Viral skin infection /Viral Exanthems

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Outline:

Viral Exanthems

Virology, Clinical sign and Symptoms, LAB diagnosis and treatment

Erythematous maculopapular rash

- Measles
- Rubella
- Roseola Infantum
- Infectious mononucleosis
- Fifth Disease
- Kawasaki syndrome ?

Vesiculopustular rash

- Herpes simplex infection
- Varicella zoster infection
- Hand foot and mouth disease

HPV and Pox virus

Exanthematous fever

- Infection : Bacteria, Virus
- Non infection: drug rash
  - ซักประวัติการรับประทานยาในช่วง 3 สัปดาห์ก่อนเกิดผื่น
  - หยุดยานั้นทันที ผื่นมักหายไปภายใน 24-48 ชั่วโมง

Erythematous maculopapular rash

- Measles
- Rubella
- Exanthem subitem (Roseola Infantum)
- Infectious mononucleosis
- Fifth disease

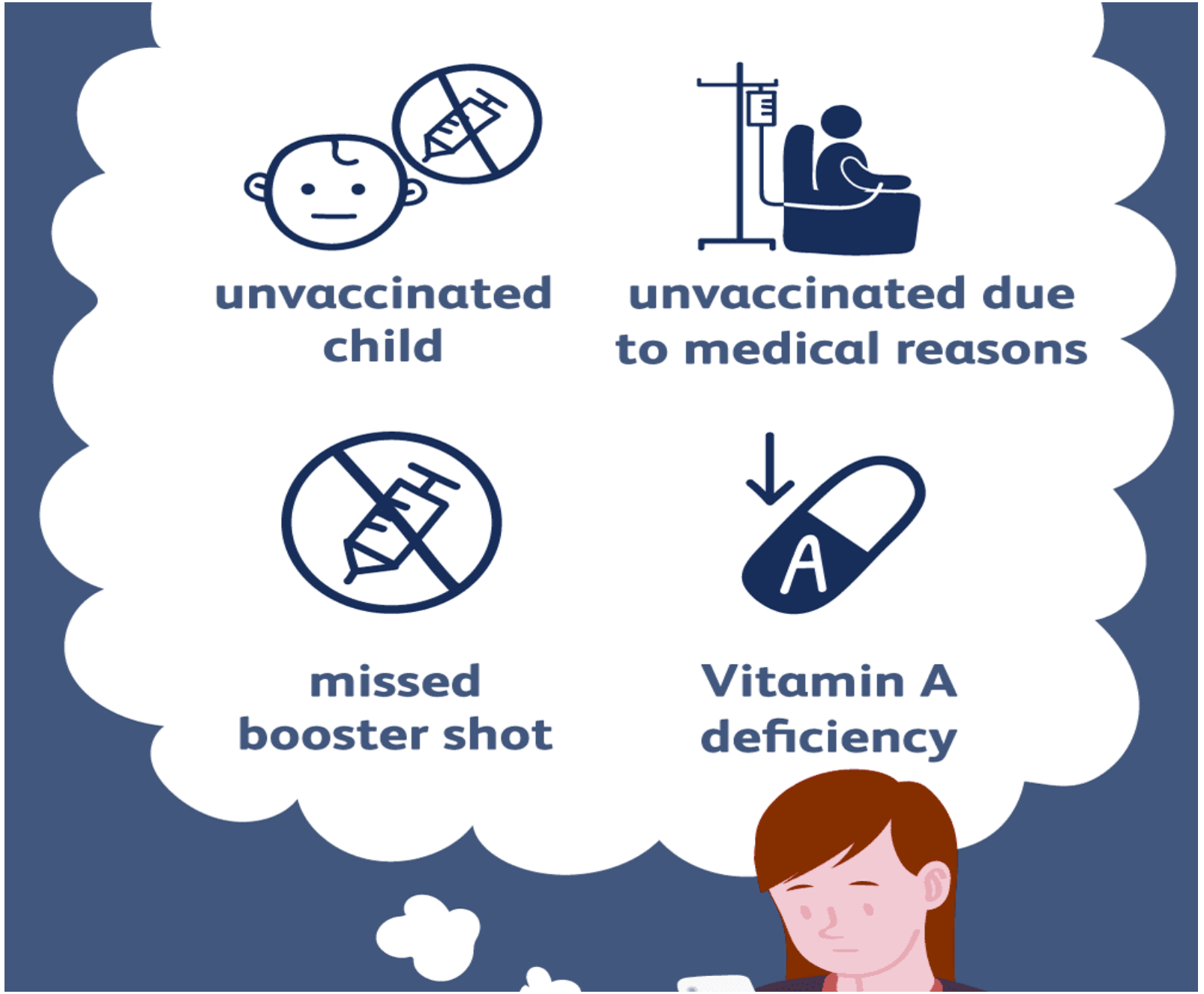
Vesiculopustular/vesiculopapular rash

- Herpes simplex infection
- Varicella zoster infection

Measles

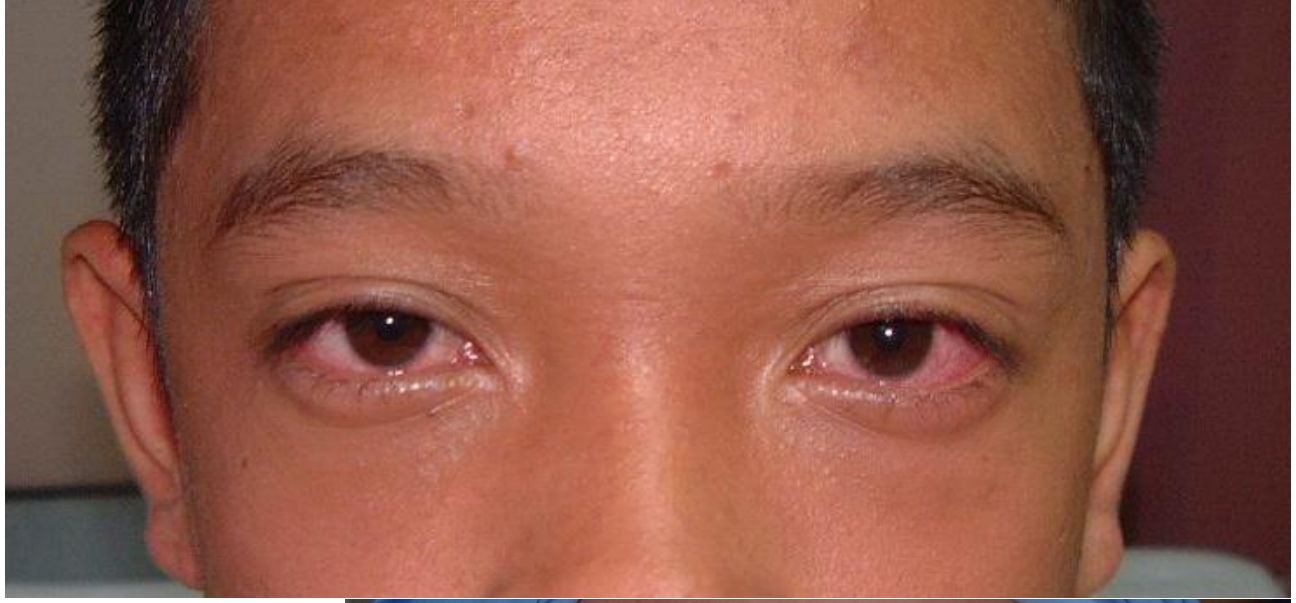
- RNA virus family paramyxovirus
- Transmission: airborne
- Pre-school age
- Incubation period: 10-12 d
- Prodromal period: 3-5 d : 3 C*
  cough ,coryza, conjunctivitis+ Koplik's spot
- Rashes 2-3 d → desquamation
- Hyperpigmentation ซึ่งเป็นผลจากการมีเลือดออกในหลอดเลือดฝอย จากนั้นจะหลุดลอกเป็นแผ่นบางๆ
- Contagious period: 4 d before and after rashes*
- Severe in malnutrition and Vit A def

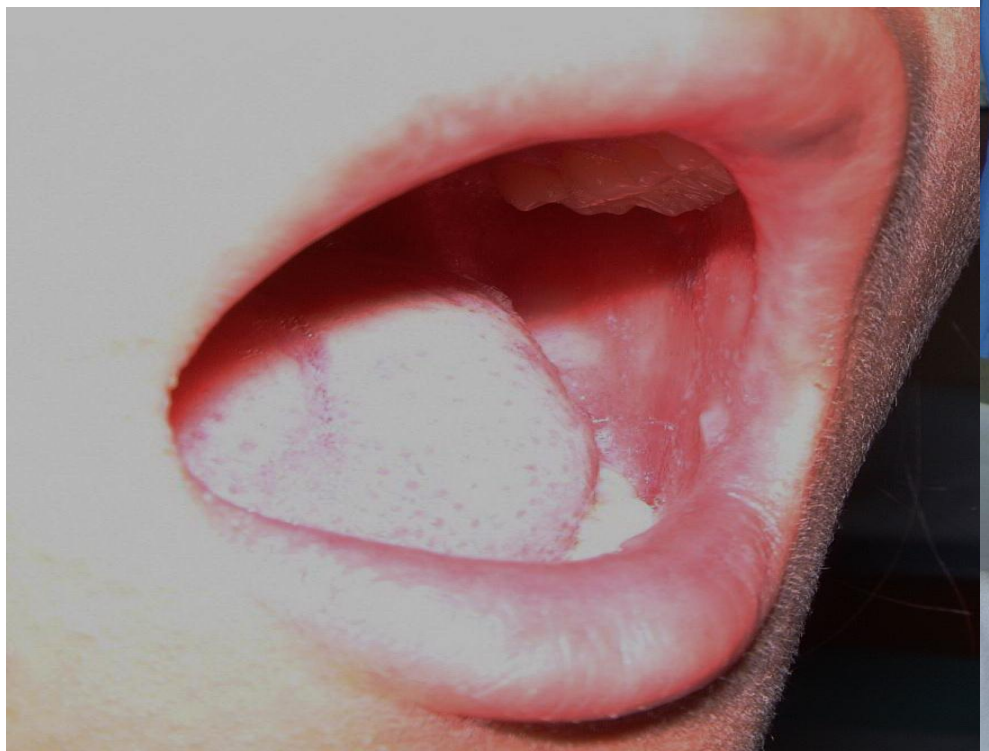
Measles

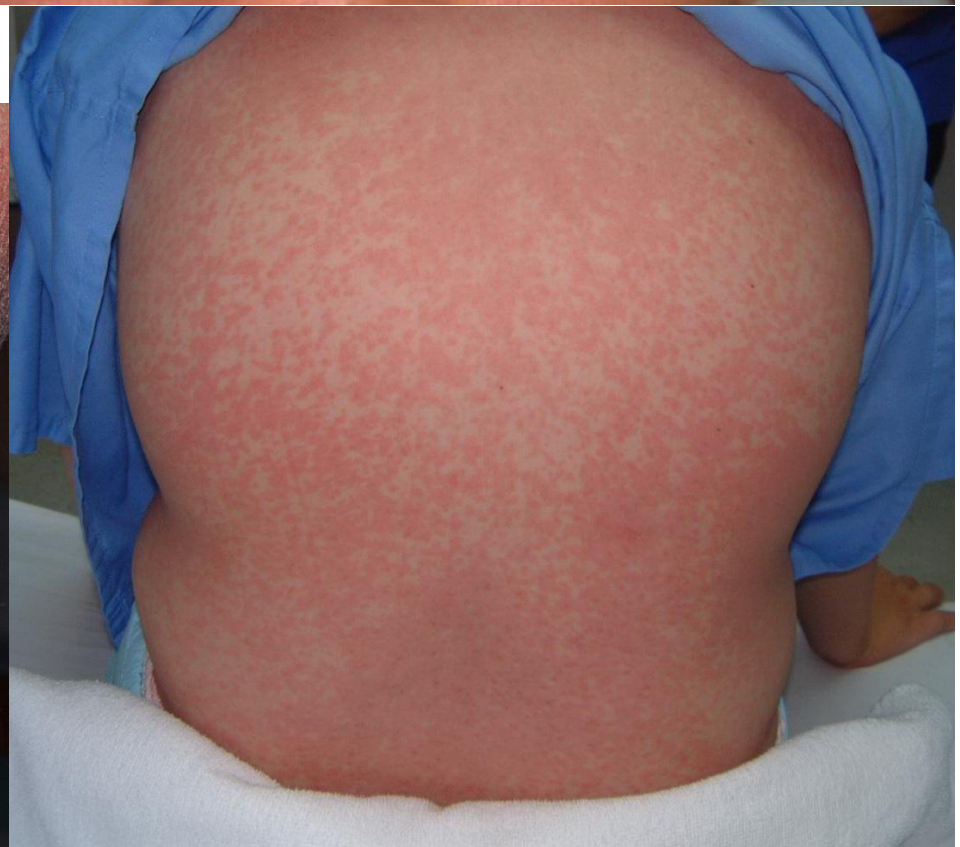

unvaccinated child
unvaccinated due to medical reasons
missed booster shot
Vitamin A deficiency
A

Measles /Rubeola

(3C)
Cough,
Coryza,
Conjunctivitis
+ Koplik's spots



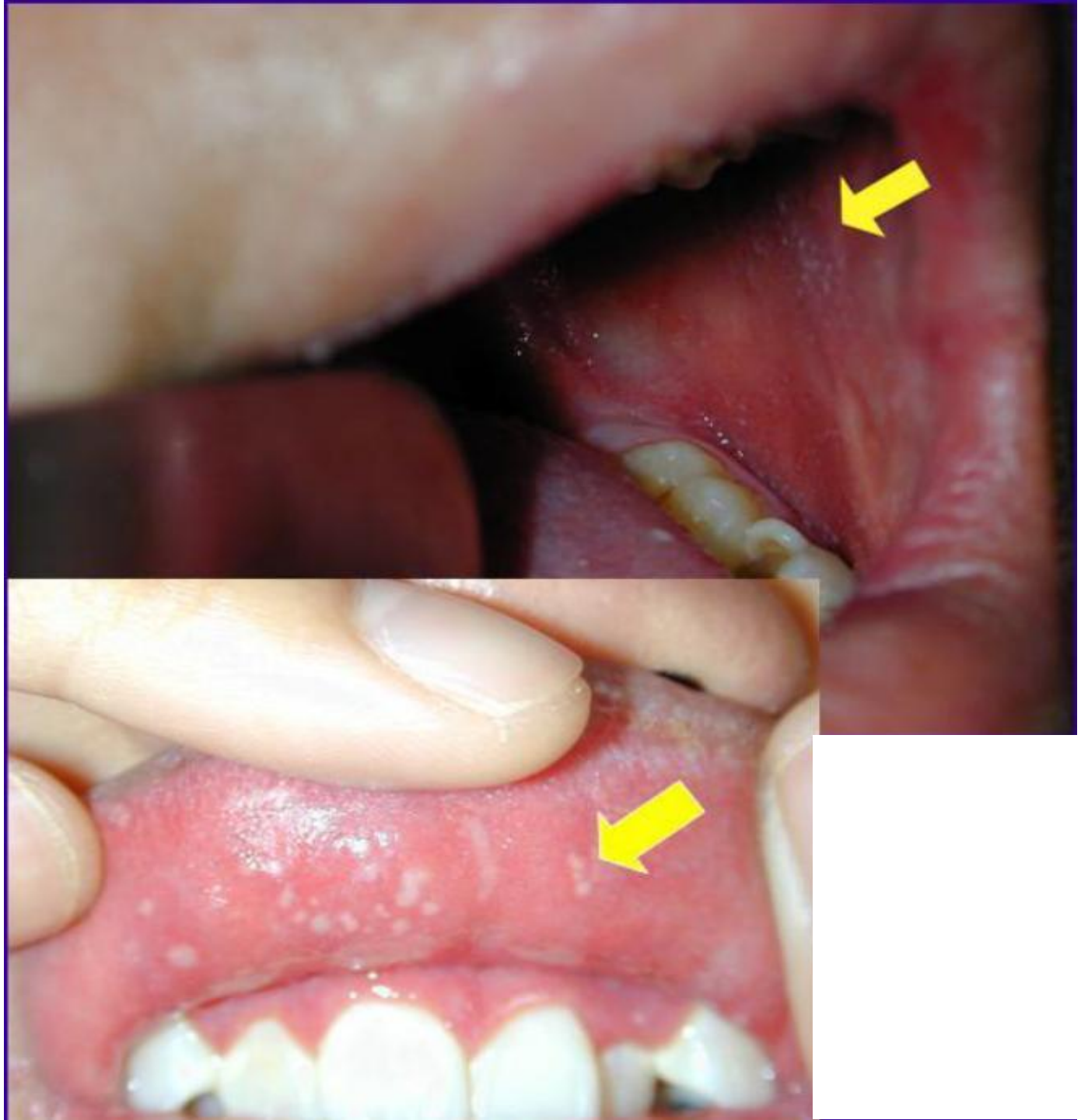




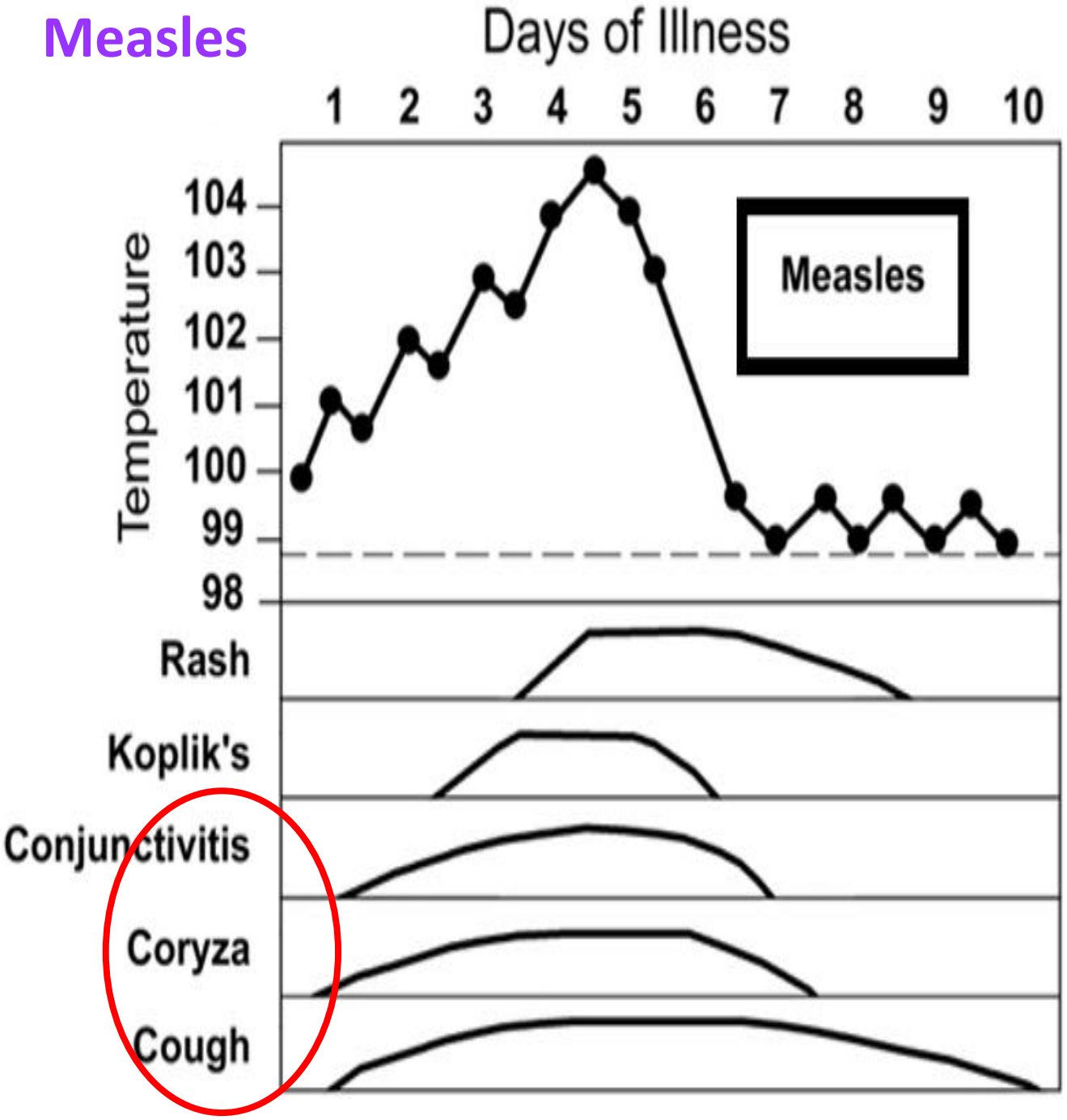
Measles

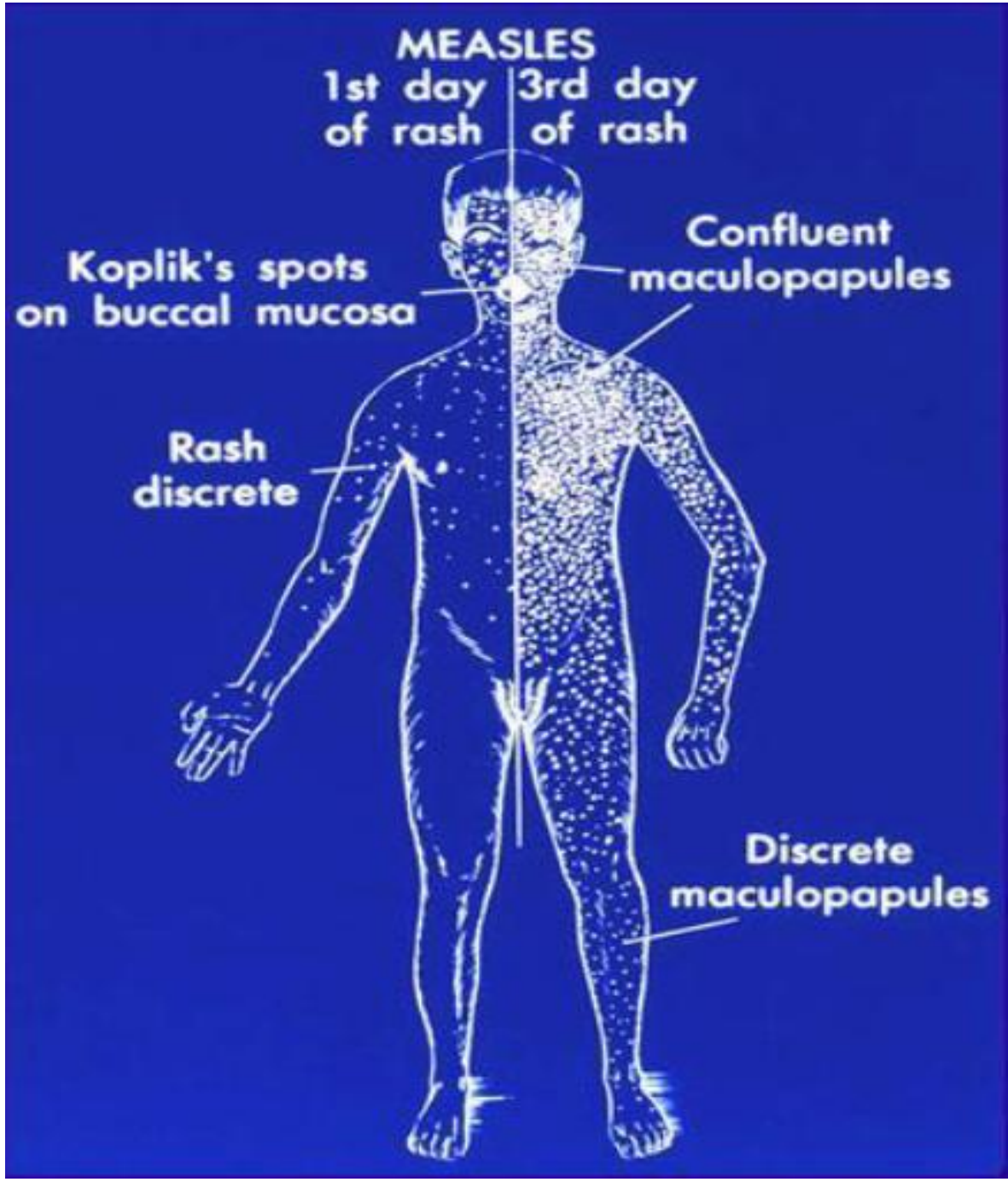
Koplik's spots

(pathognomonic)

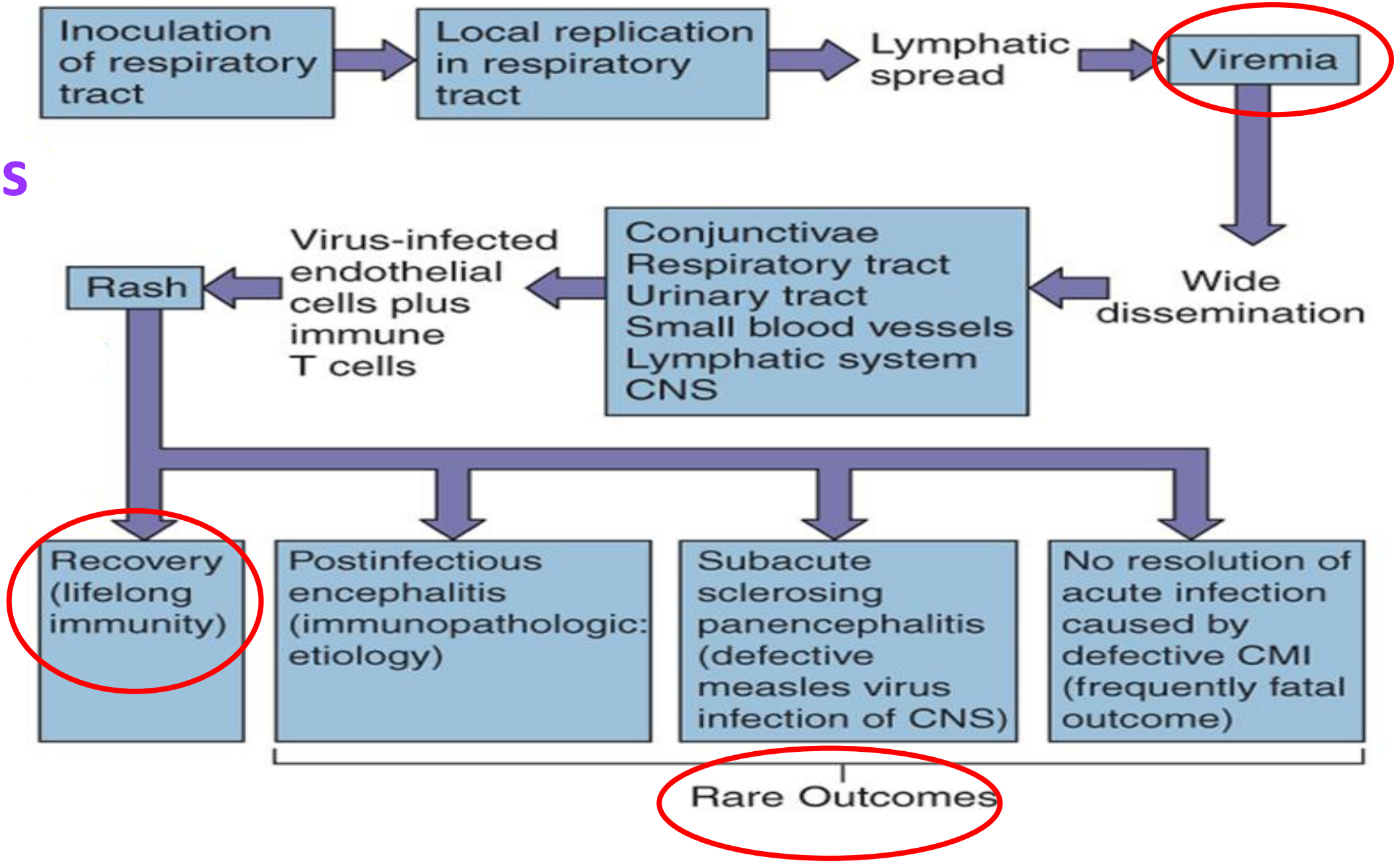


Measles


Days of Illness
1 2 3 4 5 6 7 8 9 10
Temperature
104
103
102
101
100
99
98
Measles
Rash
Koplik's
Conjunctivitis
Coryza
Cough


MEASLES
1st day of rash
3rd day of rash
Koplik's spots on buccal mucosa
Confluent maculopapules
Rash discrete
Discrete maculopapules

Measles


Inoculation of respiratory tract
Local replication in respiratory tract
Lymphatic spread
Viremia
Wide dissemination
Conjunctivae
Respiratory tract
Urinary tract
Small blood vessels
Lymphatic system
CNS
Virus-infected endothelial cells plus immune T cells
Rash
Recovery (lifelong immunity)
Postinfectious encephalitis (immunopathologic: etiology)
Subacute sclerosing panencephalitis (defective measles virus infection of CNS)
No resolution of acute infection caused by defective CMI (frequently fatal outcome)
Rare Outcomes

Measles complication

"Epithelial surface destruction and Immune suppression"

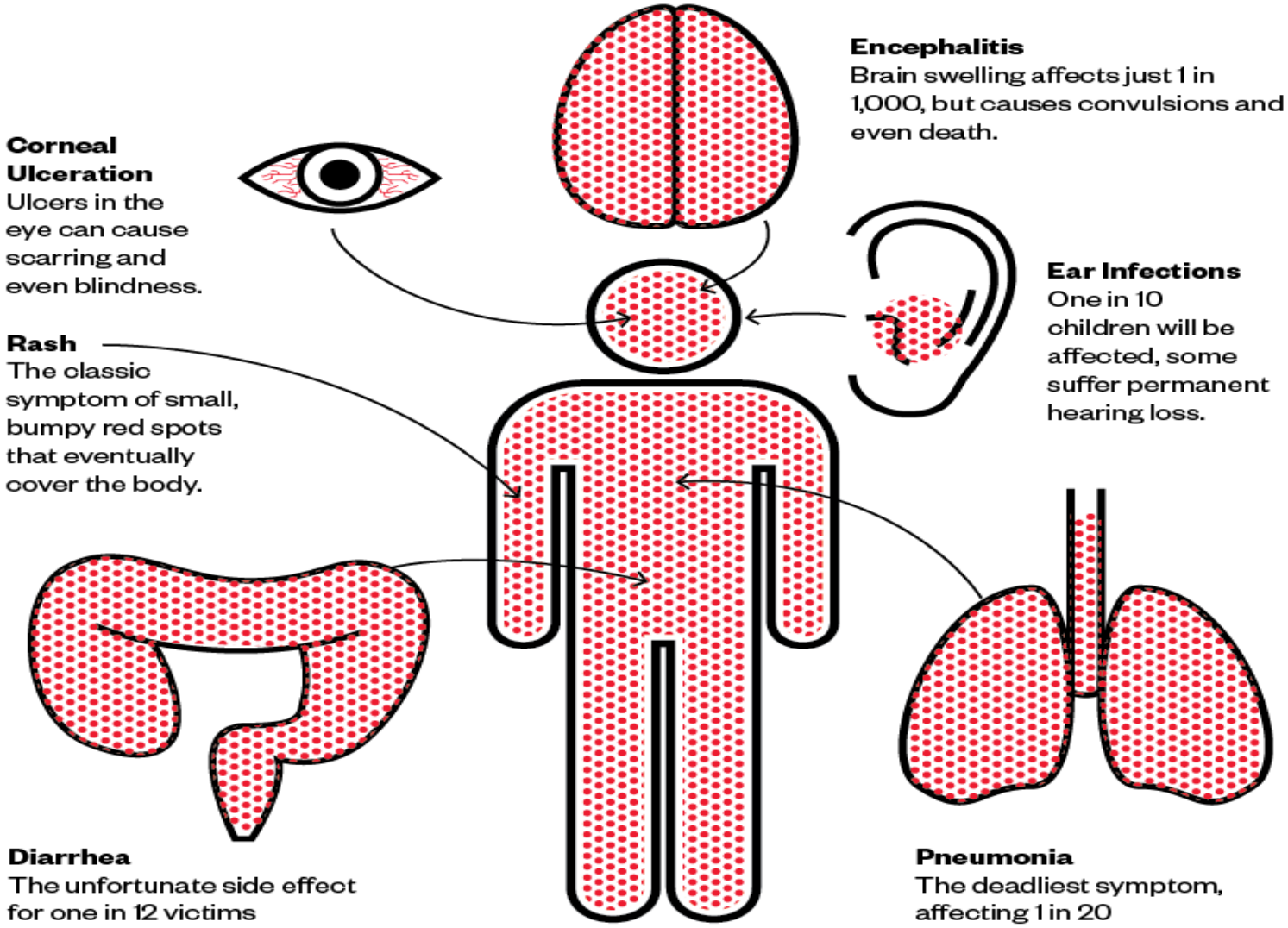
-Otitis media,

-Pneumonia,

-mesenteric adenitis,

Dx: Measles IgG, IgM

Tx: Supportive tx



Measles Prevention

- Symptomatic treatment; < 2 ปี ให้ Vit A
- Prevention: MMR vaccine
- Post exposure prophylaxis:

- Vaccine ภายใน 72 hr
- คนท้อง/ เด็ก< 1ปี /immunocompromise, HIV
- Measle IG : ภายใน 72 ชม-6 วัน
- IVIG

ในทารกอายุต่ำกว่า 6 เดือน หรือเด็กที่เคยออกหัดแล้ว ไม่ต้องทำอะไร เนื่องจากมีภูมิคุ้มกัน

ผู้ป่วยที่ให้ประวัติออกหัดมาก่อน เป็นหัดจริงหรือไม่

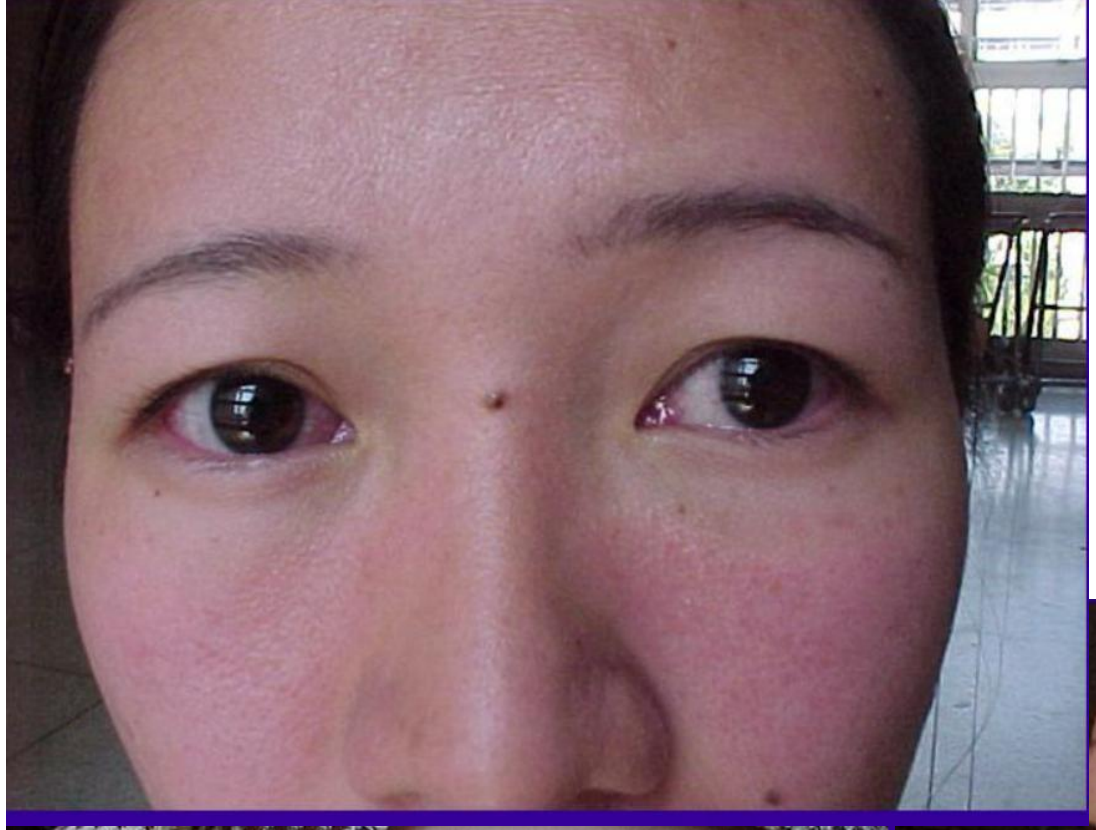
- **1.** ถ้าไม่ไอไม่ใช่หัด
- **2.** ถ้าเป็นหัดจริง วันที่ผื่นขึ้นจะต้องมีไข้อยู่ ถ้าไข้ลงแล้วไม่ใช่หัด
- **3.** เมื่อไข้ลงโรคหัดมักมี **hyperpigmentation** อีกหลายวัน
- **4.** เป็นด้วยกัน หลายคนจะช่วยสนับสนุนโรคหัดมากขึ้น
- **5.** เป็นไข้กี่วันก่อนผื่นขึ้น ในโรคหัดมักจะมีผื่นขึ้นประมาณวันที่ **3-4** หลังจากมีไข้
- **6.** อายุของผู้ป่วย ถ้าต่ำกว่า **6** เดือนมักไม่ใช่หัด

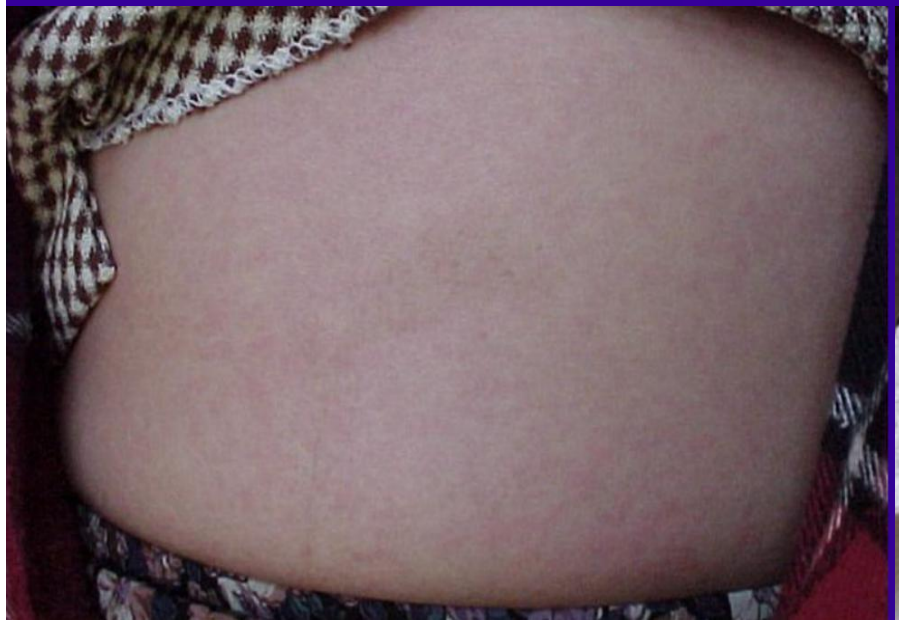
Rubella (German Measles)

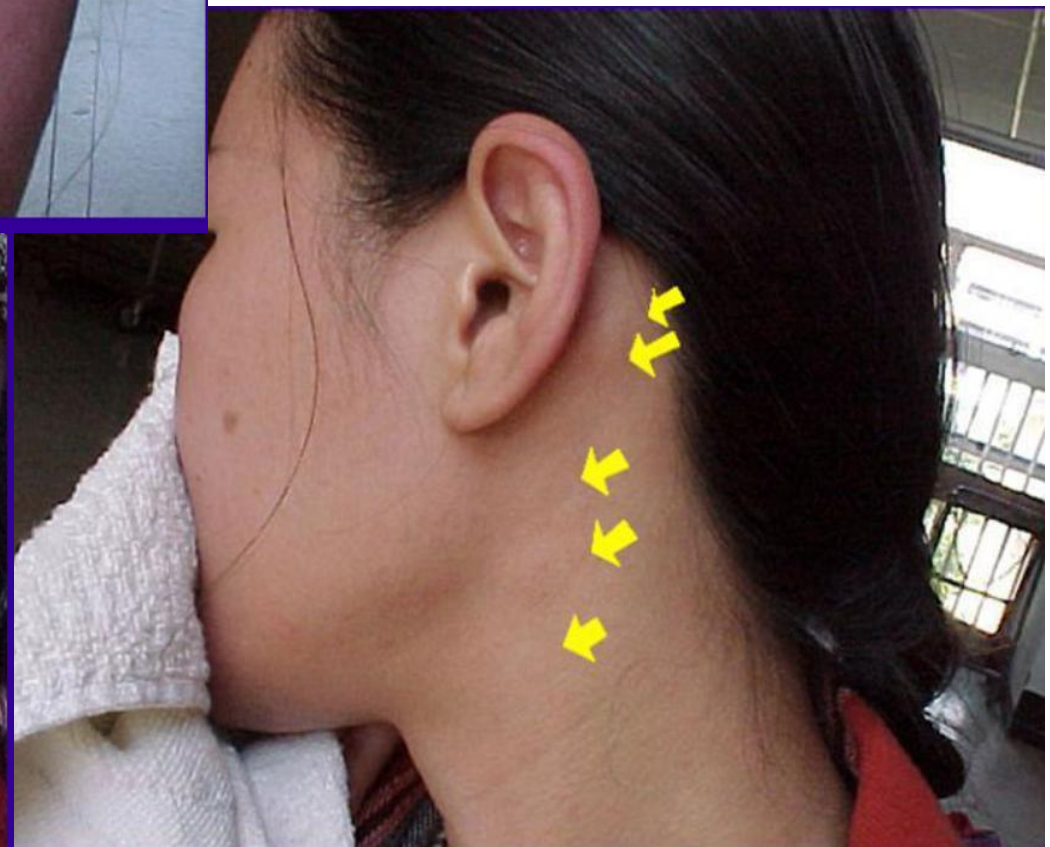
- Rubella Virus, Family Togaviridae
- Teenage
- Incubation period: 12-23 d
- Prodromal period: Low grade fever
- droplet transmission: ระยะติดต่อ 5 วัน ก่อนผื่นขึ้น จนถึง 7 วันหลังผื่นขึ้น
- Maculopapular rashes with

“ Retroauricular , posterior cervical, postoccipital lymphadenopathy”

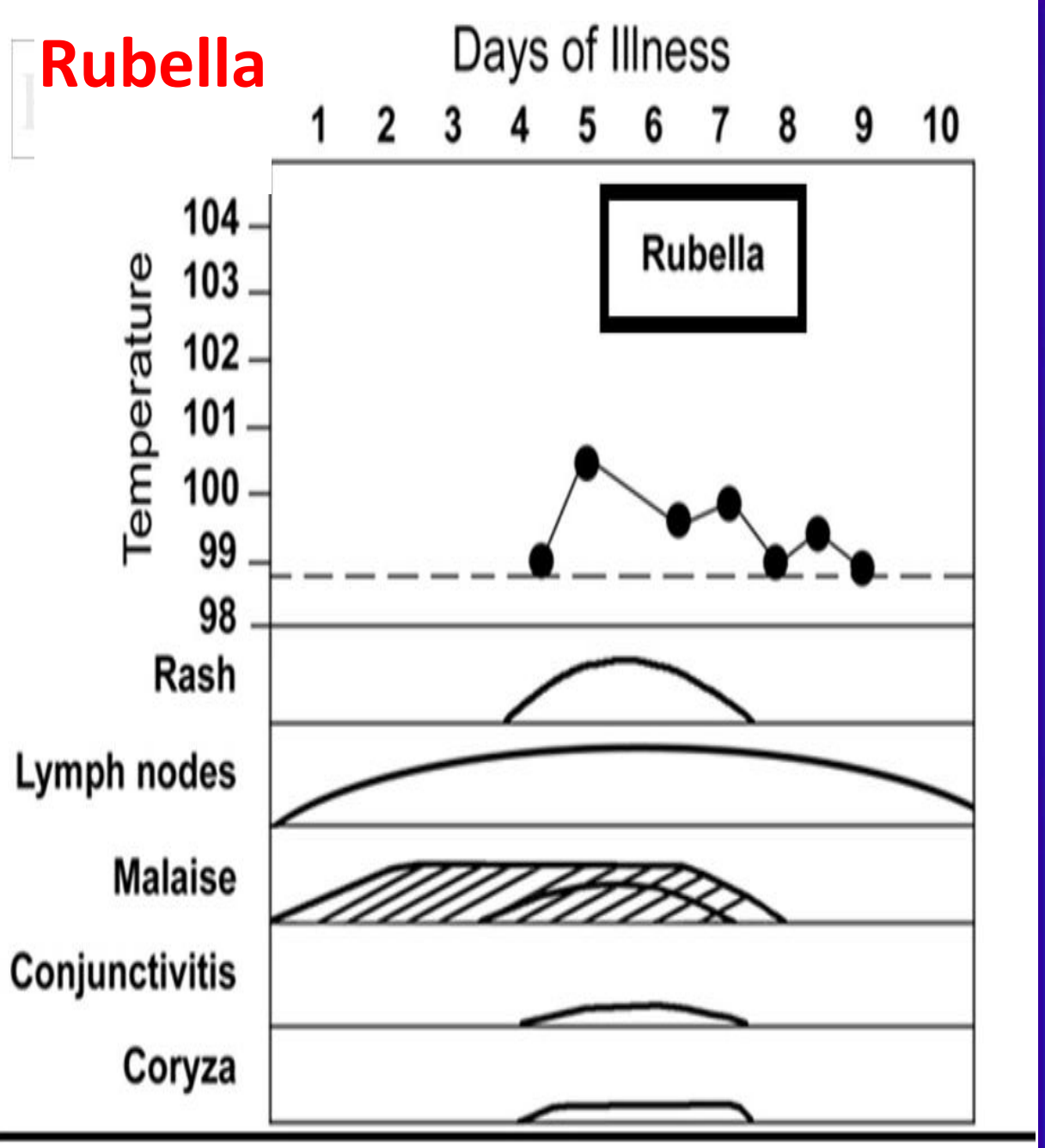
Rubella



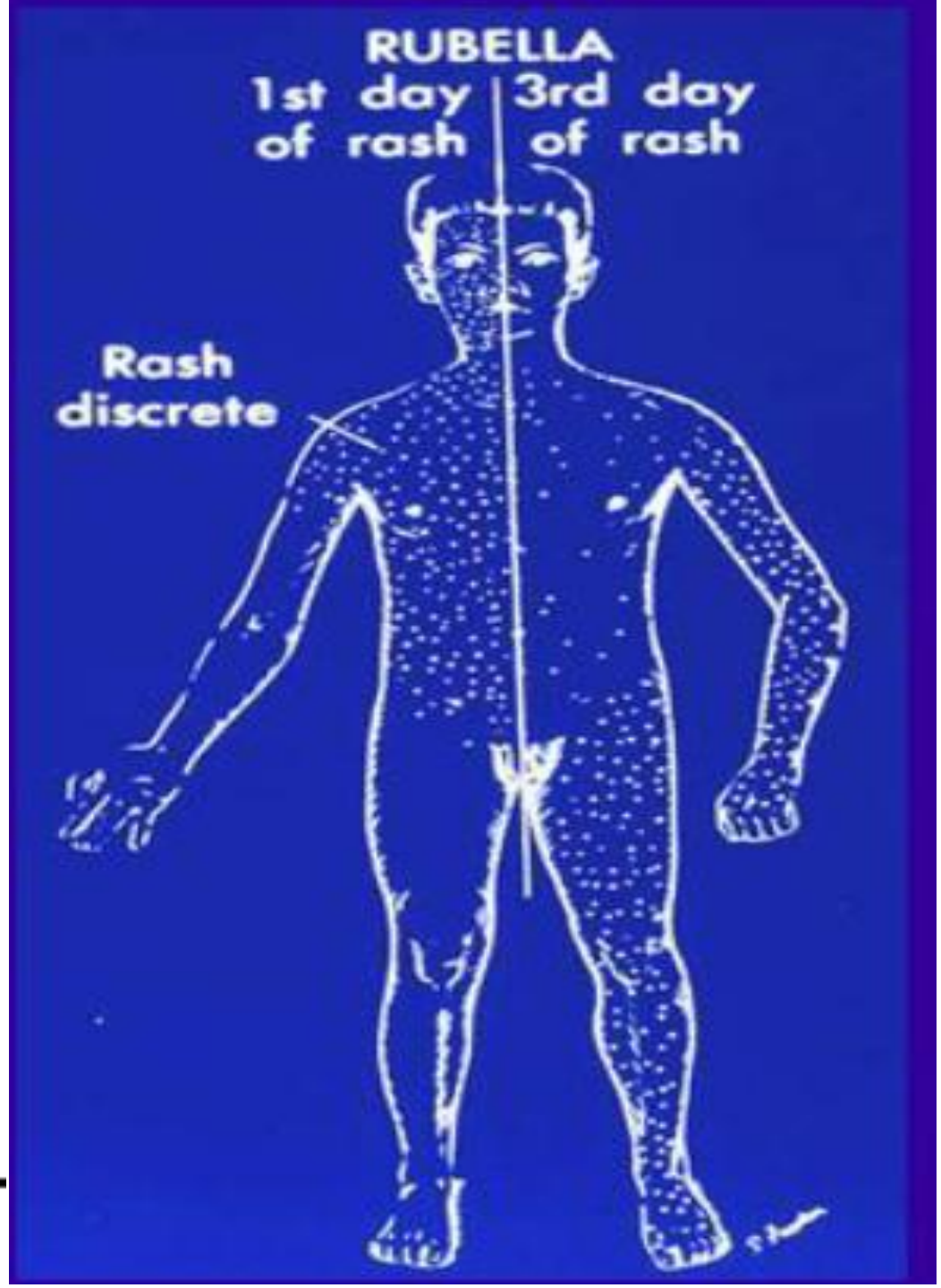




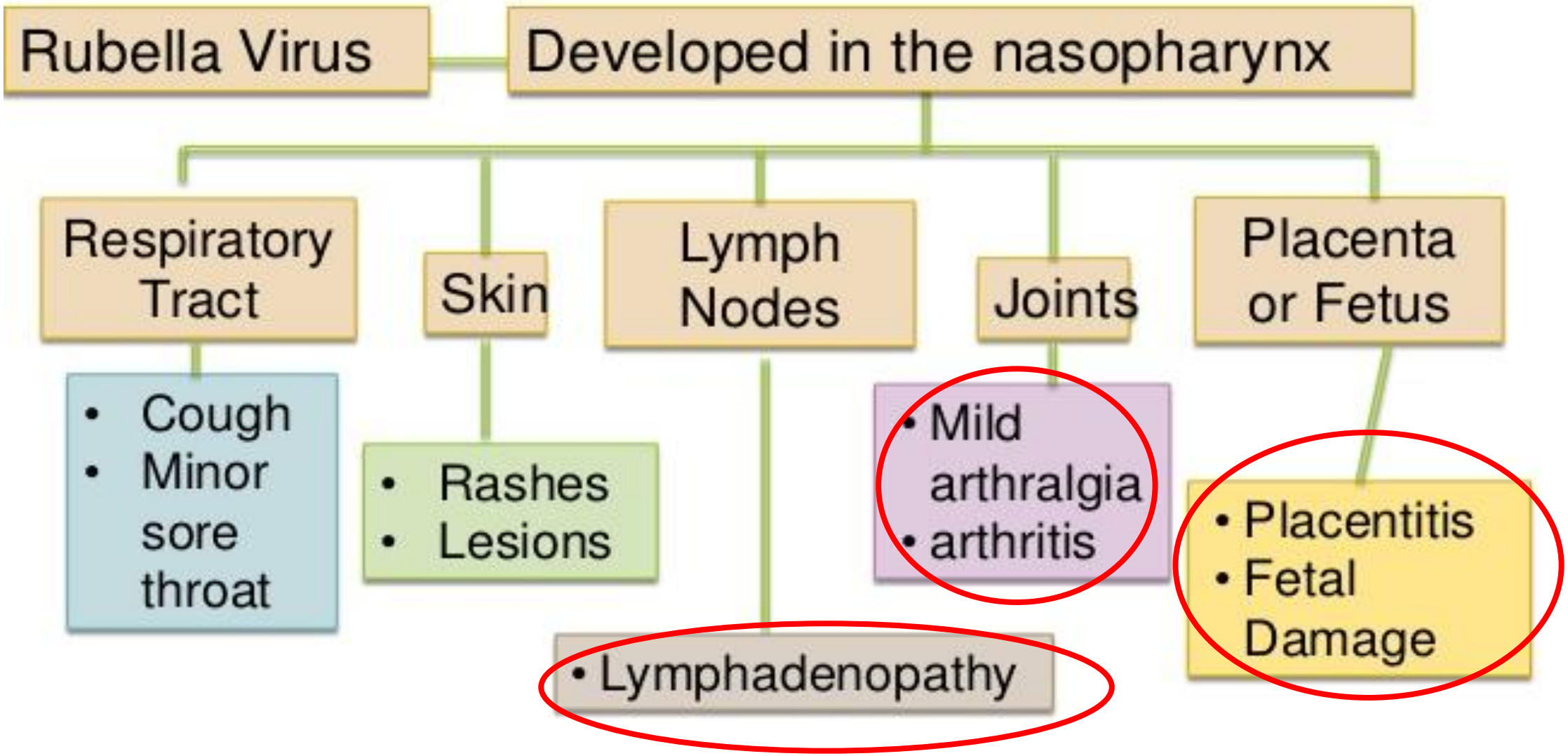
Rubella



3 days rashes



Rubella Pathogenesis



Congenital rubella syndrome

- IUGR (Intra uterine Growth retardation)
- Cataract, Glaucoma
- Deafness
- Cardiac : PDA (patent ductus arteriosus),
  PS (pulmonary stenosis)
- Blueberry Muffin Skin lesion,
- Mental retardation, microcephaly
- Bony radiolucency : Celery stalk metaphysis

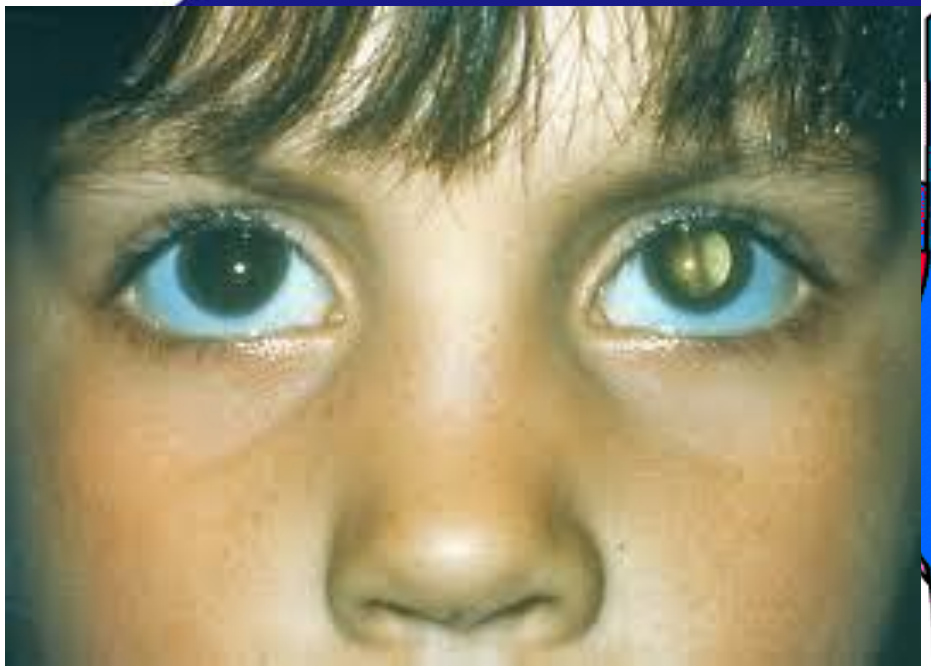
"Rubella Triad"

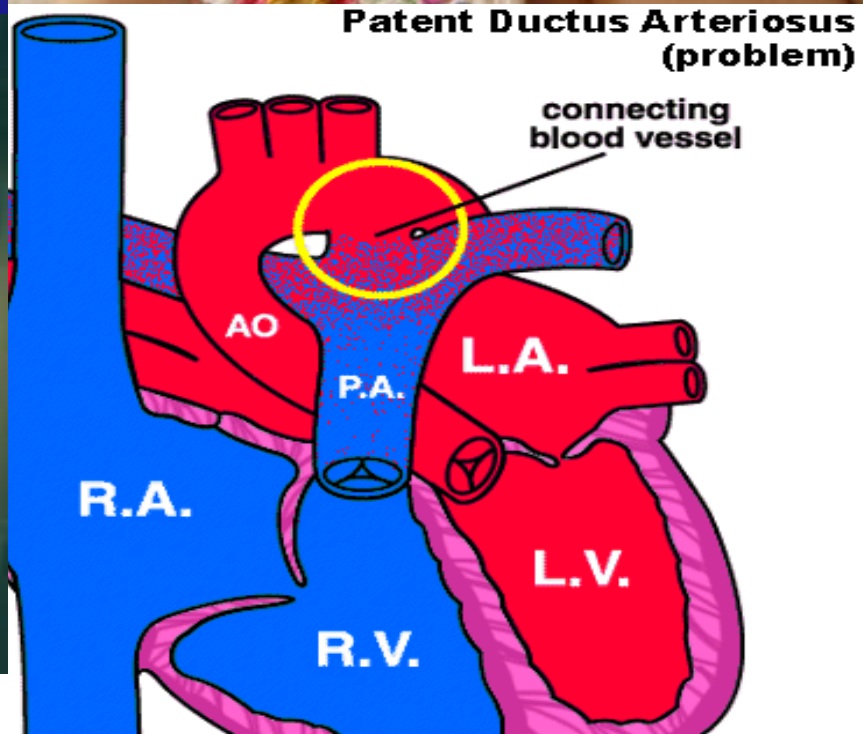
"Generalized viral induce progressive Necrotizing Vasculitis"

สามารถตรวจพบเชื้อใน nasopharyngeal secretion และปัสสาวะได้นานถึง 1 ปี

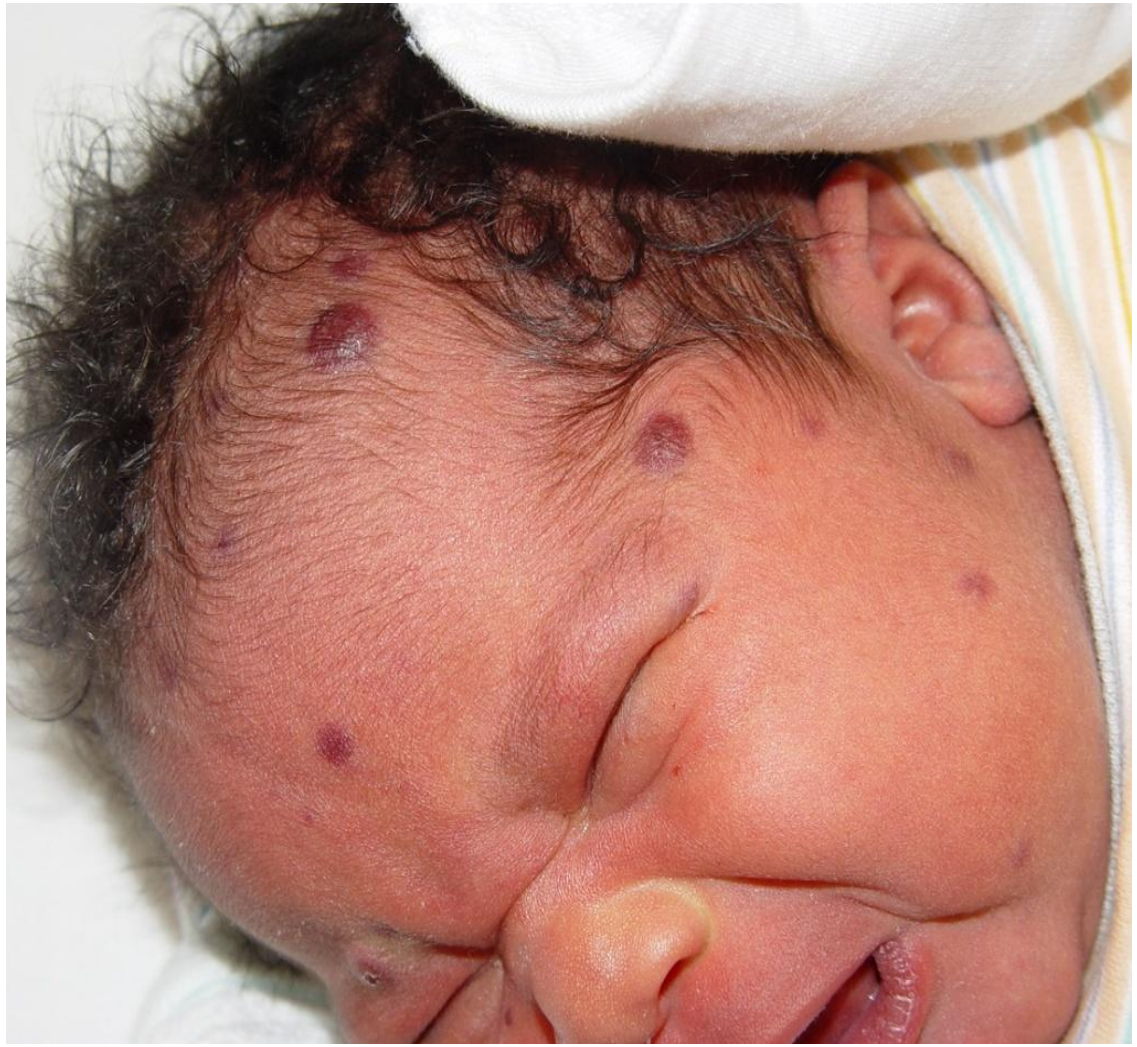
Congenital Rubella

“Generalized
viral induce progessive
Necrotizing Vasculitis”



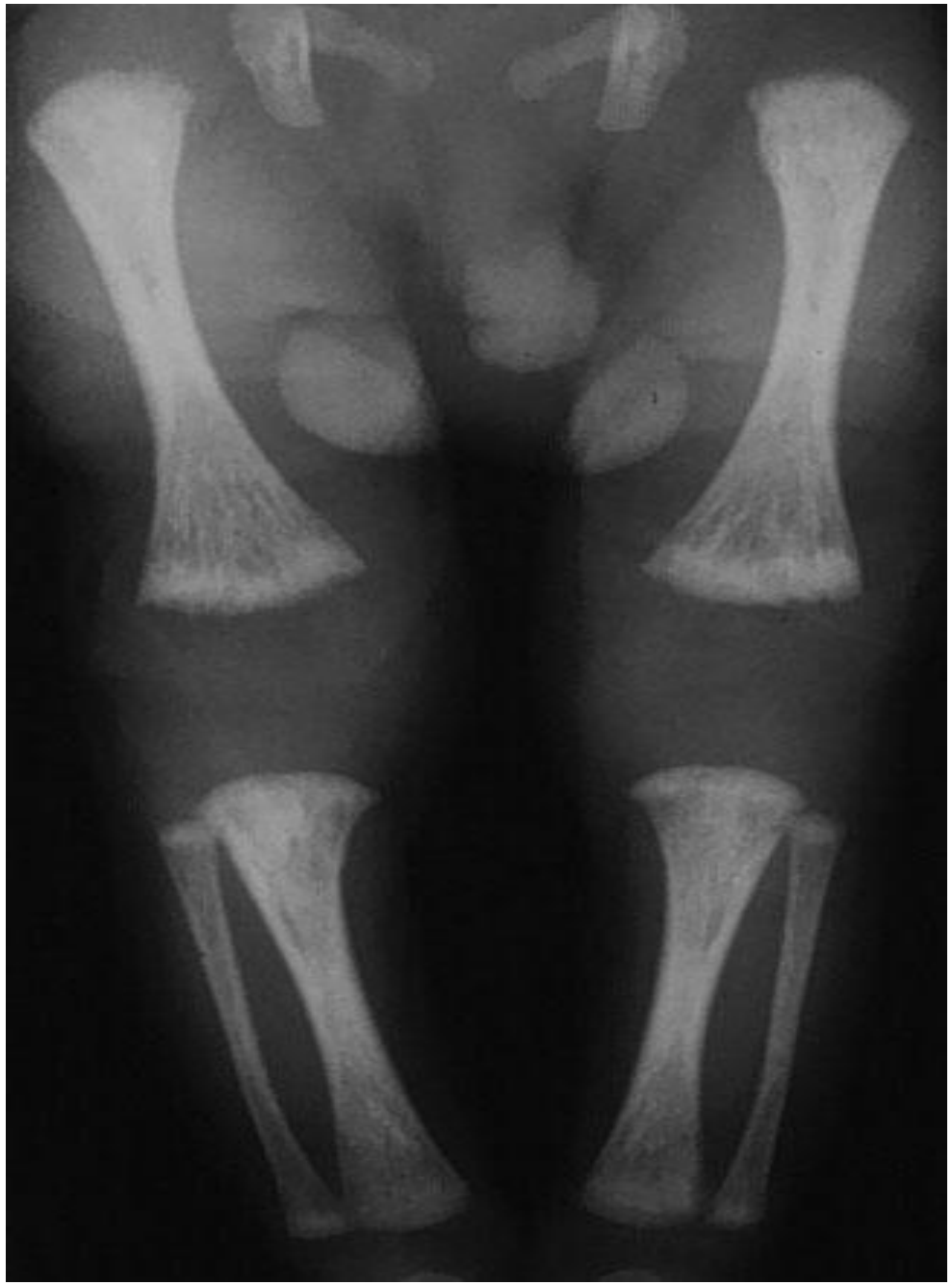


Blueberry Muffin Skin lesion



Dermal erythropoiesis

Congenital infections
(rubella, cytomegalovirus, parvovirus B19),



Congenital Rubella

Celery stalk metaphysis.

Rubella

Complication

- 1. Arthritis: adult female
- 2. Thrombocytopenia

LAB:

- ELISA, PCR

Prevention

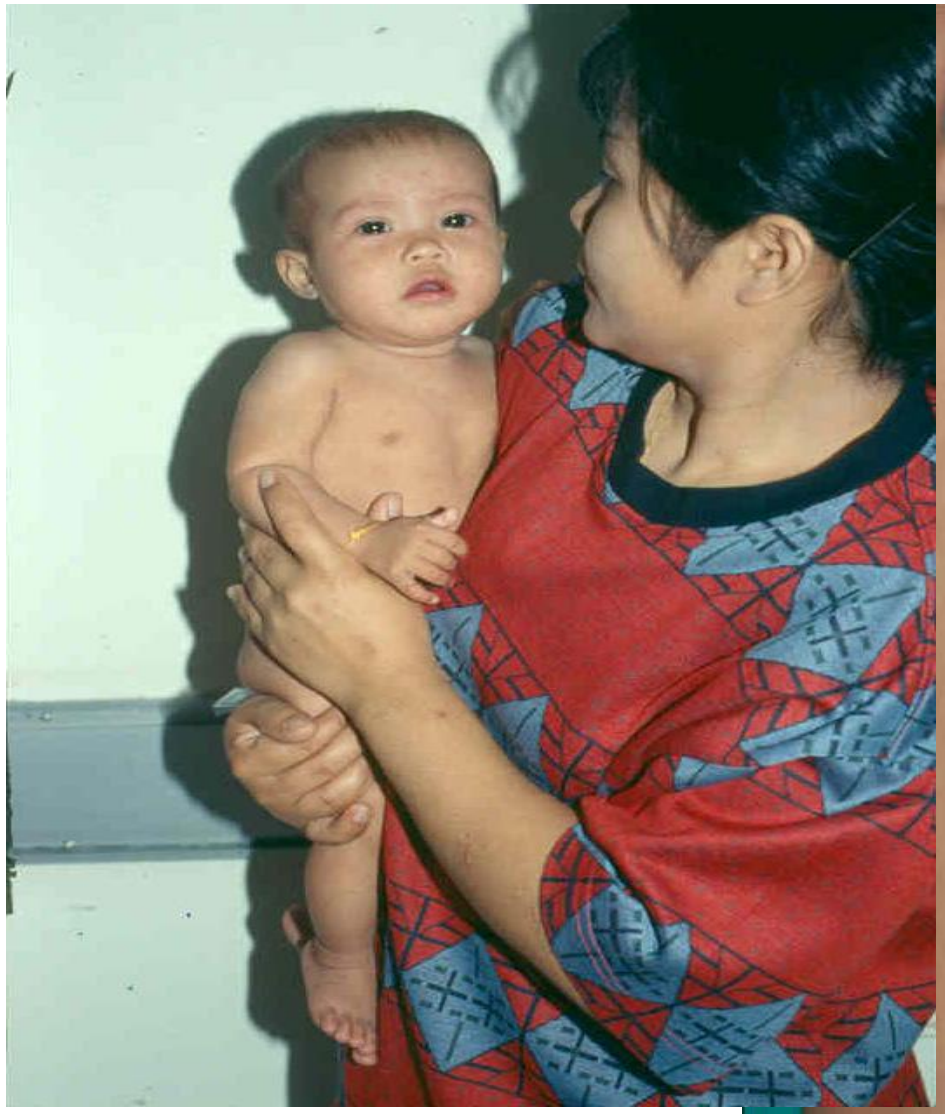
MMR vaccine

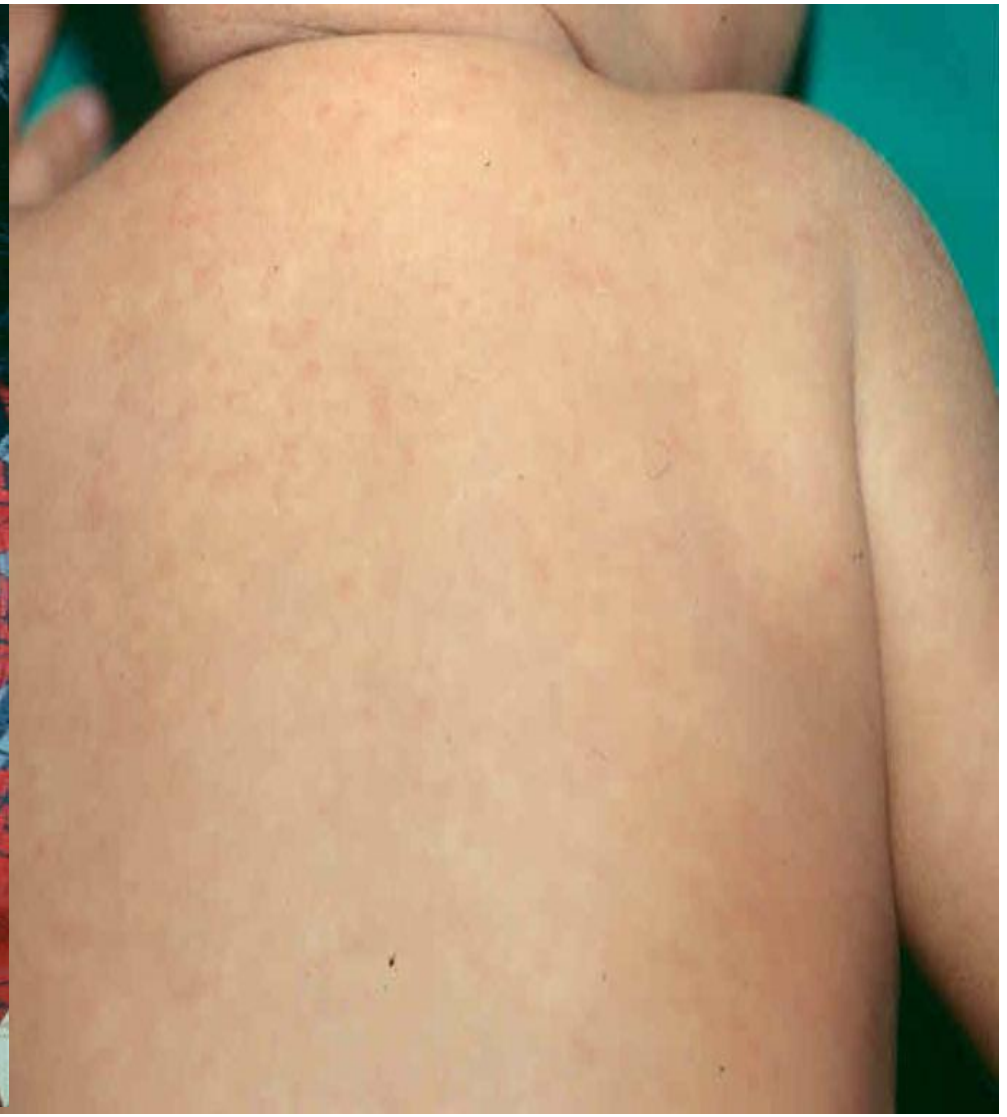
คนท้อง ถ้าสัมผัสโรค

:ให้ IG ลดอาการ แต่ไม่ลด viremia

: ตรวจ rubella Ab 2 ครั้ง

Roseola infantum



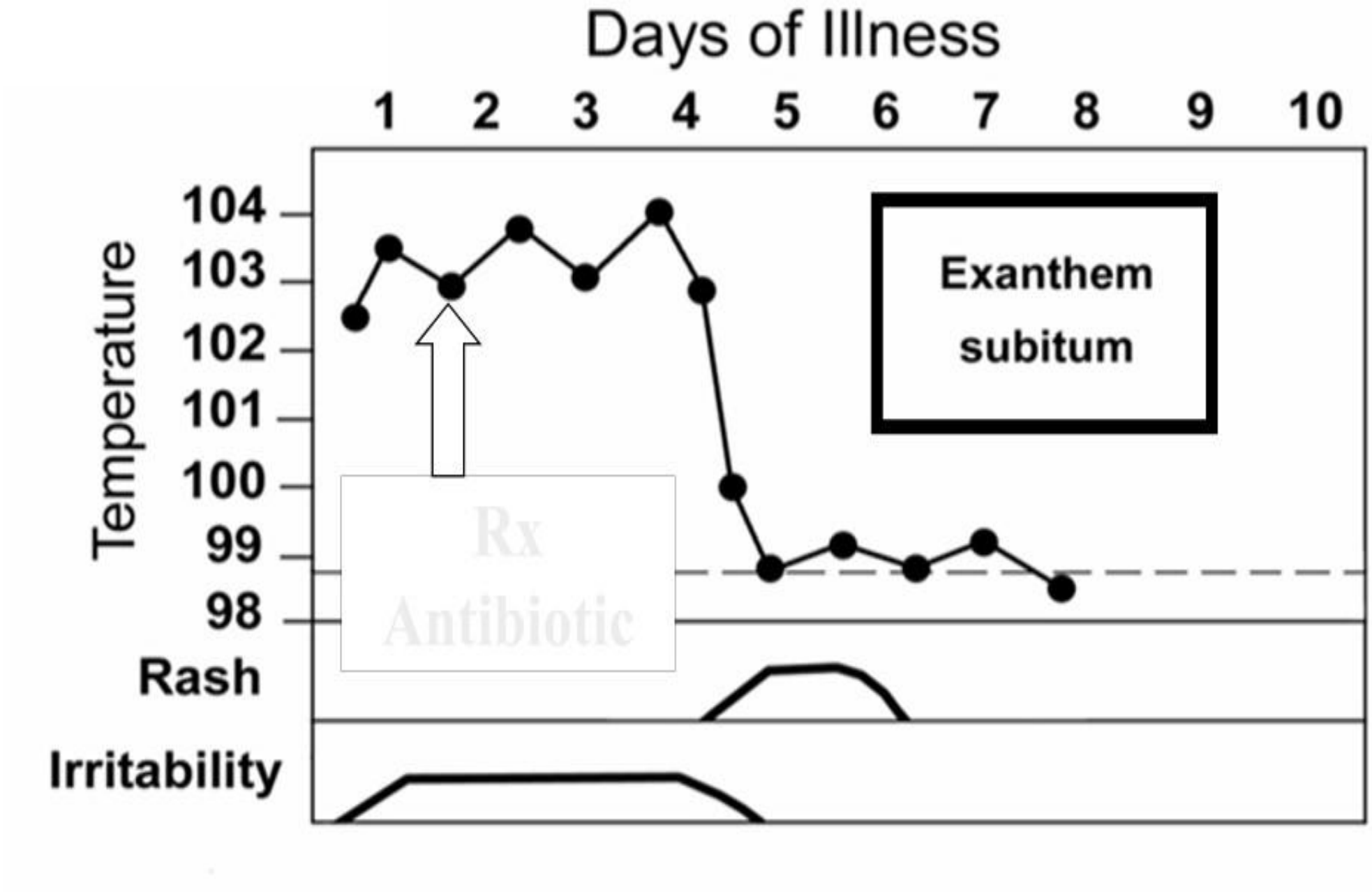


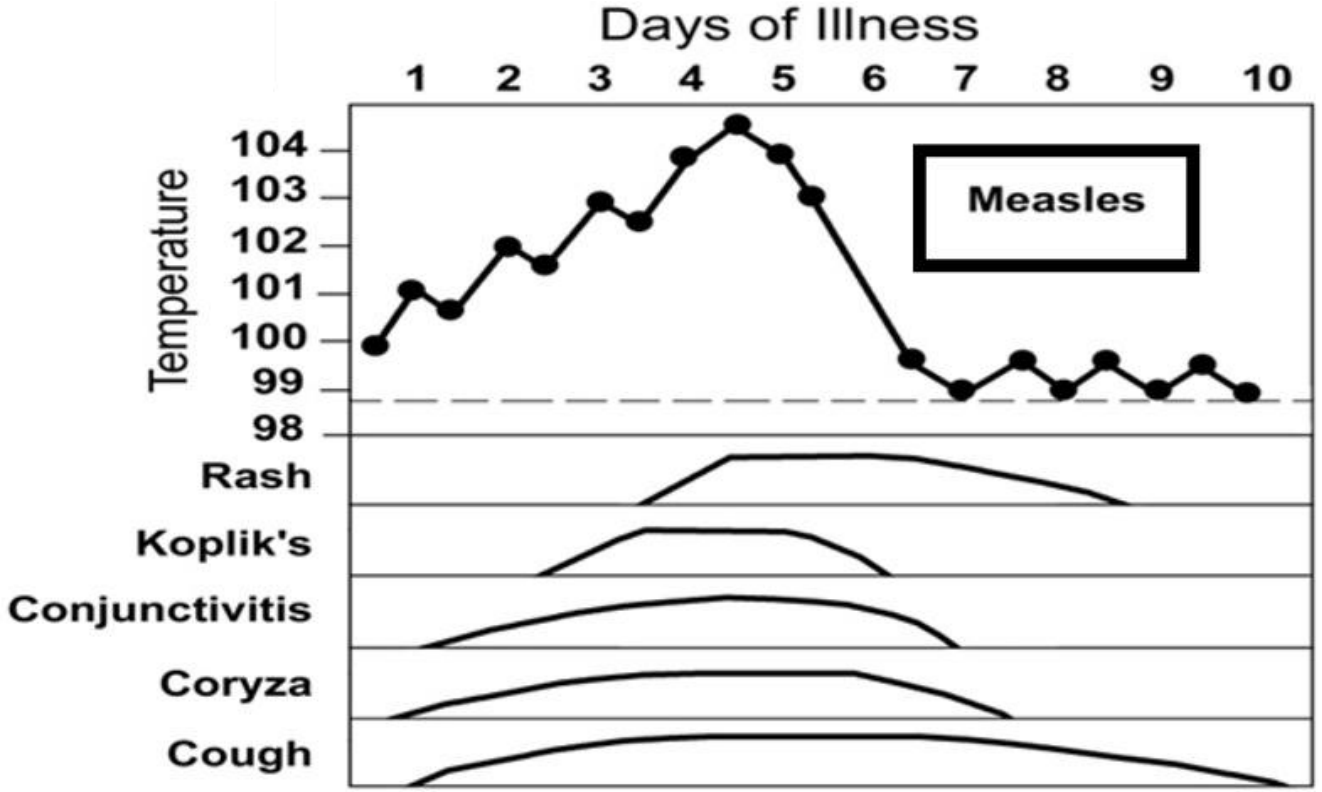
Roseola infantum

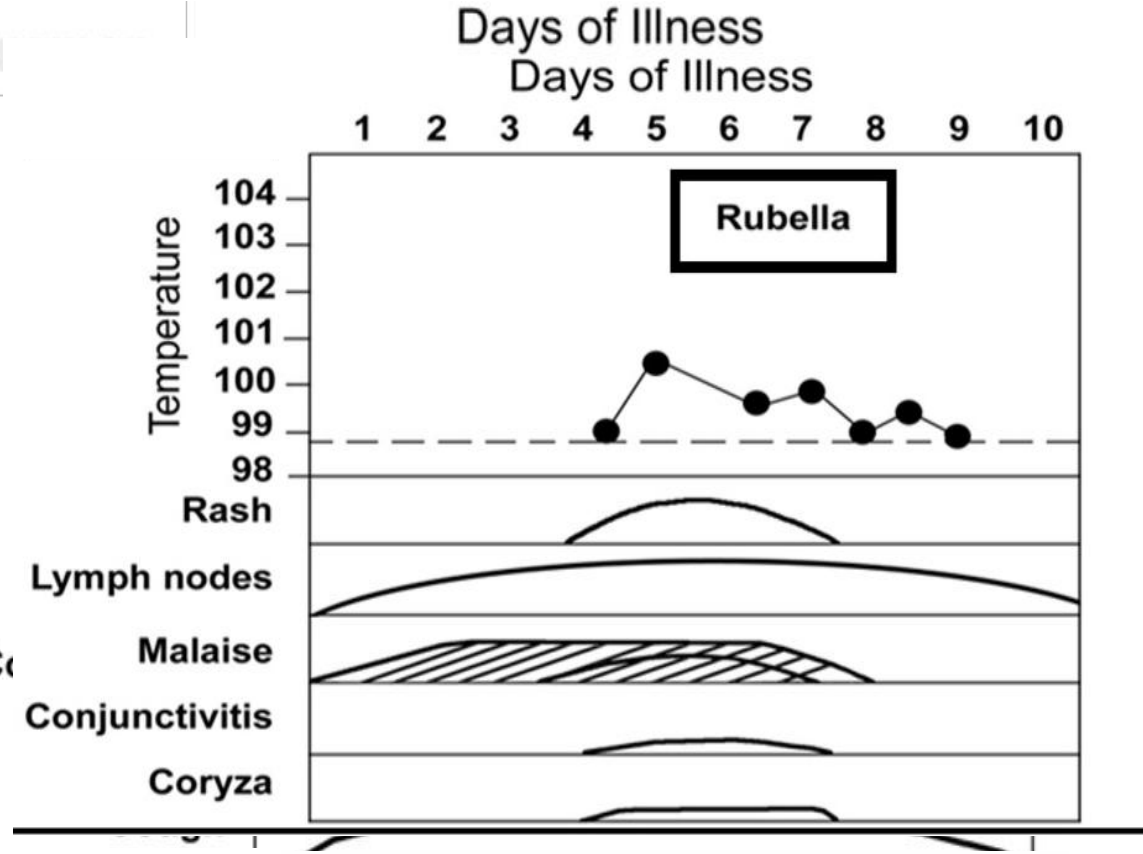
- HHV 6-7 (Human Herpes virus 6,7)
- Infant 90%
- Sudden onset of high grade fever
- Bulging anterior fontanel, convulsion
- Look well despite high fever

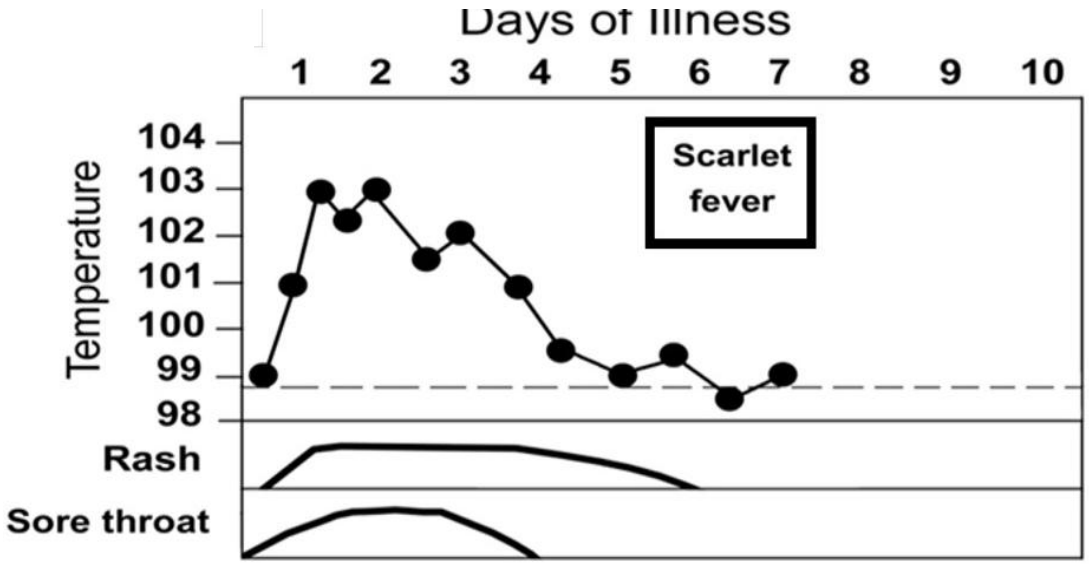
Fever fall on 3th -4th day with eruption of maculopapular rash

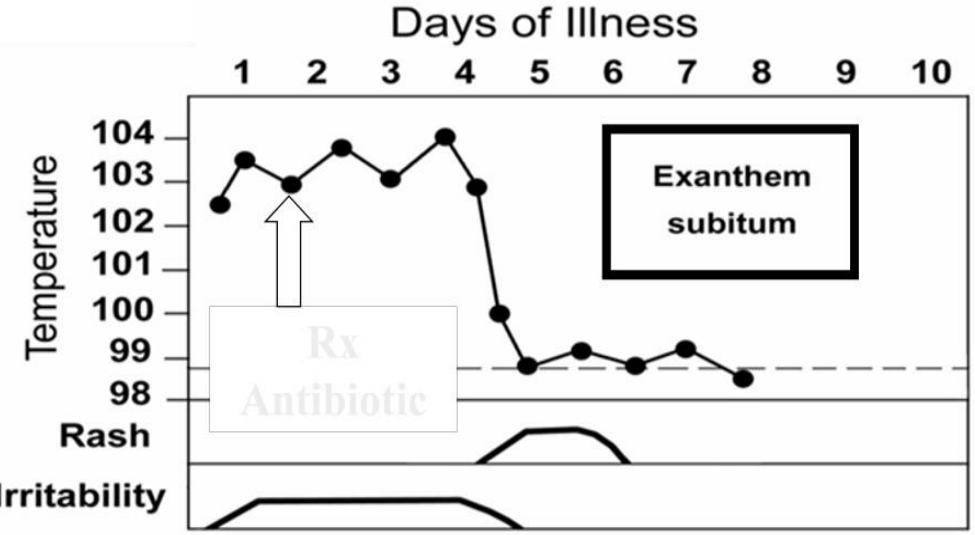
Supportive Tx.


Days of Illness
1
2
3
4
5
6
7
8
9
10
Temperature
104
103
102
101
100
99
98
Exanthem subitum
Rx Antibiotic
Rash
Irritability


Days of Illness
1 2 3 4 5 6 7 8 9 10
Temperature
104
103
102
101
100
99
98
Measles
Rash
Koplik's
Conjunctivitis
Coryza
Cough


Days of Illness
Days of Illness
1 2 3 4 5 6 7 8 9 10
Temperature
104
103
102
101
100
99
98
Rubella
Rash
Lymph nodes
Malaise
Conjunctivitis
Coryza


Days of Illness
1 2 3 4 5 6 7 8 9 10
Temperature
104
103
102
101
100
99
98
Scarlet fever
Rash
Sore throat


Days of Illness
1 2 3 4 5 6 7 8 9 10
Temperature
104
103
102
101
100
99
98
Exanthem subitum
Rx
Antibiotic
Rash
Irritability

Epstein Barr virus (EBV)

(Human herpes virus 4)

"Lymphocytotropic virus" เพิ่มจำนวน ใน WBC

Acute: Infectious mononucleosis (IM)

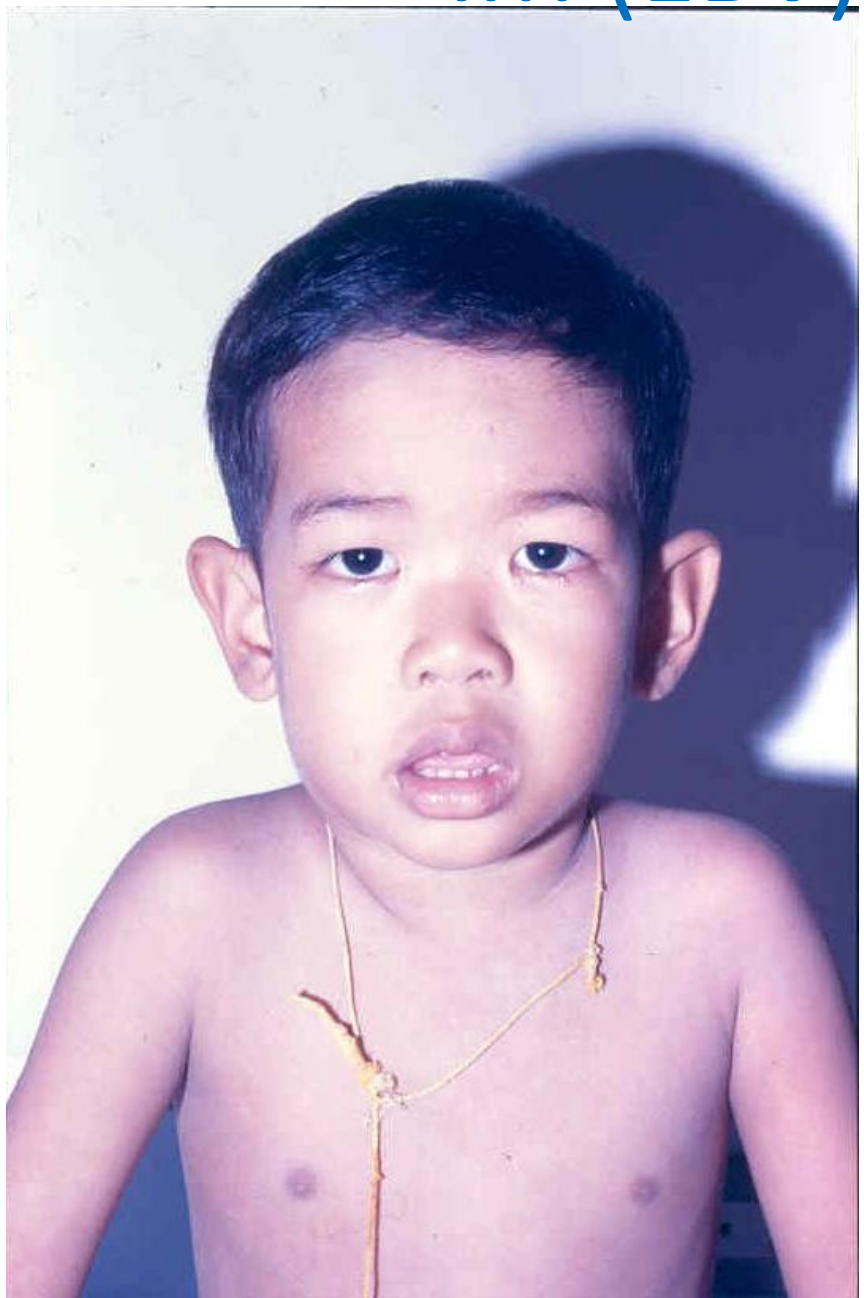
Latent:

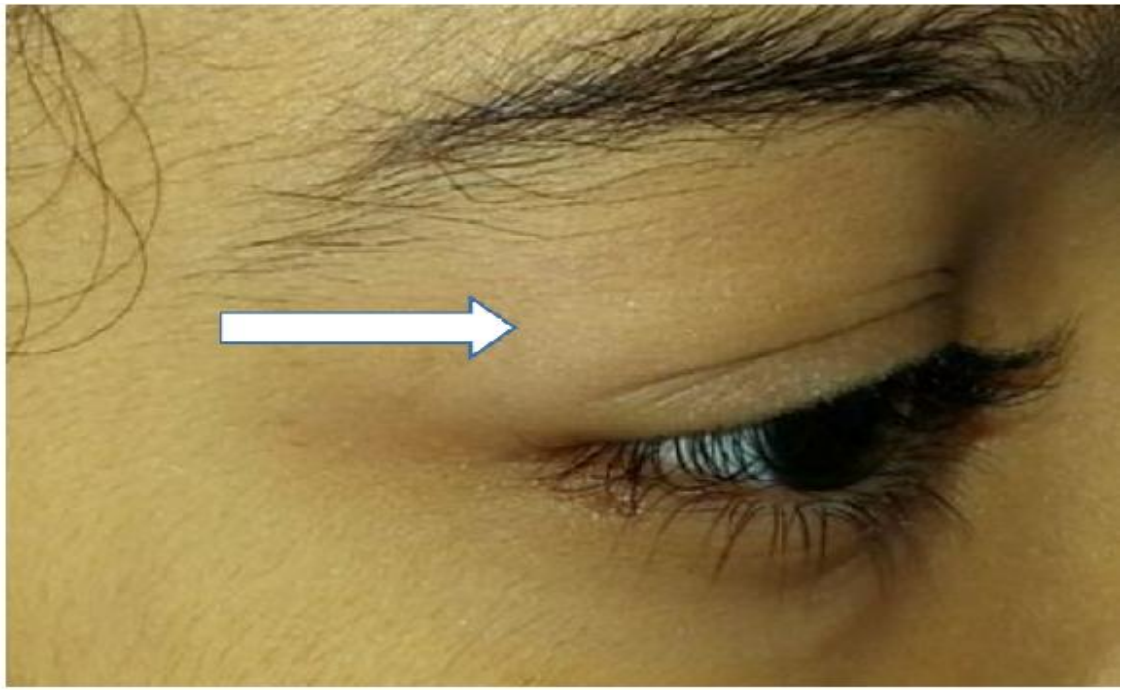
- *Burkitt's Lymphoma,*
- *CA nasopharynx*
- Lymphoproliferative disease

Infectious mononucleosis (IM)

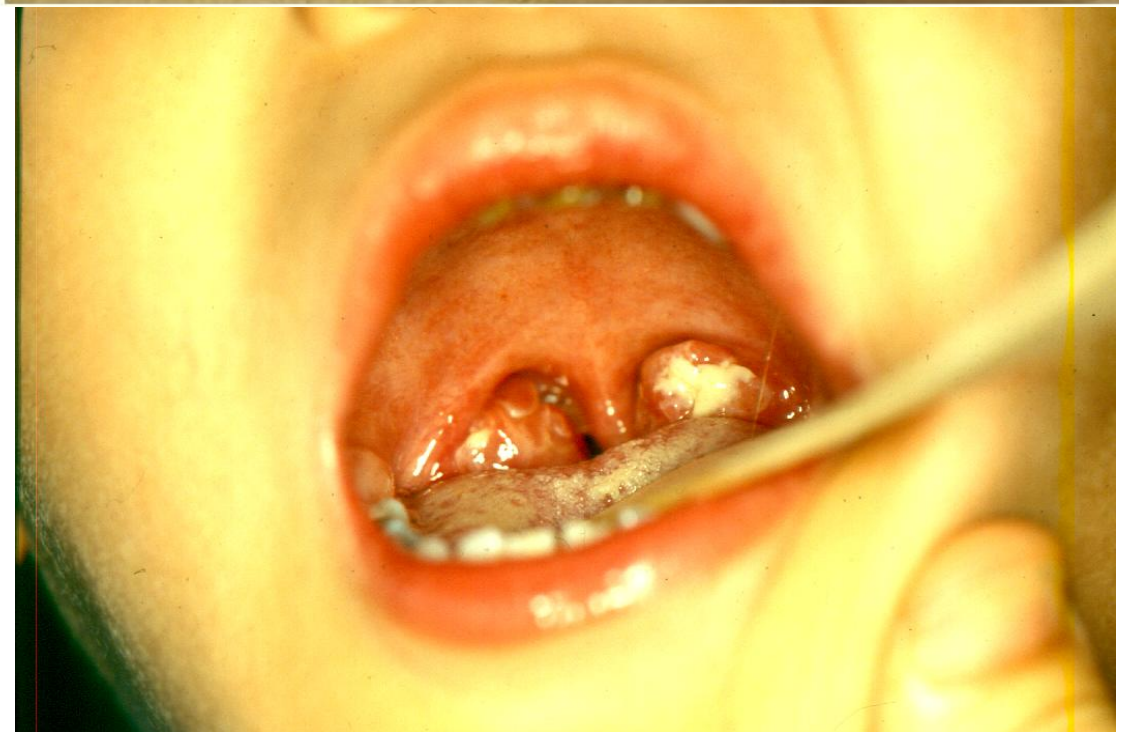
- Epstein-Barr virus **(HHV** 4)
- พบบ่อยในเด็กโต
- มีไข้สูง 4-14 วัน
- LN โต เจ็บคอ ร่วมกับมี whitish patch
- Hepatosplenomegaly, ตาบวม (Hoagland sign), ตาเหลือง
- ผื่นพบได้ในสัปดาห์แรก 10-15 %
- ได้ ยา ampicillin หรือ amoxicillin ผื่นขึ้น จะพบได้สูงถึงร้อยละ 90 ของผู้ป่วย

IM (EBV)

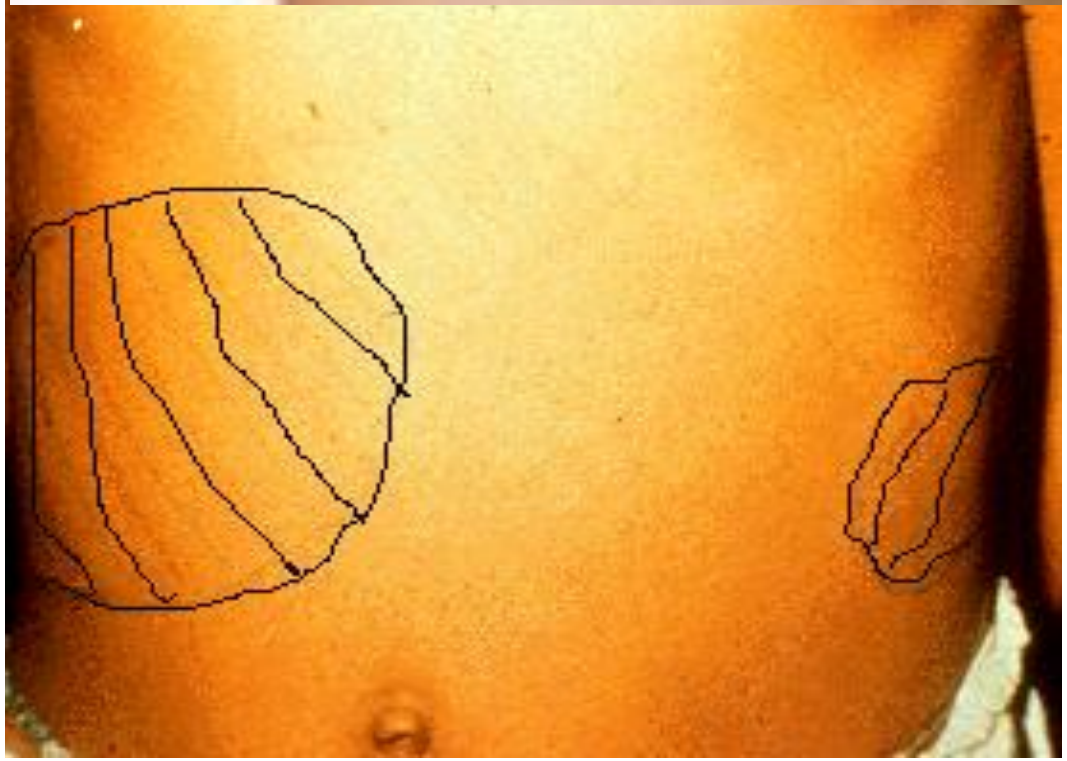


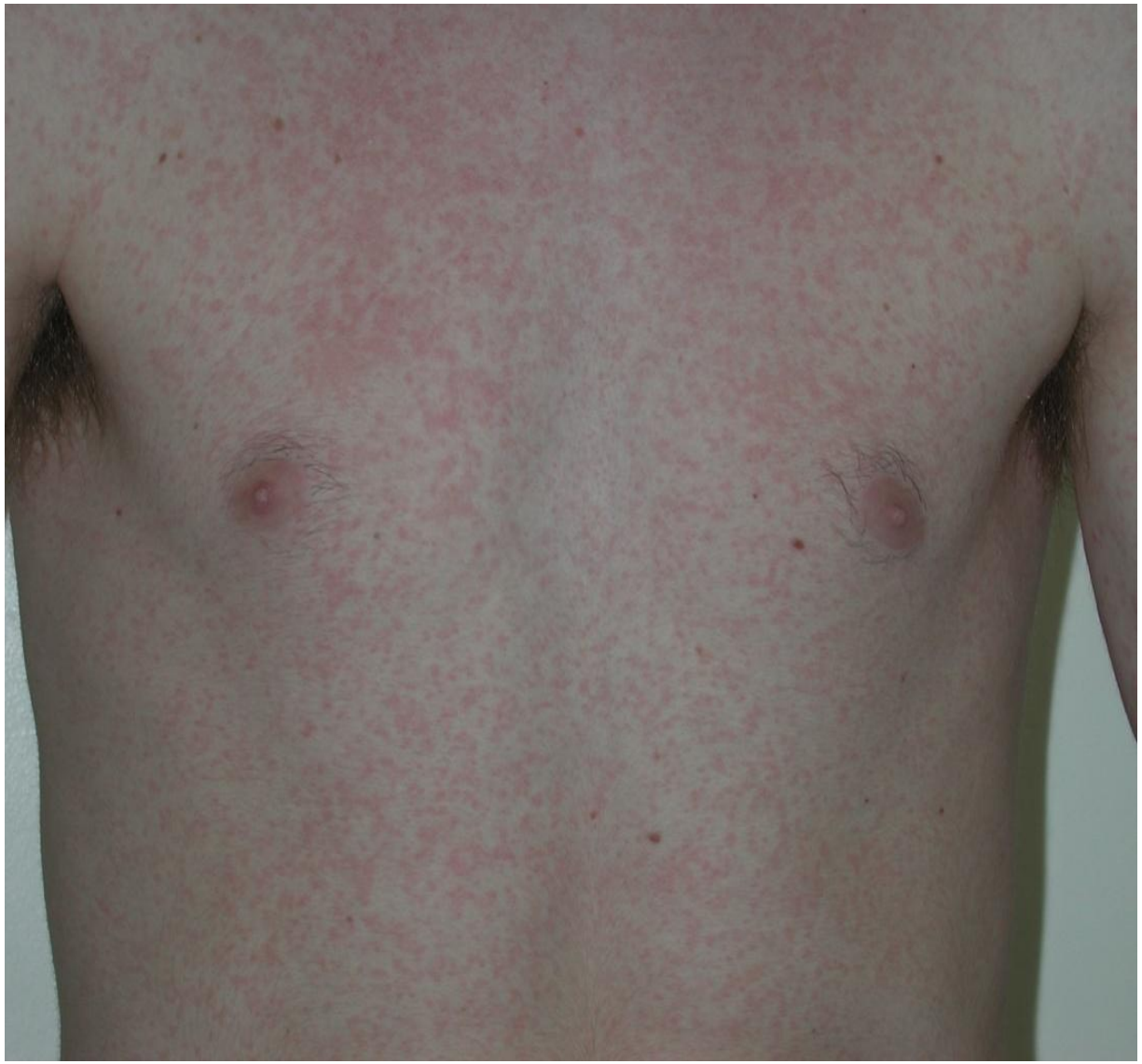


Hoagland sign

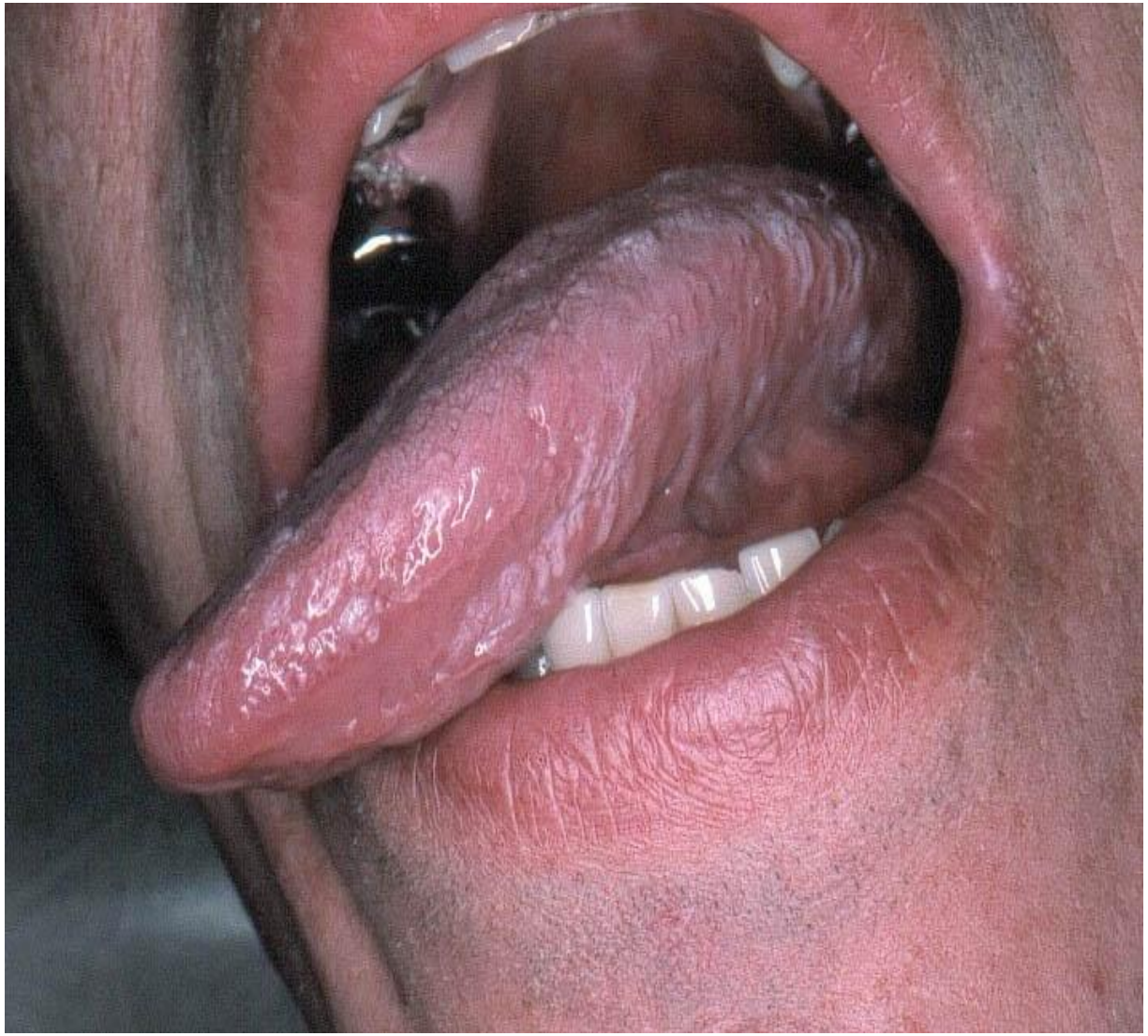


IM (EBV)



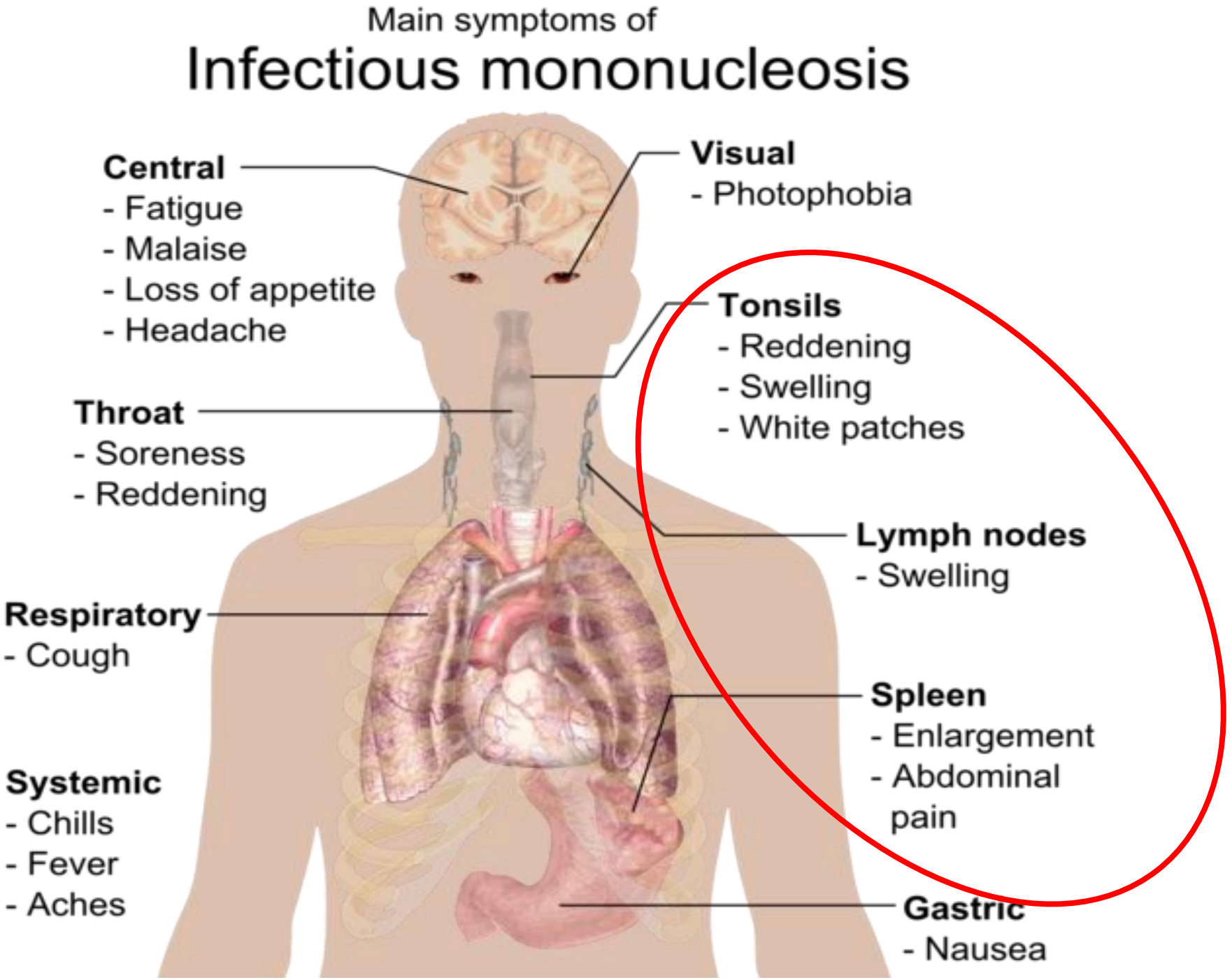


•Rashes after ampicillin in IM



EBV: Oral hairy leukoplakia in HIV

IM (EBV)


Main symptoms of
Infectious mononucleosis
Central
- Fatigue
- Malaise
- Loss of appetite
- Headache
Visual
- Photophobia
Tonsils
- Reddening
- Swelling
- White patches
Throat
- Soreness
- Reddening
Lymph nodes
- Swelling
Respiratory
- Cough
Spleen
- Enlargement
- Abdominal pain
Systemic
- Chills
- Fever
- Aches
Gastric
- Nausea

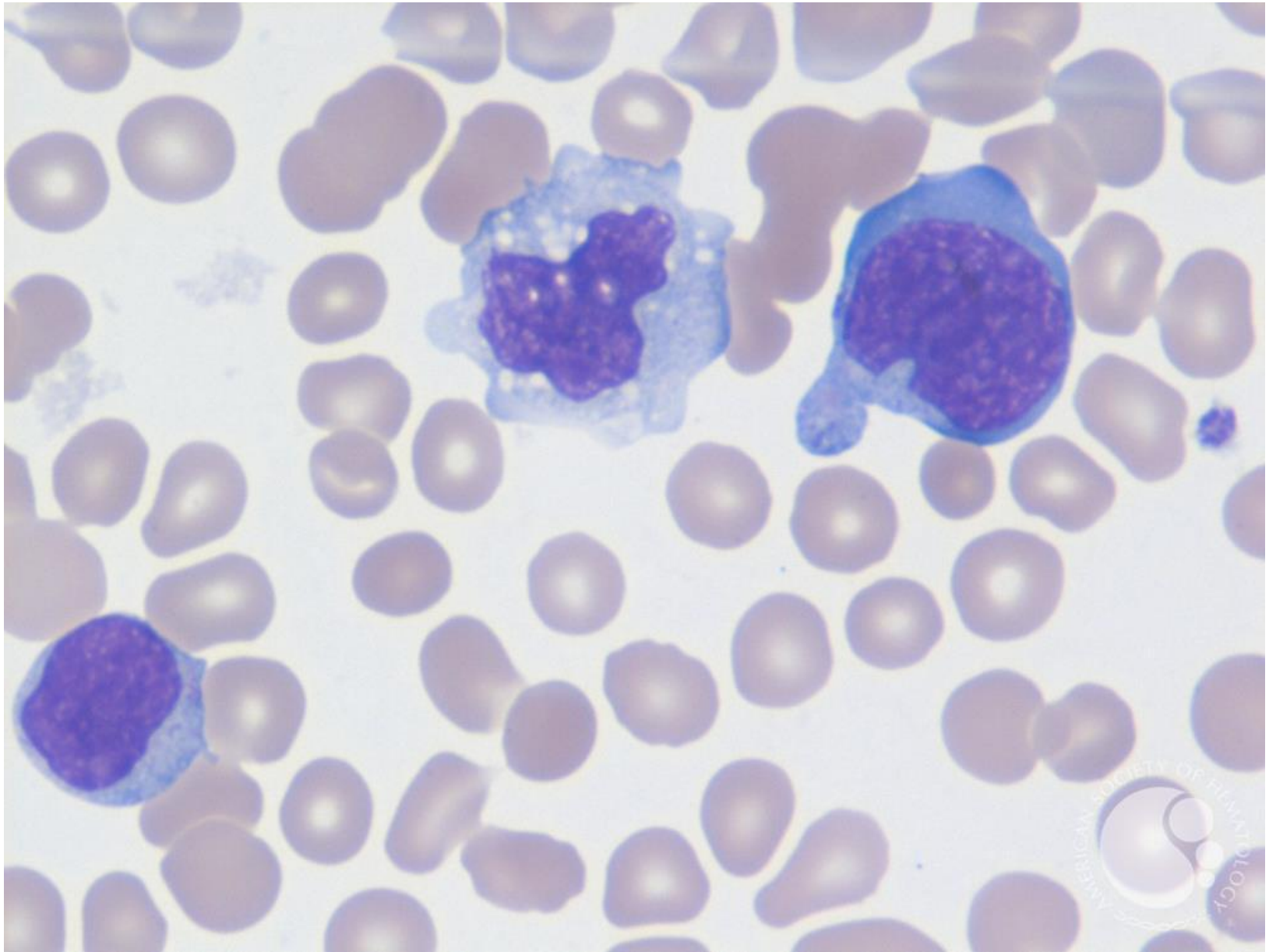
Infectious mononucleosis

- CBC : Lymphocytosis ; Atypical lymph 20-40%

  Thrombocytopenia, hemolytic anemia

- Diagnostic : PCR , anti-VCA IgM, Hetrophile Ab
- Tx: supportive
- Steroid :
  - Airway obstruction
  - Thrombocytopenia with hemorrhage,
  - Autoimmune hemolytic anemia (AIHA)
  - CNS

Infectious mononucleosis



Atypical lymphocyte

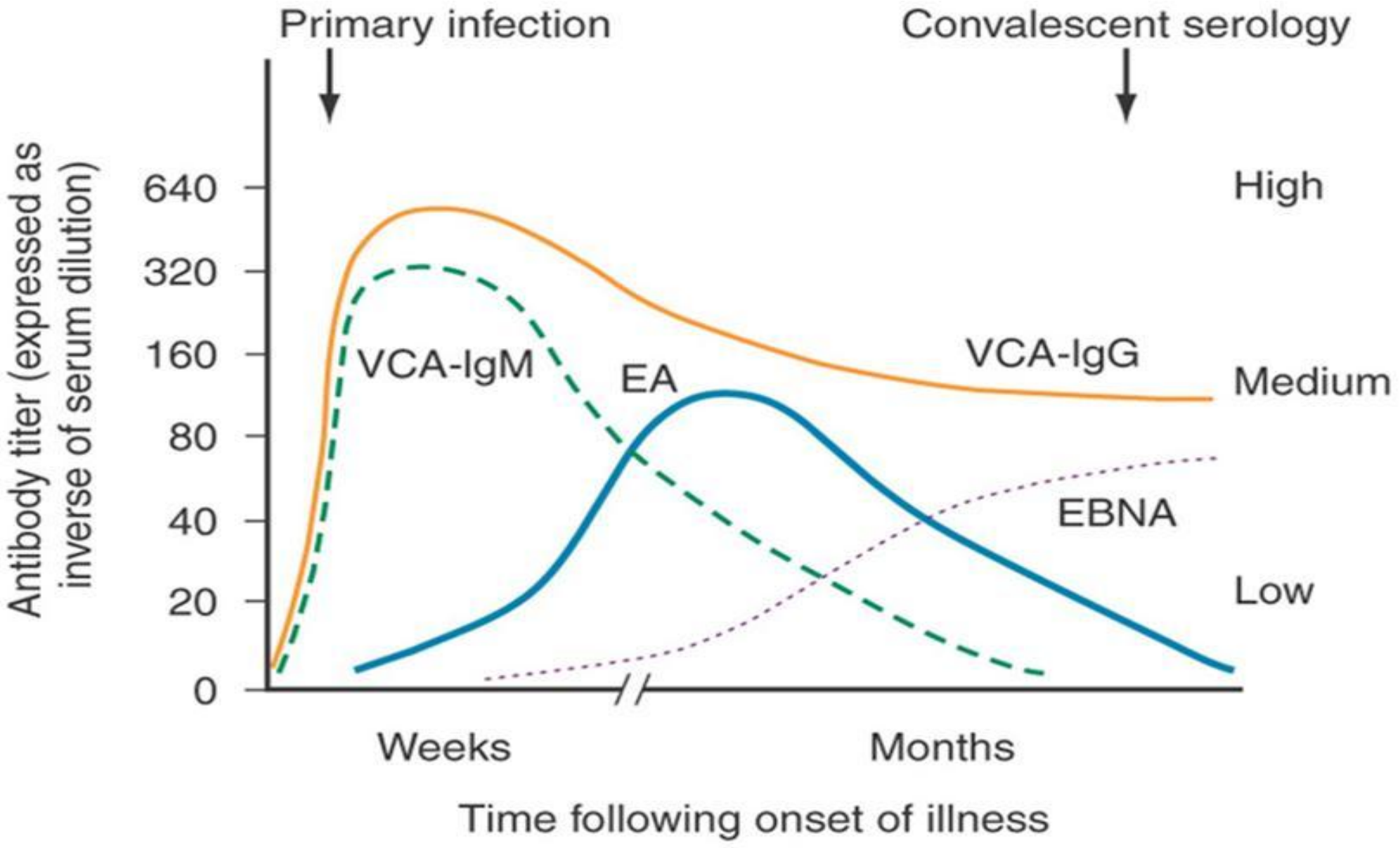
"Downey cells"

large lymphocyte

มี cytoplasm สีน้ำเงิน

และจะมี RBC อยู่รอบ ๆ -->

Infectious mononucleosis

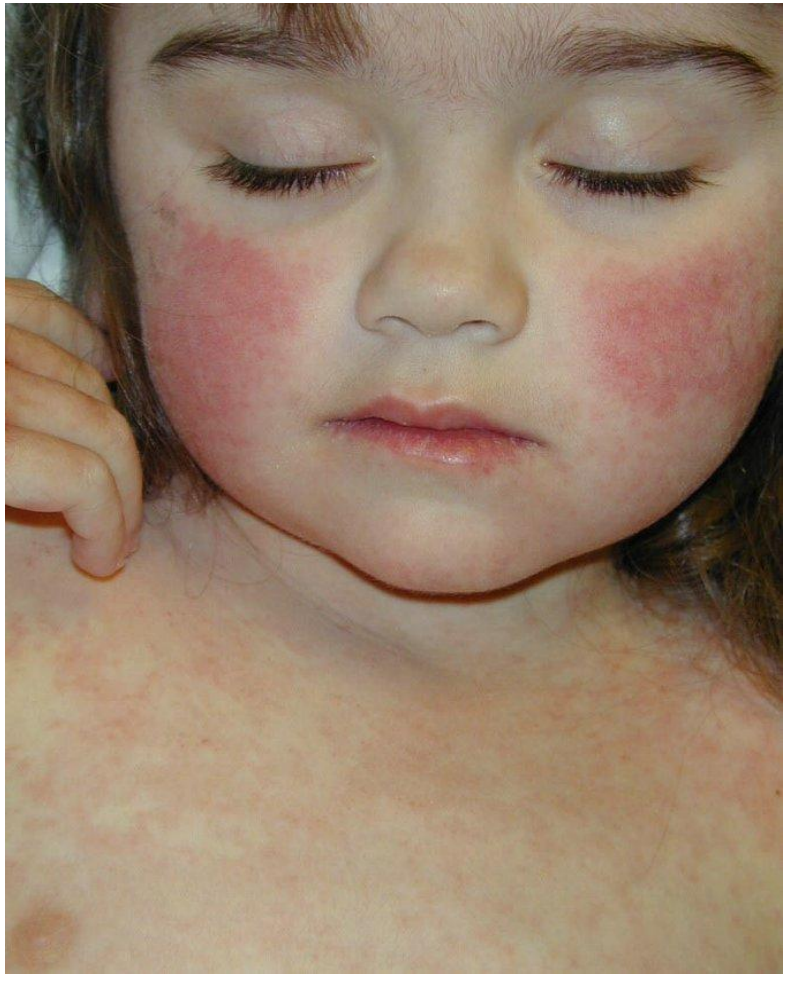


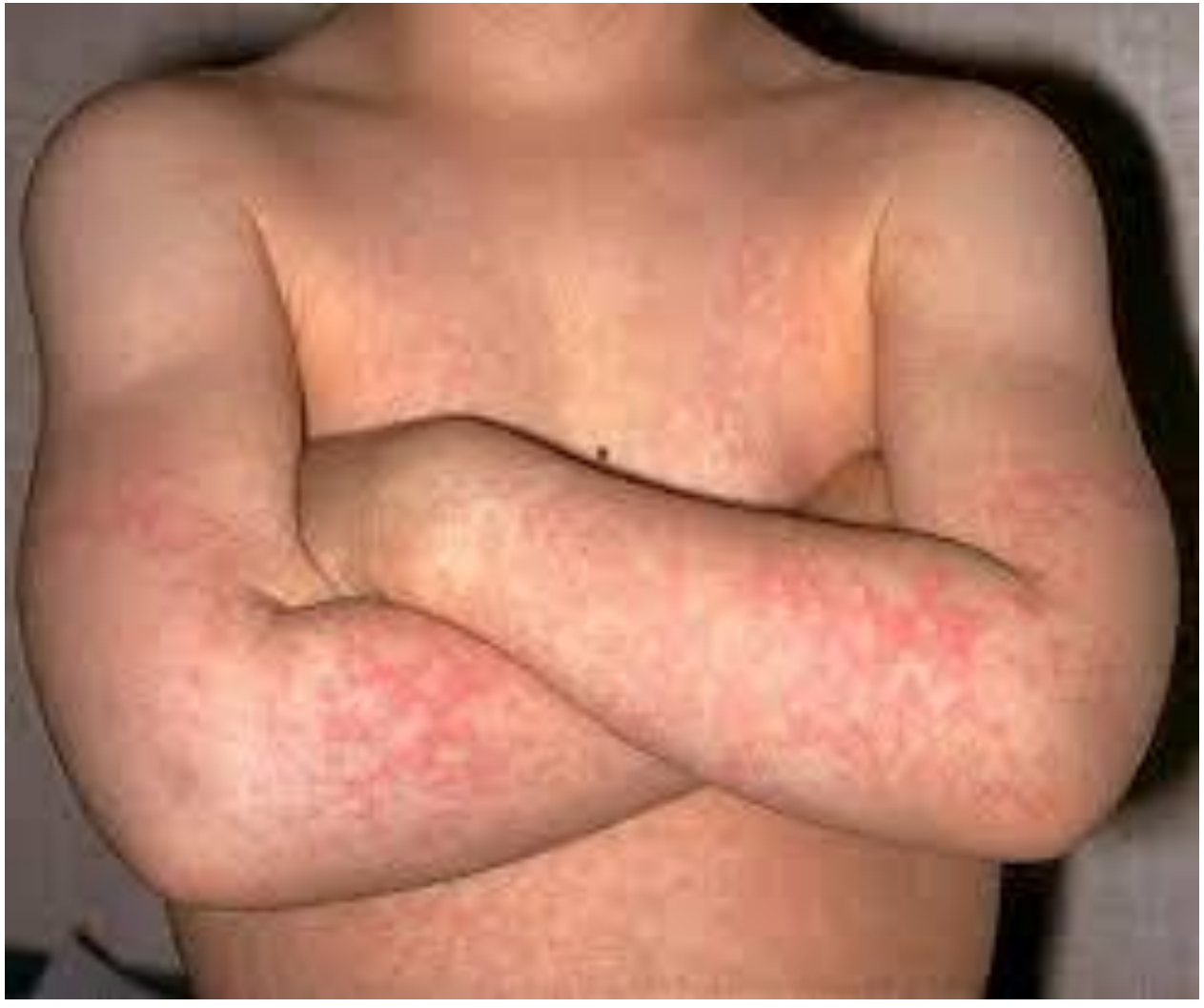
Parvovirus B19 (Fifth Disease)

erythema infectiosum

"slapped cheek"

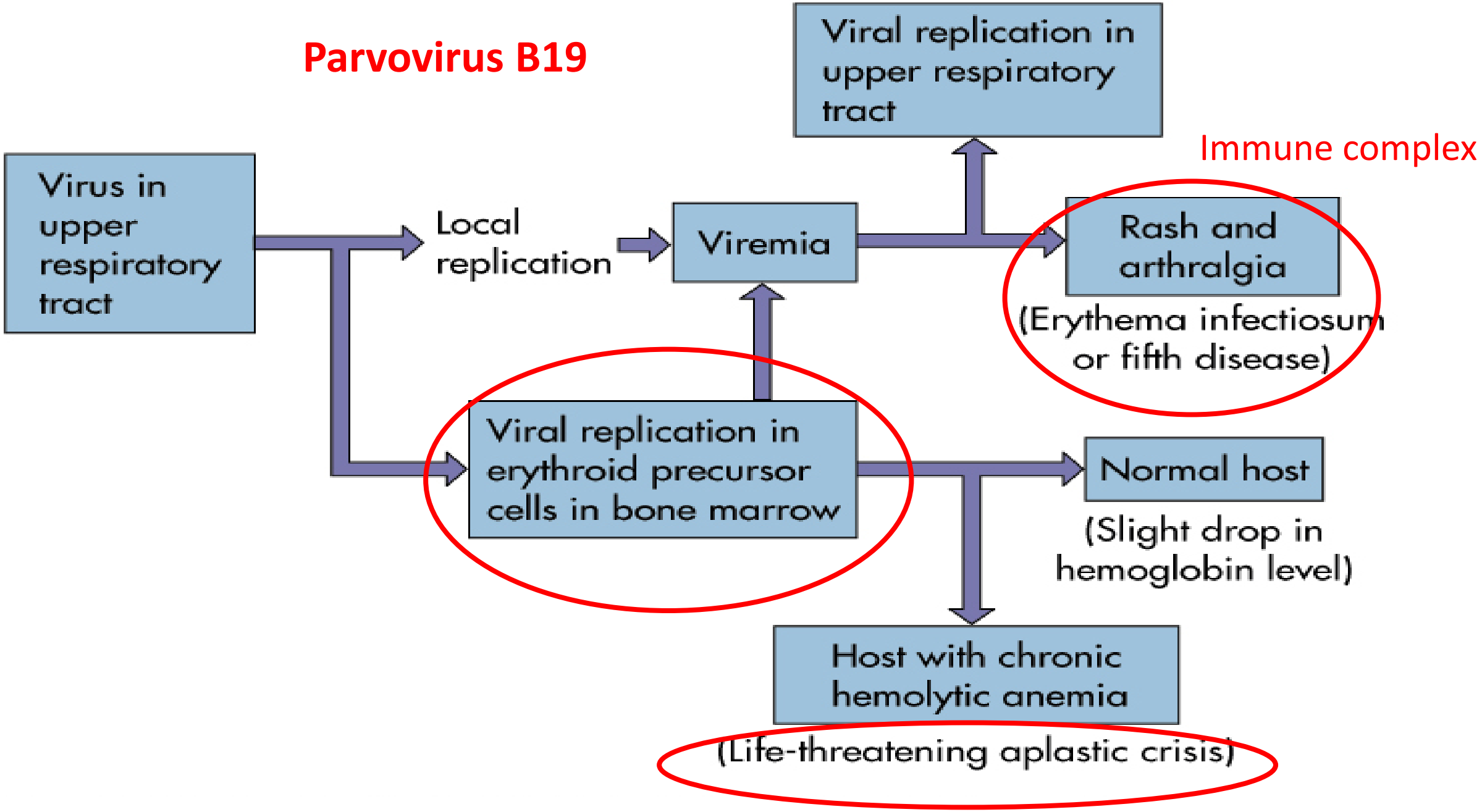
childhood



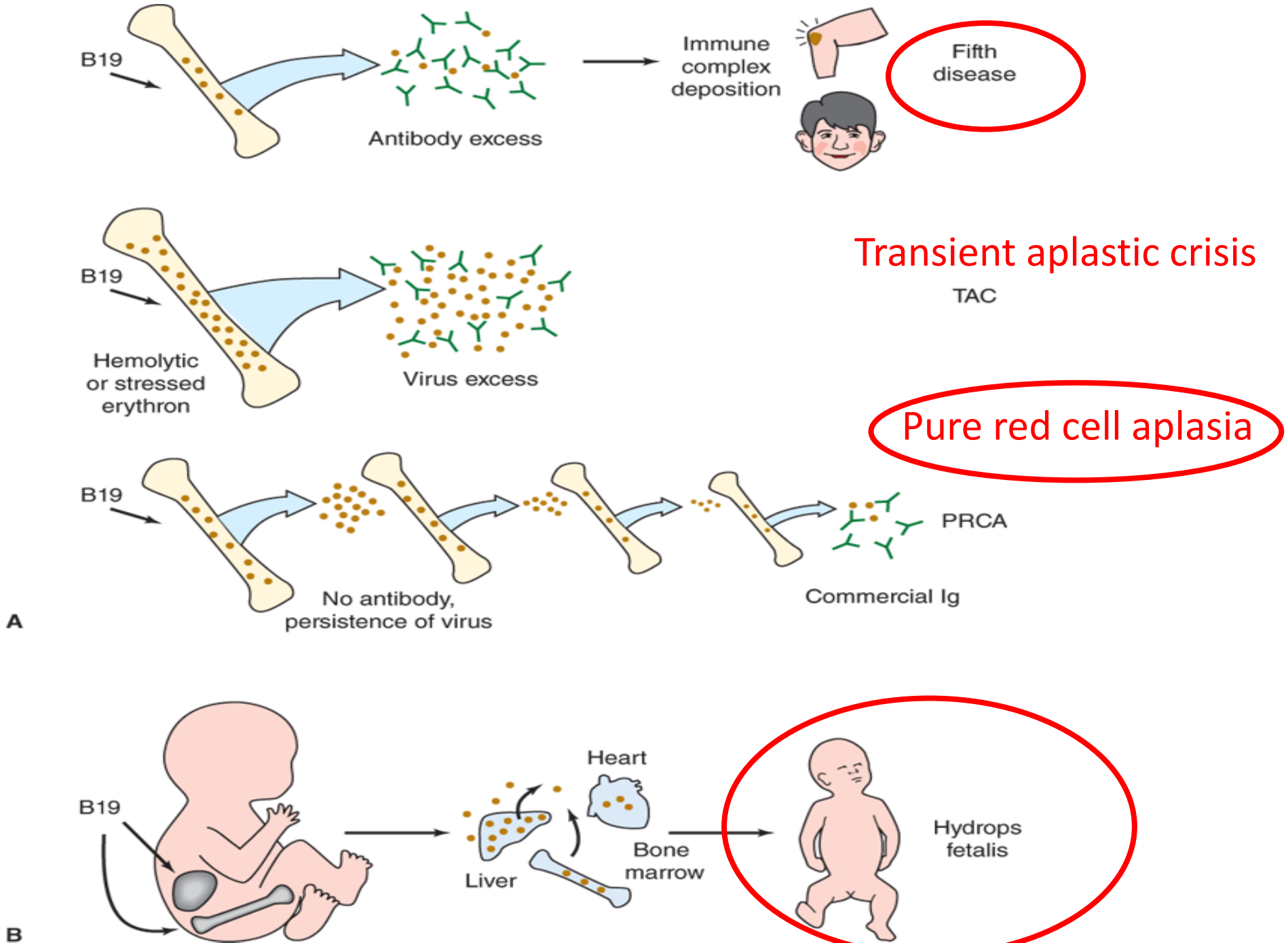


Lace like rash

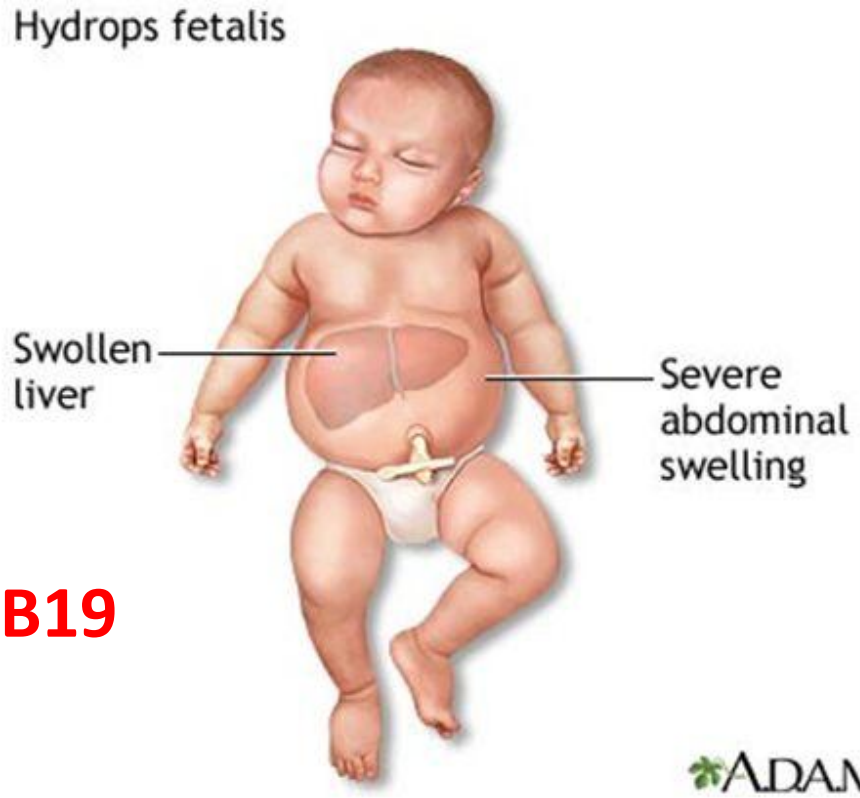
Parvovirus B19

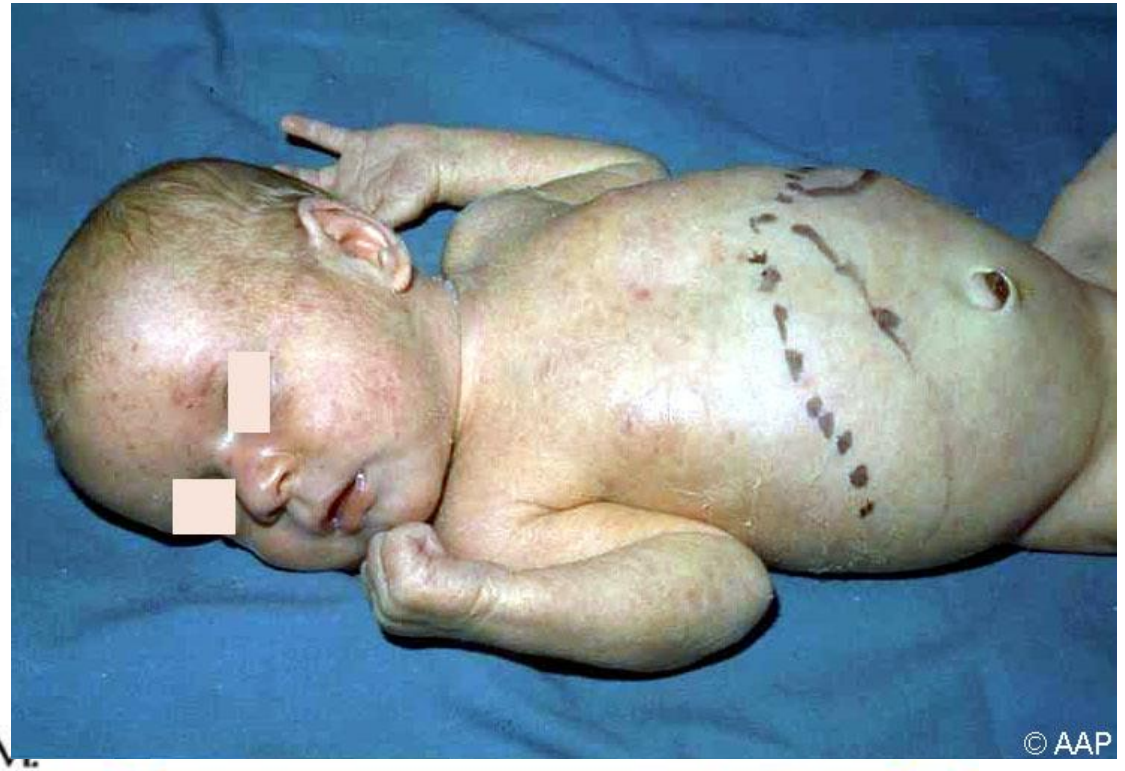


Parvovirus B19



Hydrops fetalis





Parvovirus B19

- **Human hydropic fetus and placenta after intrauterine parvovirus B19 infection**
- **Hydrops is an edema (swelling due to lymph fluid) in subcutaneous tissue**

Parvovirus B19

- Replication in erythroid progenitor cell
- Transmission : airborne, droplet
- Disease
- Fifth disease: erythema infectiosum (Fever, rash)
- Pure red cell aplasia
- Aplastic crisis
- Congenital parvovirus : Hydrops fetalis
- Associated: Encephalitis, SLE, Henoch Schoenlein purpura etc.
- Dx IgG, IgM, PCR
- Tx, supportive tx

Vesiculopustular eruption

1. Herpes simplex Virus

- Type I ; Herpes gingivostomatitis
- Type II ; Genital Herpes, Neonatal herpes

2. Varicella virus infection

- Chicken pox
- Herpes Zoster

3. Enterovirus infection

- Hand Foot and Month disease

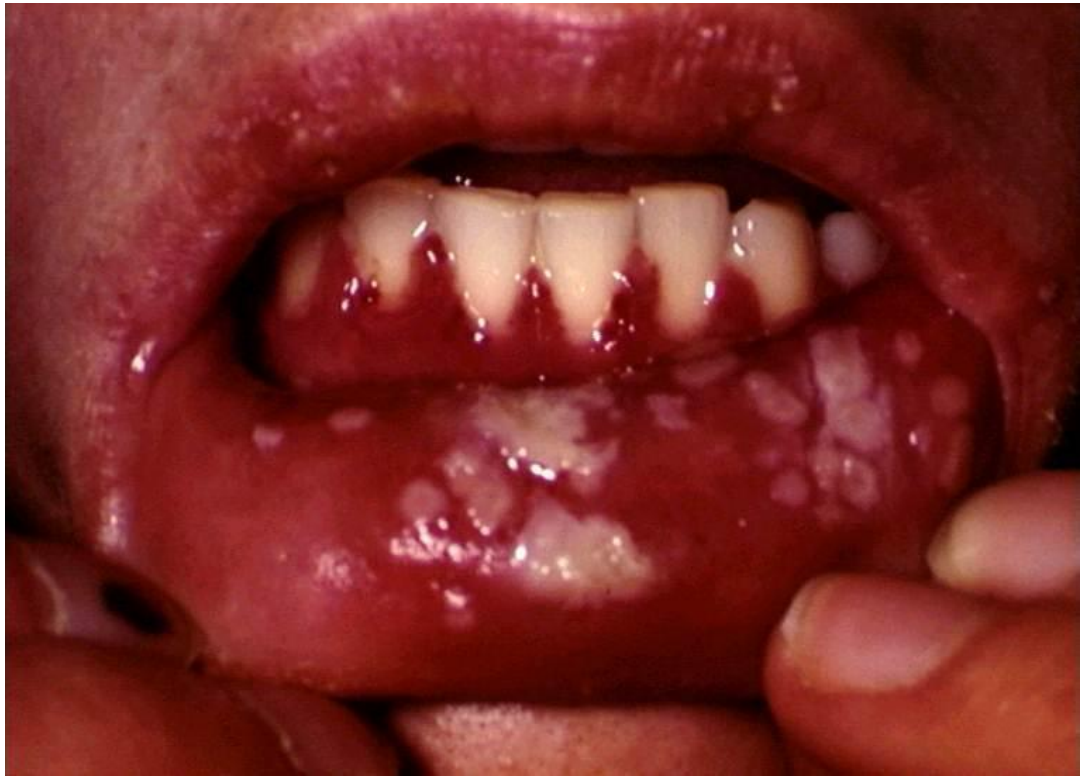
Herpetoviridae (Human herpesvirus)

DNA virus/ Inclusion body/Latent infection

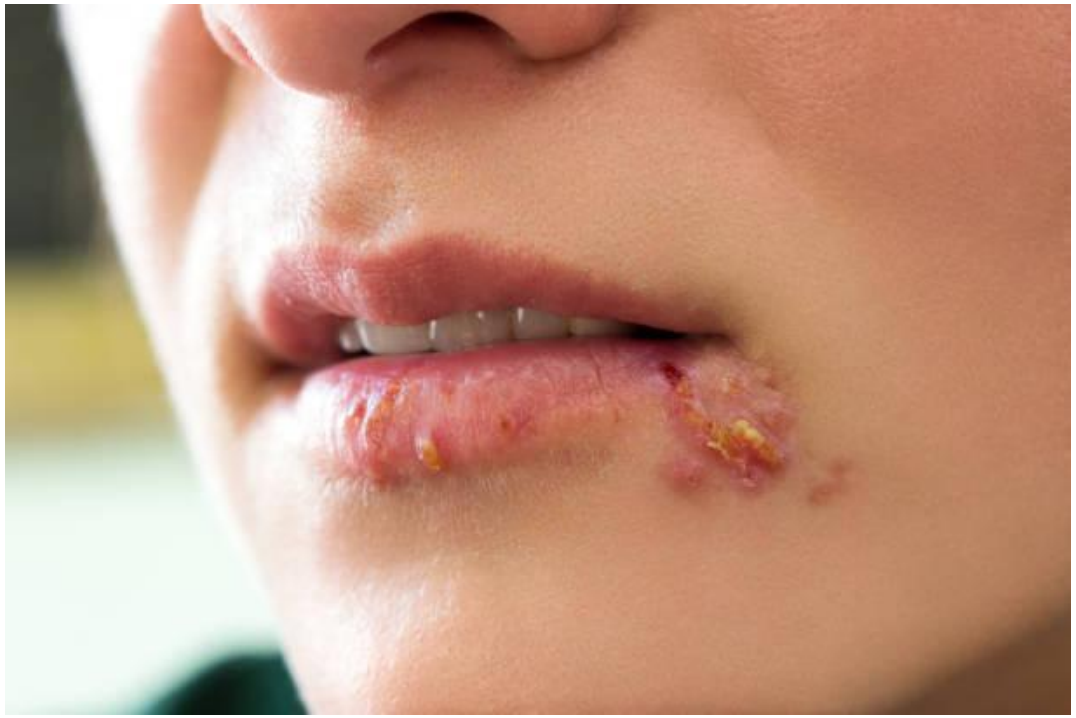
Herpes simplex virus type 1 (HSV-1)

- Herpes simplex virus type 2 (HSV-2)
- Varicella zoster virus (VZV)
- Human herpes virus 4: Epstein Barr virus(EBV)
- Human herpes virus 5: Cytomegalovirus(CMV)
- Human herpes virus 6 : Roseolar infantum
- Human herpes virus 7: Roseolar infantum(mild)
- Human herpes virus 8: Kaposi's sarcoma

Herpes simplex virus



Primary herpes gingivostomatitis



Herpes labialis

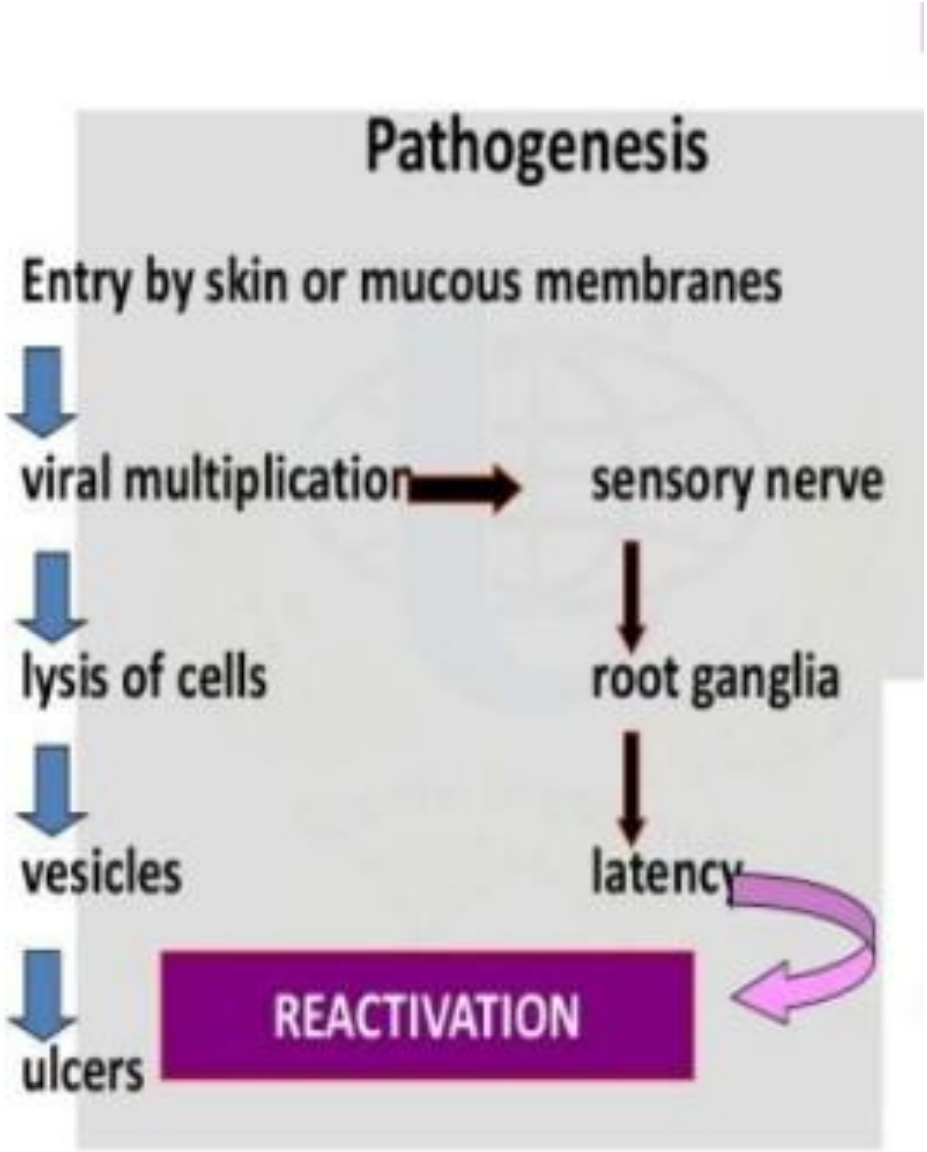
Mucocutaneous HSV: Acyclovir 400 mg x5x 7 d

	HSV - 1	HSV - 2
1. Transmission	หายใจ, สัมผัส	เพศสัมพันธ์ แม่ ⟶ ลูก (สัมผัส)
2. Clinical feature	herpes labialis gingivostomatitis, keratitis	genital,
3. การติดเชื้อซ้ำ	น้อยกว่า	บ่อยกว่า
4. Cancer	Oral cancer	Cervical cancer
5. Treatment	Acyclovir	Acyclovir

Herpes simplex virus

Pathogenesis

- Ballooning of infected cells
- Production of Cowdry type A intranuclear (Lipschutz) inclusion bodies
- Margination of chromatin
- Formation of multinucleated giant cells

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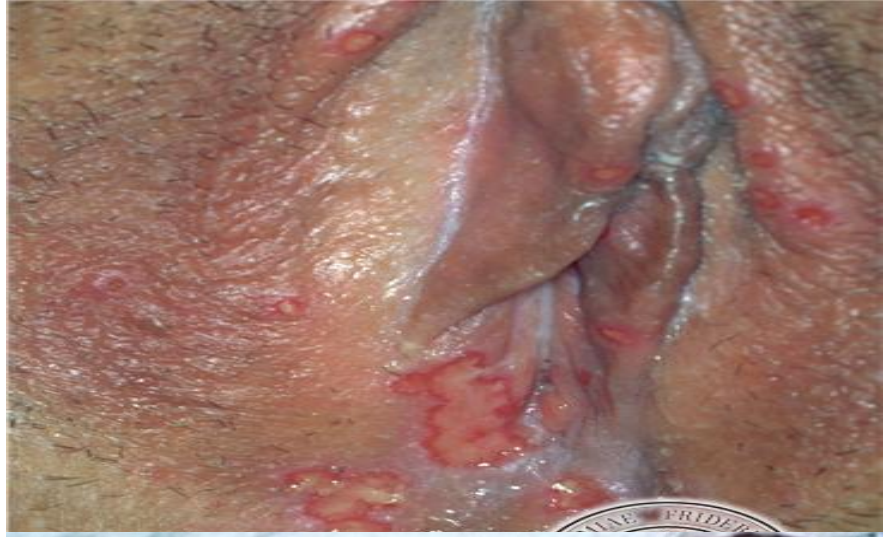
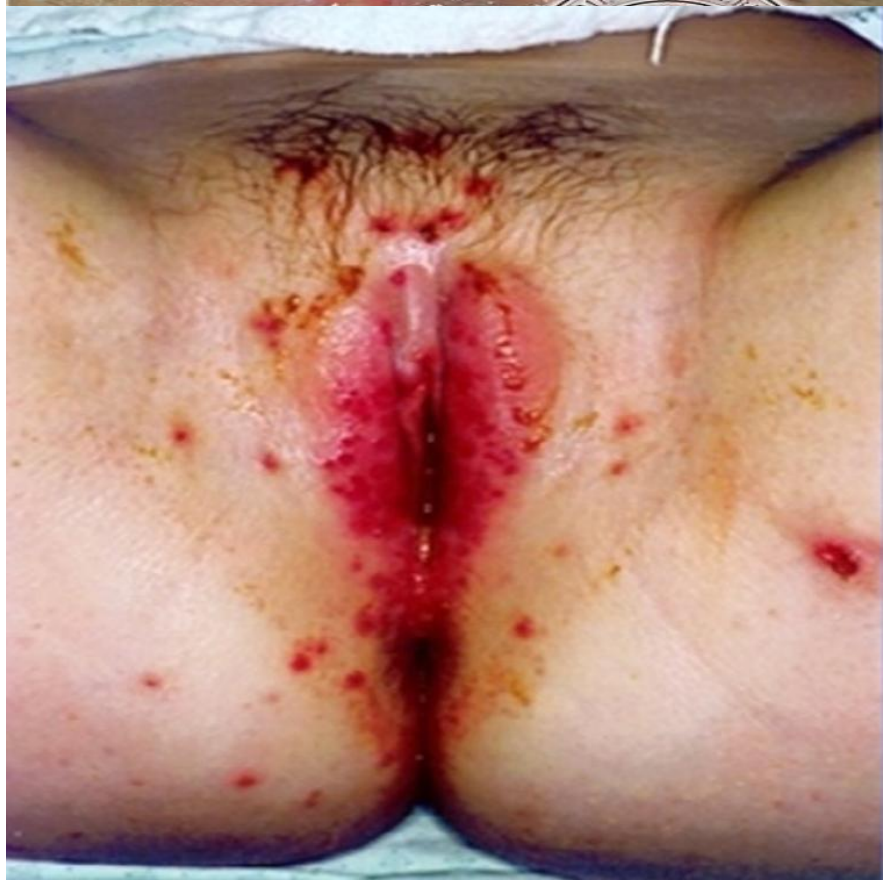
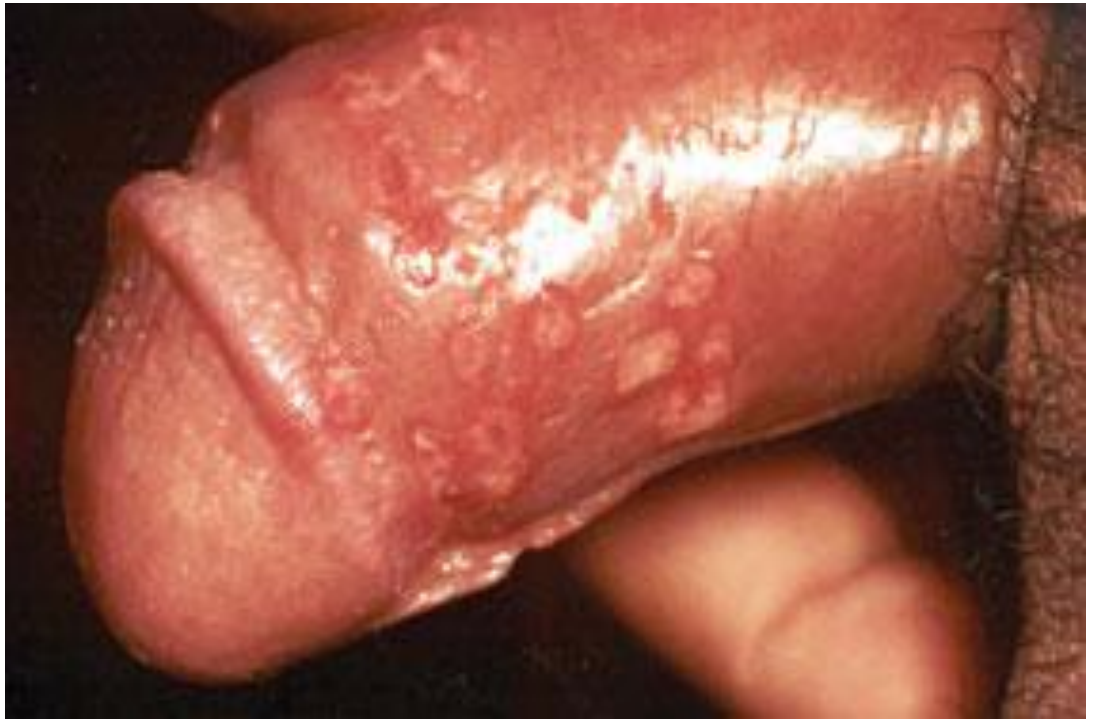
Herpes keratitis

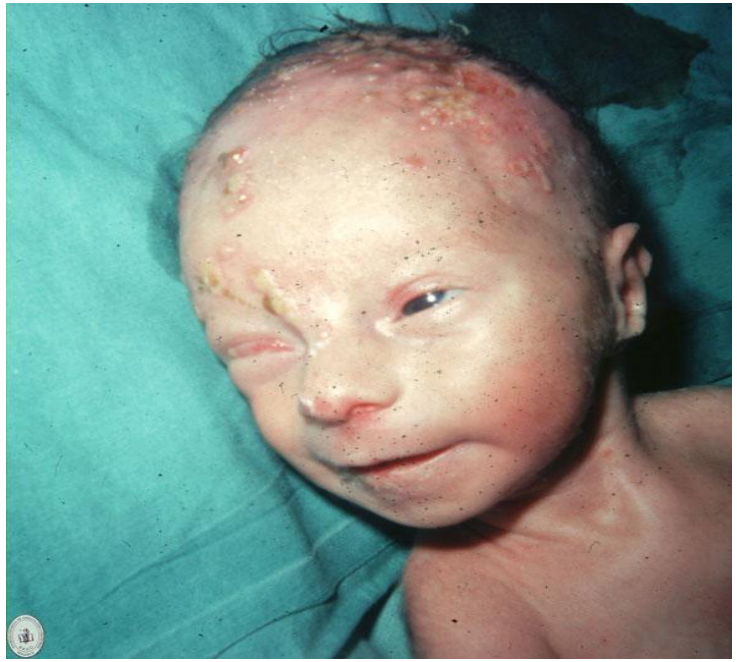

Herpes whitlow

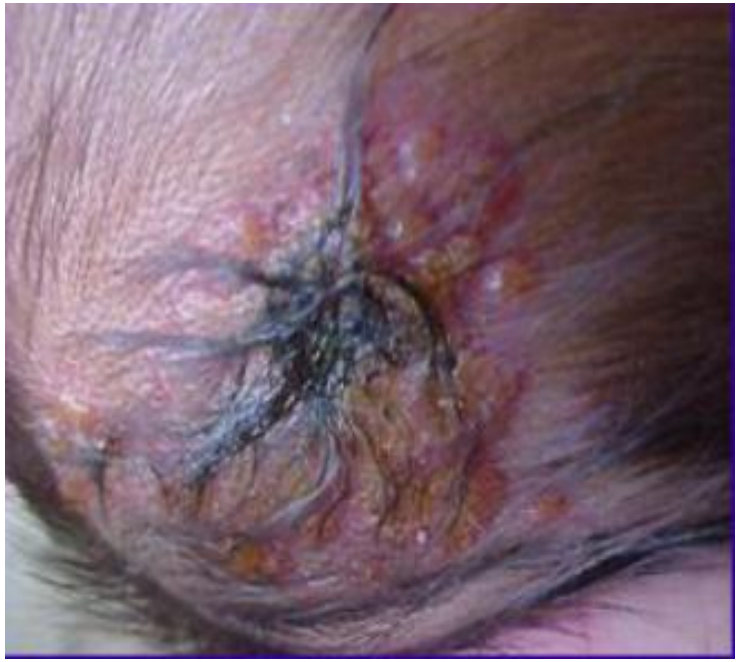

Multinucleated giant cell



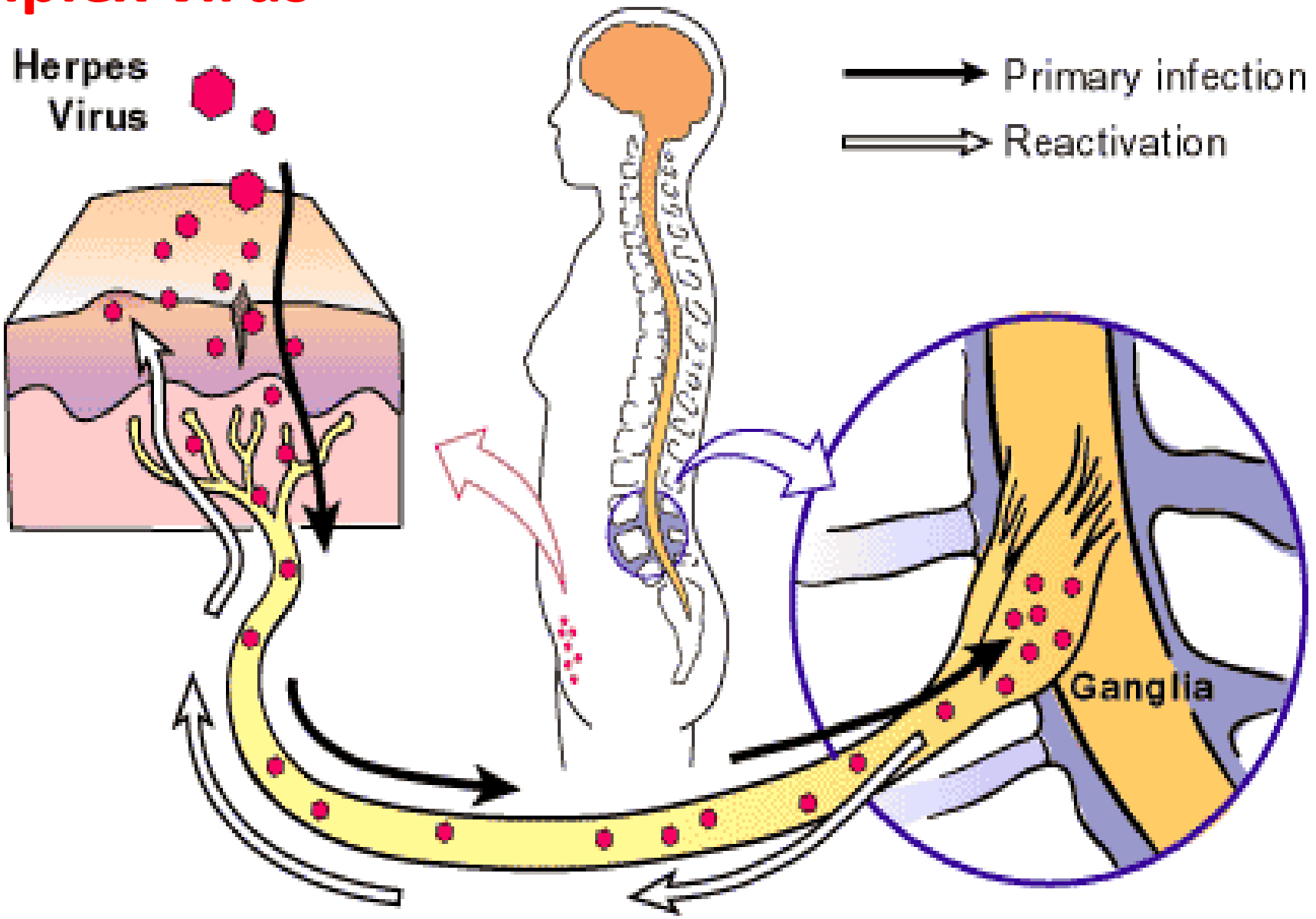








Herpes simplex virus



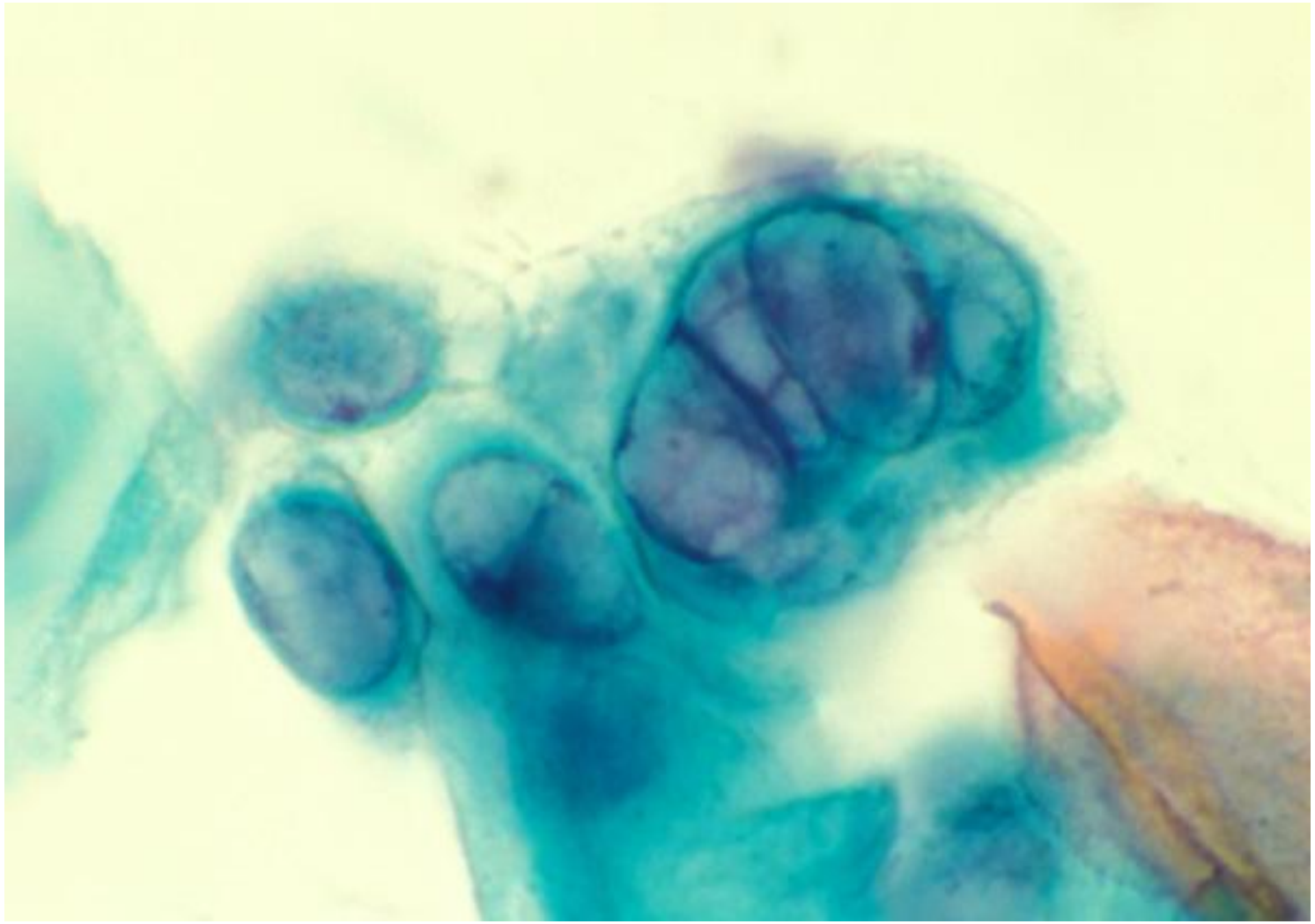
Herpes simplex virus

LAB **–PCR**

- Tzanck test

Tx: Acyclovir

Tzanck Test



Multinucleated giant cell

Varicella zoster Viruses(HHV-3)

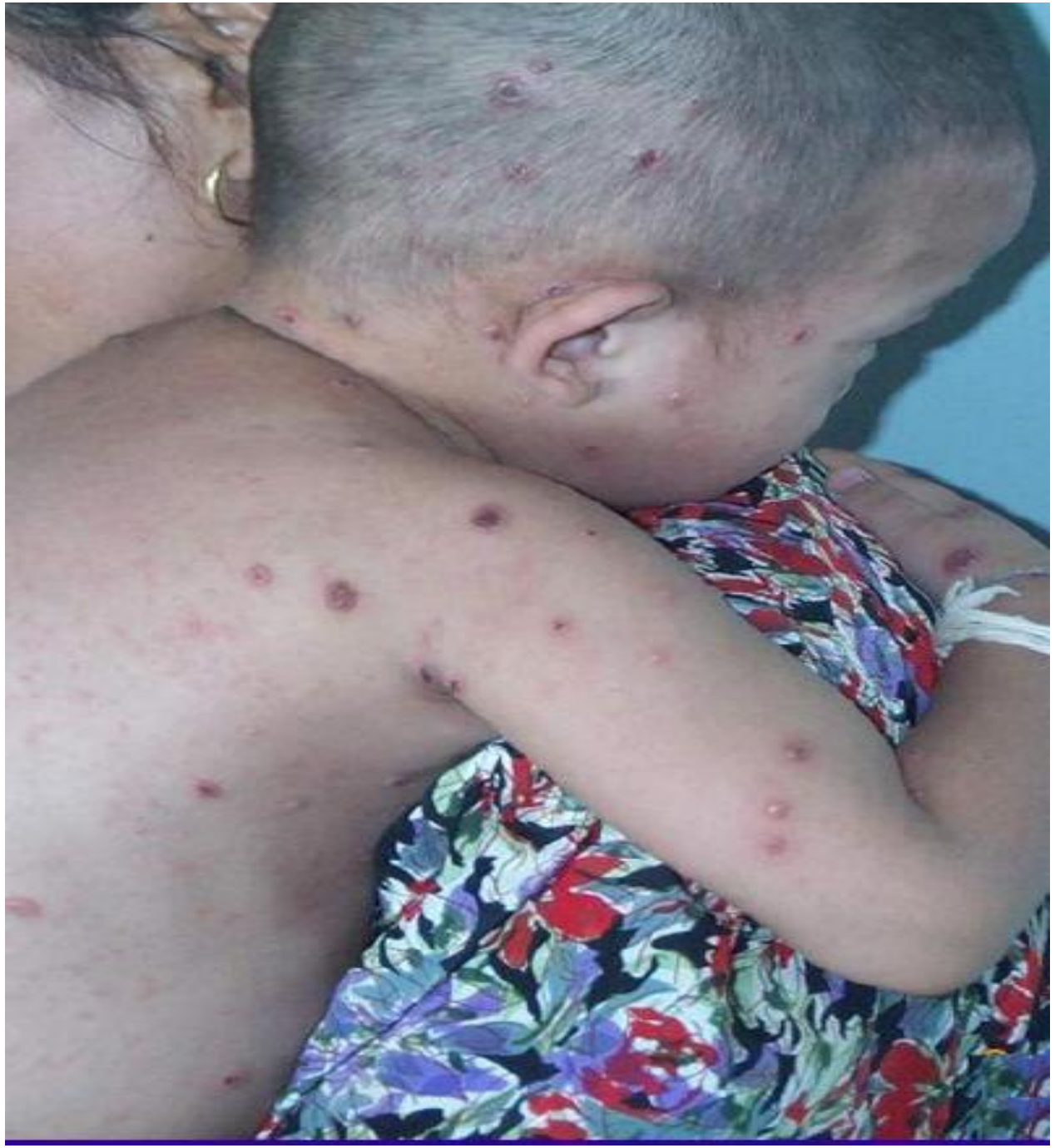
- Chicken pox - primary infection
- Herpes zoster - reactivation of infection

Chicken pox

- Rash: rapid evolution 6-8 hr, multistage, various stage
- LAB: **IgG, IgM**
- Tx Acyclovir in severe varicella
- Prevention:

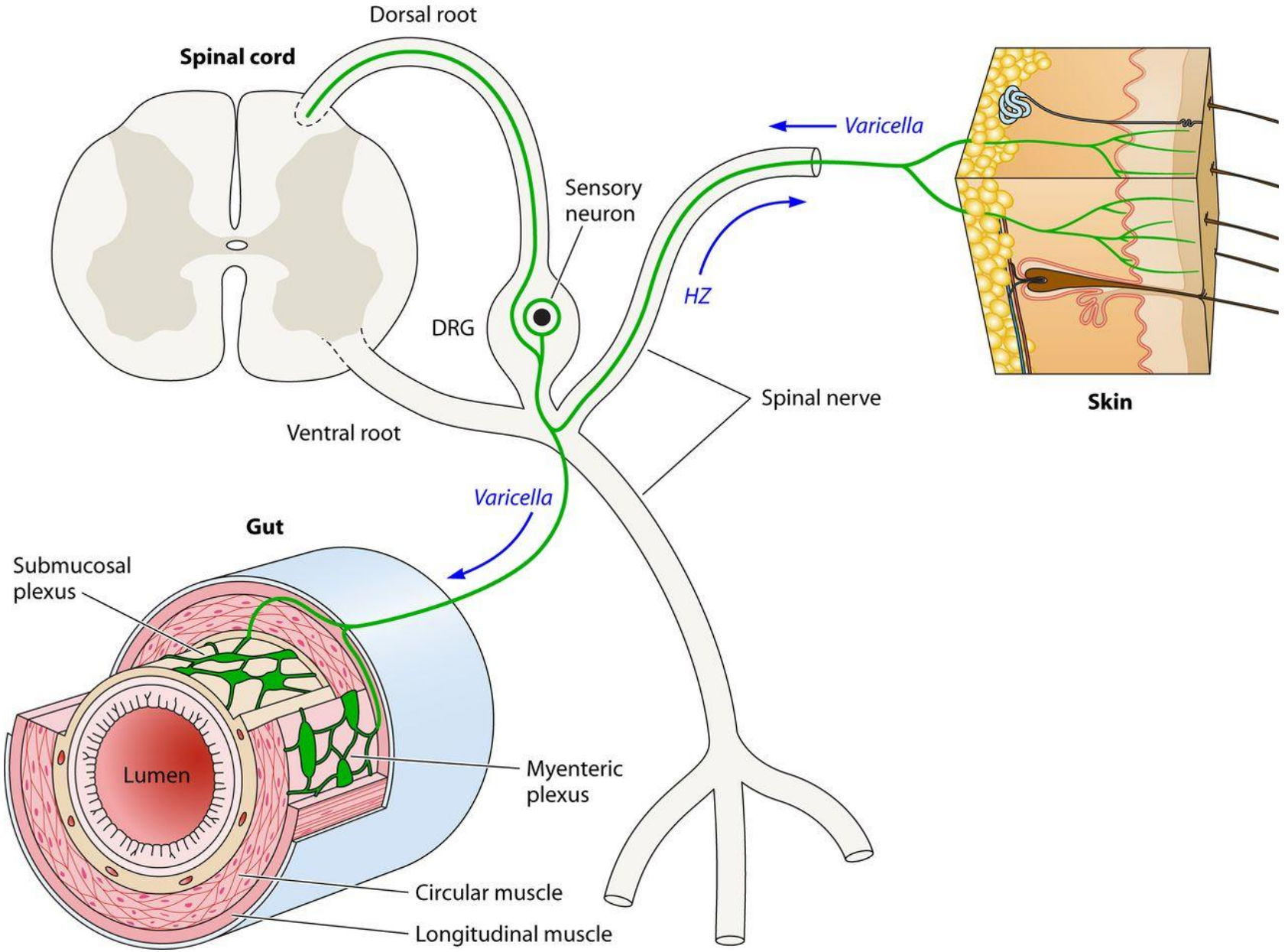
  Varicella vaccine

  Varicella Immunoglobulin: VZIG

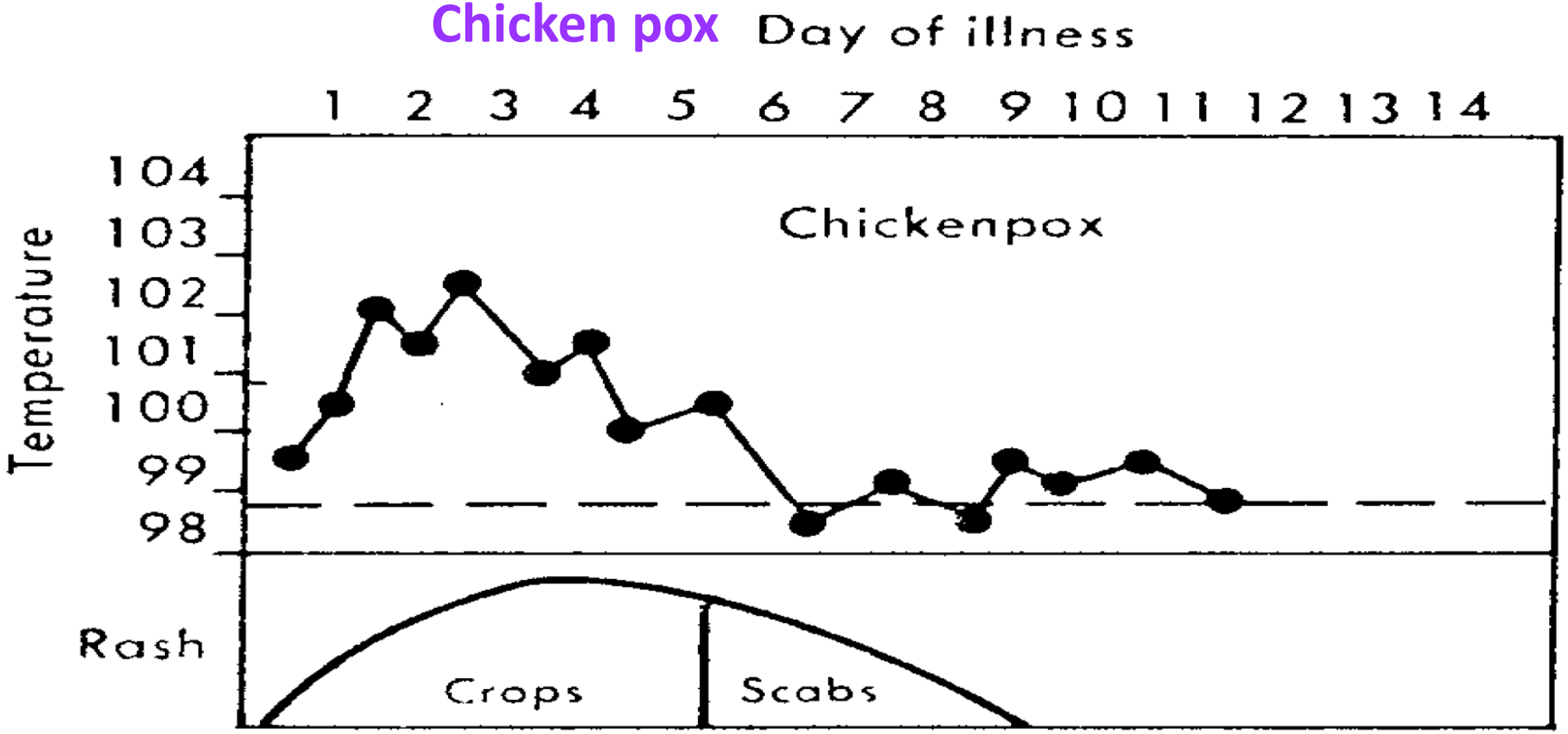


multistage, various stage rash

Potential routes taken by VZV during its life cycle.



Chicken pox

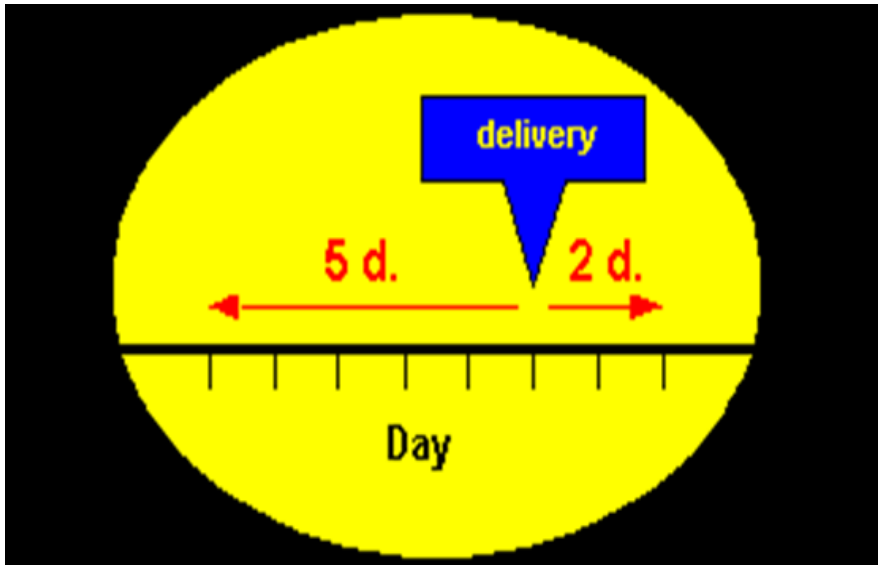

Day of illness
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Temperature
104
103
102
101
100
99
98
Chickenpox
Rash
Crops
Scabs

Neonatal chickenpox

- first 10 days of life
- mother develops varicella from 5 days before to 2 days after delivery,

Most common clinical manifestations

- Disseminated fulminant ,
- Diffuse pneumonia,
- Severe hepatitis
- Meningoencephalitis
- Approximately 1/3 die,



Herpes zoster(Shingles)

- เกิดในคนที่เคยเป็น chicken pox,

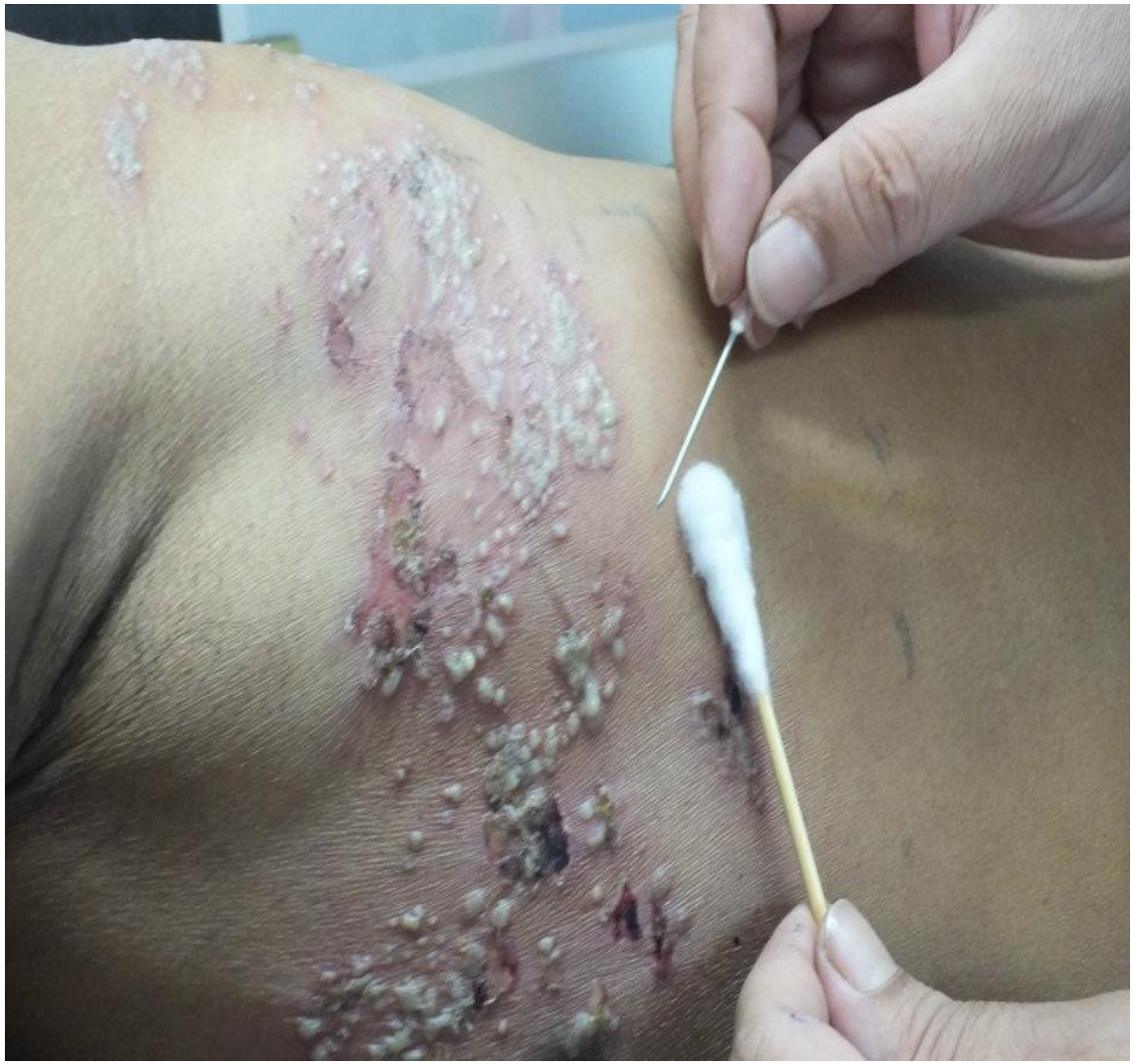
-มี vesicles ตามแนว dermatome

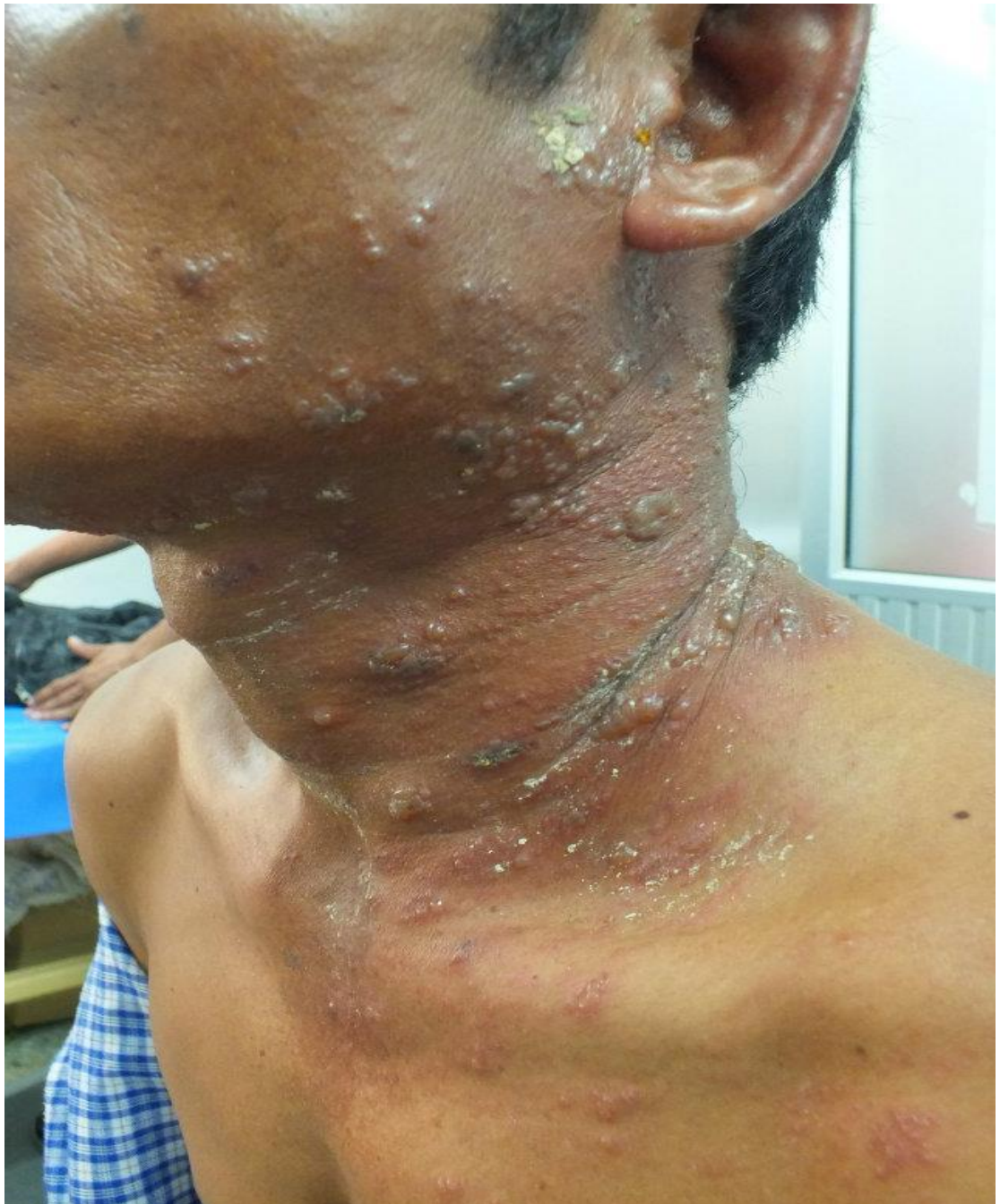
-เกิด post herpetic neuralgia

-Tx Acyclovir

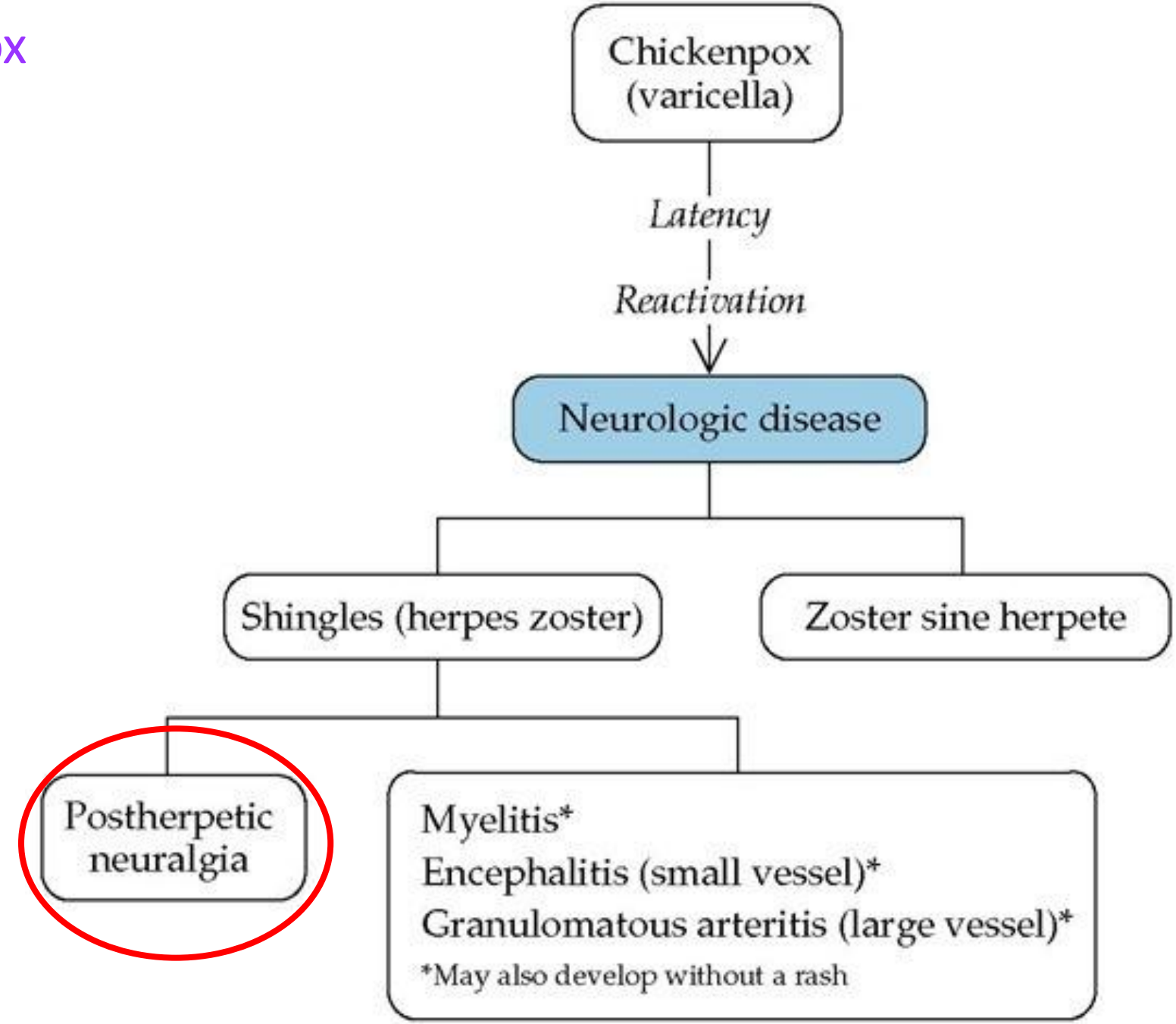
-800 mg x 5 x 7 days

Herpes zoster(Shingles)





Chickenpox


Chickenpox (varicella)
Latency
Reactivation
Neurologic disease
Shingles (herpes zoster)
Zoster sine herpete
Postherpetic neuralgia
Myelitis*
Encephalitis (small vessel)*
Granulomatous arteritis (large vessel)*
*May also develop without a rash

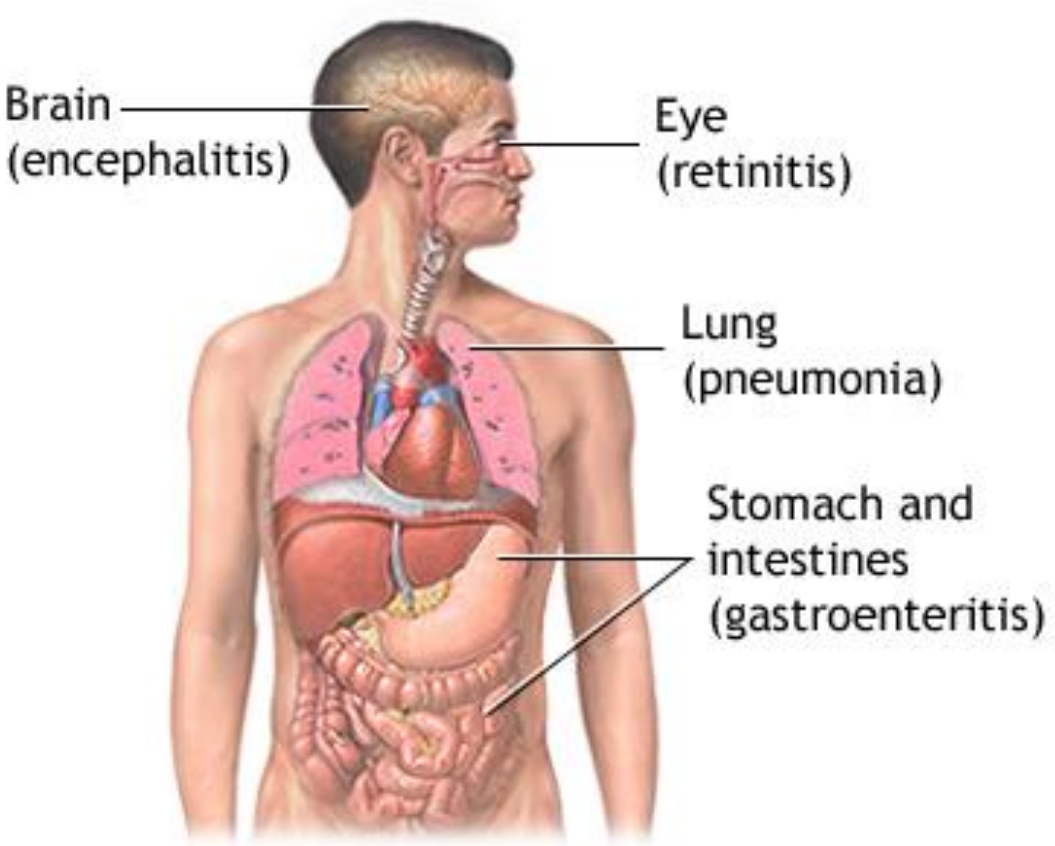
Treatment of HSV, VZV Infection

Diseases	Anti-viral agents + dose	Duration
Primary orifacial HSV	Acyclovir 200 mg 5x/d Acyclovir 400 mg 3x/d	7-10 d or until resolution
Recurrent orofacial HSV	Acyclovir 400 mg 5x/d Acyclovir cream 5x/d	4-5 d or until resolution 4 d
Primary genital HSV	Acyclovir 200 mg 5x/d Acyclovir 400 mg 3x/d	7-10 d or until resolution
Recurrent genital HSV	Acyclovir 800 mg 2x/d Acyclovir 800 mg 3x/d	5 d or until resolution 2 d
Suppressive treatment for HSV	Acyclovir 400 mg 2x/d	6-12 mo
Chickenpox	Acyclovir 800 mg 5x/d	7 d
Herpes zoster (age >50 yr, CN involvement)	Acyclovir 800 mg 5x/d	7 d

PHN, post herpetic neuralgia; TCA, tricyclic antidepressant

CMV: Cytomegalovirus /HHV-5

Latent infection : Most common → Immunocompetent : reactivation
Mononucleosis like syndrome → Immunocompetent
Tissue invasive disease : immunocompromised → Transplant , chemotherapy
30% most common in GI (CMV colitis)

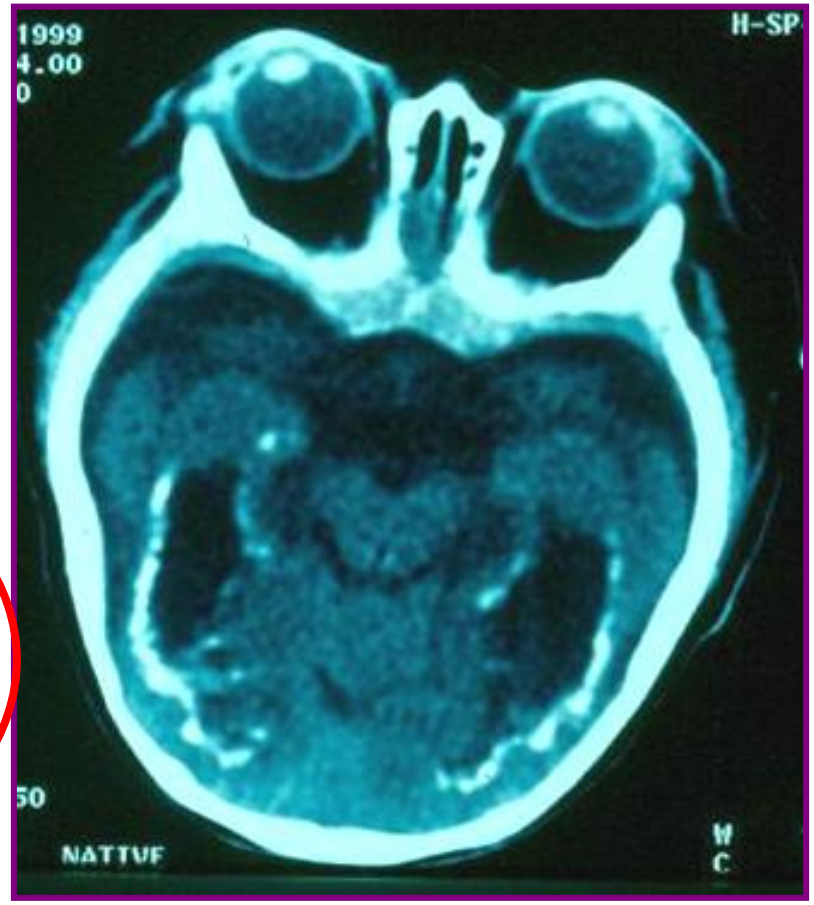


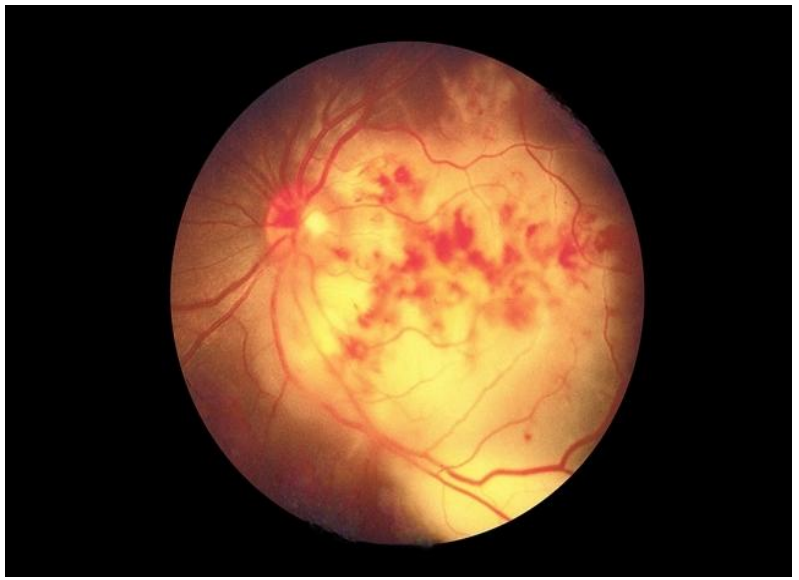
CMV spread Via

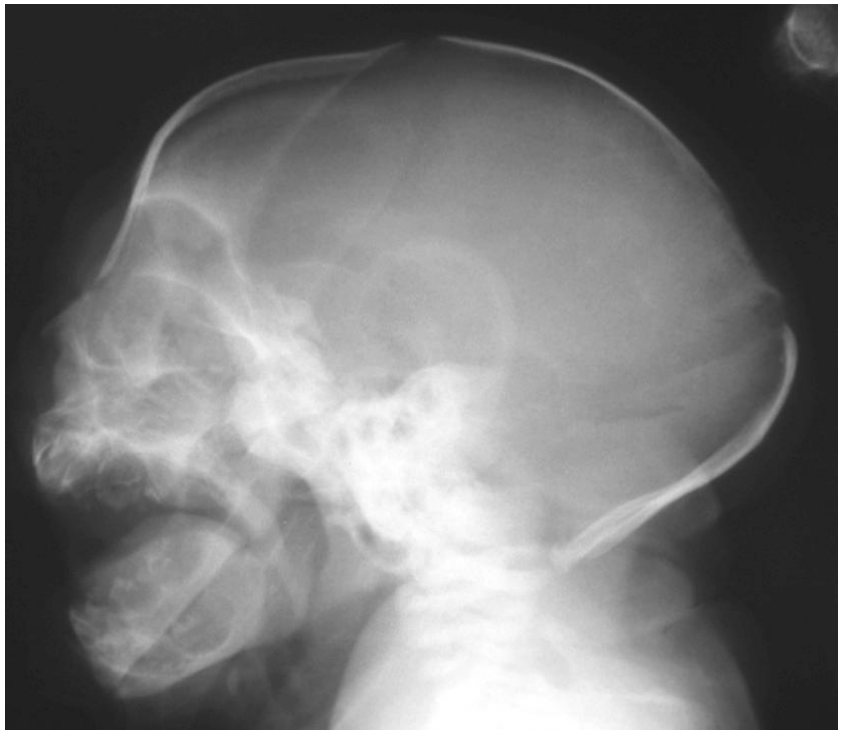
1. Sexual
2. Blood transfusion
3. Throug
4. At birth
5. Breast feeding
6. Air born

Congenital CMV
HHV-5

- Classic triad of symptoms:
  - *Chorioretinitis*
  - *Hydrocephalus*
  - *Intracranial calcifications*







- Other symptoms include fever, rash, HSM, microcephaly, seizures, jaundice, thrombocytopenia, lymphadenopathy

Congenital CMV

Transient Outcomes	Permanent Outcomes
• Hepatomegaly	• Microcephaly
• Splenomegaly	• Vision loss
• Jaundice	• Hearing loss
• Petechia and purpura	• Mental retardation
• Pneumonitis	• Motor disabilities
• Fetal growth retardation	• Seizures
• Seizures	• Death

Cytomegalovirus CMV: (HHV-5)

LABORATORY DIAGNOSIS

1. Virus Isolation, PCR

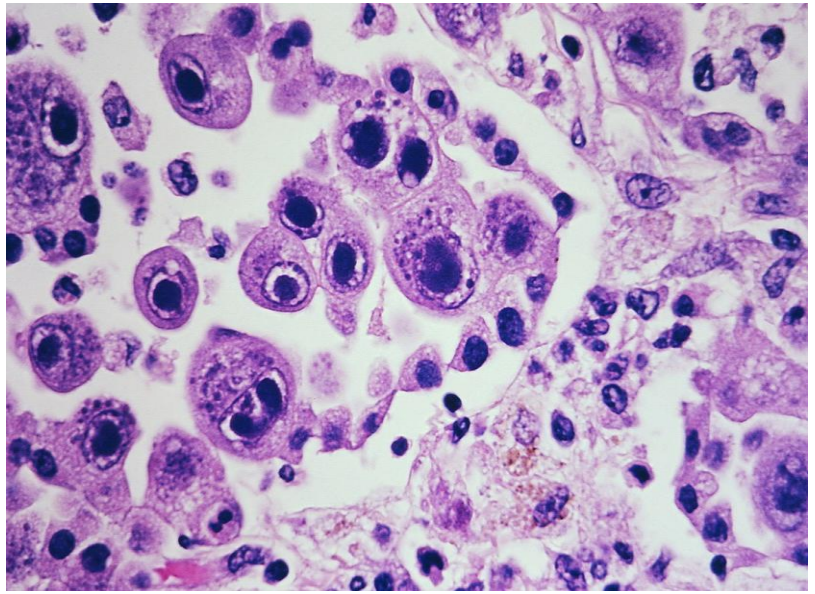
Urine, saliva, blood and biopsy

2. Serology

CMV IgM antibodies are detected in primary infection and lasts 3 - 4 months

CMV IgG is produced early in primary infection and persists lifelong.

Rising titres of IgG can be used as markers of acute infection.

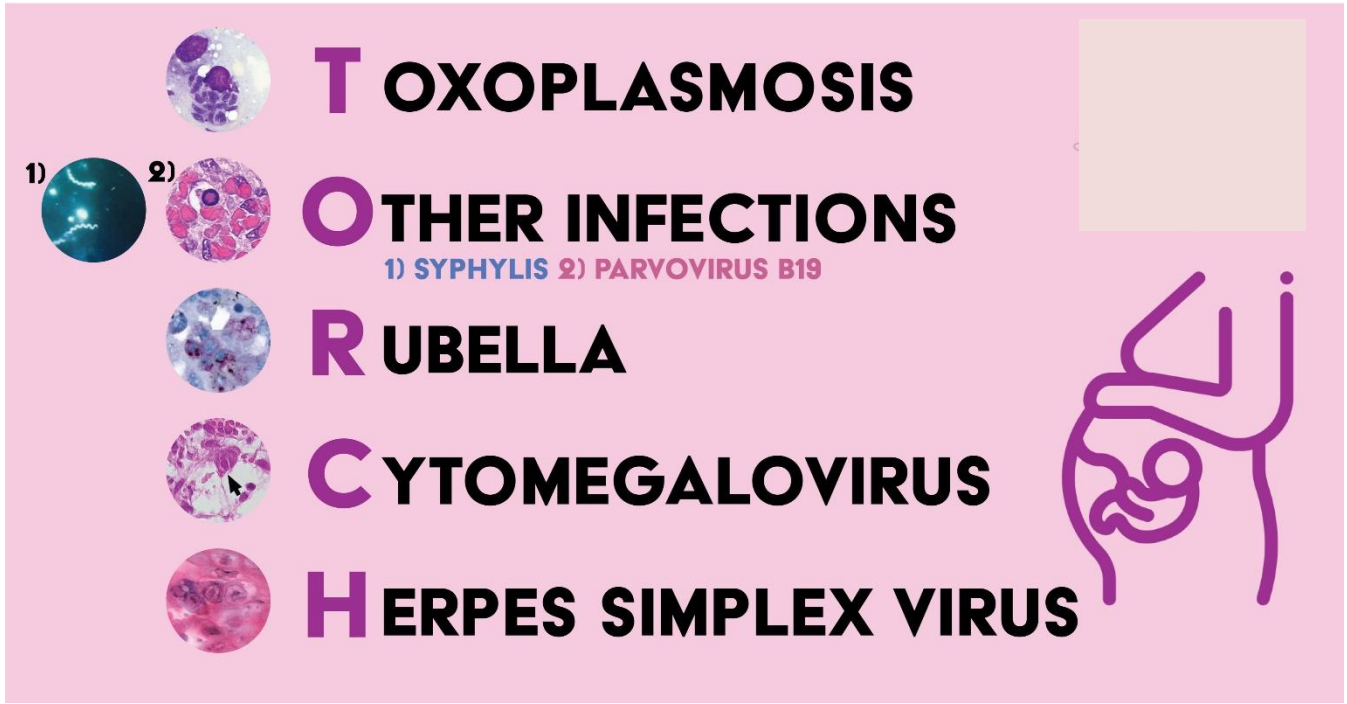


owl's eye intranuclear viral inclusions body

CMV

LAB : PCR

IgG, IgM

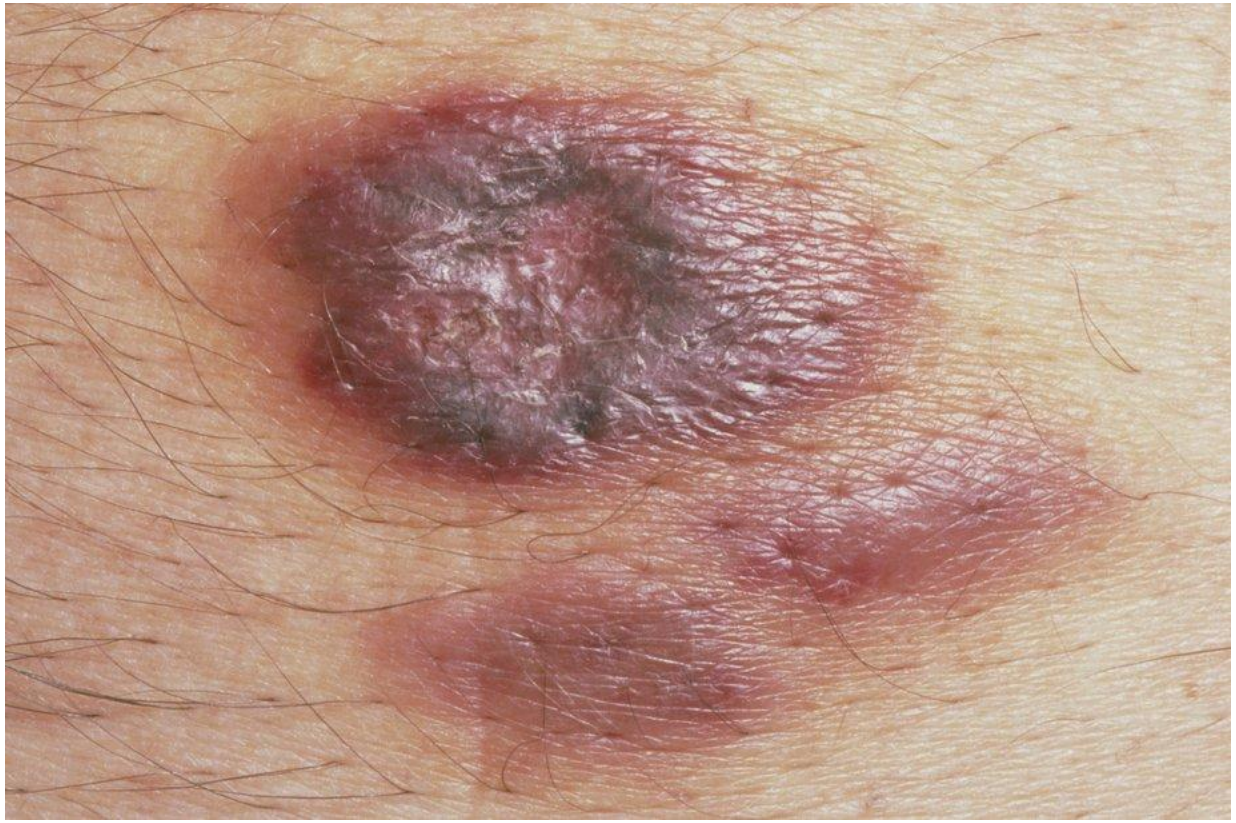


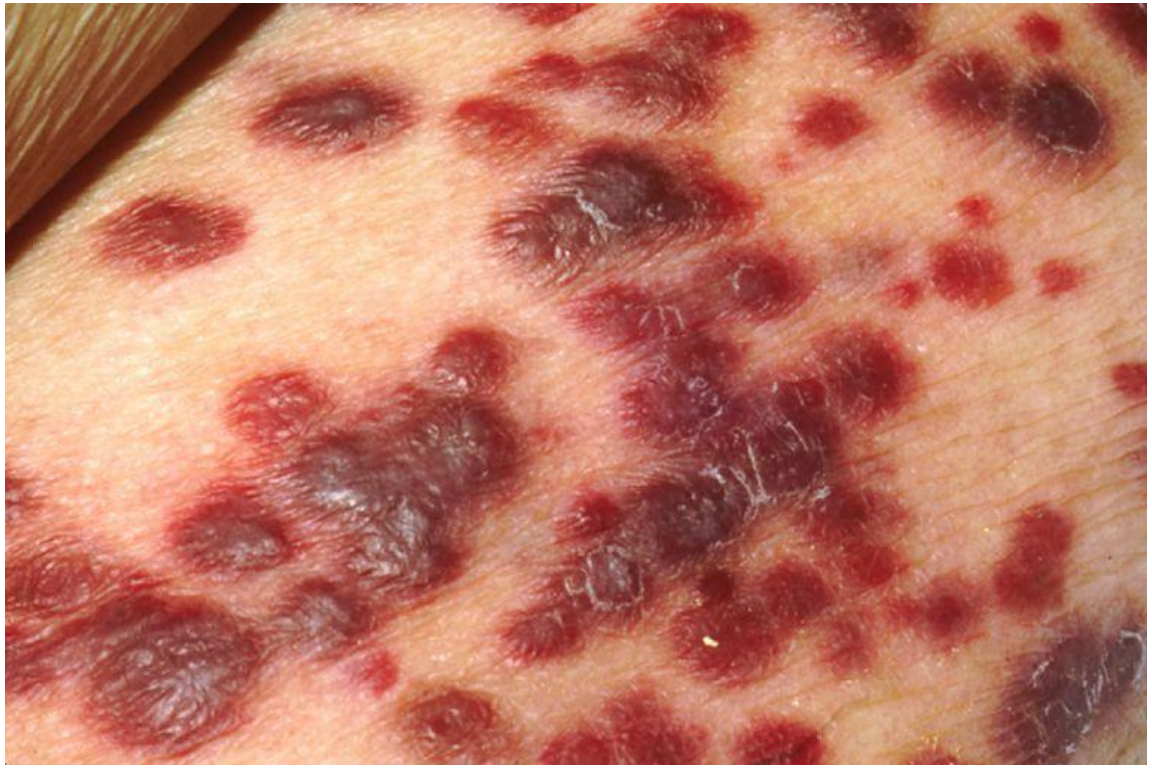
CMV : Treatment

- Ganciclovir
- Valganciclovir
- Foscarnet
- Cidofovir

Kaposi's sarcoma (HHV8)

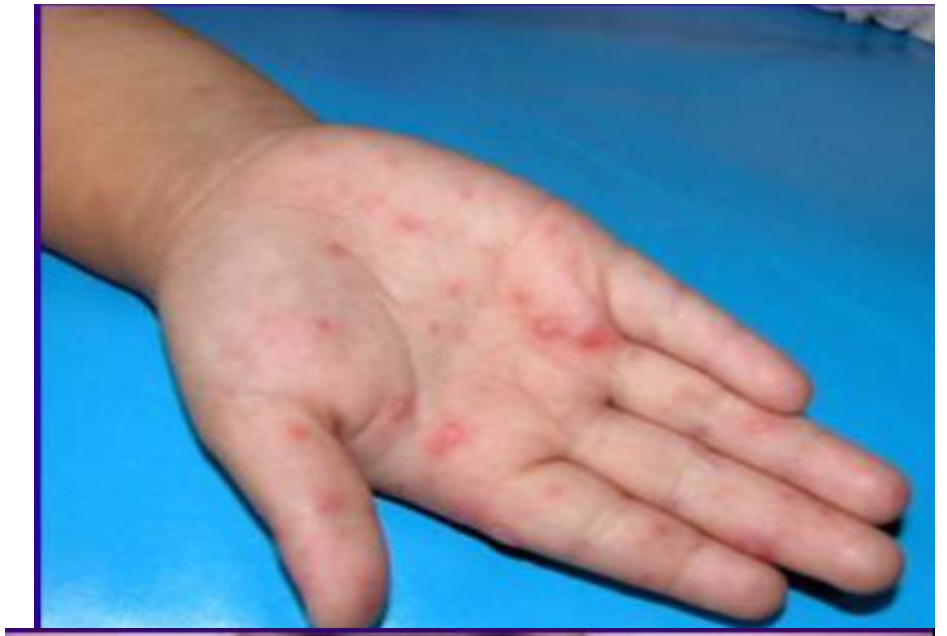
- Vascular tumor in HIV

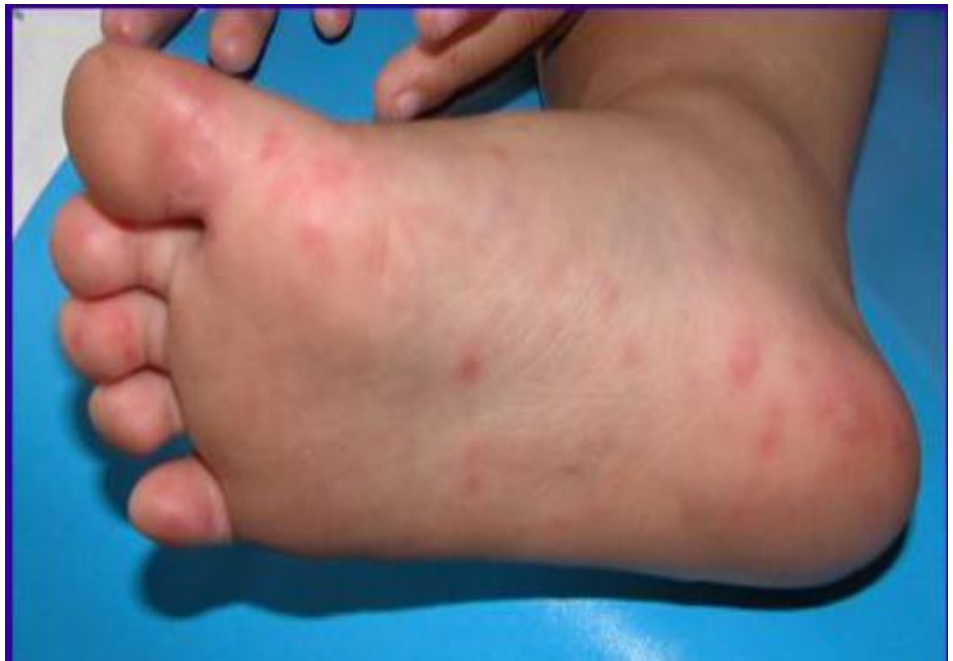


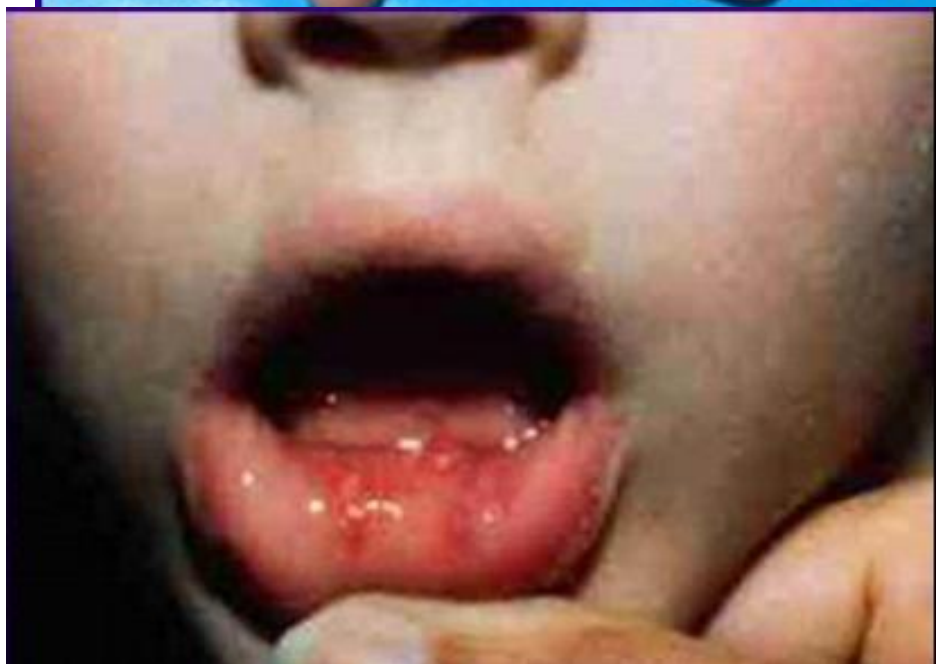


Hand Foot and Mouth Disease

- Enterovirus 71, Coxsackie A 16
- Fecal Oral route
- Fever + vesicles
- Complication :
- Brainstem encephalitis , Myocarditis,



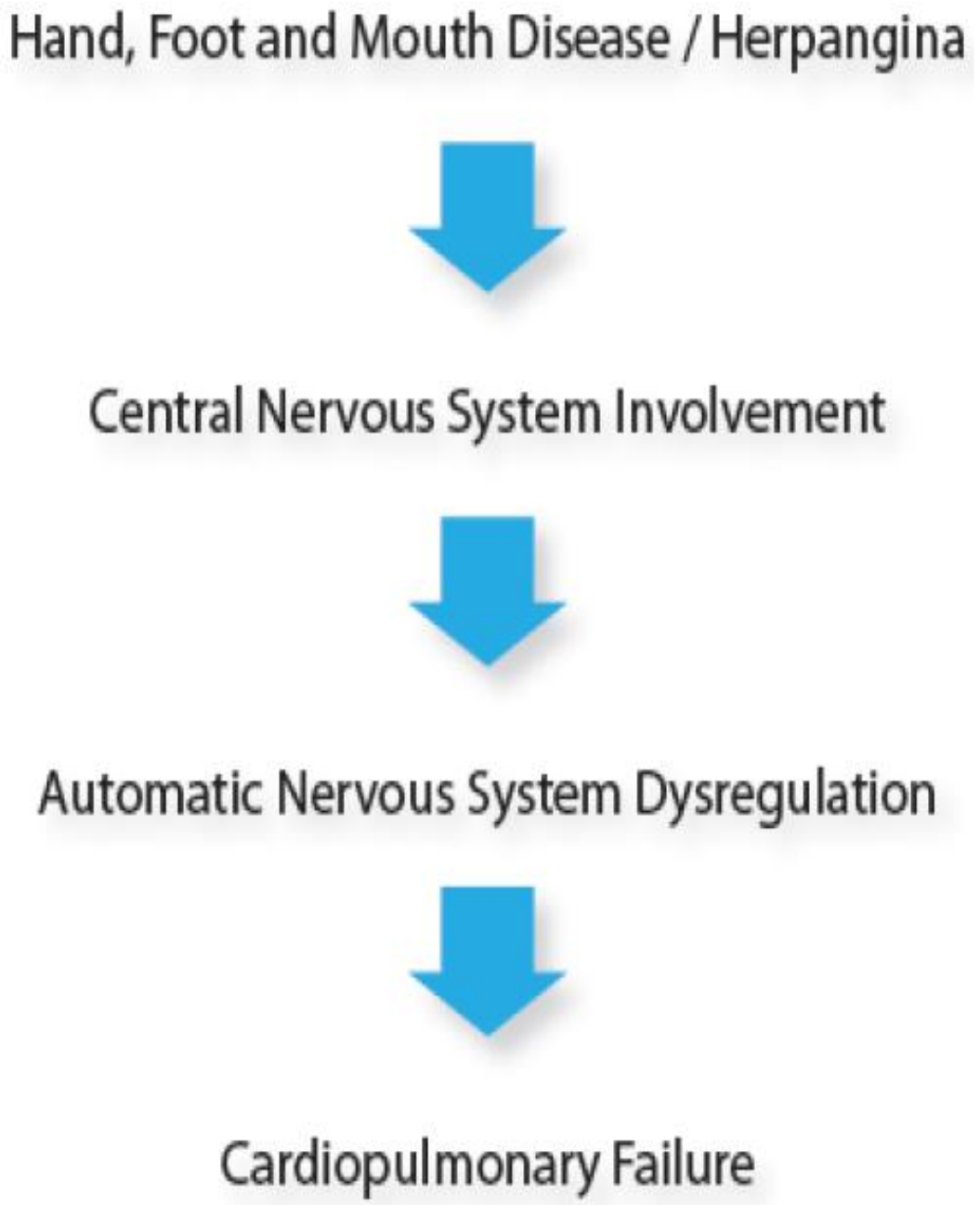




Complication
Enterovirus 71

Aseptic meningitis
Brain stem encephalitis
(Rhombencephalitis)
Autonomic nervous system
dysregulation

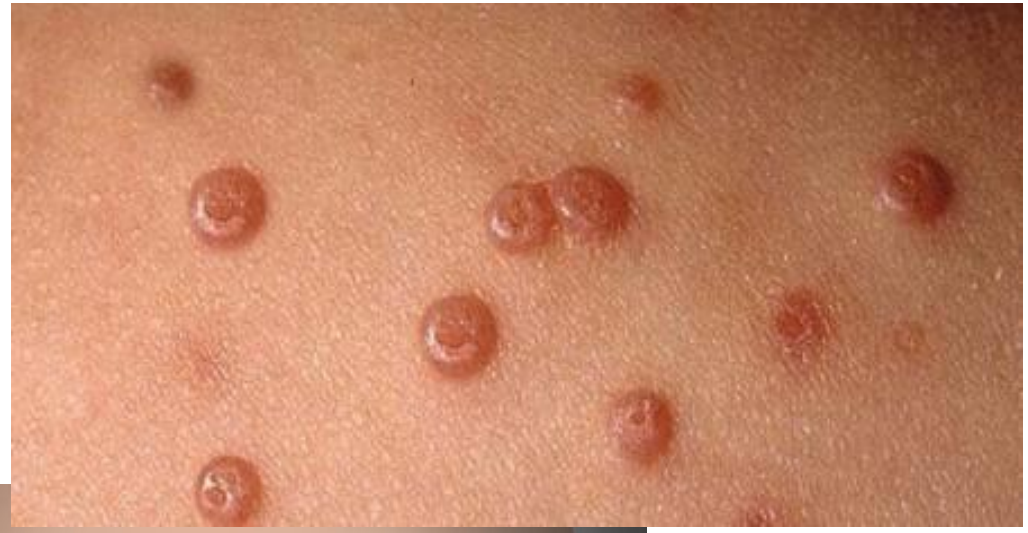
LAB: PCR
Tx IVIG

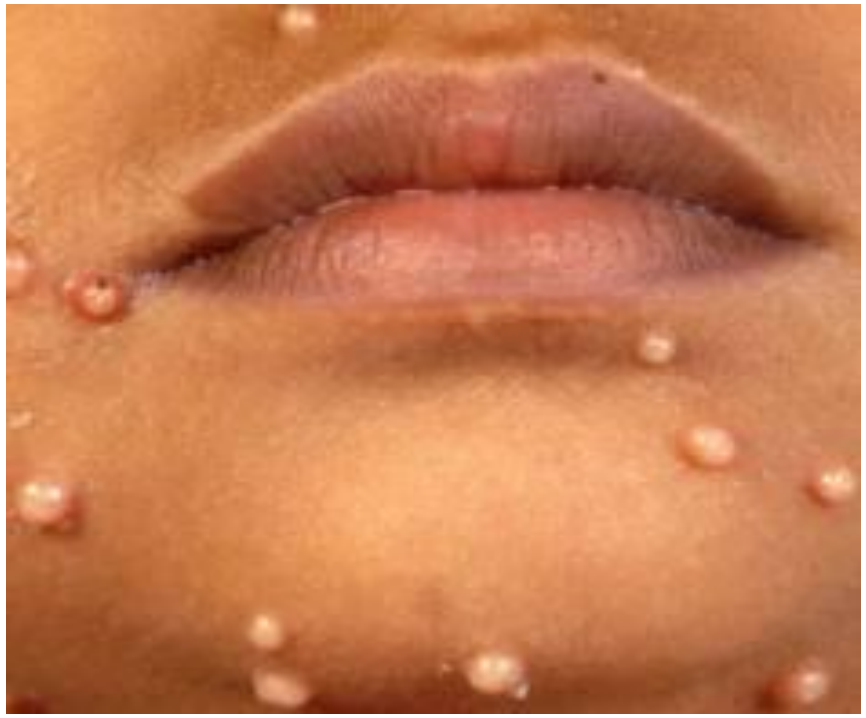


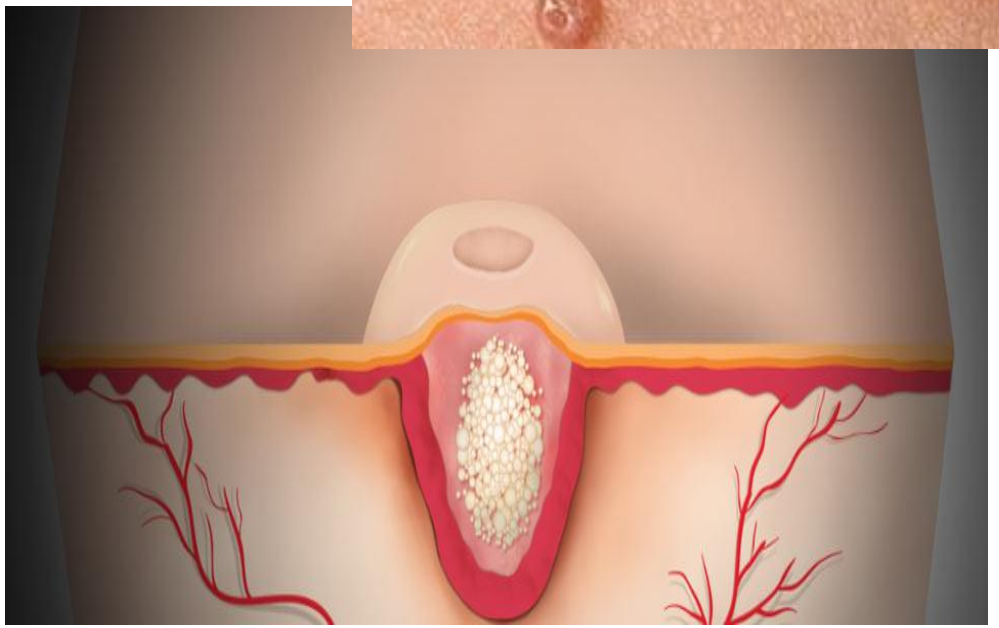
Molluscum contagiosum

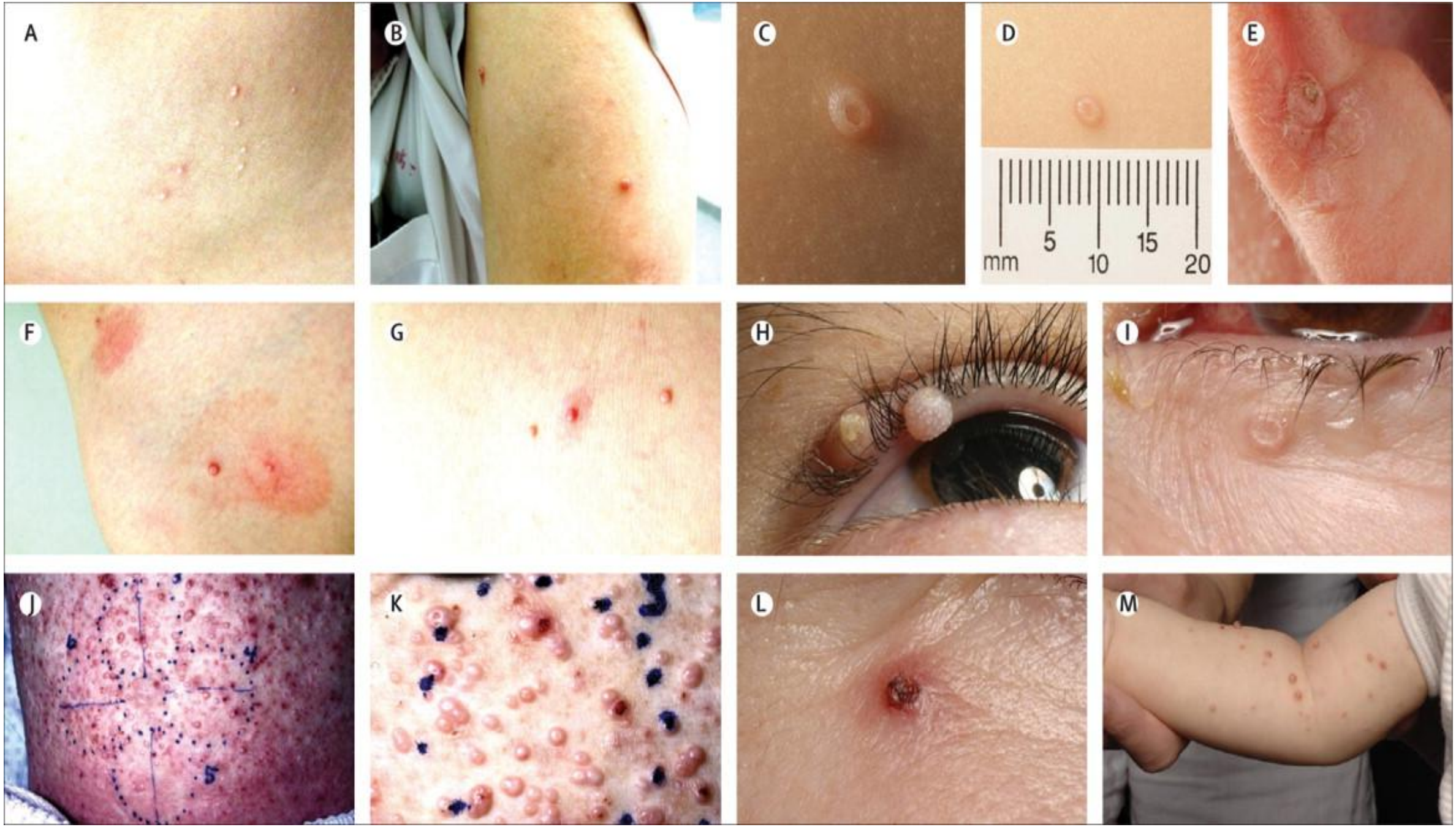
Oncogenic virus

- **Molluscum contagiosum virus**
- **Family *Poxviridae*,**
- **direct contact : sexual transmission**





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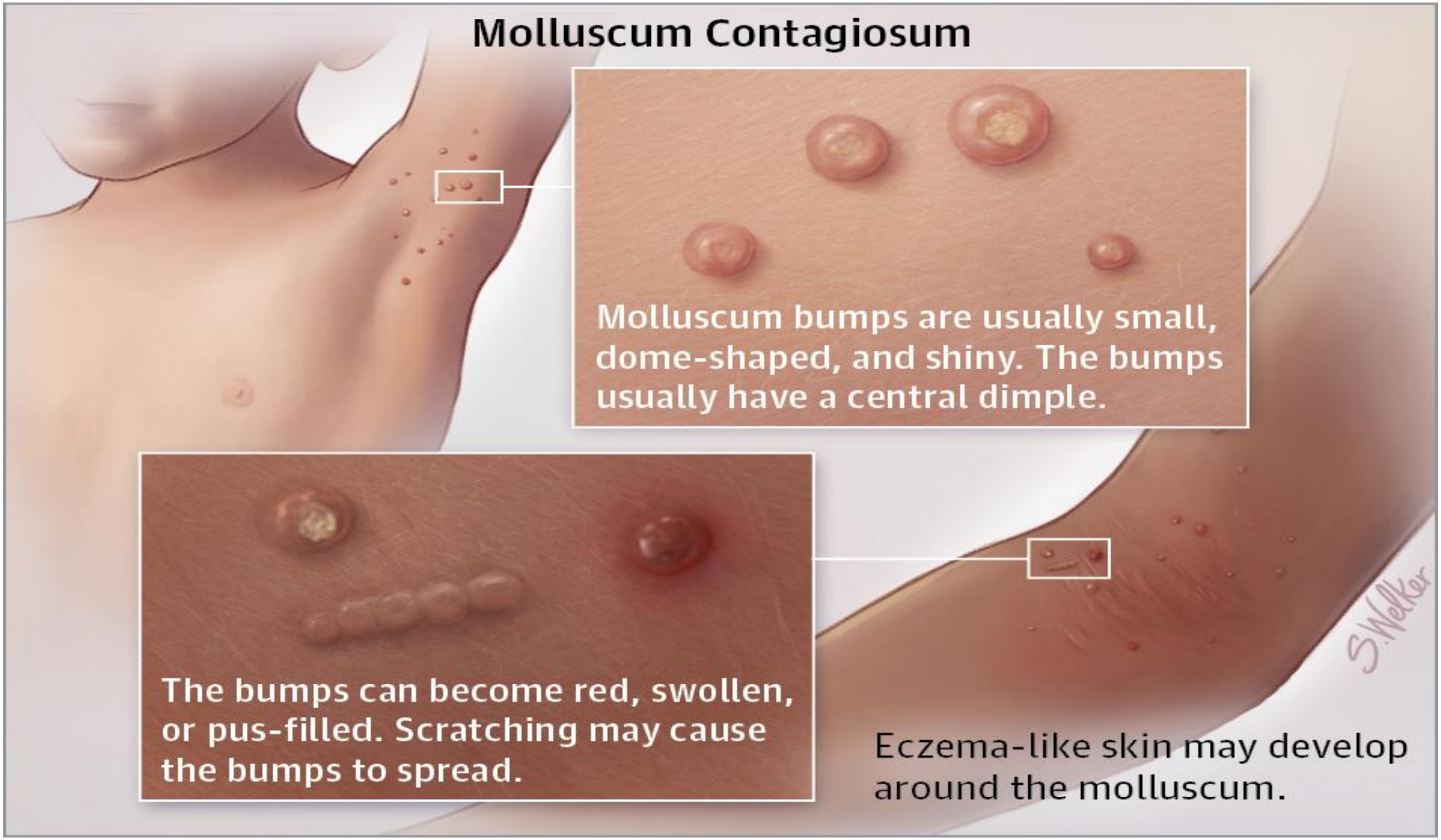
Molluscum Contagiosum

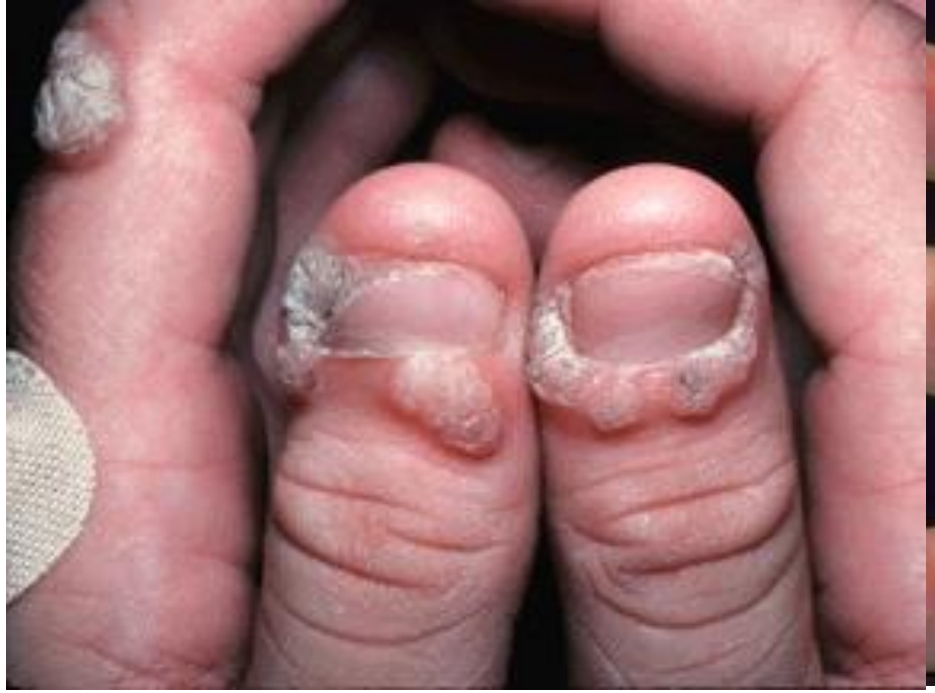


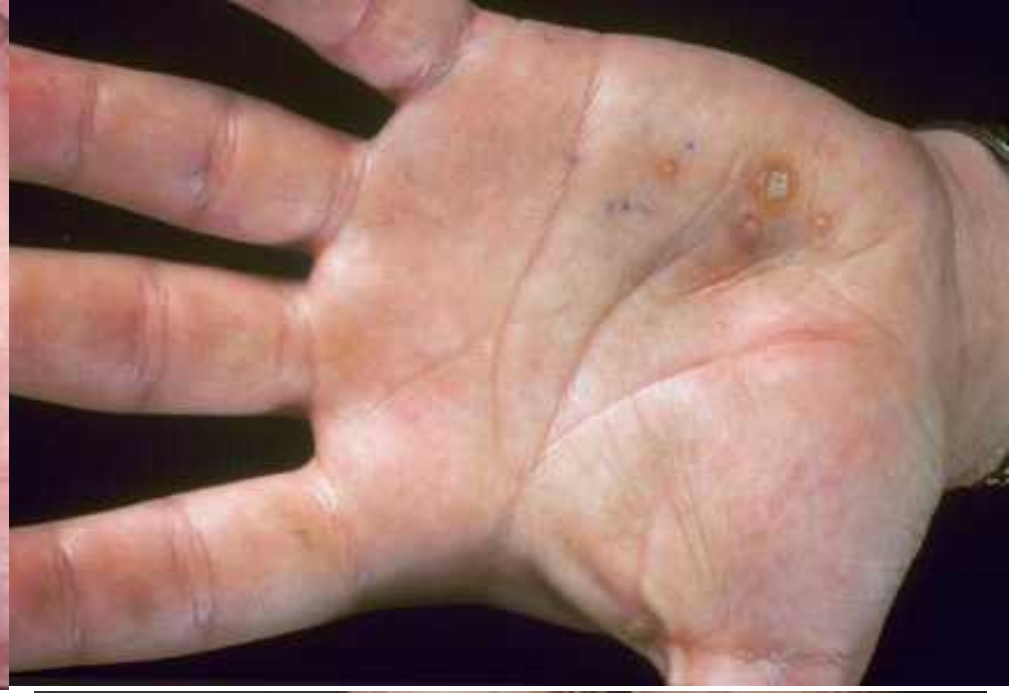
Molluscum contagiosum : Treatment

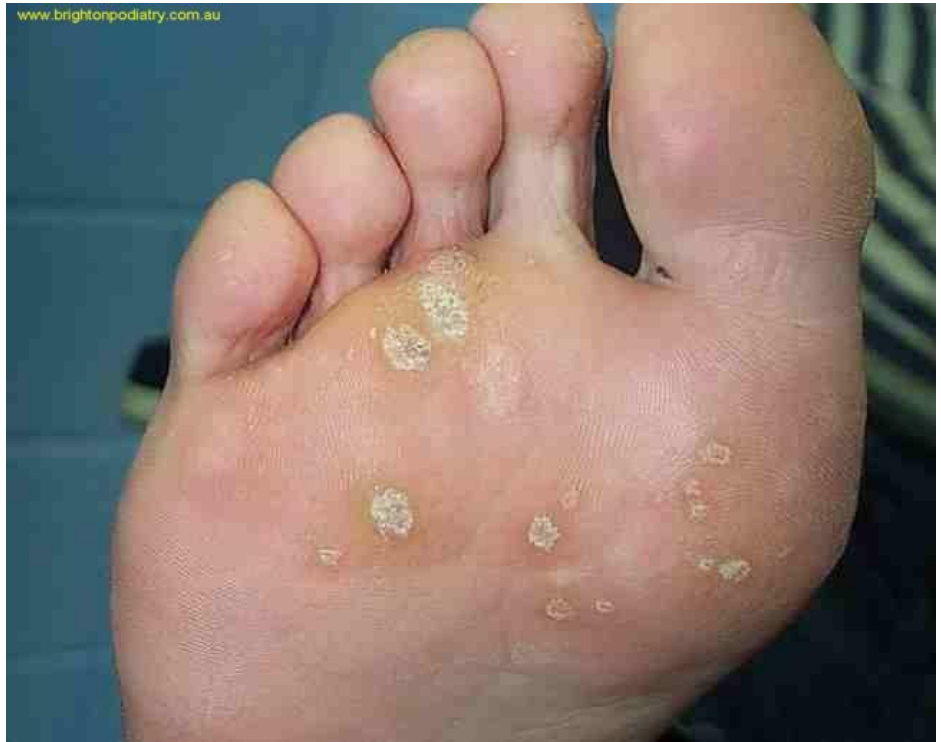
- Trichloroacetic acid
- Topical podophyllotoxin cream (Condylox)
- Imiquimod
- Cryosurgery

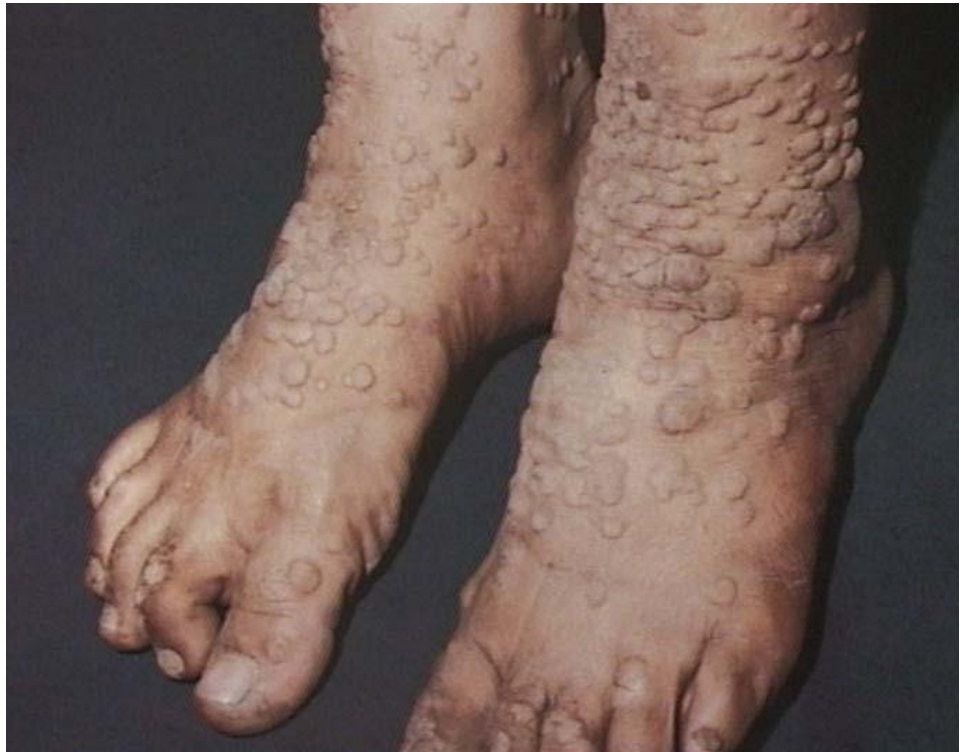
Human papillomavirus (HPV)

- *Papillomaviridae :* **Oncogenic Virus**
- HPV 16,HPV 18 (13%) : cervical cancers
- HPV 6 HPV 11 : skin lesion
- Wart (common, plantar, palmar warts)
- Condyloma acuminata (genital wart, perianal wart)
- Laryngeal papillomatosis
- Anogenital cancer
- Tx: Imiquimod, Podofilox, Podophyllin, Cryotherapy

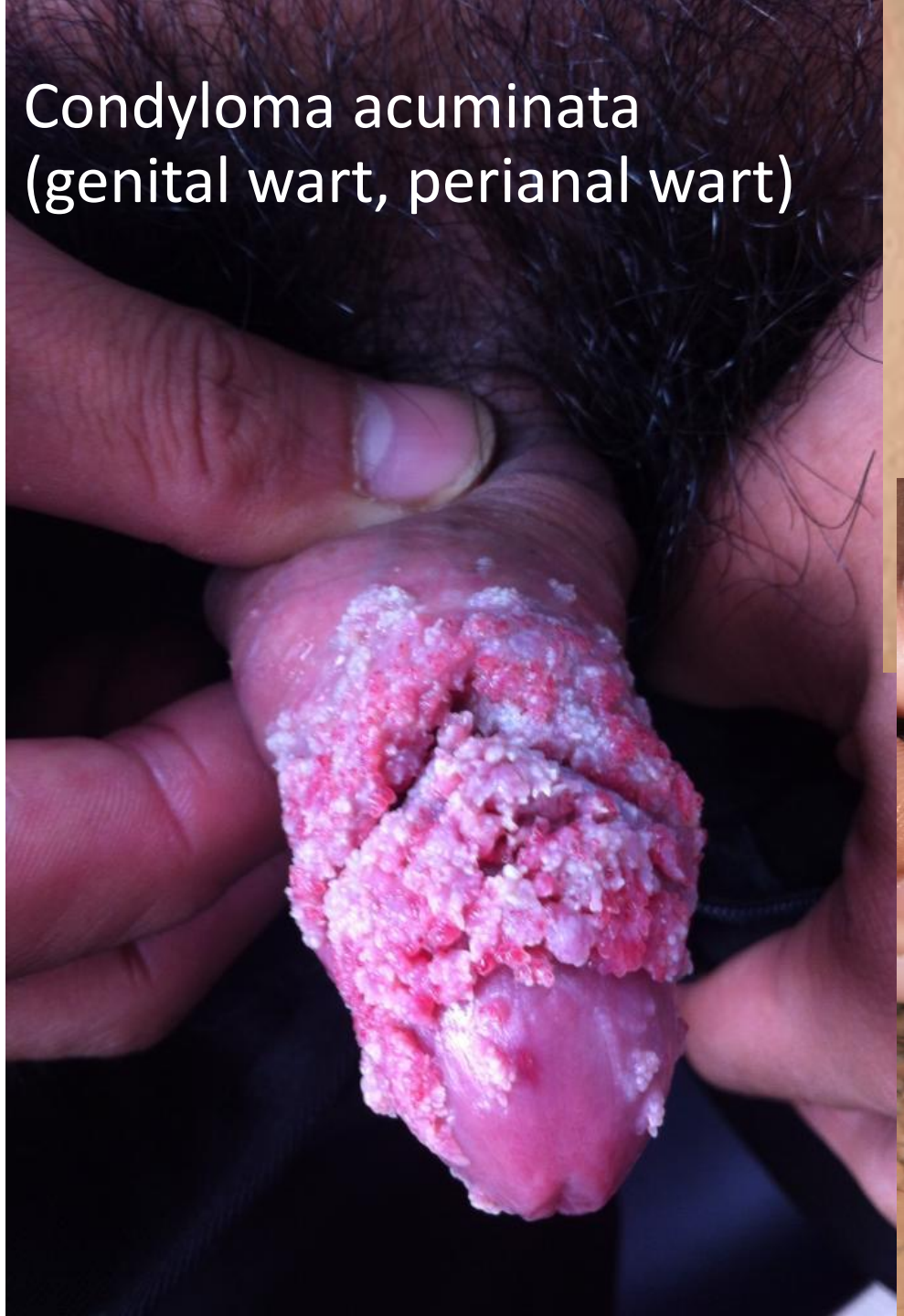


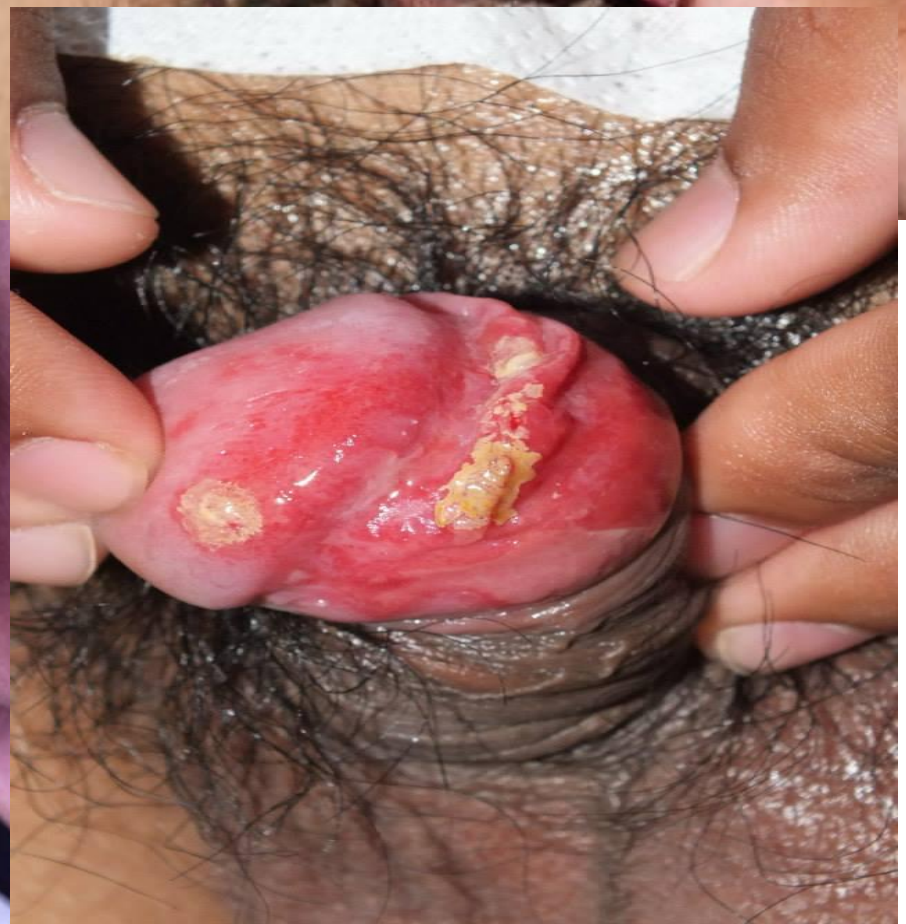


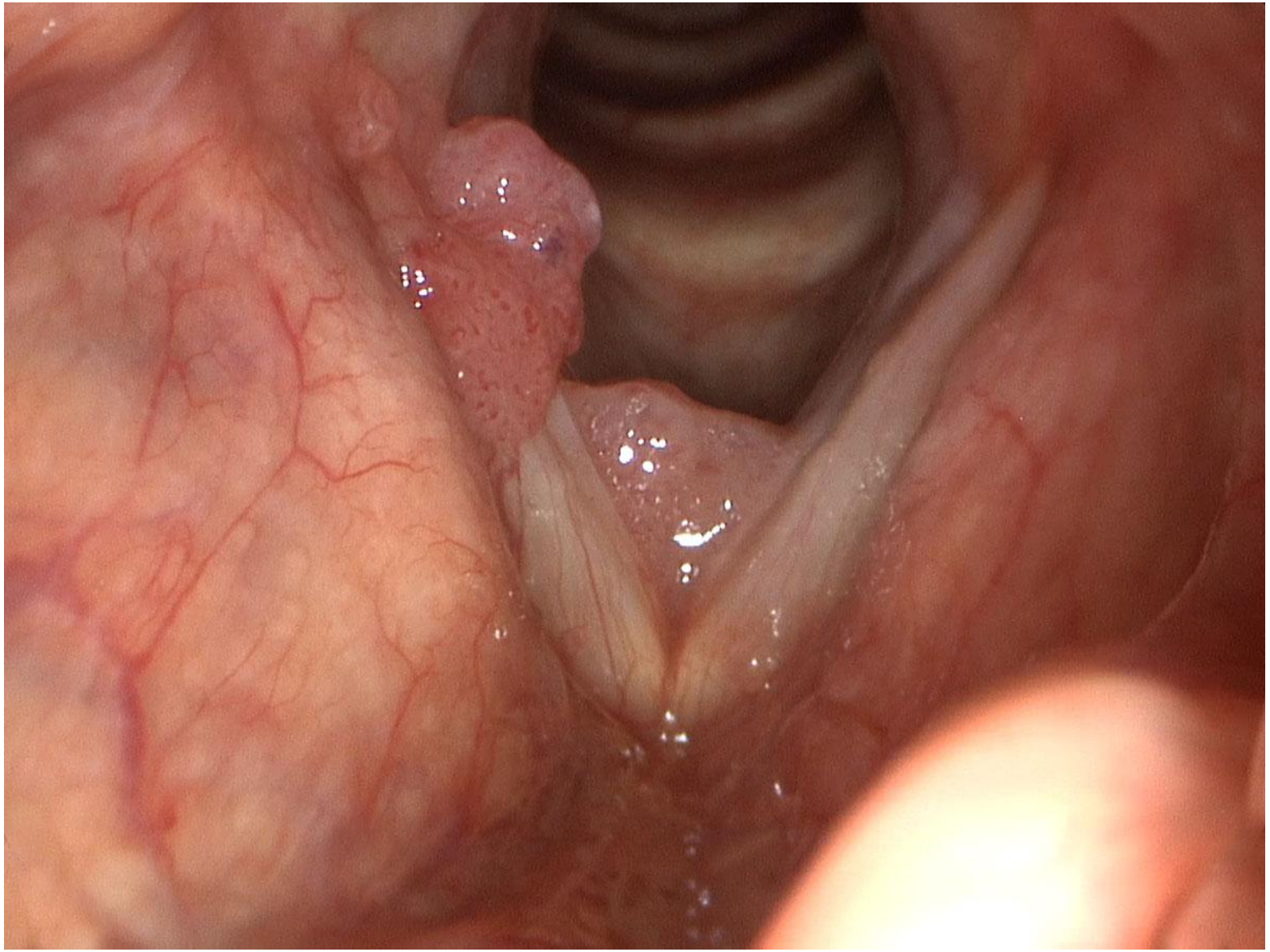

www.brightonpodiatry.com.au



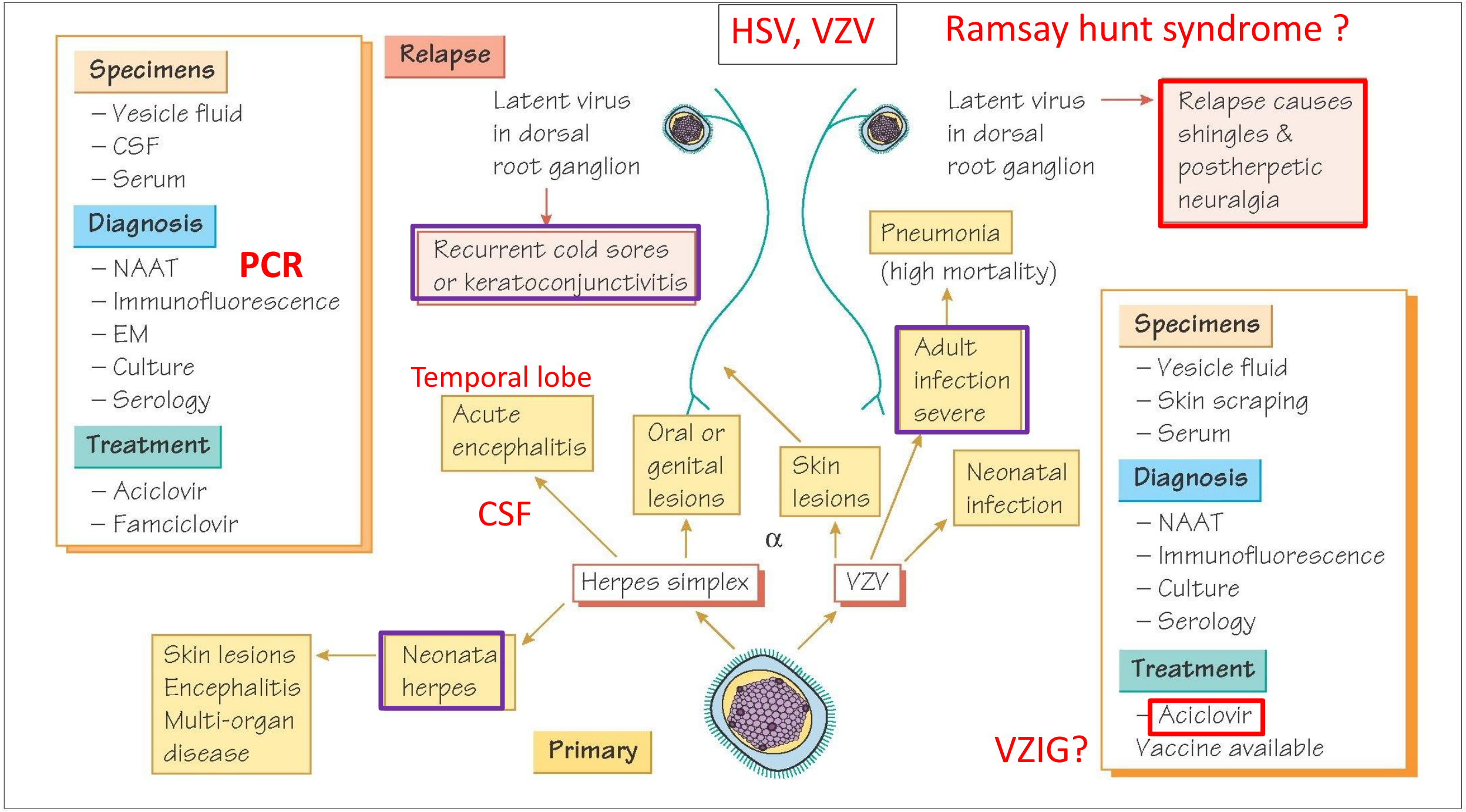
Condyloma acuminata
(genital wart, perianal wart)





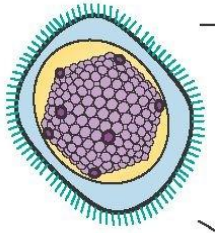


Laryngeal papillomatosis


HSV, VZV
Ramsay hunt syndrome ?
Specimens
– Vesicle fluid
– CSF
– Serum
Diagnosis
– NAAT
– Immunofluorescence
– EM
– Culture
– Serology
PCR
Treatment
– Aciclovir
– Famciclovir
Relapse
Latent virus in dorsal root ganglion
Recurrent cold sores or keratoconjunctivitis
Latent virus in dorsal root ganglion
Relapse causes shingles & postherpetic neuralgia
Pneumonia (high mortality)
Adult infection severe
Temporal lobe
Acute encephalitis
CSF
Oral or genital lesions
Skin lesions
Neonatal infection
α
Herpes simplex
VZV
Skin lesions Encephalitis Multi-organ disease
Neonata herpes
Primary
VZIG?
Specimens
– Vesicle fluid
– Skin scraping
– Serum
Diagnosis
– NAAT
– Immunofluorescence
– Culture
– Serology
Treatment
– Aciclovir
Vaccine available

CMV, EBV, HHV6-8

Infectious mononeucleosis
-Lymphadenopathy
-Atypical L
-Hepatosplenomegaly



β

- HHV-6 → Exanthem subitum — Roseolar infantum
- HHV-7 → Fever in immunocompromised
- HHV-8 → Kaposi sarcoma — HIV

β

CMV
Viral load by NAAT

Epithelial cells

Virus shed in urine & pharynx

- Severe disease in immunocompromised
  - Pneumonia
  - Retinitis
  - Enteritis
- Congenital infection
  - Fetal death
  - Hearing loss
  - Ocular disease
  - Cerebral damage

EBV γ

B-lymphocytes & epithelial cells

- Post-transplant lymphoma
- Nasopharyngeal carcinoma
- Burkitt's lymphoma

Infectious mononucleosis

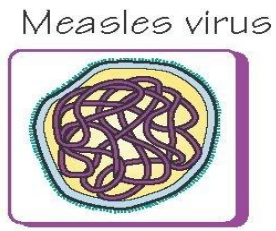
Specimens
- Blood
- Urine
- Saliva

Diagnosis
- Immunofluorescence
- NAAT
- Culture

Treatment
- Ganciclovir
- Foscarnet

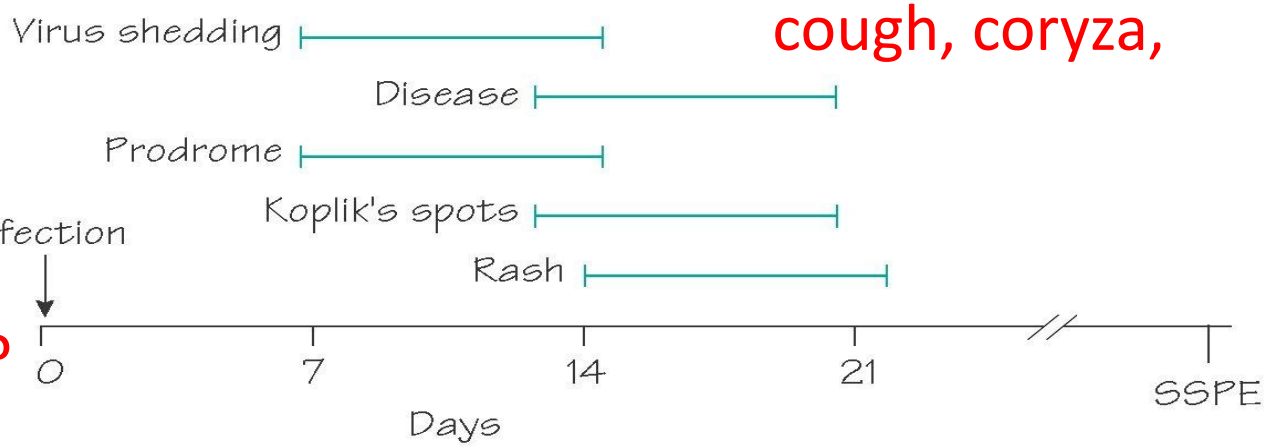
Specimens
- Serum
- Throat gargle

Diagnosis
- Serology
- NAAT
- Culture



Measles virus

3C:Conjunctivitis cough, coryza,



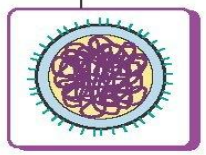
Vaccine?

Measles

Specimens
- Serum
- Nasopharyngeal secretion

Diagnosis
- IgM
- Antigen detection
- NAAT detection

Mumps,Measle, Rubella



Mumps virus

Infection

Primary viraemia

Salivary glands
– parotitis

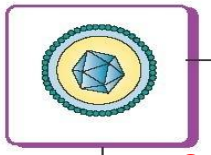
Testes
Ovaries
Pancreas
Meningitis

Secondary viraemia

Mumps

Specimens
- Serum
- Saliva
- CSF

Diagnosis
- Culture
- IgM
- NAAT detection



Rubella virus

Adults

Mild disease & postinfection arthritis

Congenital transmission
- Cataracts
- Deafness
- Hepatitis
- Thrombocytopenia

Celery stalk .
Cong rubella.

Children

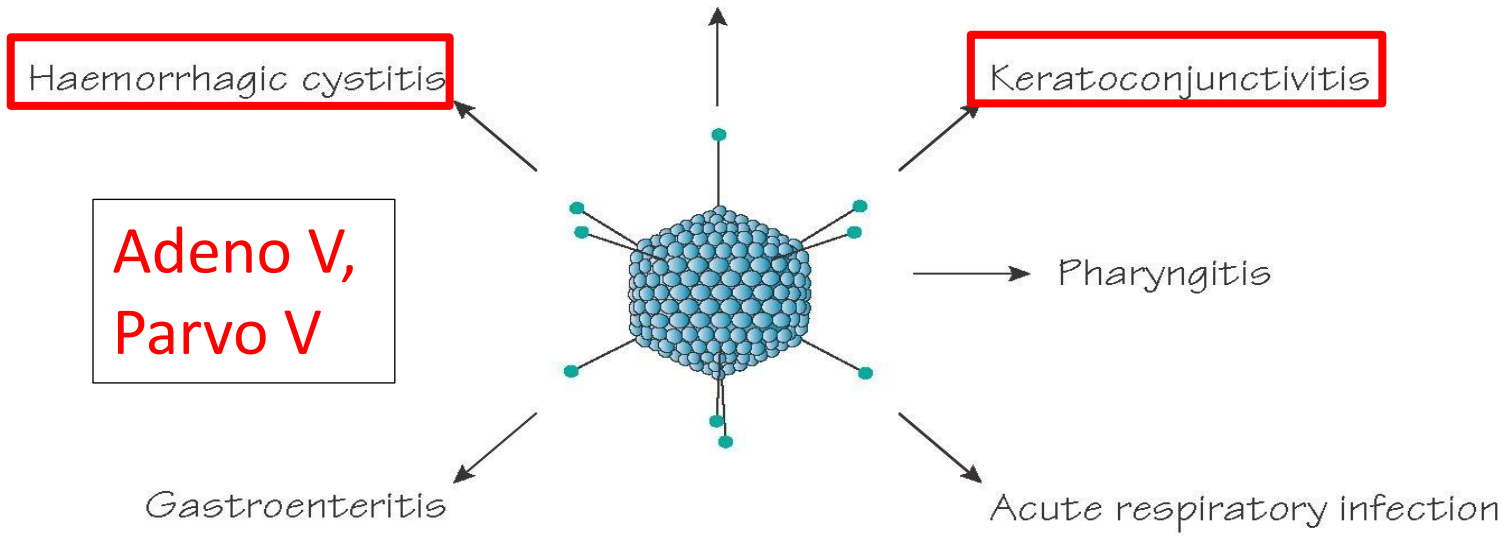
Mild infection
Fever & rash

Rubella

Specimens
- Serum

Diagnosis
- Serology (IgM)

Spectrum of adenovirus infection



Adeno V,
Parvo V

Adenovirus

Specimens

- Nasopharyngeal
- Eye exudates
- Stool
- Urine
- Biopsy

Diagnosis

- Immunofluorescence
- NAAT
- EM
- Culture
- EIA

Parvovirus

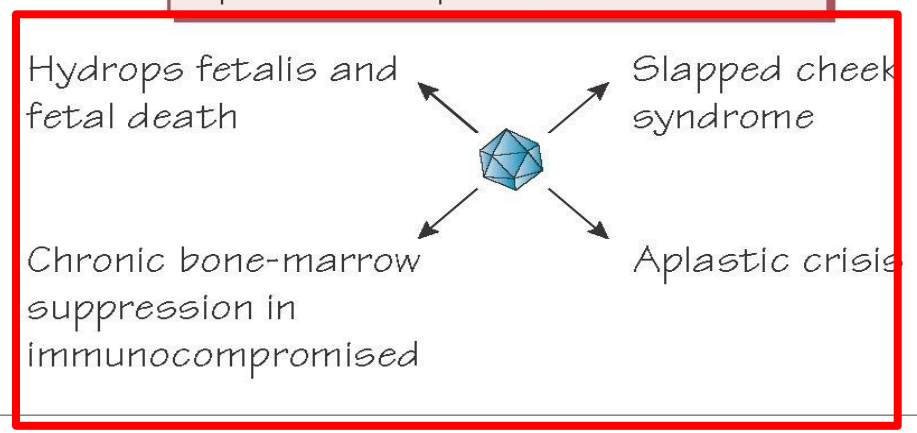
Specimens

- Blood
- Cord blood
- Nasal/throat washings
- Amniotic fluid

Diagnosis

- NAAT
- EM
- Hybridization

Spectrum of parvovirus infection



Fifth disease


Thanks!