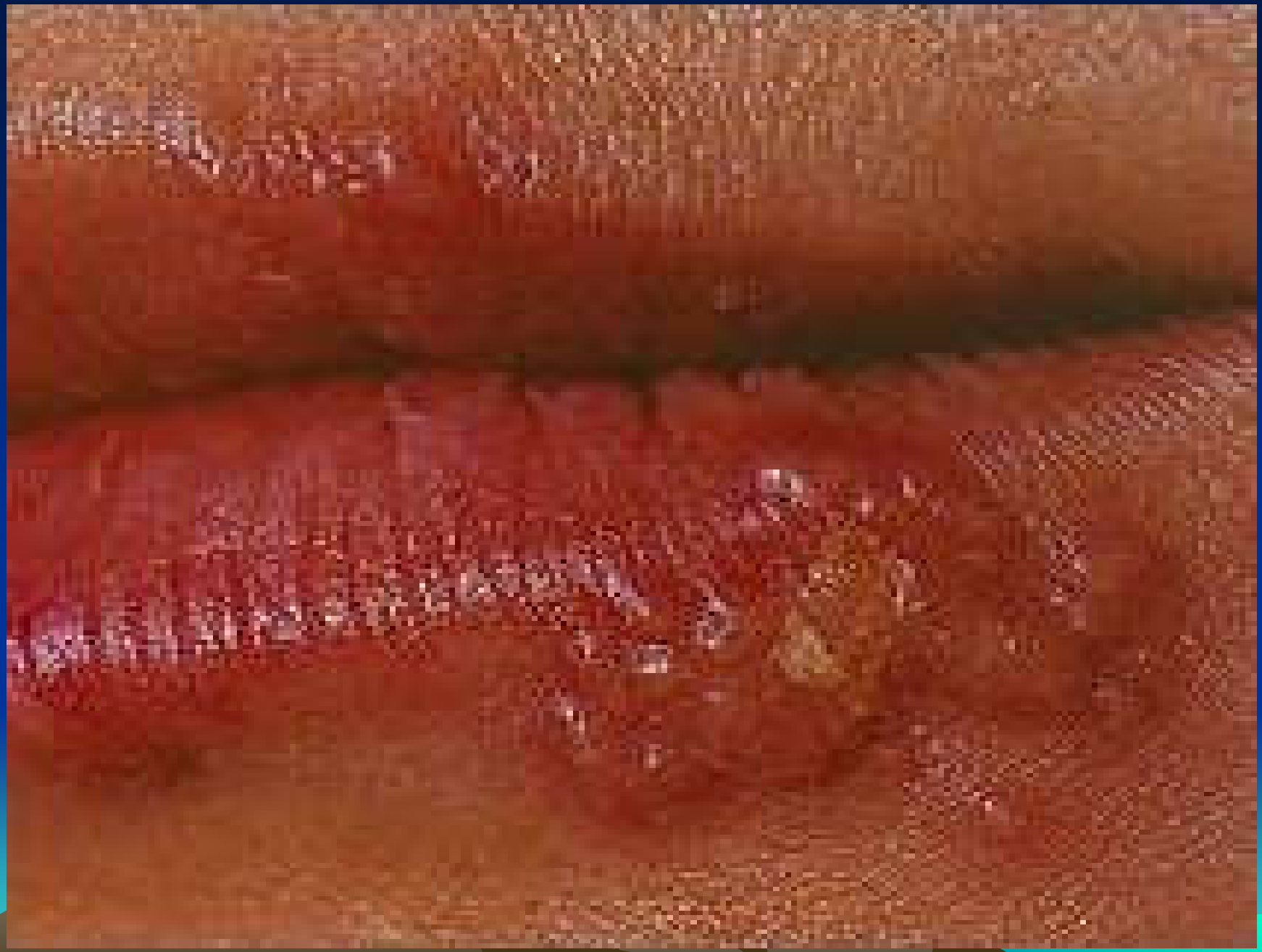

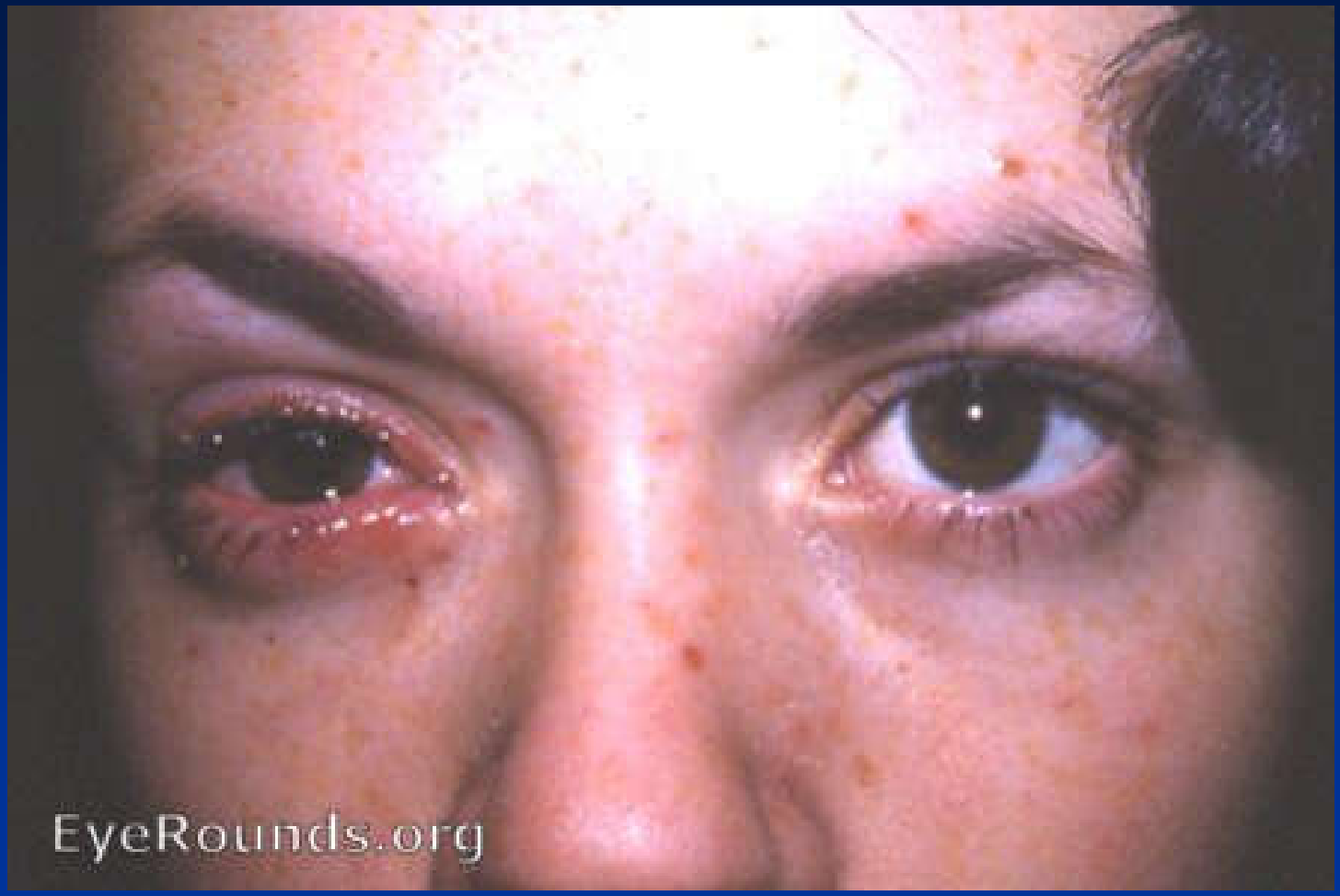
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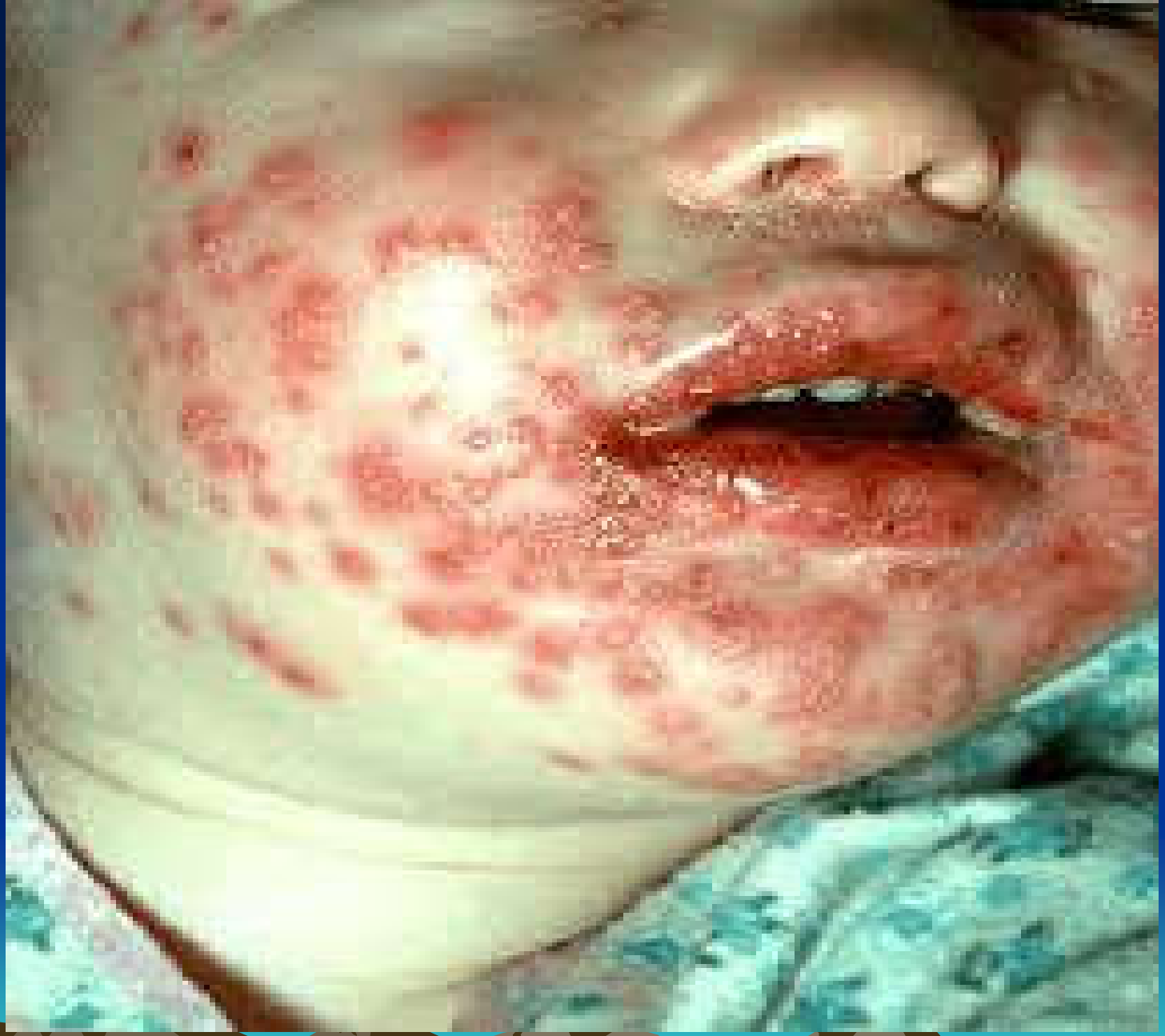


HSV-2:

Primary infection: takes one the two following forms:

1- genital herpes, which is characterized by vesiculoulcerative lesions on the external genetalia and cervix associated with fever and inguinal lymphadenopathy.

2- neonatal herpes:

Leads to disseminated disease of the newborn including meningitis and encephalitis. Delivery by CS is recommended

- Reactivation: the same clinical picture as genital herpes or just viral shedding.

Diagnosis

- Mainly clinical clinical diagnosis, laboratory diagnosis is needed when the clinical picture is unclear.
- 1- T zanck smear: scrapings from the base of skin lesions are stained with Geimsa , the presence of multinucleated giant cells with intranuclear inclusions is suggestive of HSV infection.

2- vesicular fluid: detection of viral antigens by ELISA or viral DNA by DNA probes.

3- PCR: specially for rapid diagnosis of viral encephalitis.

4- isolation of the virus:

- Cytopathic effect.
- ELISA
- Direct immunoflorescence

5- Serology: rise in antibody titre, or the presence of specific IgM specially in newborn

Treatment

- Acyclovir is used for all herpetic infections and is useful if given early and IV in encephalitis, disseminated systemic infections, and neonatal infections.
- Foscarnet is used for acyclovir resistant cases
- Topical ointements for herpetic keratitis and orolabial infections such as idoxuridine and trifluridine

Prophylaxis

- Recombinant HSV-2 glycoprotein vaccine, which is only active in sero-negative women.
- Delivery by CS for prevention of HSV-2

Varicella-zoster virus (VZV)

- There is only one type of the virus.
- It causes two distinct clinical conditions:

1- Varicella: which is the primary form and is characterized by generalized eruptions.

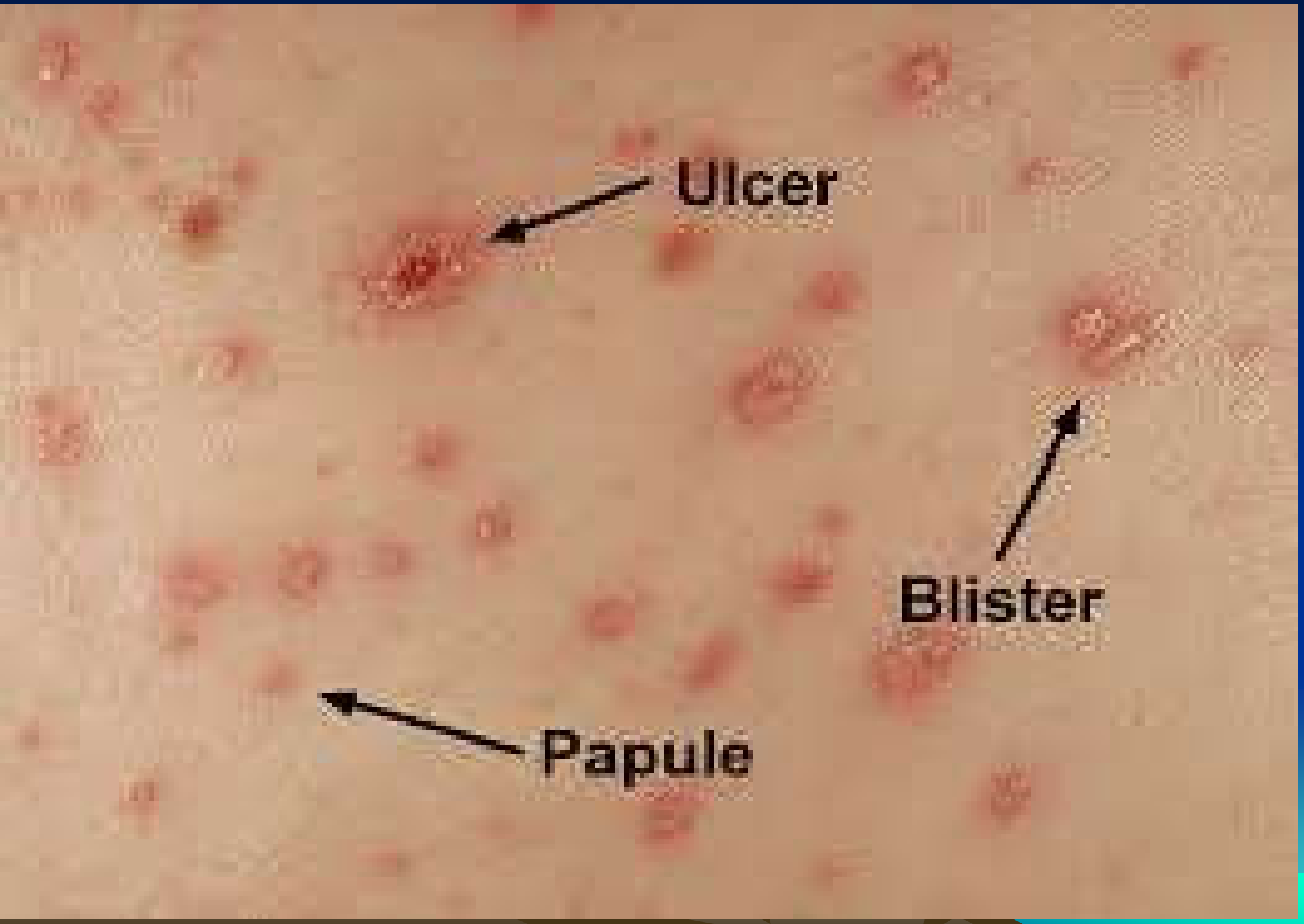
2- Zoster is the recurrent form and is characterized by localized painful eruption

Clinical picture varicella

- Usually affect children
- Highly contagious
- Restricted to the epidermis
- Infection is acquired by droplet or by contact with lesion

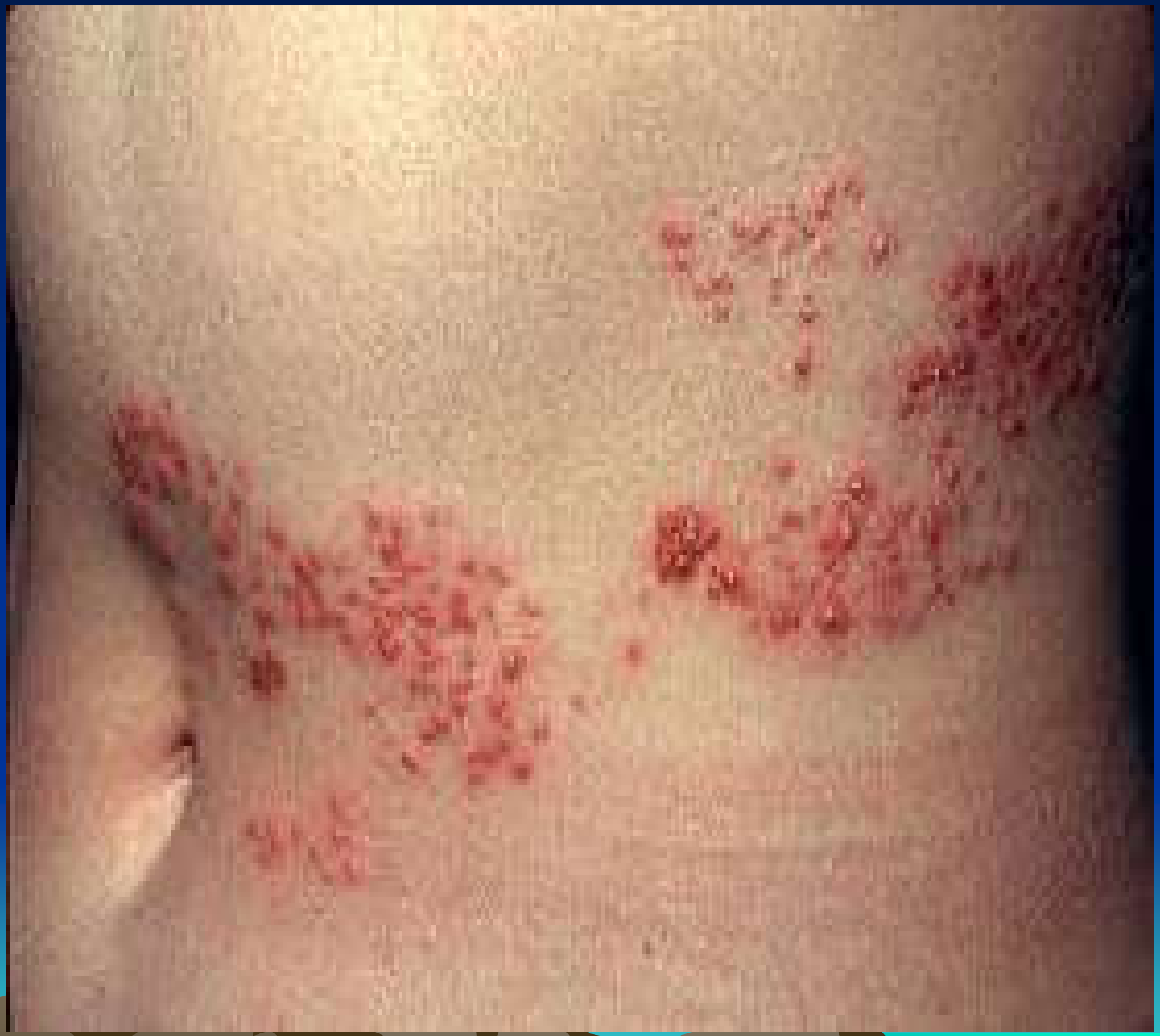
I.P. is 2-3 weeks, the initial multiplication occur in the respiratory tract, then the virus spread through the blood to skin causing the typical rash. papule, vesicle, pastule , crust without scar formation

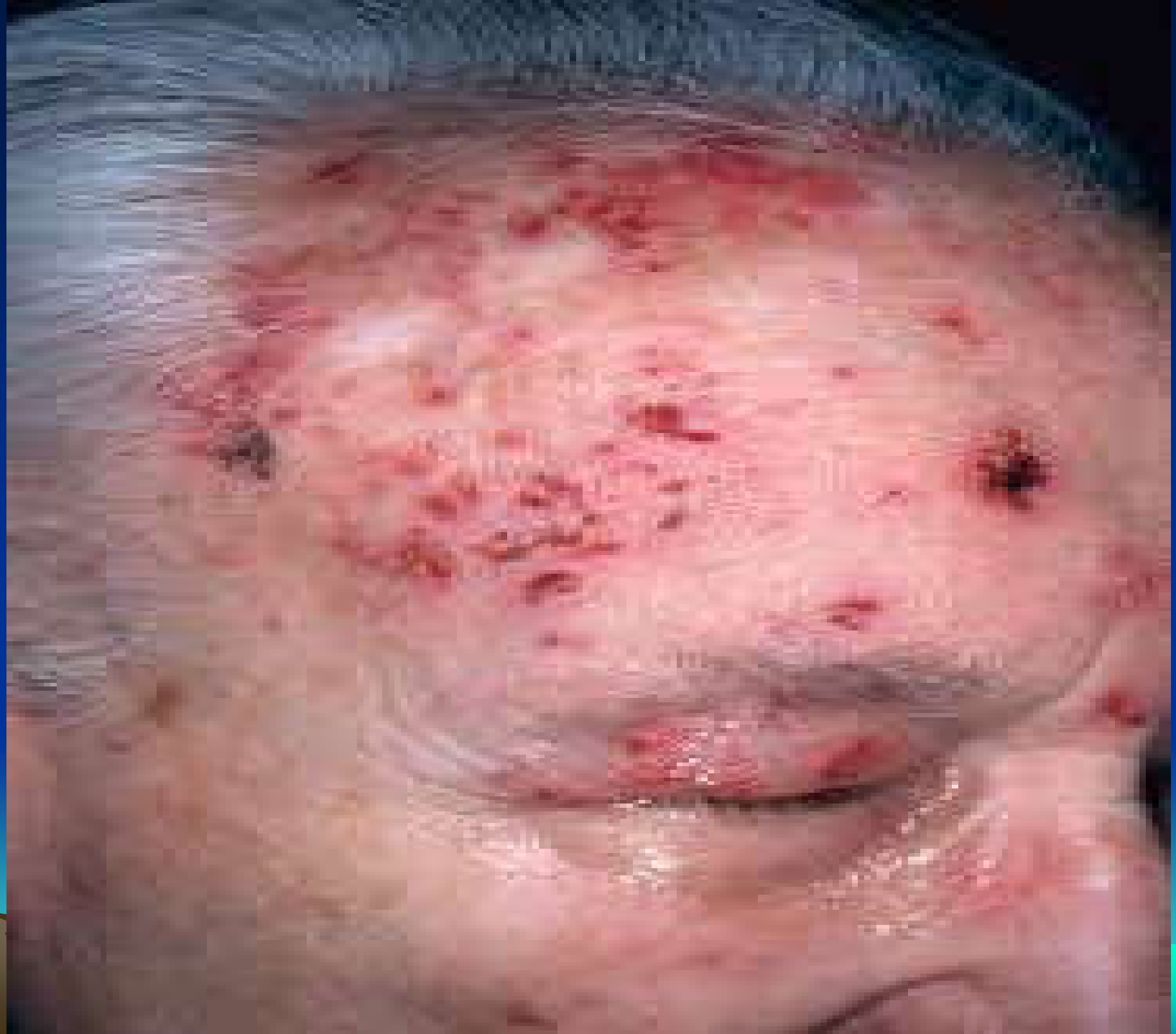
- The rash begin in the trunk and spread to the face and the limbs. After recovery the virus remain latent in the dorsal root ganglia. The disease is usually mild in children and more sever in adults and immunocompromized.
- Congenital varicella syndrome: it occurs following maternal chicken box during pregnancy or just after birth and it has a fatal outcome.
- Immunity following varicella is life long but zoster can occur in spite of this immunity


Ulcer
Blister
Papule

zoster

- It is the reactivation form of varicella that occur in adults and immunocompromized patient. It affects the sensory nerves and their ganglia to sever pain in the area of skin supplied by these nerves, then crops of vesicles appear over the area supplied by these nerves.
- The eruption is unilateral affecting the trunk and the and the neck, specially the ophthalmic division of trigeminal nerve.
- Susceptible children develops varicella on exposure to an adult zoster patient





prophylaxis

- Isolation of the affected children for 5-7 days.
- **Varivax:**

Living attenuated vaccine that

Recommended for children 12-15 month and second dose at 4-6 years, it is given by SC injection.

Not given to immunosuppressed patients and pregnant women.

- Zostavax:

A new living attenuated vaccine . Given as a single subcutaneous dose to old individuals 60 years or more. It reduces the risk of getting zoster.

- Acyclovir and varicella zoster immunoglobulin are used in preveting varicella and disseminated zoster in immunocompromized persons.

treatment

- Soothing agent for the vesicles.
- Antipyretic
- Antibiotic to prevent secondary bacterial infection presence of multinucleated giant cells
- Acyclovir, valacyclovir, and foscarnet: used in adults with varicella, and in disseminated varicella disease

CMV

- It is one of the herpes virus family
- Is causes massive enlargement of the infected cells, hence its name.
- It is transmitted by the following routes :

1- congenital

2- through the birth canal.

3- by breast milk.

4- sexually.

5- blood transfusion.

Clinical picture

In normal host:

- * asymptomatic latent infection with virus persistence in the leucocytes and kidney. Intermittent shedding in saliva and urine may occur.
- * hetrophil antibody negative infectious mononucleosis like syndrome.
- * restenosis of coronary artery angioplasty due to proliferation of smooth muscle cells

In immunocompromized host:

- It causes systemic infection , pneumonia, retinitis, graft rejection. Usually infection is due to reactivation of latent infection.

Congenital infection:

- After primary infection or reactivation in the muscle. It causes abortion, stillbirth, and cytomegalic inclusion disease which is characterized by congenital anomalies such as blindness, deafness, mental retardation, or microcephaly. Hepatosplenomegally, jaundice, and purpura may occur

diagnosis

- 1- detection of intranuclear cytoplasmic inclusions in tissues and in desquamated epithelial cells in urine.
- 2- detection of CMV DNA in tissues and body fluids by PCR , used also for determination of viral load.
- 3- serology: detection of IgM and rising titre of IgG, DIAGNOSIS OF INTRAUTRINE INFECTION THROUGH IgM

TREATMENT

- Gancyclovir is used for systemic infection
- Valgancyclovir (oral)
- Foscarnet and cidofovir used in treatment of viral retinitis.
- Blood transfusion and organ transplatation should CMV negative specially in neonate

Epestien- Barr virus (EBV)

It causes the following clinical conitions:

1- infectious mononucleosis

2- nasopharyngeal carcinoma.

3- Burkitts lymphoma.

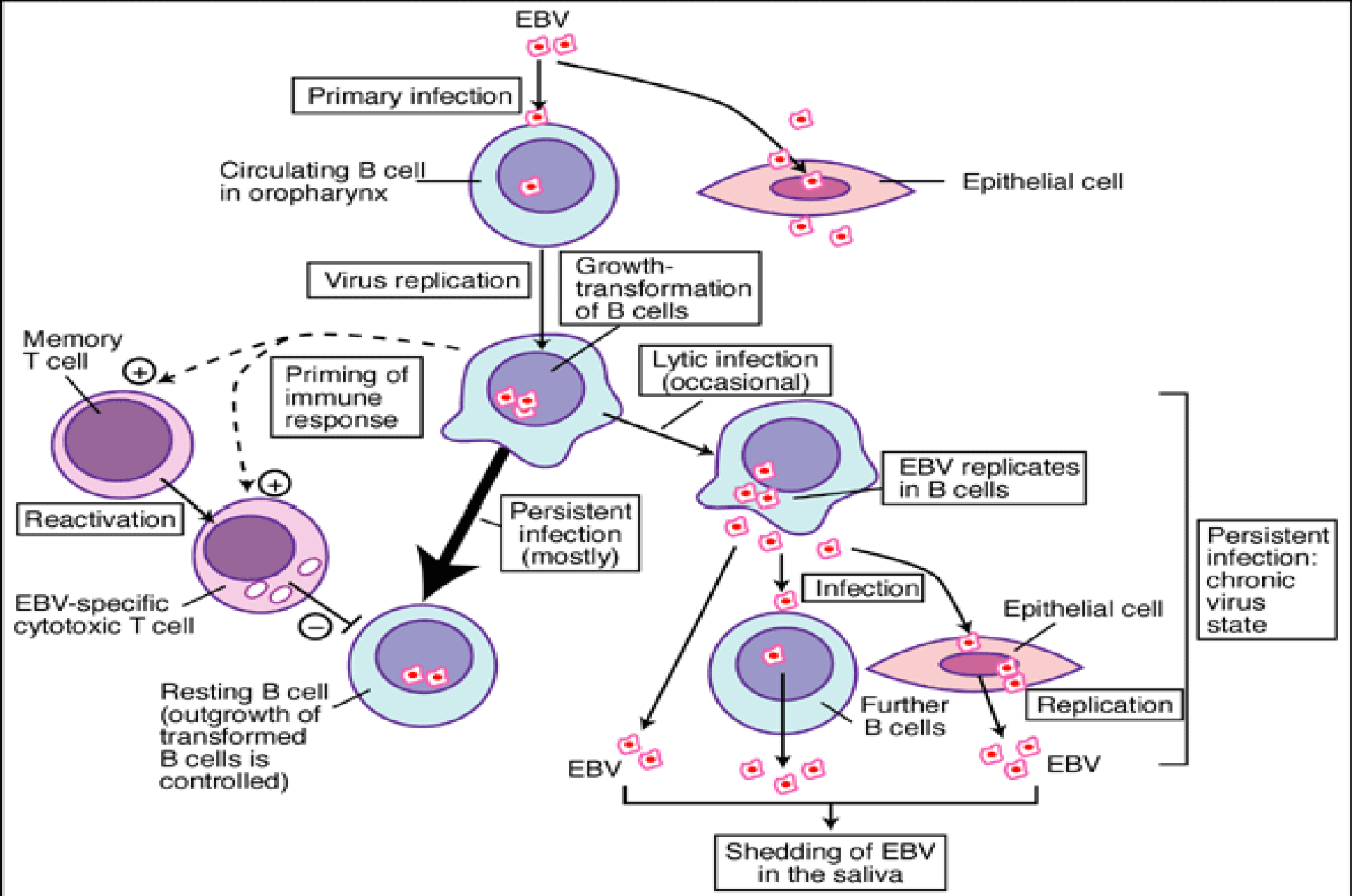
4- In immunodiffient patients it causes oral hairy leucoplakia and immunoproliferative disorders.

Antigenic structure

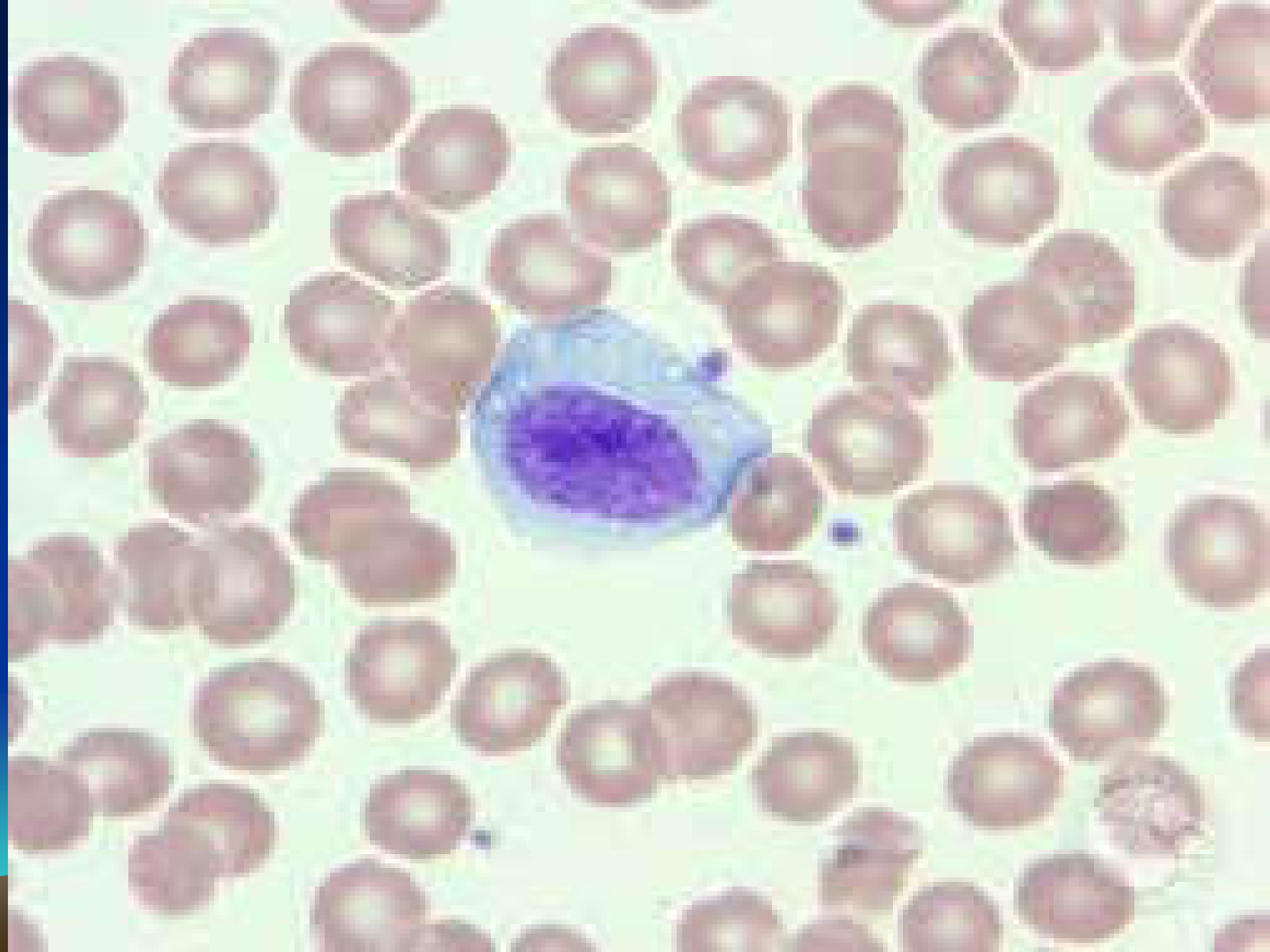
- Viral capsid antigen (VCA).
- Early antigen (EA).
- Epestien-Barr nuclear antigen (EBNA).
- Membrane antigen (MA)

pathogenesis

- It is transmitted by infected saliva, very rarely by blood transfusion.
- Infection starts in the oropharynx then spread to blood where B lymphocytes are infected. Cytotoxic T cells react against infected infected B lymphocytes and appear as atypical lymphocytes.
- The virus remain latent in B lymphocytes and leads to theirtransformation and immortalization.



Epstein–Barr virus (EBV) infection in normal healthy virus carriers

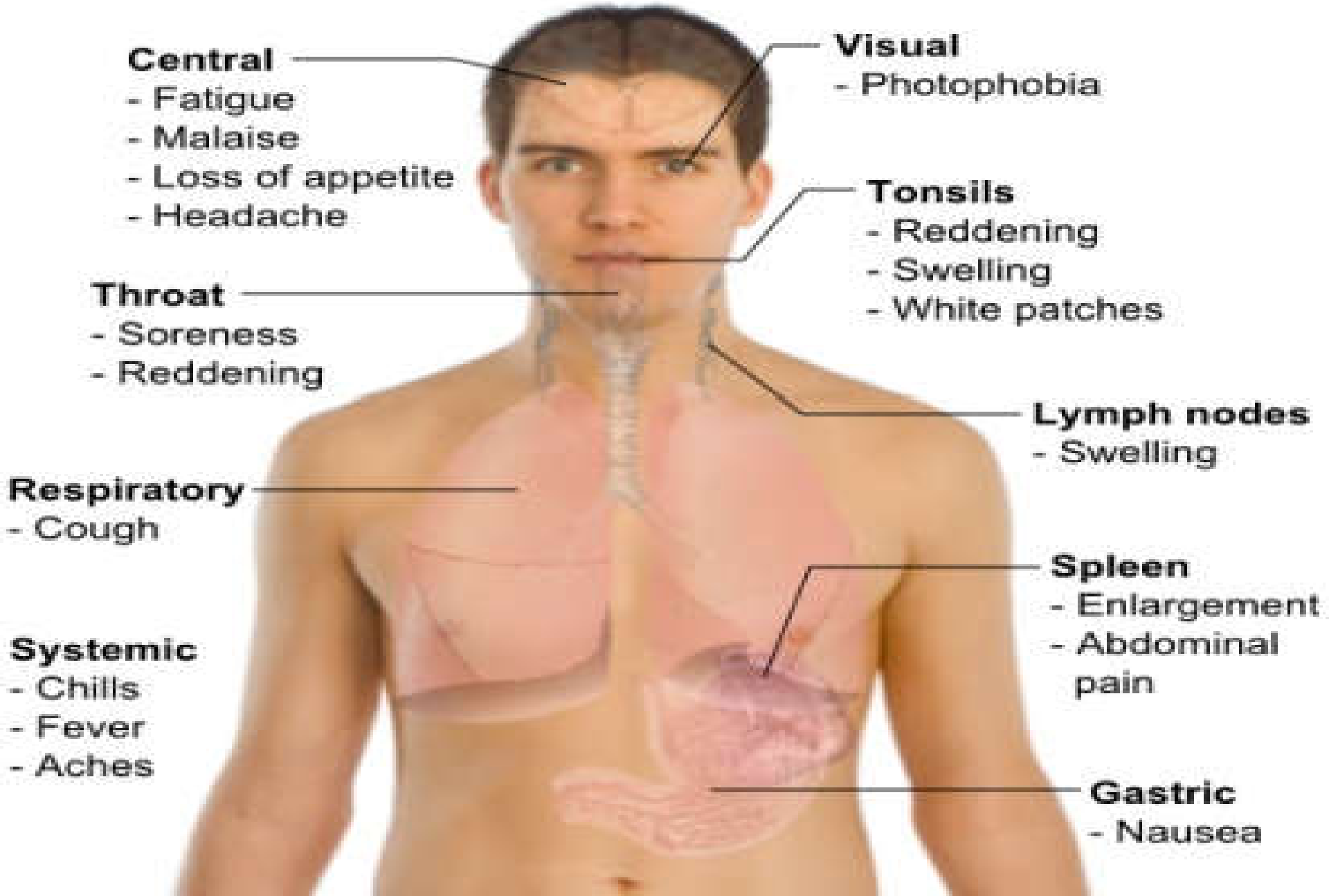


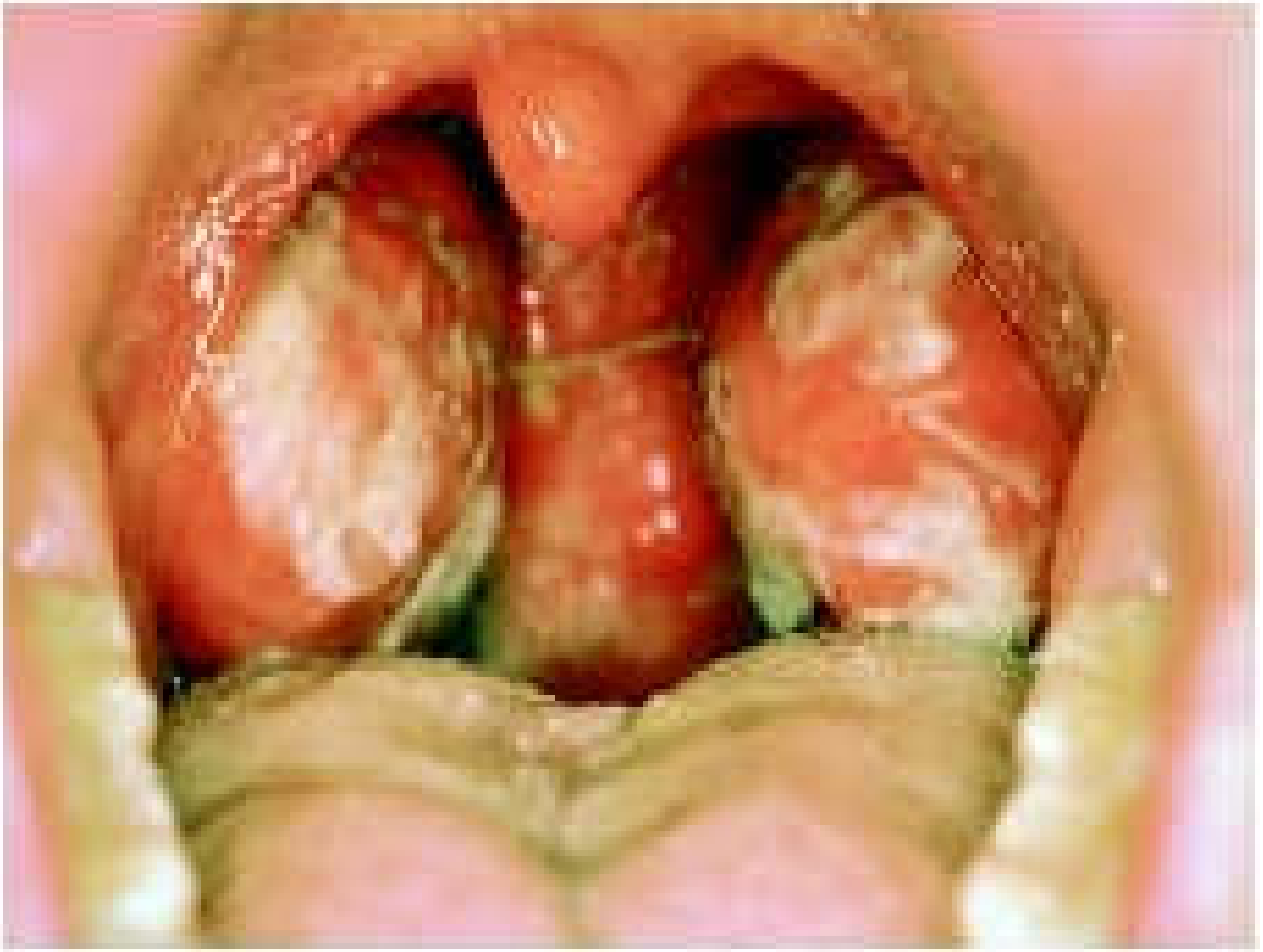
Clinical picture of infectious mononucleosis

- IM manifested by fever, rash, sorethroat, enlarged lymph nodes and spleen, hepatitis. The disease is self limitting.
- IM in children having inherited immunodifficiency disorders resulting x-linked lymphprolipherative syndrome.

Main symptoms of

Infectious mononucleosis





diagnosis

- 1- blood picture:
- Increased leucocytic count (25,000/cmm) with absolute lymphocytosis, monocytosis, and atypical lymphocytosis.
- 2- PCR: Detection of EBV DNA by PCR in saliva, thraot washing, and lymphatic tissue.
- 3- Serology: detection of heterophil antibodies (mono-spot or Paul Bunnel test). These antibodies are nonspecific.

- 4- Detection of specific antibodies by ELISA or immunoflore:
- IgM to VCA indicates recent infection, while IgG to VCA or EBNA indicates past infection.
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Thank you