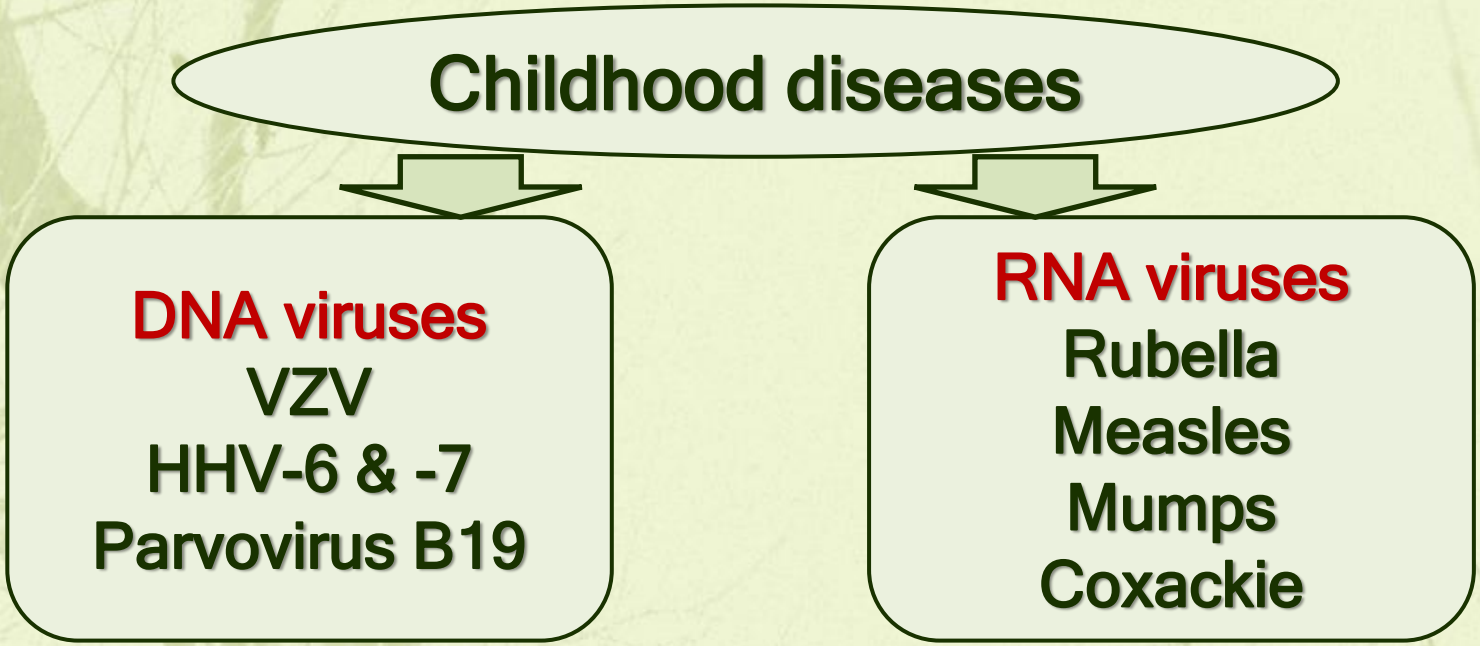
Childhood diseases

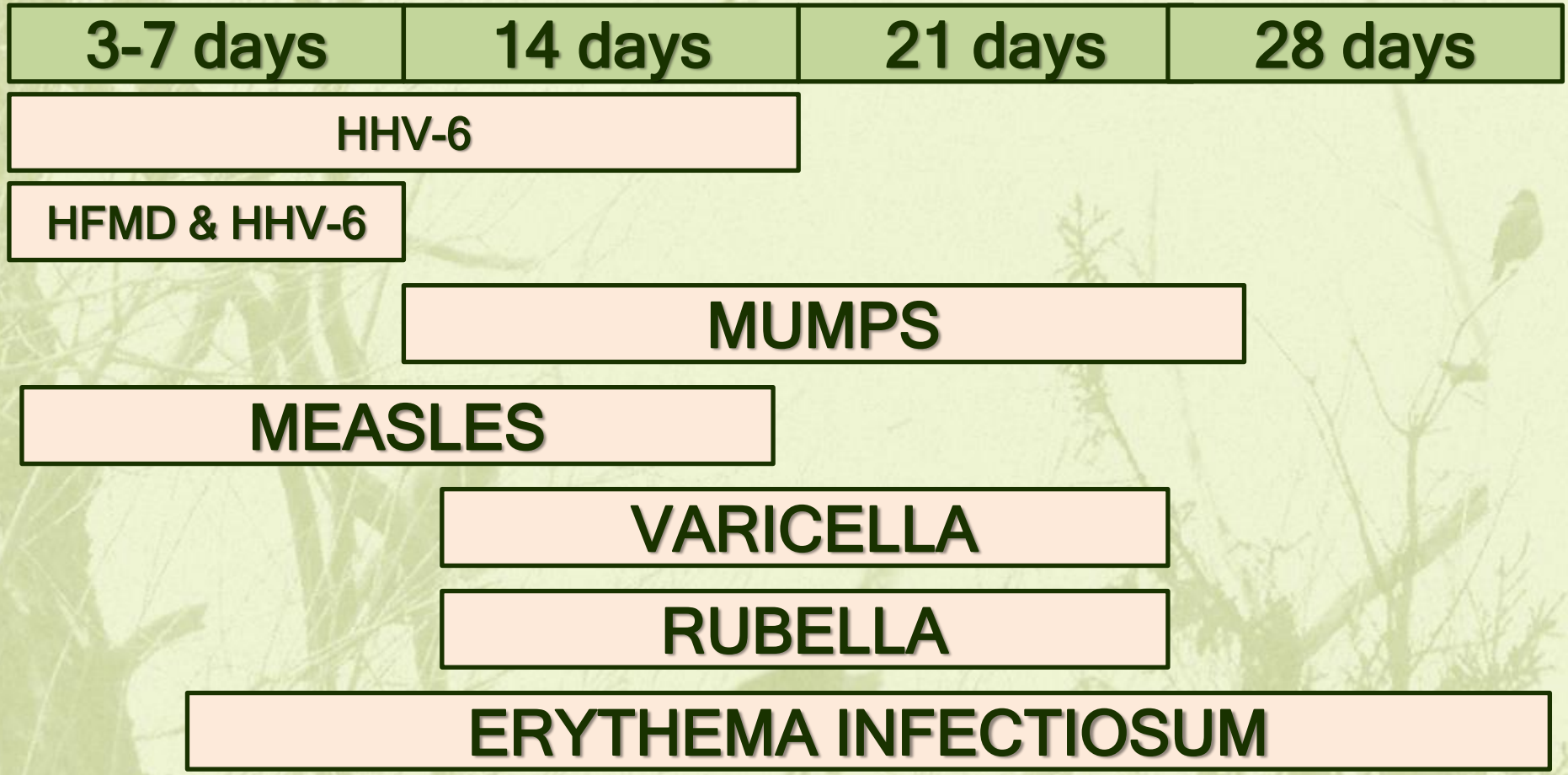
Prof. dr hab. Beata Sobieszczańska
Department of Microbiology
Wrocław Medical University



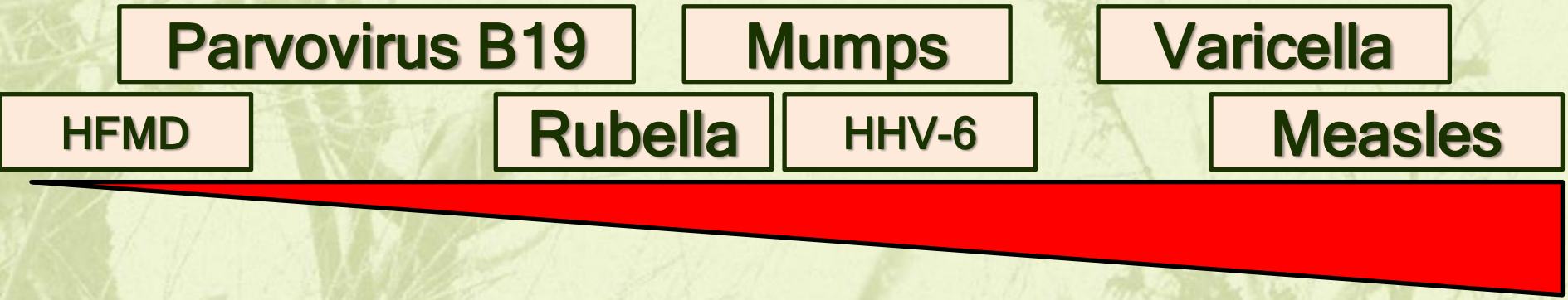
Common characteristics:

- Air-borne route (exception – HFMD)
- Rash (exception – mumps)

Incubation period



Severity of the disease



Prevention (vaccine)

MMR = mumps, measles, rubella

MMRV = mumps, measles, rubella, varicella

Varivax - varicella

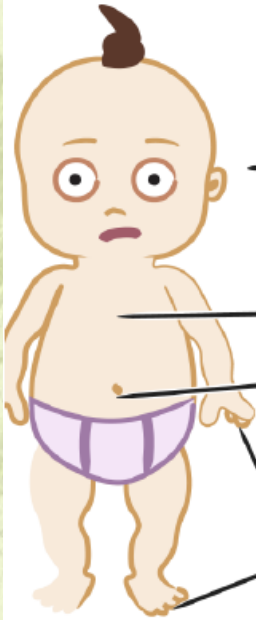
Treatment: Acyclovir, gancyclovir (varicella, HHV-6)

Seasonality

winter	spring	summer	fall
			
Measles	Rubella	HFMD	
Varicella			
	Parvovirus B19		
Mumps			
HHV-6			

Helpful Distinguishers

Initial Location & Pattern



FACE & TRUNK

- Measles
- Rubella
- Erythema infectiosum
- Chickenpox (Face & Trunk)
- Roseola infantum- Trunk

EXTREMITIES

- Hand, foot, and mouth disease

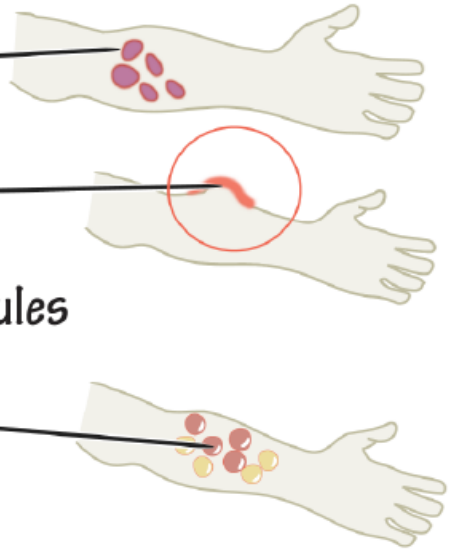
Timing of Rash/Other symptoms

- ✓Presence & timing of other symptoms:
  Fever, malaise, respiratory...
- ✓Incubation period

Rash types

Multiple rash types can exist at once.

- ✓Macules
  Colored flat spots
- ✓Papules
  Solid, raised area
  Large papules = Nodules
- ✓Vesicular
  Raised "pockets" of fluid in the skin.

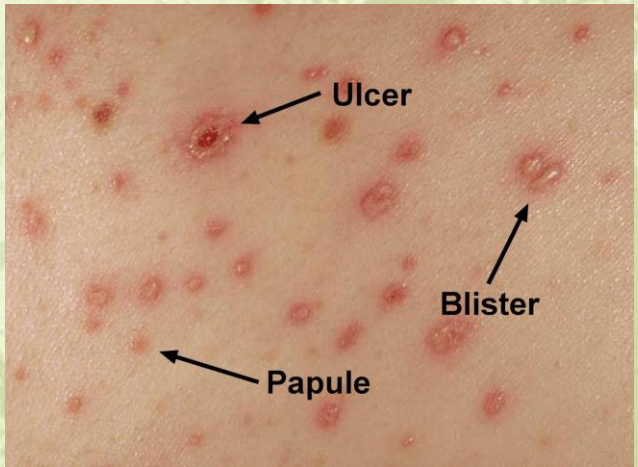


Rash

maculopapular
Rubella
Parvovirus B19
HHV-6
Measles

vesicular
HFMD

Macules-papules-vesicles
Varicella



No rash
Mumps

(Smallpox rash)

(Chicken pox rash)

Chickenpox

The same spot over 15 days.

maculopapular

vesicular

Varicella (chickenpox)

Varicella-zoster virus
dsDNA icosahedral with an envelope

Human is the only reservoir

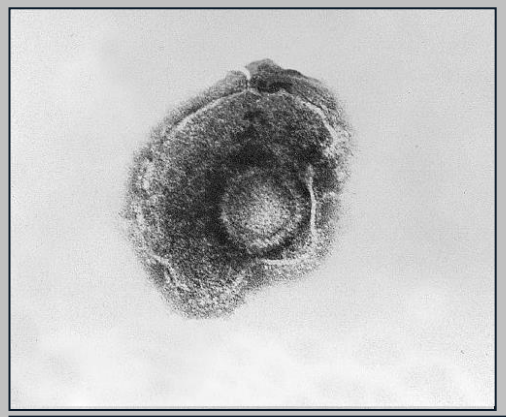
Transmission:

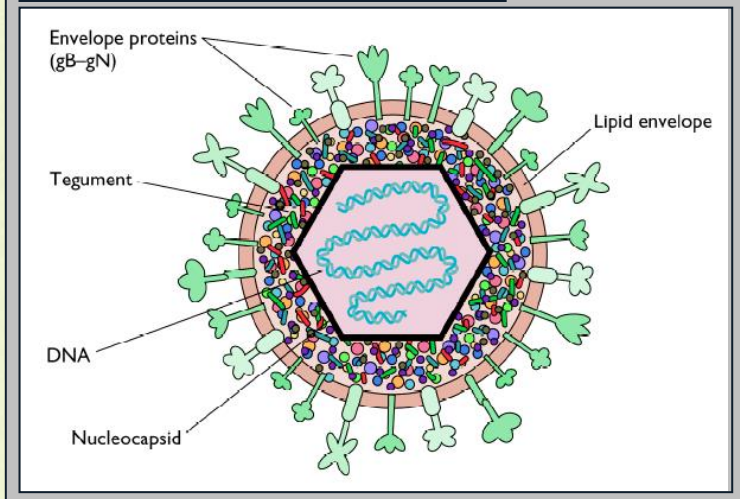
- Air-borne respiratory droplets
- Direct contact with the rash
- Vertical transmission during pregnancy

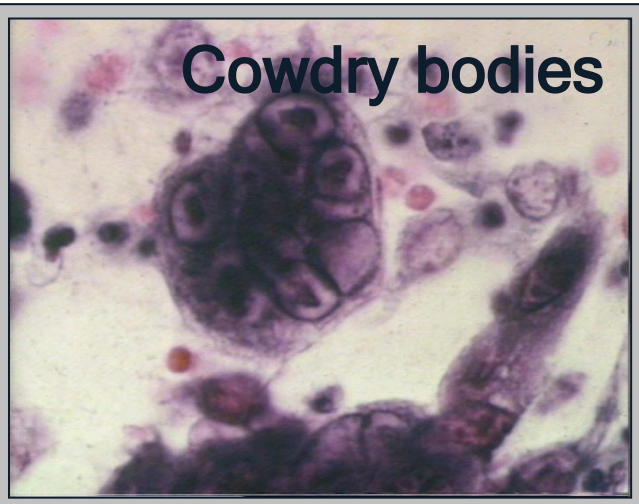
VZV is highly contagious

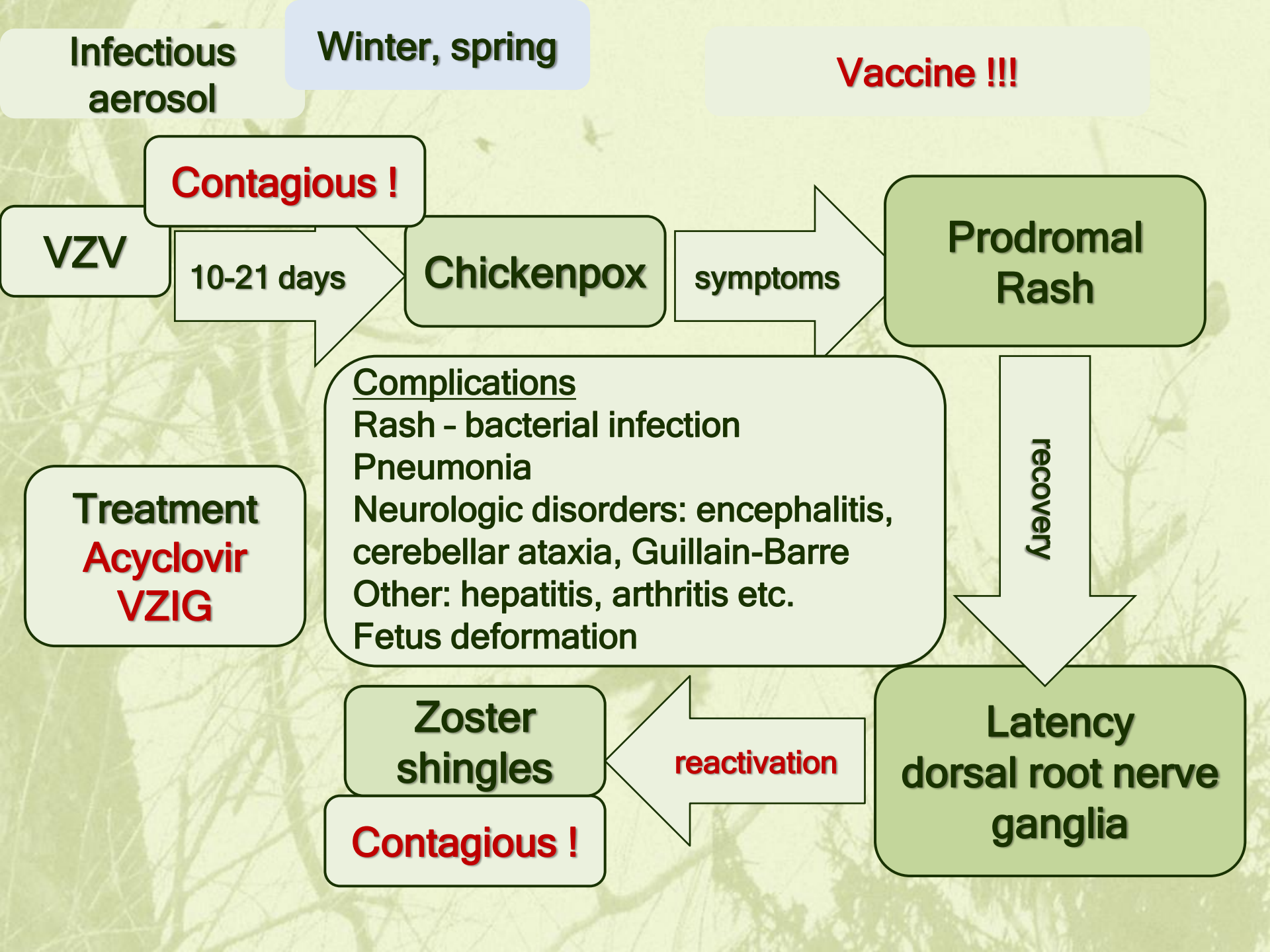
Almost all children will be infected by the age of 10 years

Lower prevalence in tropical and subtropical countries



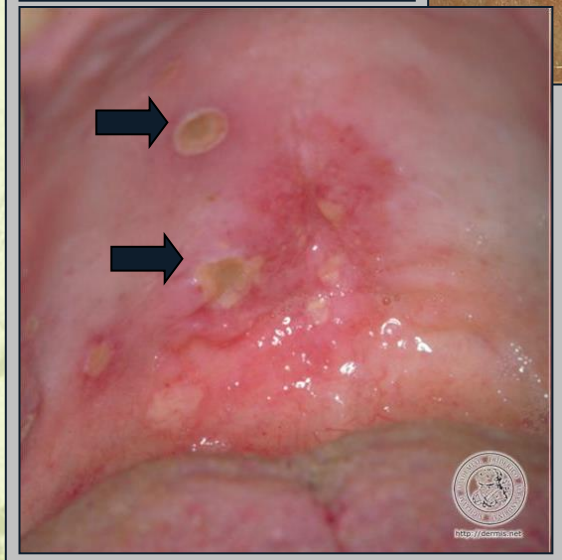





Infectious aerosol
Winter, spring
Vaccine !!!
Contagious !
VZV
10-21 days
Chickenpox
symptoms
Prodromal Rash
Complications
Rash – bacterial infection
Pneumonia
Neurologic disorders: encephalitis, cerebellar ataxia, Guillain-Barre
Other: hepatitis, arthritis etc.
Fetus deformation
recovery
Treatment
Acyclovir
VZIG
Zoster shingles
Contagious !
reactivation
Latency dorsal root nerve ganglia

Varicella (chickenpox)

- Rash (face, scalp, trunk)
  lasts 3 to 5 days:
  macules – papules – vesicles – pustules - crusts
- Contagious from 2 days prior to the eruption of the rash until all the spots have crusted over
- Clinical course in healthy children - generally mild
- Immunosupressed children – severe progressive form with complications



RAPID EVOLUTION

Macule Papule Vesicle Pustule

VARICELLA (Chickenpox); Vesicles on child

Varicella (shingles)

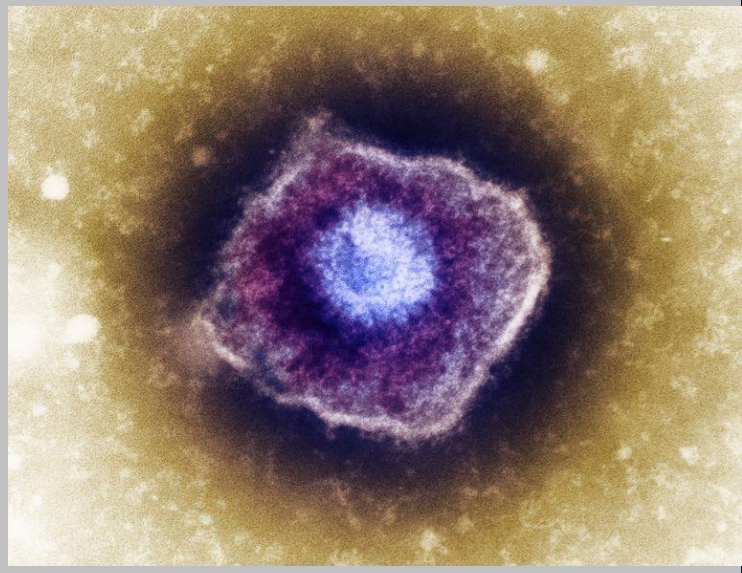
- Reactivation of chickenpox
- Virus remains dormant for many years in the dorsal root nerve ganglia
- Localised, painful, red blistering rash
- Less common in children than in adults

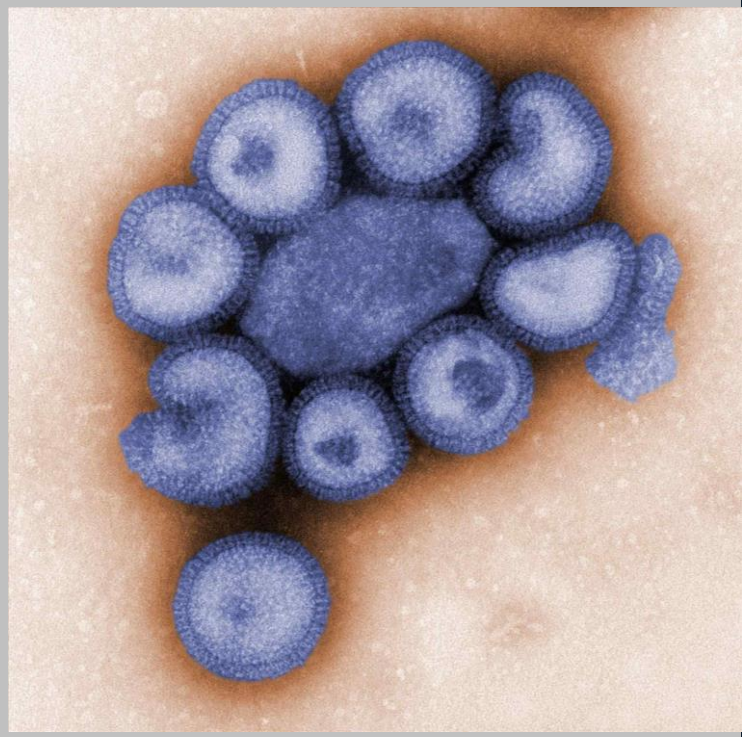
Latency

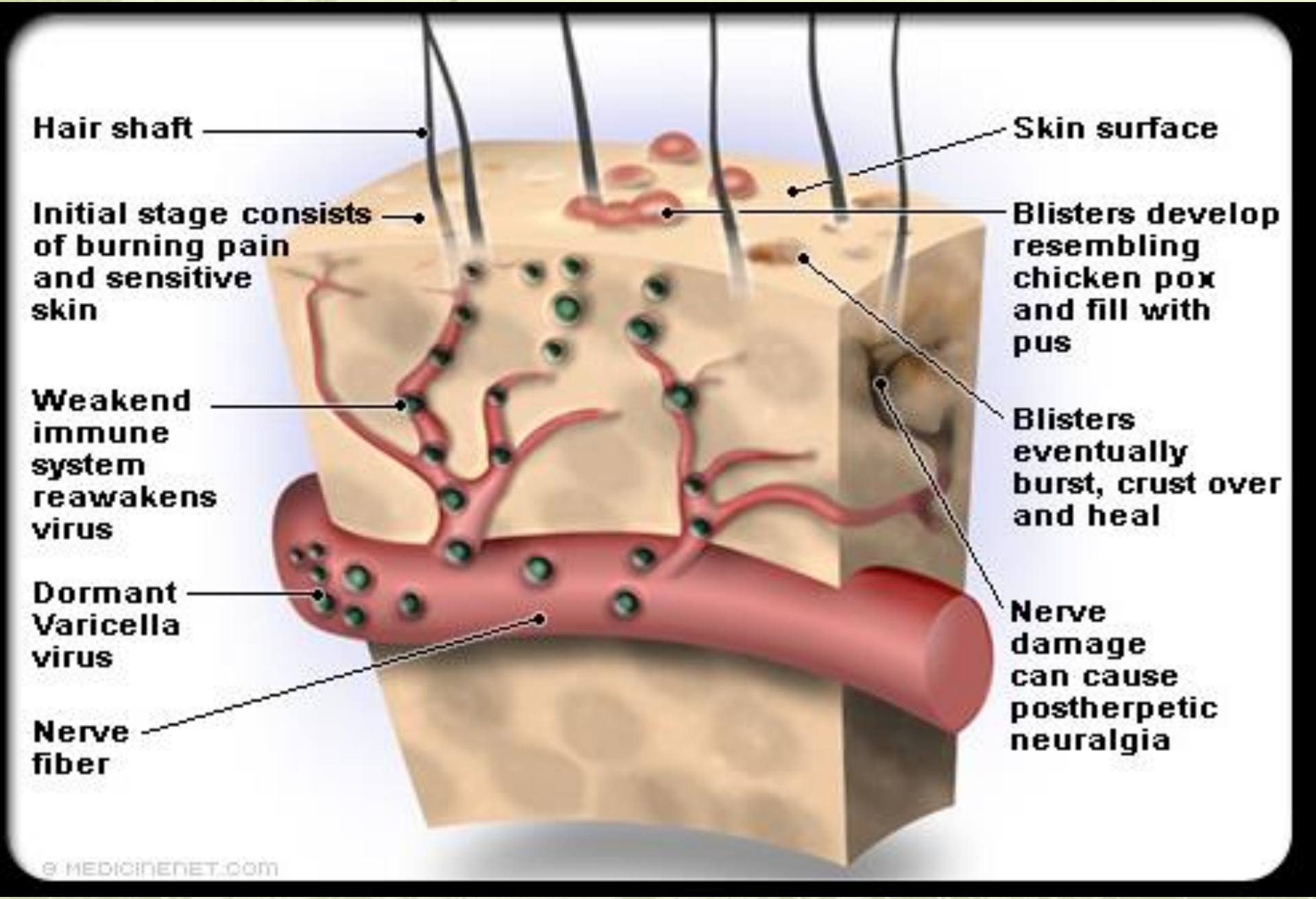
- Pathogenic virus lies dormant (latent) within a cell – does not replicate

Viral DNA as episome in the cell or integrated with host cell DNA

Result: virus can reactivate and replicate






Hair shaft
Initial stage consists of burning pain and sensitive skin
Weakend immune system reawakens virus
Dormant Varicella virus
Nerve fiber
Skin surface
Blisters develop resembling chicken pox and fill with pus
Blisters eventually burst, crust over and heal
Nerve damage can cause postherpetic neuralgia
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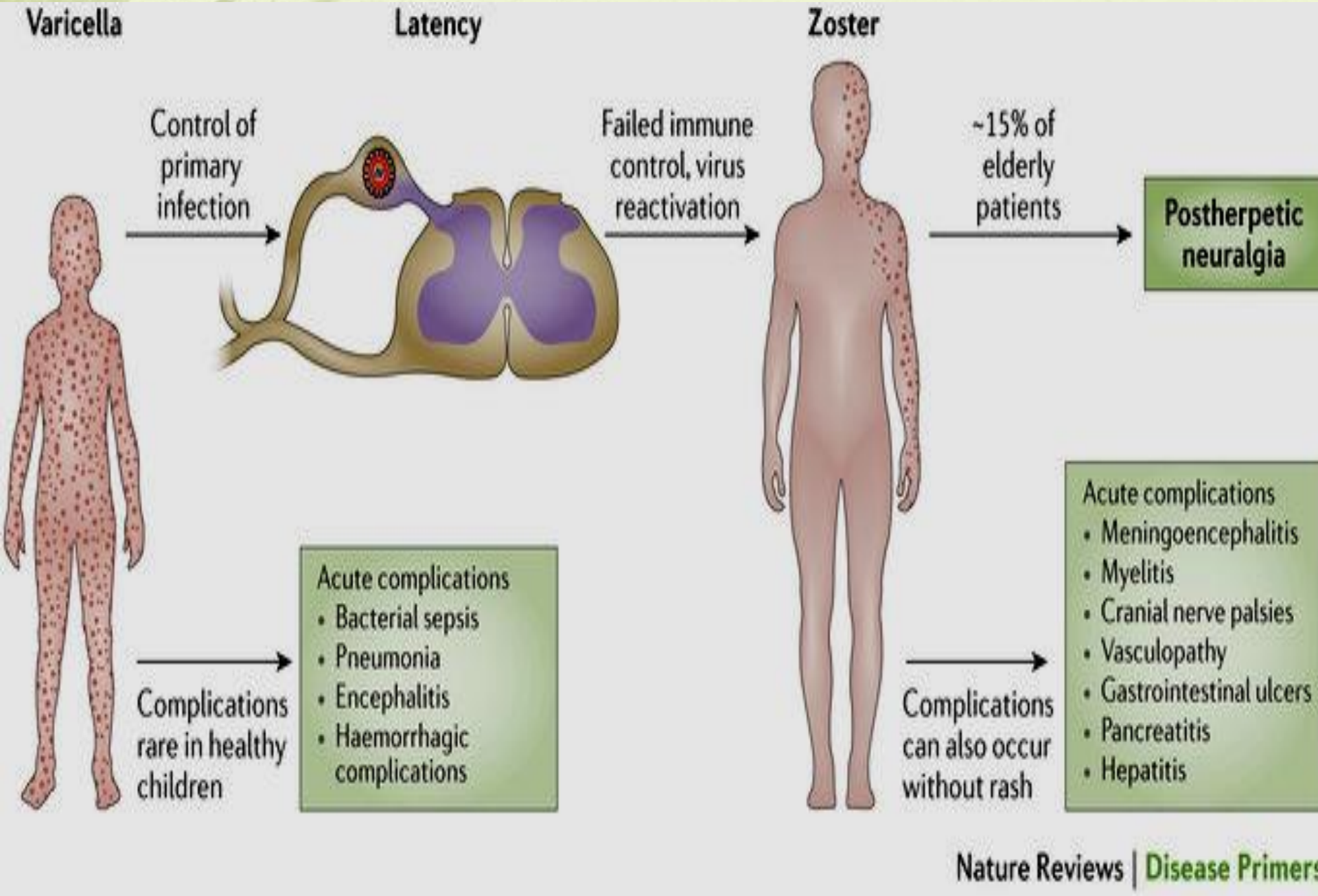

Varicella
Latency
Zoster
Control of primary infection
Failed immune control, virus reactivation
~15% of elderly patients
Postherpetic neuralgia
Complications rare in healthy children
Acute complications
• Bacterial sepsis
• Pneumonia
• Encephalitis
• Haemorrhagic complications
Complications can also occur without rash
Acute complications
• Meningoencephalitis
• Myelitis
• Cranial nerve palsies
• Vasculopathy
• Gastrointestinal ulcers
• Pancreatitis
• Hepatitis
Nature Reviews | Disease Primers

VZV risk of maternal infection during pregnancy

The risk of the mother passing VZV onto her baby is extremely low

If the mother contracts chicken pox – 2% chance that the baby will develop congenital varicella syndrome (CVS)

Most CVS cases - mothers infected between 13 and 20 weeks gestation

Maternal shingles are not associated with CVS

The fetal risk associated with maternal varicella include development of:

- congenital varicella syndrome
- severe varicella in infant
- occurrence of zoster in infancy or early childhood

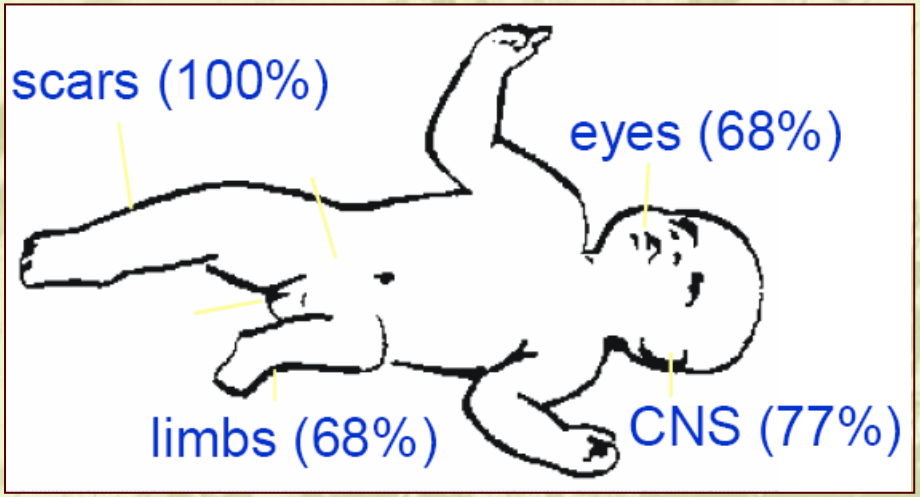
Factors influencing: timing of maternal varicella regarding gestation

Congenital VZV infection

Table 1: Sequelae of varicella fetopathy

Damage to sensory nerves	Cutaneous manifestations Cicatricial (zig-zag) scarring Hypopigmentation
Damage to optic nerve and lens vesicles	Microphthalmia Cataracts Chorioretinitis Optic atrophy
Damage to cervical and lumbosacral cord	Hypoplasia of extremities Motor/sensory deficits Absent deep tendon reflexes Anisocoria/Horner's syndrome Anal/vesical sphincter dysfunction
Damage to brain	Encephalitis Microcephaly Hydrocephaly Aplasia of brain

Horner's syndrome refers to a constellation of signs produced when sympathetic innervation to the eye is interrupted



Congenital VZV infection

Scaring skin lesions	100%
hypoplasia or aplasia of limbs	86%
low birth weight	82%
damage to the eyes	64%
neurological disorder	30%
retarded psychomotor development	50%

Maternal varicella in the period around the expected birth date

The clinical course of the infection in the neonate depends on the time of transmission (intrauterine or postnatal) and the presence or absence of maternal VZV-specific antibodies

Transplacental transmission in the case of maternal viremia can lead to a high inoculum in the absence of maternal antibodies

VZV prevention

VARIVAX vaccine for the prevention of chicken pox in non-immunized children and adults

ZOSTAVAX vaccine for the prevention of shingles

designated to elicit an immune response in adults whose immunity to VZV wanes with advancing age

Reduces the incidence of shingles by almost 50%

Winter, spring

Infectious aerosol

Parvovirus B19

4-28 days

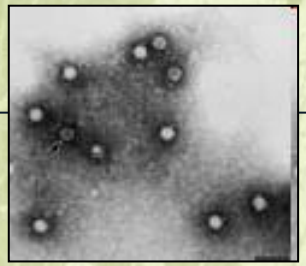
Erythrema infectiosum
Slapped check disease
Self-limiting

Pregnant women
Hydrops fetalis

Miscarriage, stillbirth

Treatment
No specific
No vaccine

Erythema infectiosum



Seroprevalence increases with age: 15-60% by age 5-9

Transmission:

- respiratory droplets,
- vertical (from mother to fetus)

The most characteristic feature of the disease is the prominent red rash on the face followed by a generalized rash

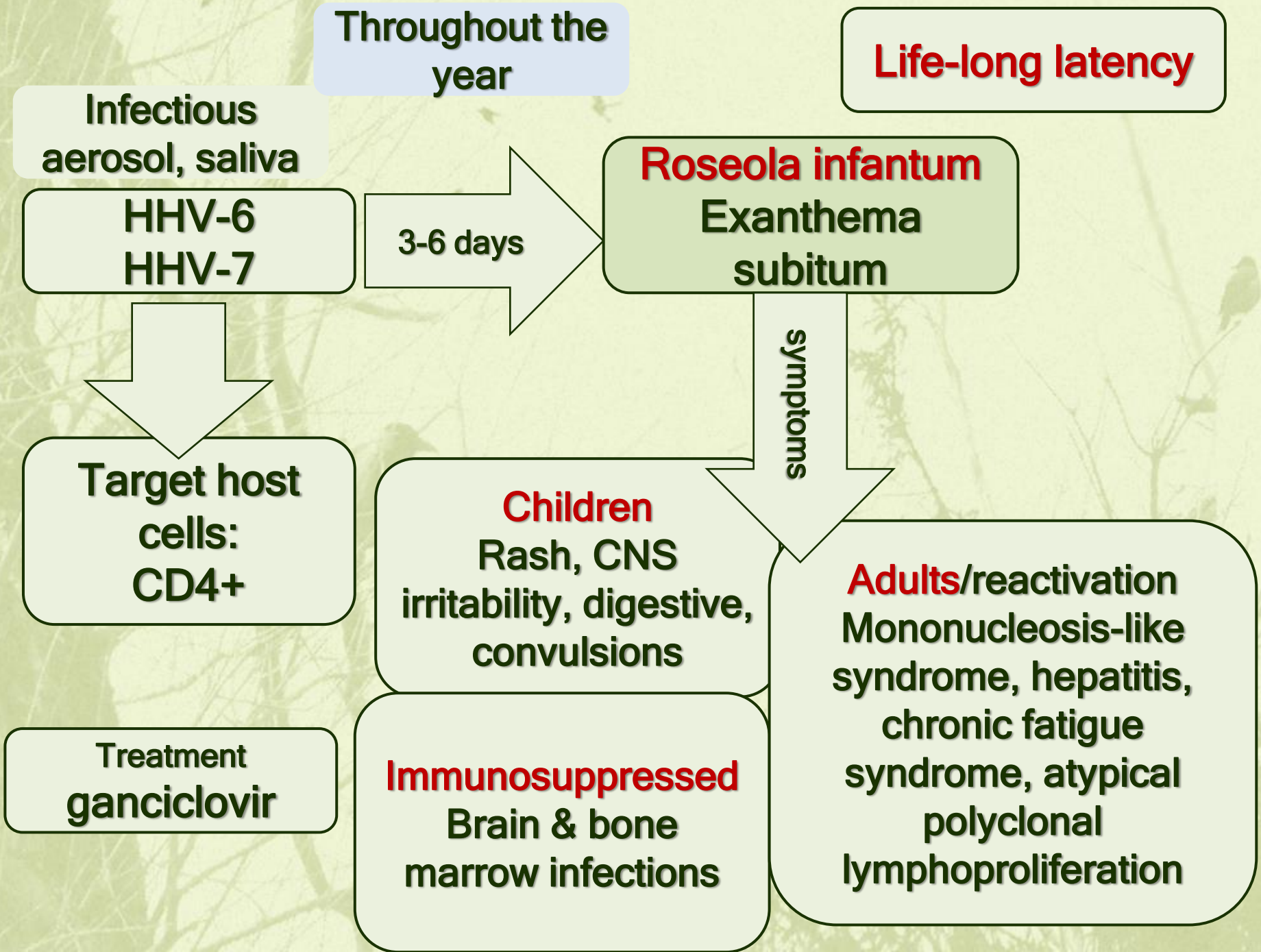
Parvovirus B19

- ssDNA, a nonenveloped virus of the Parvoviridae family
- Parvovirus B19 can easily overcome the placental barrier
- Embryocidal – destroys the dividing cells
- Incidences of intrauterine infection - unknown

Clinical presentations of symptomatic infection:

- erythrema infectiosum, arthropathy, hematological complications (congenital anemia), hydrops fetalis, fetal death
- congenital abnormalities: neurological, cardiac, ophthalmological, myocarditis, vasculitis

Slapped cheek disease


Throughout the year
Life-long latency
Infectious aerosol, saliva
HHV-6
HHV-7
3-6 days
Roseola infantum
Exanthema subitum
symptoms
Target host cells:
CD4+
Children
Rash, CNS irritability, digestive, convulsions
Adults/reactivation
Mononucleosis-like syndrome, hepatitis, chronic fatigue syndrome, atypical polyclonal lymphoproliferation
Treatment
ganciclovir
Immunosuppressed
Brain & bone marrow infections

Infectious aerosol, direct contact

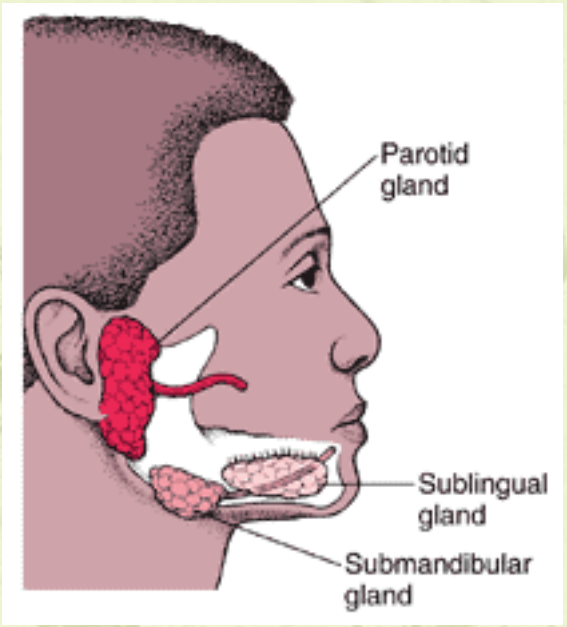
Winter / spring

MMR vaccine

Mumps virus

16-18 days

MUMPS



symptoms

20% no symptoms

50% respiratory symptoms

60% parotid salivary glands swelling

10% submandibular salivary glands swelling

Complications:

Meningitis, encephalitis, orchitis, pancreatitis, acute unilateral deafness, arthritis

In adults the disease is more severe

summer / fall

direct contact
air-borne

Coxackie A16,
(rare: Coxackie A6,
enterovirus A71)

3-7 days

Hand Foot Mouth Disease
HFMD

symptoms

Rash on palms, soles,
in mouth, low grade
fever
Lasts 7-10 days

spring

Air-borne route

MMR vaccine

Rubivirus

12-23 days

Rubella

symptoms

Rash – face, generalized

Complications benign & rare:
Arthritis, encephalitis, orchitis, neuritis
Congenital disease

Rubella virus (RBV)

- RNA virus, member of Togaviridae family
- Rubella = German measles or 3-days measles – mild, self-limited infection
- Primary rubella infection during pregnancy – fetus death, miscarriage, congenital abnormalities

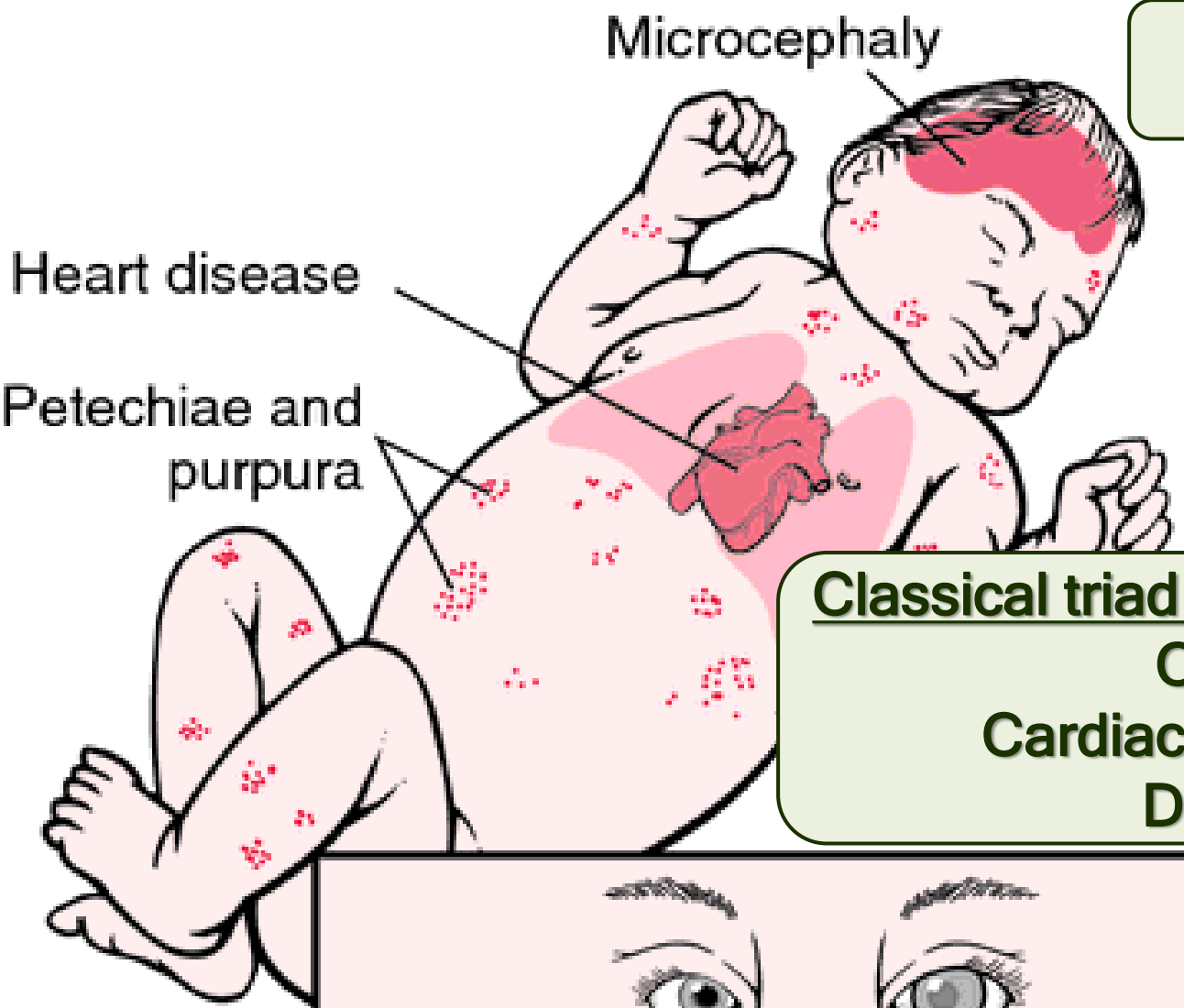
RBV - Risk of congenital infection

Intrauterine transmission of rubella occurs during viremia in the mother

Women without preexisting immunity are at risk for congenital infection

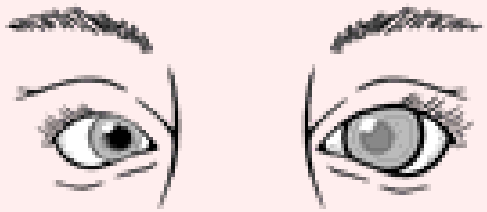
Reinfection during pregnancy – risk of fetal infection very low

Congenital rubella



Classical triad of congenital rubella

- Cataract
- Cardiac abnormalities
- Deafness



Eye anomalies may include cataracts, glaucoma, strabismus, nystagmus, microphthalmia, and iris dysplasia.

Risk of congenital infection (RBV)

- The rate of infection in infants whose mother had exposure before 11th week of gestation = about 90%
- Maternal infection during II & III trimester: the rate of infection in neonates – 39% & 53%
- Risk for defects in neonates infected during the first trimester – very high (85%)
- Risk for defects in neonates infected during the 2nd & 3rd trimester – 20% & 5%

RBV – congenital infection

Intrauterine infection with rubella can affect any organ system & infants often have multiple organ involved

Spectrum of clinical abnormalities: ophthalmological (cataracts, retionopathy, congenital glaucoma), cardiac (patent ductus arteriosus), auditory, neurological (meningoencephalitis, microcephaly)

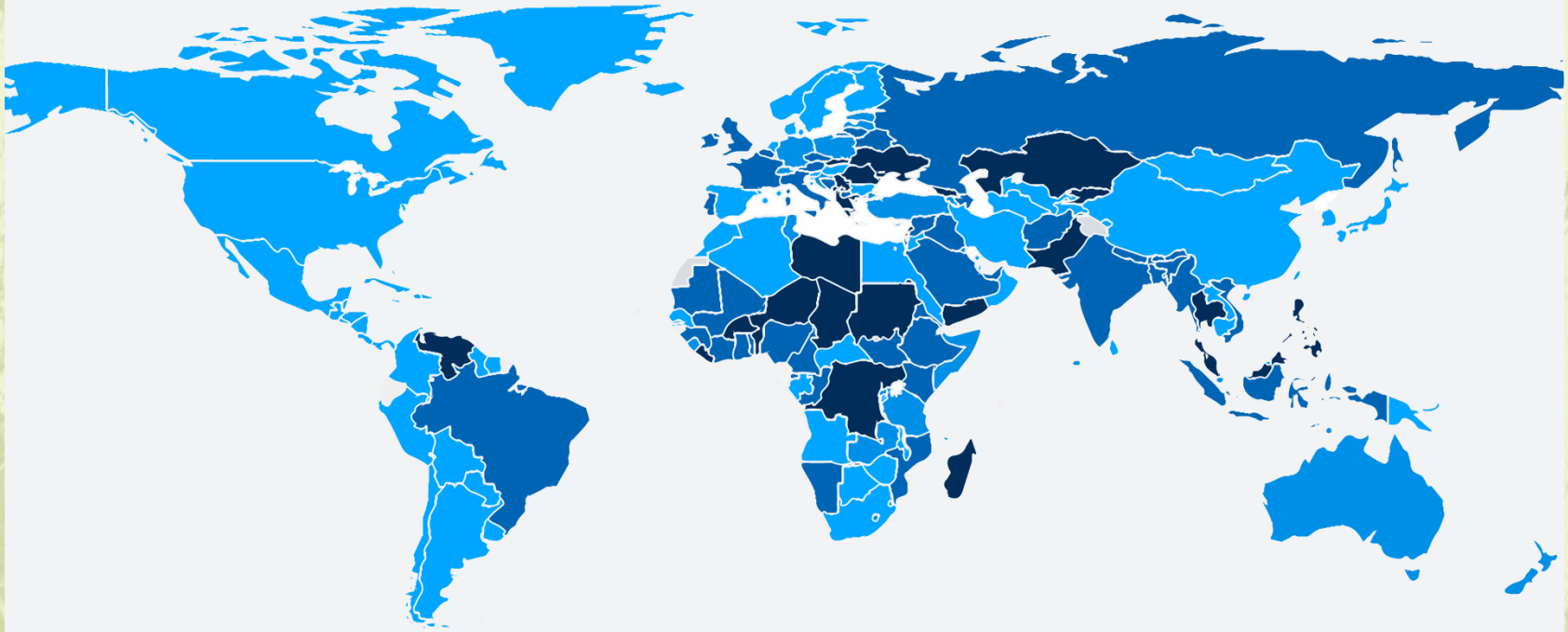
RBV – congenital infection

Teratogenic agent

An agent that causes developmental defects during pregnancy through a direct effect on the embryo or fetus (this includes severe abnormalities that may lead to embryonic or fetal death)

TORCH: Toxoplasma gondii, Others (syphilis, mumps, VZV, Parvovirus B19, HIV), Rubella virus, Cytomegalovirus, HSV

Measles cases worldwide*



* Rate per million, 12 month period

Source: WHO, March 2019

Europe Still Struggling With Major Measles Outbreak

Measles cases in Europe from January 2018 to August 2018

Source: World Health Organization

Winter

Air-borne
direct contact

Measles
virus

10-12 days

Measles
(Greman rubeola)

symptoms

Prodromal: 3xC's:
coryza, cough, conjunctivitis

Maculopapular rash: face then generalized

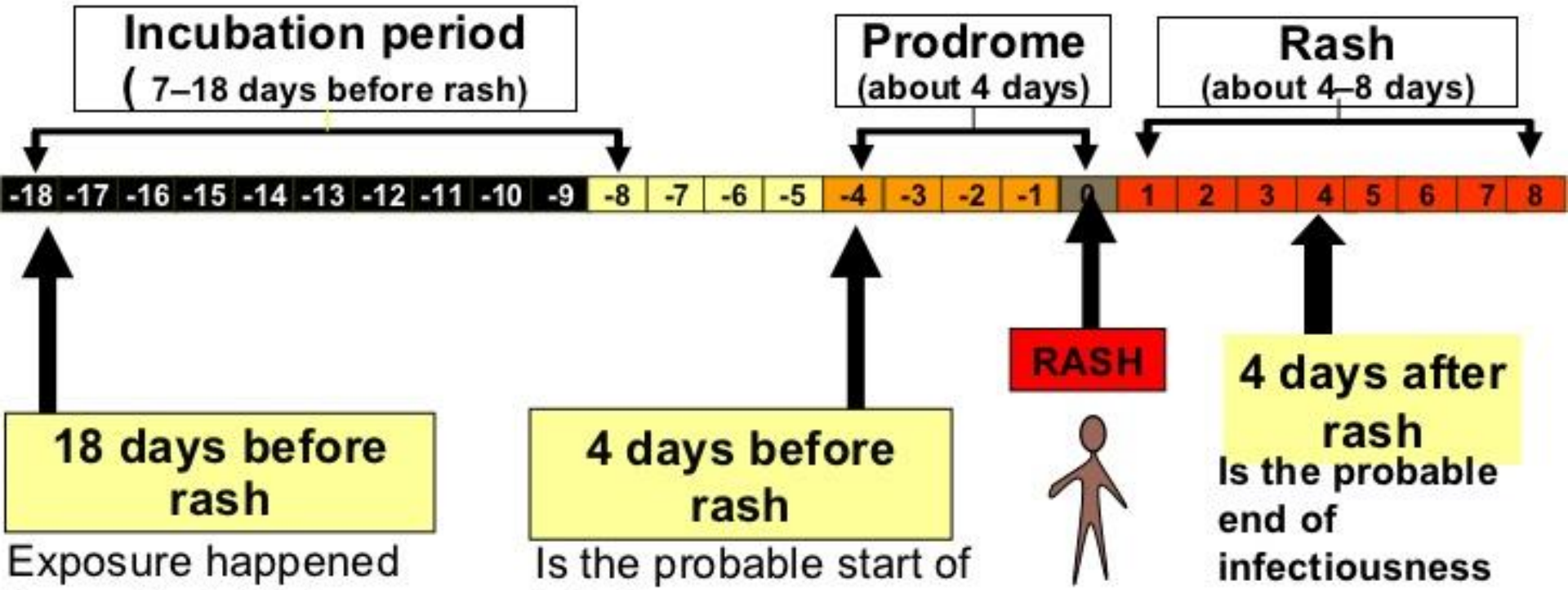
Koplik's spots in mouth

<u>Complications:</u>
Blindness, diarrhea, pneumonia (60% deaths)

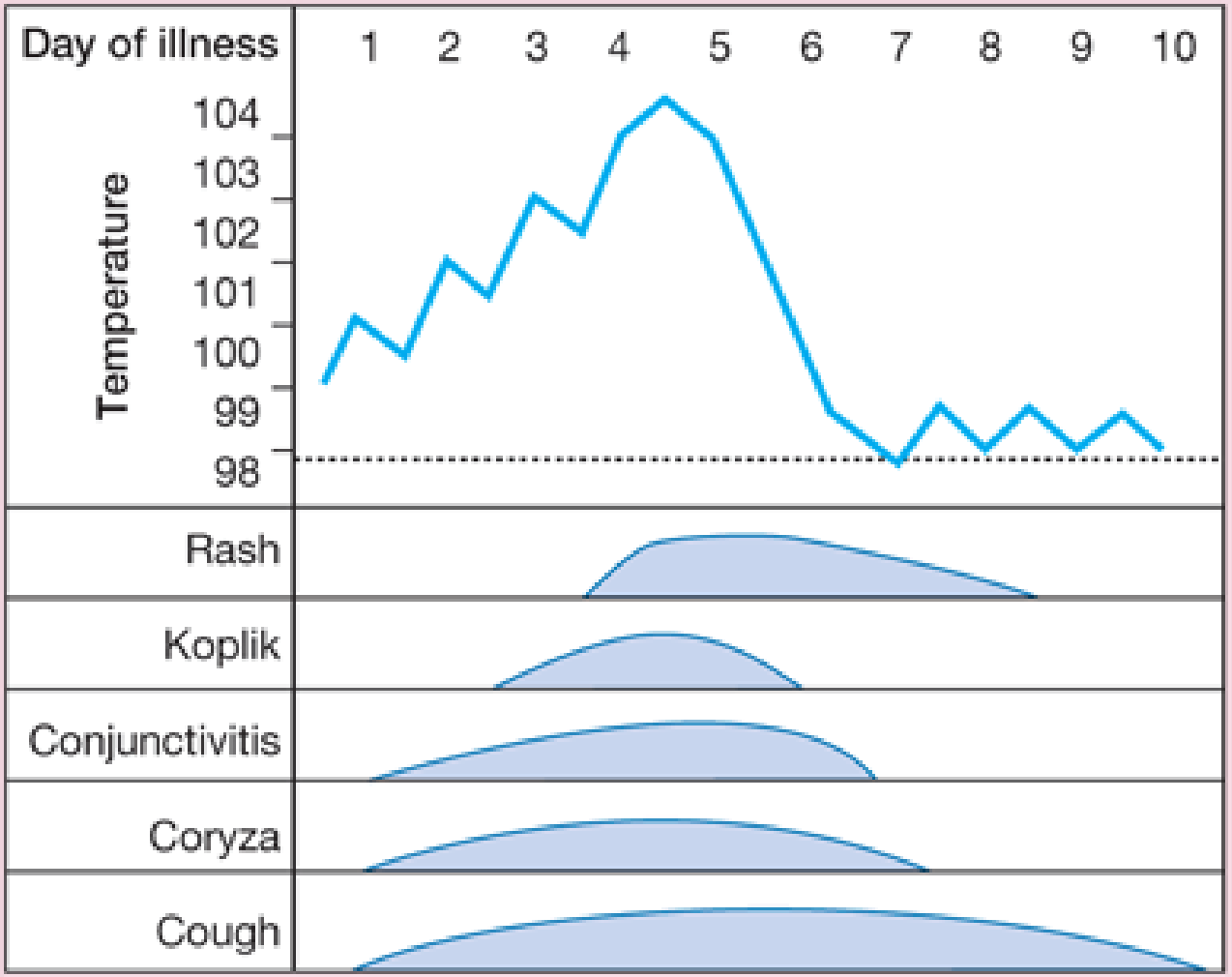
CNS disordres

MMR vaccine

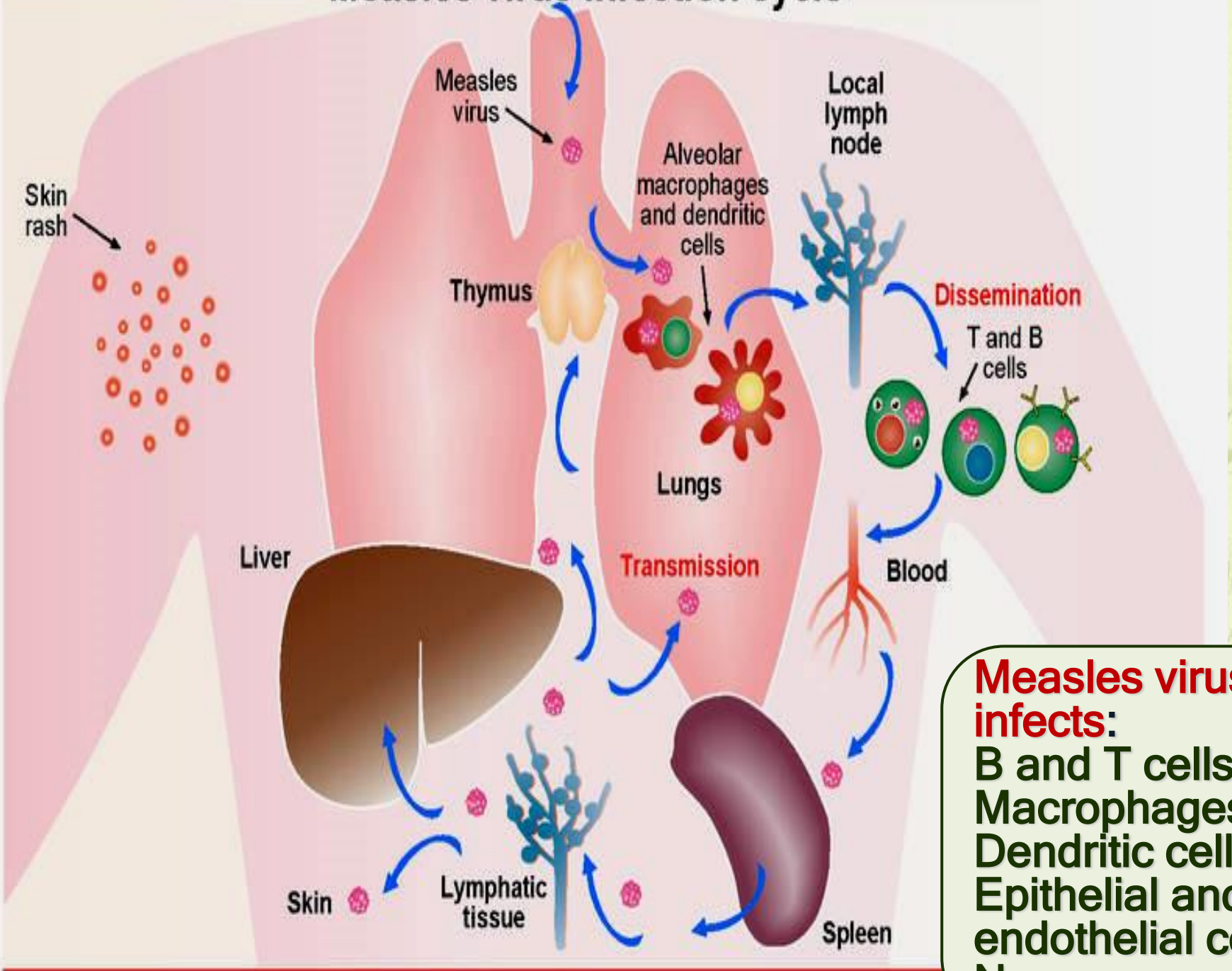
Clinical course of measles



Clinical course of typical measles



Source: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K: *Fitzpatrick's Dermatology in General Medicine, 8th Edition*: www.accessmedicine.com

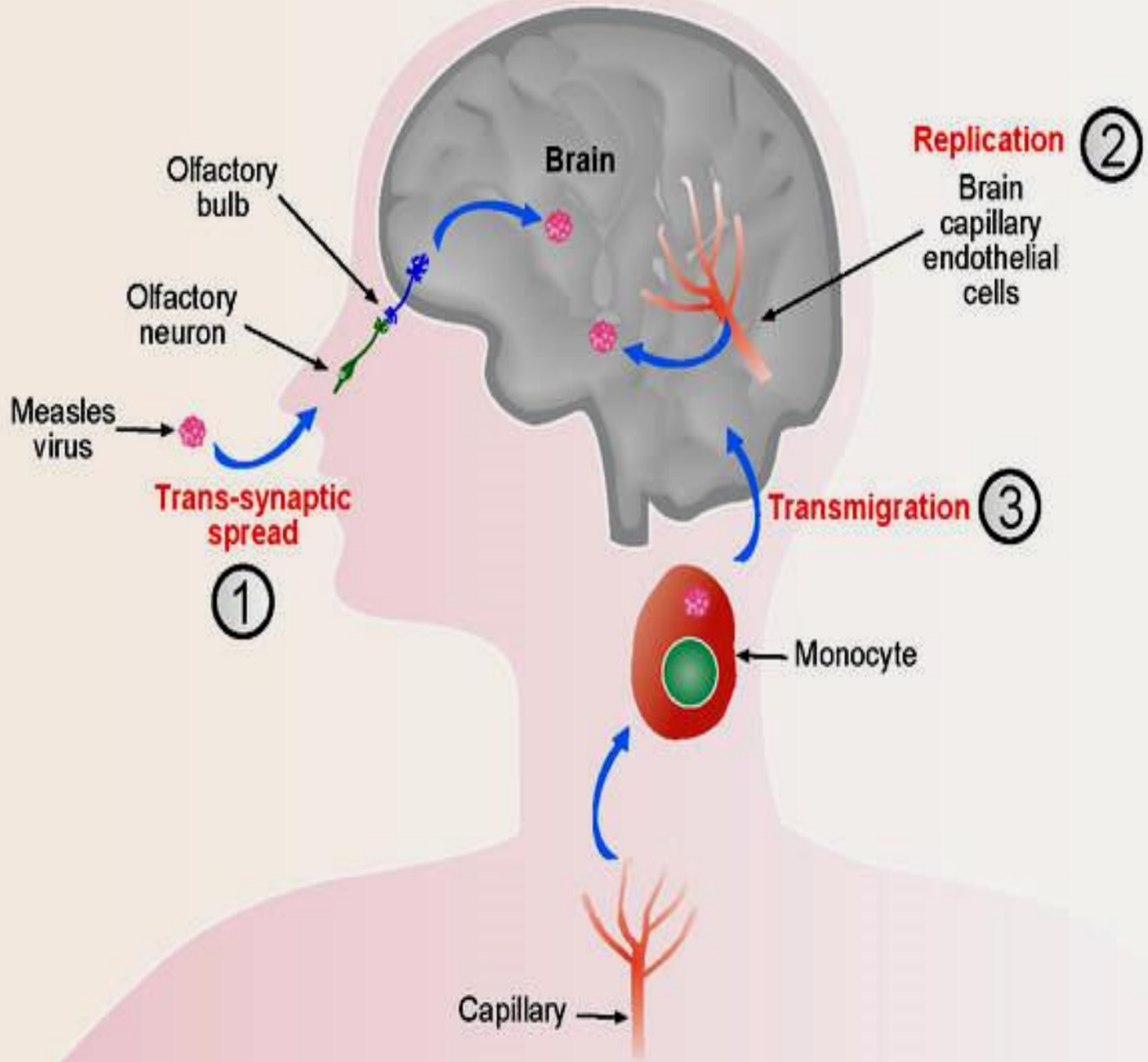


Measles virus infects:

B and T cells
Macrophages
Dendritic cells
Epithelial and endothelial cells
Neurons

Measles virus is transmitted between humans by aerosal inhalation or contact with respiratory s
cells are immune cells such as T and B cells, macrophages and dendritic cells that express CD150

Potential routes of measles virus dissemination to the brain



Acute viral encephalitis
(brain swelling)

During rash in 1-3/1000 cases

MR 10-15% children; 25% adults

Acute disseminated encephalomyelitis (ADEM) most frequent
(immune-mediated brain inflammation + demyelinization)

After 2-30 days post disease

1/1000 cases / infants

1-2/1.000.000 post vaccination

MR 5% children; 25% adults

SSPE (subacute sclerosing encephalitis)
virus persistence & mutation

6-15 years after disease

1/25.000 cases

but children <1 year 1/5000

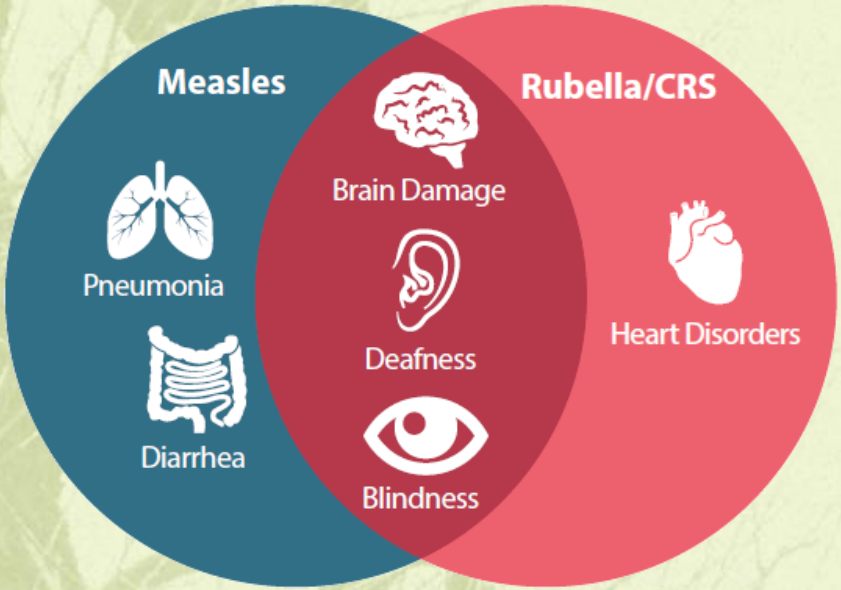
Death within 3 years MR 100%

Measles inclusion body encephalitis (MIBE)
Virus persistence

in immunosuppressed after disease or vaccination

MR 75%

Ribavirin for treatment



In 2020, reported measles cases and deaths were lower than previous years

Measures to mitigate COVID-19, such as social distancing and mask use, may have helped prevent measles transmission

Surveillance for measles also declined, and the number of specimens submitted for testing was the lowest in a decade

Disruptive outbreaks were still reported in 26 countries


Thank you for your attention