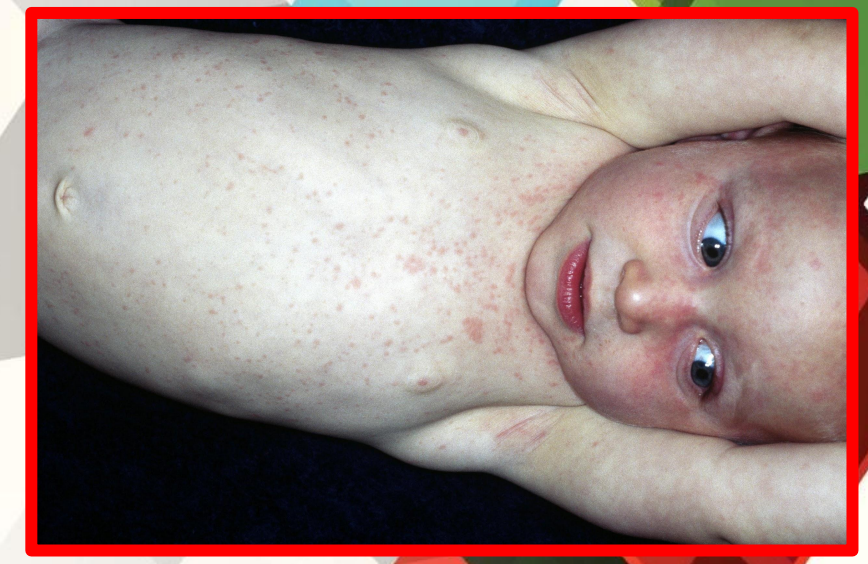
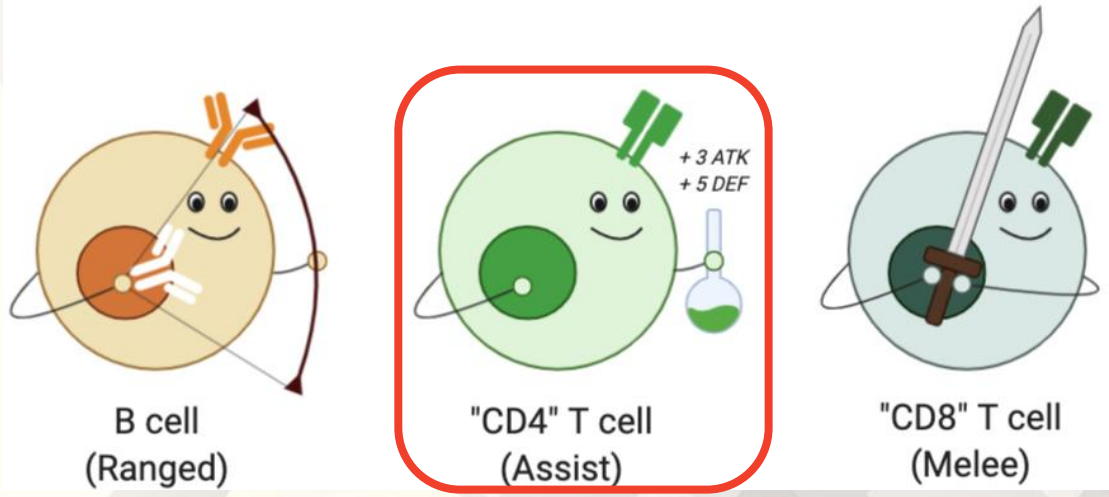
- Cause roseola infatum (Sixth disease)

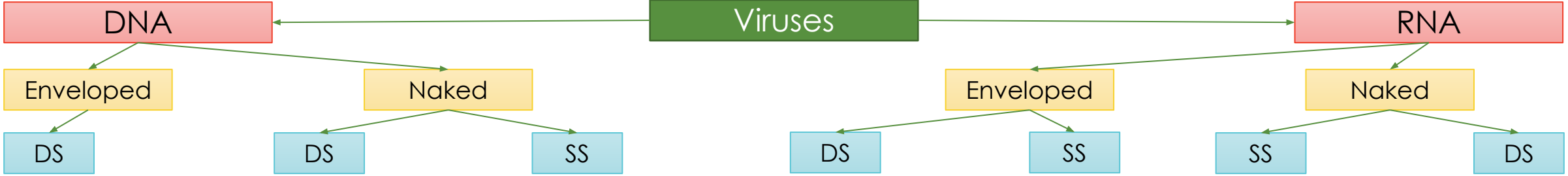


- Infect mainly CD4+ T cells



Herpesvirus 6 & 7

Done by: Abdelhadi Okasha



Herpesviridae (Ic)

-Herpes simplex virus 1&2

-Varicella-zoster

-Epstein-Barr virus

-Cytomegalovirus

-HHV 6 (A & B)

-HHV 7

Adenoviridae (Ic)

Adenovirus

Parvoviridae (Ic)

Parvovirus B19

Bocaviruses

Guidelines:
SS: single stranded
DS: Double stranded
Ic: Icosahedral 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

HHV-6 & 7

1- Structure & general info's

 Isolates of HHV-6 segregate into two closely related but distinct antigenic groups (designated A and B).
 The virus exhibits a limited cross-reactivity with HHV7

2- Pathogenesis & clinical manifestations

 The mode of transmission of HHV-6 is presumed to be via oral secretions.
Cells in the oropharynx must become infected because virus is present in saliva.
The virus is transmitted then to lymph nodes by dendritic cells and infect CD4+ T cells their where they replicate best (by CD46 receptors)
 Other cell types also support viral replication, including B cells and cells of glial, fibroblastic, and megakaryocyte origin.
 It is not known which cells in the body become latently infected.
 Clinical pathways may be one of the followings:
1) Asymptomatic
2) roseola infantum (exanthem subitem or sixth disease)
3) Special manifestations in reactivation
4) Encephalitis

3- Epidemiology

 Sero-epidemiologic studies using IF tests for serum antibodies or PCR assays for viral DNA in saliva or blood cells have shown that HHV-6 is widespread in the population. It is estimated that more than 90% of children older than age 1 year and adults are virus positive.
 Infections with HHV-6 typically occur in early childhood

4- HHV-7

A T-lymphotropic virus, first isolated in 1990 from activated T cells recovered from PB lymphocytes.
HHV-7 is immunologically distinct from HHV-6, although they share about 50% homology at the DNA level.
Most infections occur in childhood but later than the very early age of infection noted with HHV-6.
Persistent infections are established in salivary glands.
In a longitudinal study of healthy adults, 75% of subjects excreted infectious virus in saliva one or more times during a 6-month observation period.
Like HHV-6, primary infection with HHV-7 has been linked with roseola infantum in infants and young children. Any other disease associations of HHV-7 remain to be established.

1- Structure & general information HHV-6

- The T-lymphotropic HHV-6 was first recognized in 1986.
- Initial isolations were made from cultures of PBMCs from patients with lymphoproliferative disorders
- The viral DNA is about 160– 170 kbp. The genetic arrangement of the HHV-6 genome resembles that of CMV.
- Isolates of HHV-6 segregate into two closely related but distinct antigenic groups (designated A and B).
- The virus exhibits a limited cross-reactivity with HHV-7


Arch Virol
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BRIEF REVIEW

Classification of HHV-6A and HHV-6B as distinct viruses

Dharam Ablashi · Henri Agut · Roberto Alvarez-Lafuente · Duncan A. Clark · Stephen Dewhurst · Dario DiLuca · Louis Flamand · Niza Frenkel · Robert Gallo · Ursula A. Gompels · Per Höllsberg · Steven Jacobson · Mario Luppi · Paolo Lusso · Mauro Malnati · Peter Medveczky · Yasuko Mori · Philip E. Pellett · Joshua C. Pritchett · Koichi Yamanishi · Tetsushi Yoshikawa

2- Pathogenesis & clinical manifestations

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CD46: act as a receptor for the Edmonston strain of measles virus, *human herpesvirus-6* (HHV-6), group B adenoviruses, and type IV pili of pathogenic *Neisseria*.

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GUEST COMMENTARY

Four Viruses, Two Bacteria, and One Receptor: Membrane Cofactor Protein (CD46) as Pathogens' Magnet

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2- Pathogenesis & clinical manifestations

- Clinical pathways may be one of the followings:
  1) Asymptomatic
  2) roseola infantum (exanthem subitem or sixth disease)
  3) Special manifestations in reactivation
  4) Encephalitis
- 2) roseola infantum: mild common childhood disease characterized by a high fever and skin rash.
  The 6B variant appears to be the cause of this disease. The virus is associated with febrile seizures in children.
- Additional note: exanthema diseases are
  1.Measles (first disease) 2.Scarlet fever (second disease)
  3.German measles (third disease) 4.Variant of scarlet fever 5.Erythema infectosum
  6.Roseola which is caused by HHV 6B

ROSEOLA INFANTUM

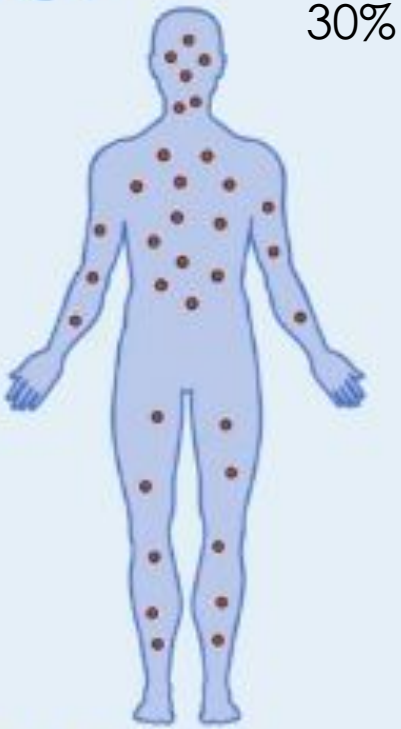
INCUBATION
* 1-2 wks

AFTER INCUBATION
* HIGH FEVER
  - ~ > 40°C (104°F)
  - ~ 3-5 days

FEBRILE
* PERIORBITAL EDEMA
* ACUTE OTITIS MEDIA
* RHINORRHEA
* COUGH
* VOMITING
* DIARRHEA
* BULGING FONTANELLE
* CERVICAL, OCCIPITAL or POSTAURICULAR LYMPHADENOPATHY
* NAGAYAMA SPOTS
  - ~ SOFT PALATE
  - ~ UVULA

AFTER FEVER
* MACULOPAPULAR RASH

30%



- ~ 1-2 days
- ~ MAY GO AWAY 2-4 hrs

2- Pathogenesis & clinical manifestations

- 3) Special manifestations in reactivation:
- Reactivation appears to be common in transplant patients and during pregnancy. The consequences of reactivated infection remain to be determined.
- HHV-6 reactivation occurs in close to half of patients who undergo hematopoietic stem cell transplantation. Those reactivations occur soon after transplant and have been associated with delayed engraftment, CNS dysfunction, and increased mortality.

3- Epidemiology

- Sero-epidemiologic studies using IF tests for serum antibodies or PCR assays for viral DNA in saliva or blood cells have shown that HHV-6 is widespread in the population. It is estimated that more than 90% of children older than age 1 year and adults are virus positive.
- Infections with HHV-6 typically occur in early childhood

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- Like HHV-6, primary infection with HHV-7 has been linked with roseola infantum in infants and young children. Any other disease associations of HHV-7 remain to be established.

Finally, let's review with a question!

In human herpes virus 6 infection:

a. Multiple sclerosis will follow in the majority of cases
b. The majority of cases occur in adulthood
c. Rose-like rash appears in the majority of cases
d. Transmission occurs via oral secretions
e. Almost all cases are symptomatic