

Exanthematic viruses



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Viral exanthematic diseases

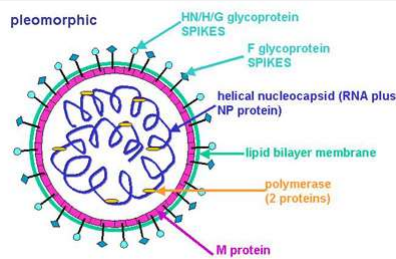
Childhood exanthema diseases

Classical name	„systematic exant. name“	Pathogen
Measles (rubeola)	1 st childhood disease	morbillivirus
Scarlet fever	2 nd childhood disease	Streptococcus pyogenes
Rubella (German measles)	3 rd childhood disease	Rubivirus
Filatov-Duke's disease (pseudoscarlantina)	4 th childhood disease	Coxackie and Echoviruses
Erythema infectiosum	5 th childhood disease	Parvovirus B19
Exanthema subitum – Roseola infantum	6 th childhood disease	HHV-6 and HHV-7
Hand, Foot and Mouth disease	7 th childhood disease	Coxackie A-16

Chicken pox - VZV

Paramyxoviridae

Members of the Paramyxovirus Family			
SUB-FAMILY	GENUS	MEMBERS	GLYCOPROTEINS
Paramyxovirinae	Respirovirus	Human parainfluenza virus1 (HPIV 1) Human parainfluenza virus3 (HPIV 3)	HN, F
	Rubulavirus	Human parainfluenza virus2 (HPIV 2) Human parainfluenza virus4 (HPIV 4) Mumps virus	HN, F
	Morbillivirus	Measles	H, F
	Henipavirus	Hendravirus Nipahvirus	G, F
Pneumovirinae	Pneumovirus	Respiratory syncytial virus Metapneumovirus	G, F



- ss (-) RNA virus
- genome length 15-16 kb
- coding 8 proteins
- spherical symmetry of capsid and diameter of 100-300 nm

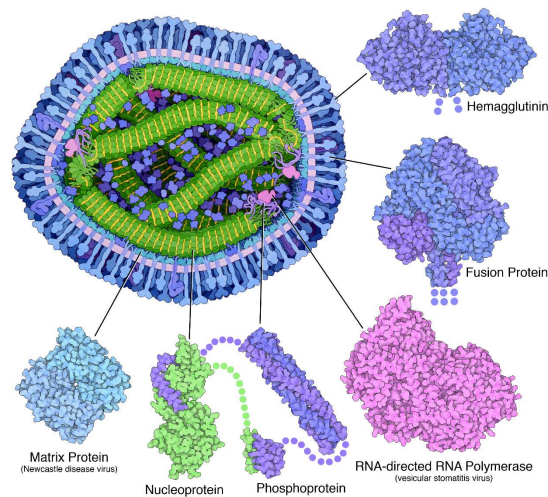
<https://www.microbiologybook.org/mhunt/mump-meas.htm>

Paramyxoviridae

Measles

Before the introduction of measles vaccine in 1963 and widespread vaccination, major epidemics occurred approximately every 2-3 years and caused an estimated 2.6 million deaths each year.

An estimated 128 000 people died from measles in 2021 – mostly children under the age of five years, despite the availability of a safe and cost-effective vaccine.



Estimated cases – 20,000,000 / year.

<https://pdb101.rcsb.org/motm/231>

Paramyxoviridae

Measles

Measles Cases and Outbreaks

January 1 to August 29, 2014*†

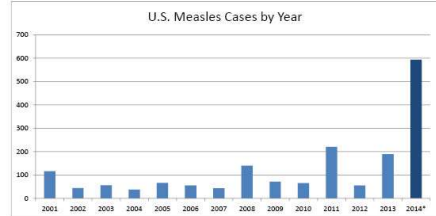
592 reported in 21 states: Alabama, California, Connecticut, Hawaii, Illinois, Indiana, Kansas, Massachusetts, Minnesota, Missouri, New Jersey, New York, Ohio, Oregon, Pennsylvania, Tennessee, Texas, Utah, Virginia, Washington, Wisconsin

Cases

18

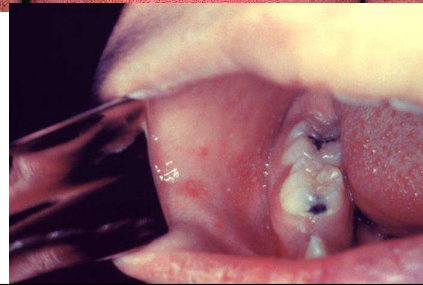
representing 89% of reported cases this year

Outbreaks



*Provisional data reported to CDC's National Center for Immunization and Respiratory Diseases

†Updated once a month



Estimated cases – 20,000,000 / year.
Estimated kills - 128,000 people in world/year.

Paramyxoviridae

Measles



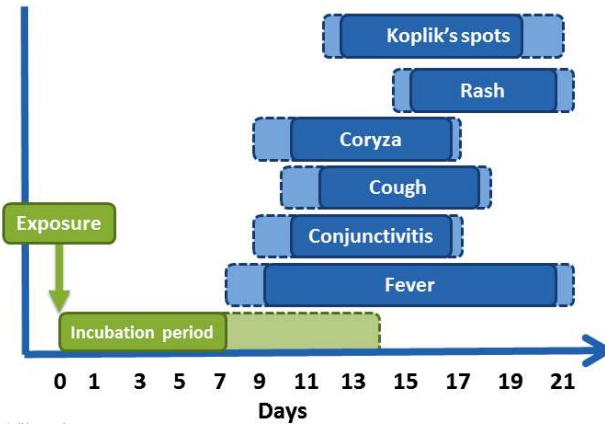
https://o.quizlet.com/Zw7Q_J7v4Lrq4L7cWY7u1w.png

Measles

- Droplet spread infection. It is so contagious that any child who is exposed to it and is not immune will probably get the disease.
- Measles virus normally grows in the cells that line the back of the throat and lungs
- incubation period 8-12 days

Symptoms

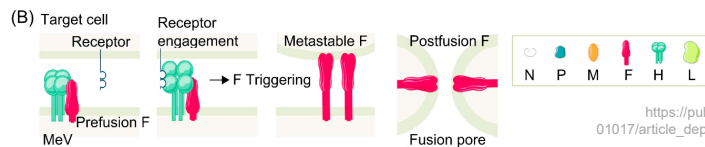
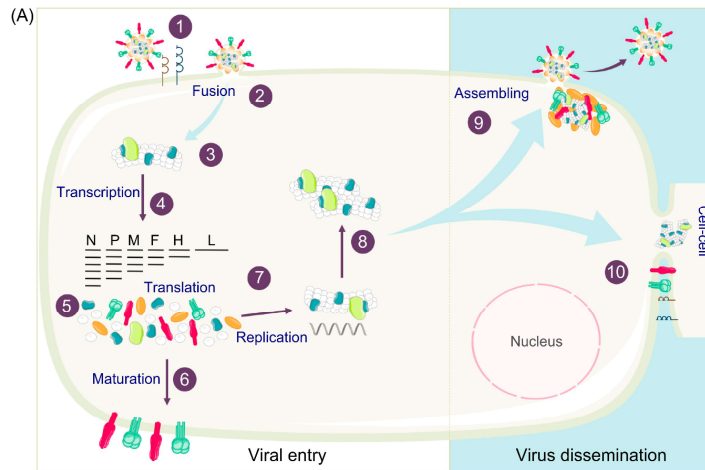
- Measles starts with fever, runny nose, conjunctivitis, white spots in the cheeks.
- Rash starts 7-18 days after exposure at head and neck and spreads from this areas to whole body (3 days); 5-6 days of fading.



<https://www.who.int/news-room/fact-sheets/detail/measles>

https://www.wikidoc.org/index.php/File:Measles_Symptoms.png

Measles



https://pub.mdpi-res.com/viruses/viruses-11-01017/article_deploy/html/images/viruses-11-01017-g001.png?1574991076

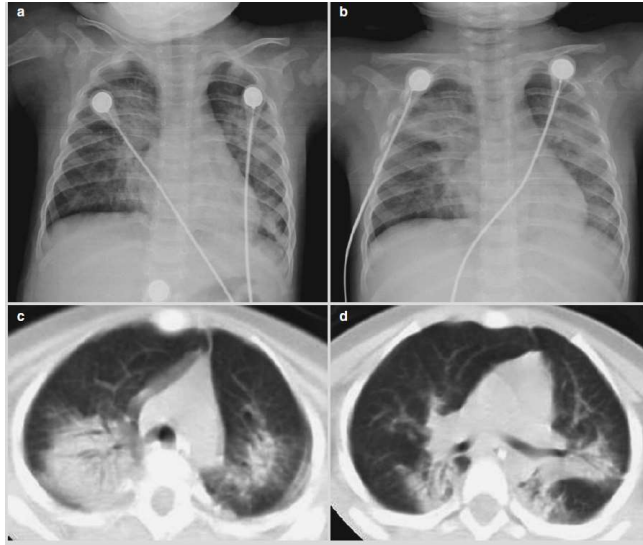
Measles

Headache, cough, myalgia...

Complications

- About 1 / 10 children gets an ear infection
- 1 out of 20 gets pneumonia.
- 1 out of 1,000 gets encephalitis,
- **1-2 out of 1,000 die.**

There is vaccination against measles.



https://pub.mdpi-res.com/viruses/viruses-11-01017/article_deploy/html/images/viruses-11-01017-g001.png?1574991078

Measles

Subacute sclerosing Panencephalitis
Rare, slowly progressive neurological disorder caused by the persistent infection

First described by Dawson 1934

Mutant measles virus infection of neuron

Subacute encephalitis

Children and young adults

Inflammatory demyelination and gliosis

Nuclear inclusions in oligodendroglial cells

#royopath histopathology-india.net

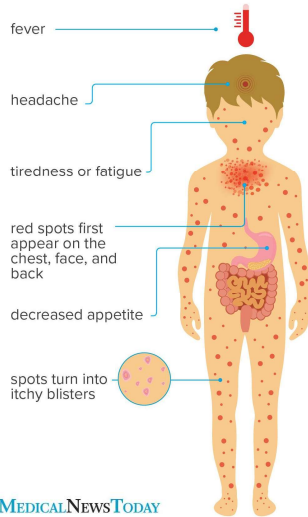
The infographic features several elements: a cartoon doctor at a desk, a red spherical virus particle with spikes, a neuron with a long process, a profile of a head with a brain showing viral activity, and three histological images. The first histological image shows purple-stained tissue with inflammatory cells. The second shows blue-stained cells with dark purple nuclear inclusions. The third shows a green-stained field with dark spots.

<http://www.histopathology-india.net/SSPE.htm>

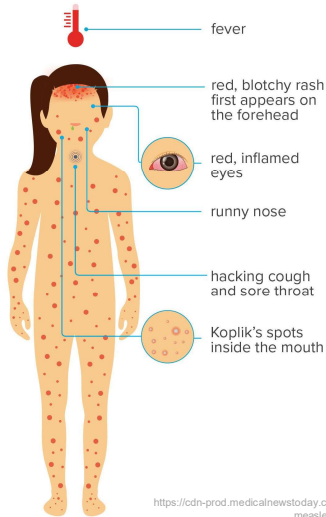
Paramyxoviridae

Chickenpox vs. Measles

Chickenpox



Measles




MEDICALNEWS TODAY


<https://cdn-prod.medicalnewstoday.com/content/images/articles/322/322637/chickenpox-vs-measles-infographic-br-image-credit-stephen-kelly-2018-br.jpg>

MEASLES & RUBELLA INITIATIVE A global partnership to stop measles & rubella


1.1 Billion Vaccinated since 2001



78% FEWER CHILD DEATHS because of measles vaccine




330 children still die of measles every day




that's **14** every hour


13.8 Million deaths averted 2000 - 2012



1 in 5 child lives saved since 1990 due to measles vaccine



It costs about **\$1** to protect a child from both measles & rubella



MEASLES MOVES FAST WE MUST MOVE FASTER

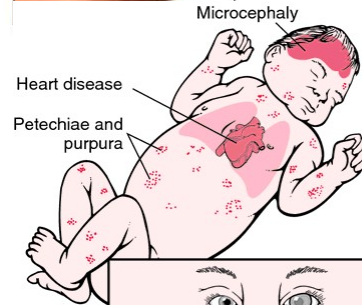
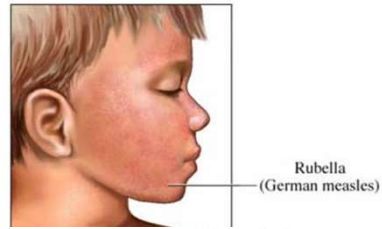
Follow @measlesrubella www.measlesrubellainitiative.org

American Red Cross CDC UNITED NATIONS FOUNDATION unicef World Health Organization

Rubella - German measles

WHAT IS RUBELLA?

- An infection that affects your skin and lymph nodes.
- Can be known as "German measles"
- "The Scarlet Scourge"
- A rash that normally spreads from your face and anything below



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

- Rubivirus (RNA)
- incubation period avr. 18 days (12-23)
- viraemia 5th-7th day after exposition with subsequent spreading to the organs

Rubella - German measles

The infection is usually mild with fever and rash. In pregnancy the virus can cause serious birth defects.

Symptoms:

In 25-50% of rubella cases the disease is usually so mild there may be few or no signs or symptoms.

In typical cases the incubation period is between 12-23 days, most people show symptoms within 16-18 days after exposure.

Common symptoms include: Slight fever, sore throat, runny nose and malaise (may occur prior to appearance of rash, more so in adults than in children).

Tender or swollen glands almost always accompany rubella, most commonly behind the ears (retroauricular) and at the back of the neck (occipital and posterior cervical lymph nodes). Lymphadenopathy may occur in patients with rubella that do not have a rash.

Mucosal involvement results in the Forchheimer sign, in which pinpoint or larger petechiae are noted on the soft palate and uvula during the prodromal period of rubella.

Rash begins on the face that spreads to the neck, trunk and extremities.

Appear as pink or light red spots about 2-3 mm in size. Lasts up to 5 days (average is 3 days). May or may not be itchy.

As rash passes, affected skin may shed in flakes. Usually not as widespread as in MeV.

Other symptoms include pain and swelling in joints (arthralgia and arthritis). This is more common in adults, particularly women, and may persist longer than 2 weeks. The arthritis may become chronic and persist for months or years.

Togaviridae

Rubella - German measles



<https://dermnetnz.org/topics/rubella>

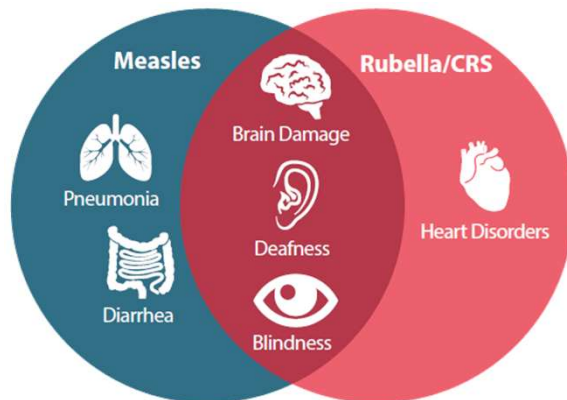
Togaviridae

Rubella - German measles

About 1/2 of the people do not have symptoms.

In rare cases, serious problems can occur. These include brain infections and bleeding problems.

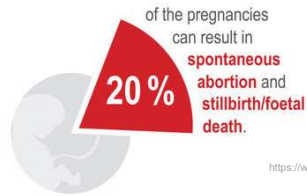
Spreading: through coughs or sneezes; most contagious when the person has a rash. But it can spread up to 7 days before the rash appears. People without symptoms can still spread rubella.



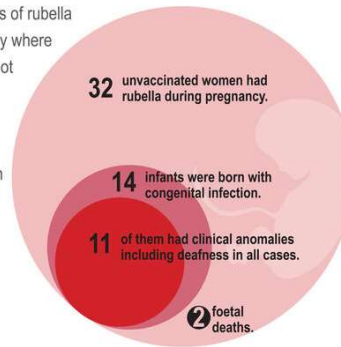
<https://www.cdc.gov/globalhealth/measles/about/index.html>

Rubella

Rubella and pregnancy



Consequences of rubella in a community where people were not vaccinated (example from the Netherlands in 2004/2005).



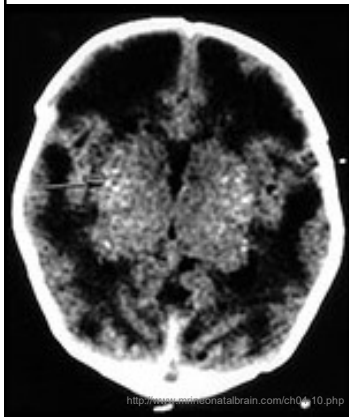
<https://www.ecdc.europa.eu/en/publications-data/infographic-protect-unborn-babies-rubella>

In pregnancy: miscarriage or birth defects like deafness, intellectual disability, and heart defects. 85% of babies born to mothers who had rubella in the first 3 months of her pregnancy will have a birth defect.

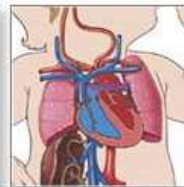
Togaviridae

Rubella - German measles

Rubella syndrome



Microcephaly



PDA



Cataracts

Box 1: Clinical features of congenital rubella syndrome

Classic triad

- **Congenital heart disease** (e.g., patent ductus arteriosus, pulmonary artery stenosis, pulmonary valvular stenosis)
- **Ocular defects** (e.g., congenital cataracts, microphthalmos, pigmentary retinopathy, congenital glaucoma)
- **Hearing loss**

Congenital rubella syndrome is usually associated with a failure to thrive and developmental delay as well as microcephaly. Other common presentations at birth include:

- purpuric rash
- hepatosplenomegaly
- meningoencephalitis
- radiolucent bone
- hepatitis
- thrombocytopenia

<http://www.cmaj.ca/content/172/13/1678/F1.expansion.html>

Infection between 8th-10th week of gestation leads to development of congenital rubella syndrome in 90%.

Congenital infections with Venezuelan Equine Encephalitis Virus are symptomatically similar.

Rubella - German measles

Congenital Rubella

Crosses placenta when **mother has acute infection**.
The earlier the fetus is infected -> more serious disease.
May result in serious congenital abnormalities

- Intrauterine growth retardation
- Hepatosplenomegaly
- Cataracts
- Mental retardation
- Sensorineural hearing loss
- Heart- Patent ductus arteriosus
- Pulmonary stenosis
- Thrombocytopenic purpura



Cataracts



Blueberry Muffin Rash



PDA

- Classic triad:**
- PDA
 - Cataracts, and deafness
 - +/- "blueberry muffin" rash

https://pbs.twimg.com/media/ERid_0yWAAAMZ9r.jpg

Rubella and measles



The MMR vaccine protects against rubella.

Details e.g. also in:

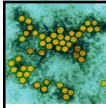
<http://ecdc.europa.eu/en/publications/Publications/systematic-review-incubation-period-shedding-children.pdf>



SCIENTIFIC ADVICE

Systematic review on the incubation and infectiousness/shedding period of communicable diseases in children

www.ecdc.europa.eu



Picornaviridae

Filatov-Duke's disease

Called also *unreal scarlet fever*, *pseudoscarlatina*, *Filatov-Duke's disease*, or *Fourth child's disease*.

Caused by coxsackie and echoviruses.



Parvovirus B19

Described in Australia in 1975 by Yvonne Cossart, in microtitration plate „B19“.

Proliferation in erythroid cells of bone marrow (dysregulation of cell cycle through NS1 protein).

Transmission by droplets, mainly. Incubation: 2 weeks (4-28 day) lasting for a week.

Erythema infectiosum („slapped cheek“) – „Fifths disease“.

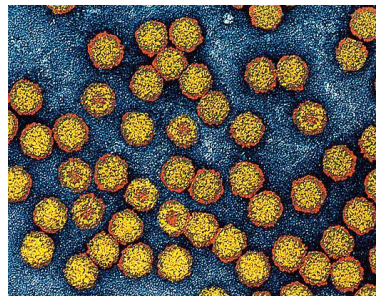
Teenage - "Papular Purpuric Gloves and Socks Syndrome".

Adults – urticas; Pregnant hydrops foetalis

Immunosupressed patients - „pure red cell aplasia“.



Described possible related complication of B19 infection is myocarditis.



<http://infofly-noses.com/images/parvovirus.b19>

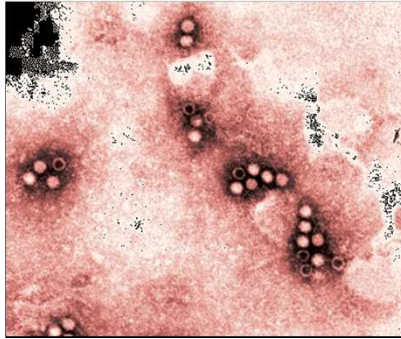
http://www.sciencenote.com/images/download_0_res.html?id=770500728

Parvovirus B19

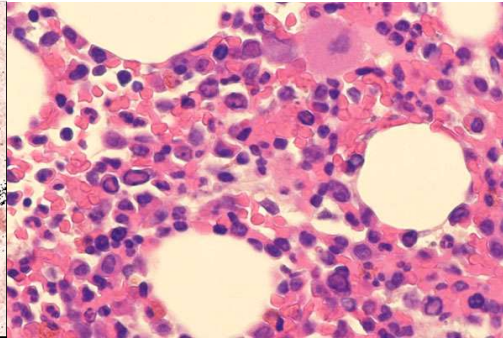


- small ss DNA +/-
- Capsid 20-26 nm, genome: 5 kbp
- E.g. Aplastic anaemia...

<http://fai.unne.edu.ar/biologia/virologia/images/virolo6.jpg>



<http://www.wadsworth.org/databank/hircz/gradyp2.gif>



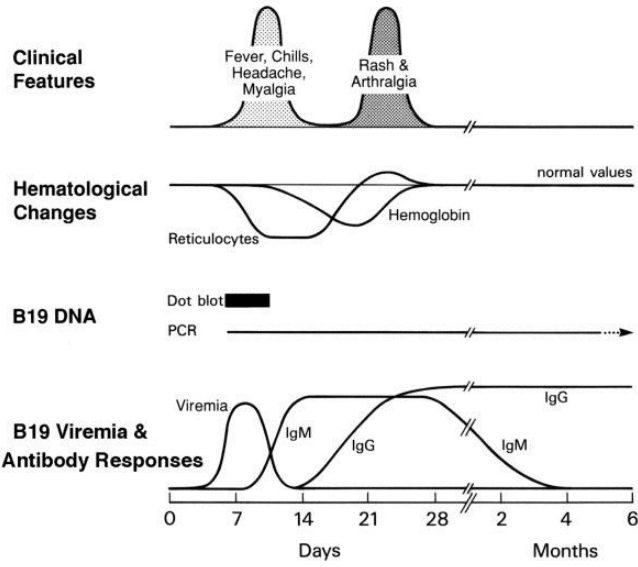
<http://www.yamagku.co.jp/pathology/image/210/1.jpg>

Parvovirus B19



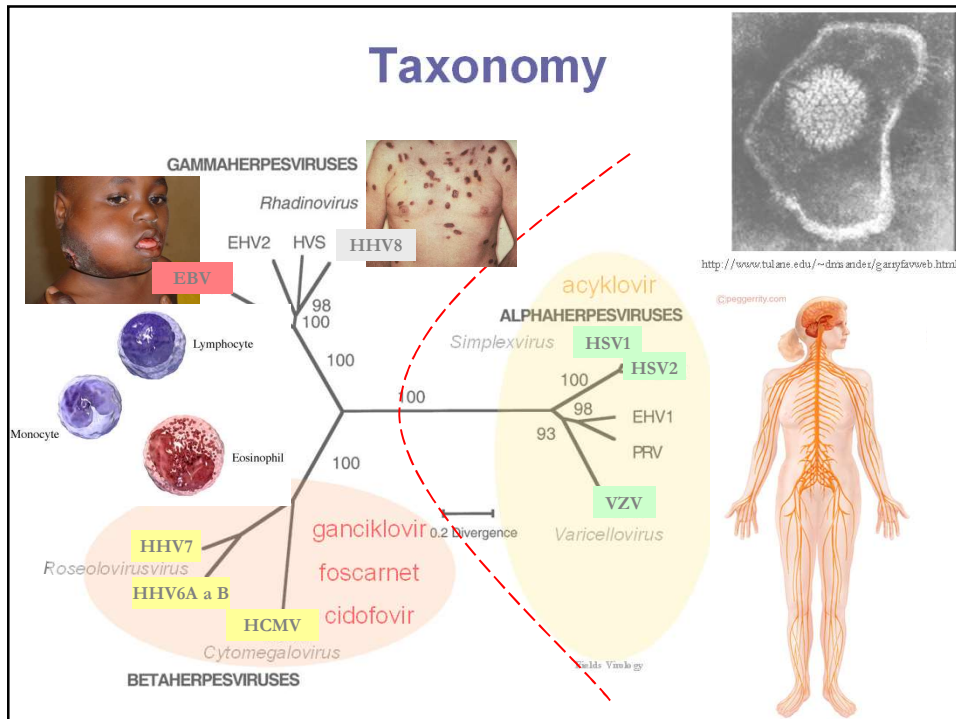
<https://www.mayoclinic.org/content/dam/media/global/images/2023/04/05/parvovirus-infection-face-rash.jpg>

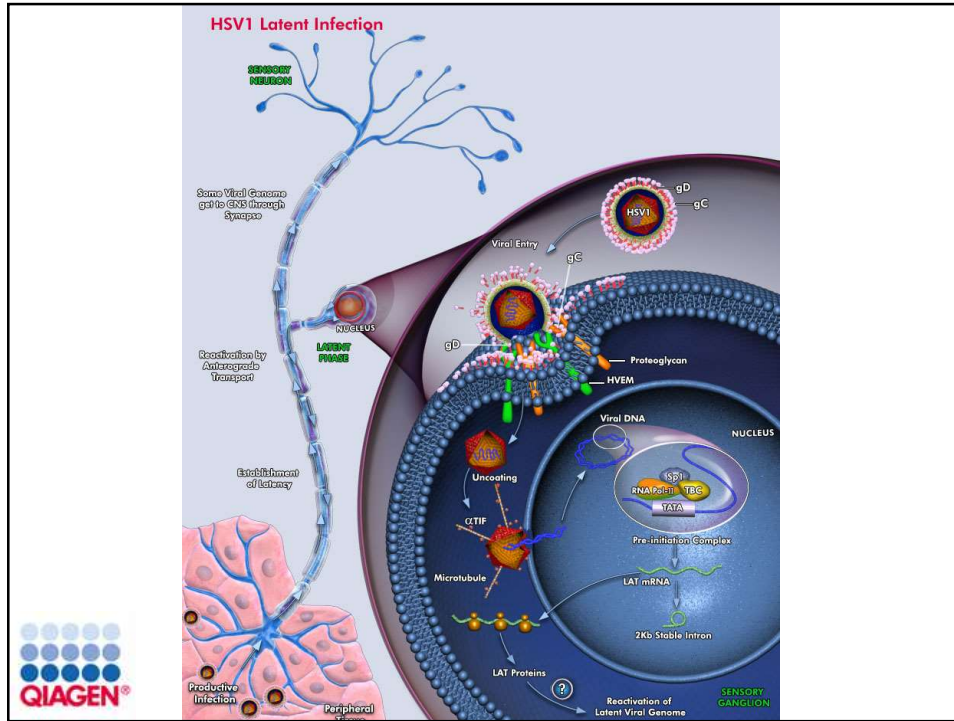
Parvovirus B19





<https://www.nejm.org/doi/10.1056/NEJM200404300430840>
<https://www.nejm.org/doi/10.1056/NEJM200404300430840>

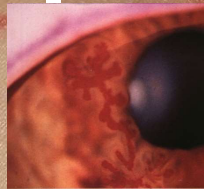




Pathological impact of HSV and VZV

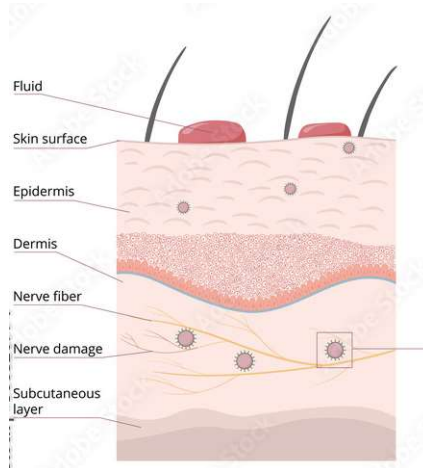
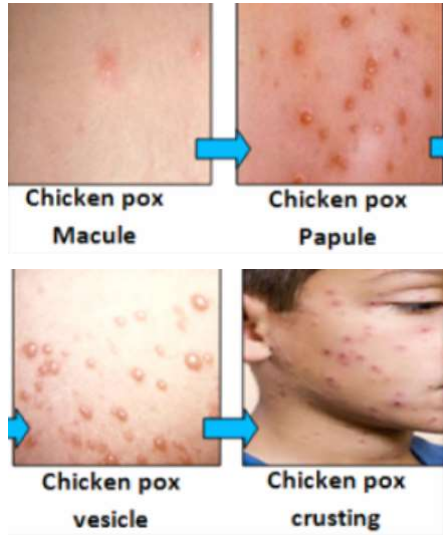
- HSV – herpes simplex, benign crbl. ataxia, gingivostomatitis, faryngotonsillitis, **encefalitis, pneumonie, hepatitis**
- VZV – varicella, herpes zoster, encefalitis, pneumonie, hepatitis

– *In allogeneic HSCT setting less frequently in case of acyclovir prophylaxis; reactivation of HSV without ACV prophylaxis in 80% of patients*



Varicella – chicken pox

VZV and HSV



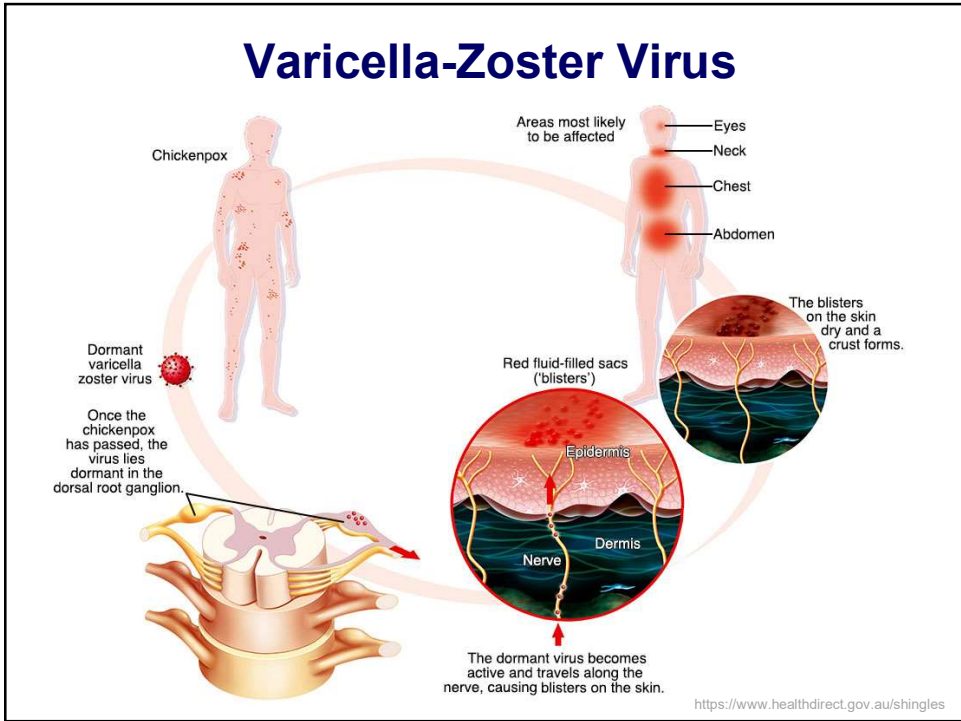
<https://allenkeyanocollege.weebly.com/clinical-manifestations-and-treatment.html>

https://as2.ftcdn.net/v2/jpg/05/08/32/09/1000_F_508320994_kOwtpylLC11OFQFYLDQhOZD1SPNF1dtj.jpg

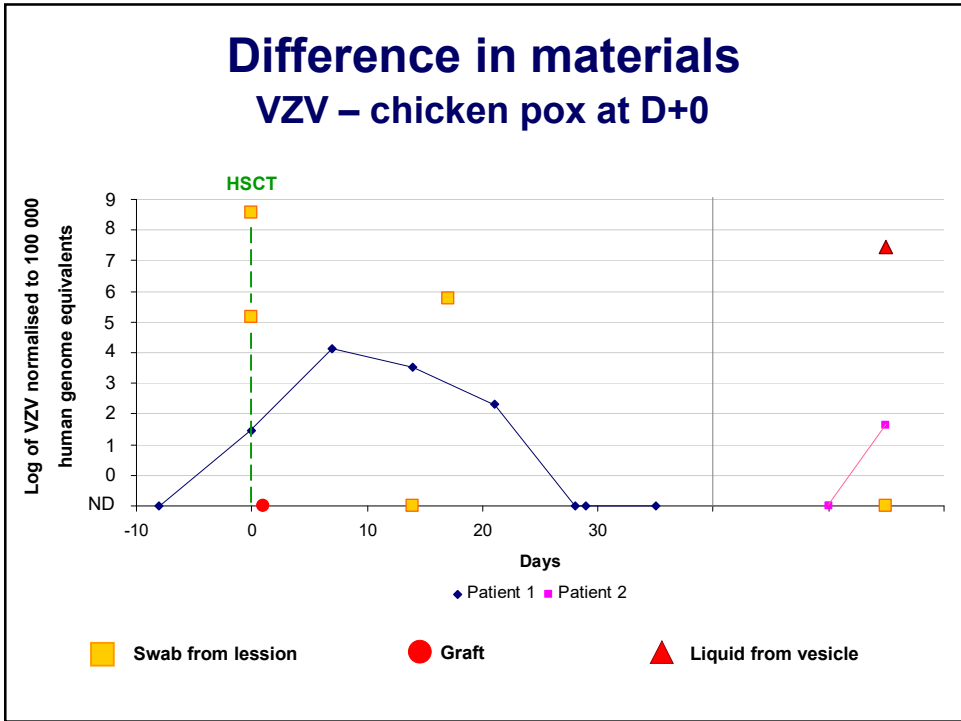


https://www.youtube.com/watch?v=Jl8OeAh_Q8Y

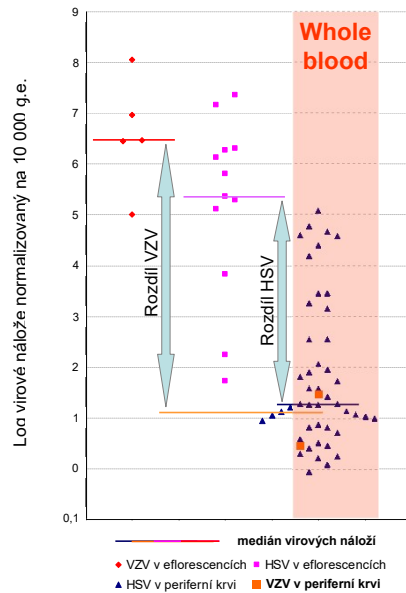
Varicella-Zoster Virus



Difference in materials VZV – chicken pox at D+0



Source for viral detection



January 2004 to August 2011

- HSV in **735** samples from 266 patients
- VZV in **587** samples from 148 patients
- 569 whole blood samples
- **43** swab samples from skin, mucousal tissue and aspirates from vesicles (from 15 p.)
- 227 samples from other biological materials (stool, urine, CSF, tissues)

HSV detected

- in **12** samples from efflorescence from **9** pts; median of quantity **439,465 NVC** (range 53-23,380,000 NVC)
- **6** pts in whole blood samples; median of viral load **18.7 NVC** (range 0.88 – 1,216,650 NVC)
- **4** in stool with median **53,662 NVC** (range 1,248-900,000 NVC)

VZV detected

- in **8** samples from skin eruption from **5** pts; median of quantity **2,856,124 NVC** (range 13,939-114,464,380 NVC)
- in **2** pts. In whole blood (quantity **30 and 2.9 NVC**)

Human herpesvirus 6

Previously two variants of HHV-6.
Recently 2 distinct viral species

HHV-6 A

Unknown
„Orphan virus“



HHV-6 B

Immunocompetent host

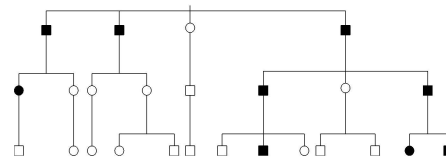
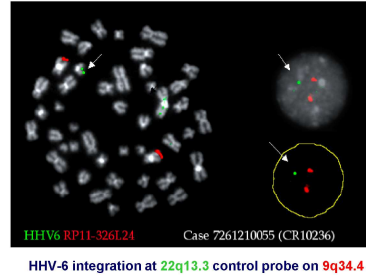
- **Sixth disease**
- **Febrile seizures**
- **Encephalitis**

Immunocompromised host

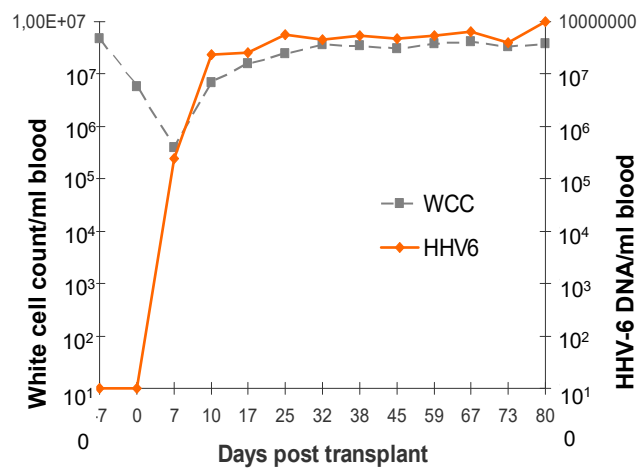
- **Encephalitis**
- **Myelosuppression**
- Hepatitis
- Pneumonitis
- Pericarditis
- **Delayed engraftment after HSCT**

Chromosomally integrated HHV-6 (CI-HHV-6)

- Viral DNA integrated into human chromosomes
 - Inherited from parents to child
 - Viral DNA is present in every body cell (e.g. hair roots, nails)
 - Ratio of viral DNA : human DNA = 1:1
- Described frequency in population between 0.2-2.9% (Tanaka-Taya 2004, Ward 2007)
- Both variants (A or B) integrates
- No clear observed reactivation CI-HHV-6 to active infection in vivo
- In vitro reactivations are doubtful

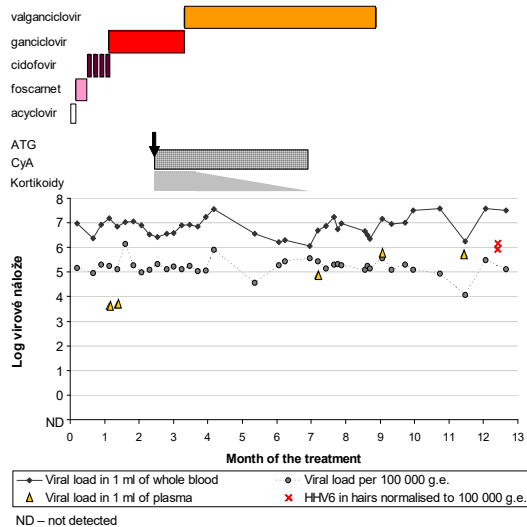


HHV6 DNA in blood after HSCT donor with Ci-HHV-6



Clark et al., JID 2006

Chromosomally integrated HHV-6 (Ci-HHV-6)



Patient with SAA

50 years

After start of the IS therapy – partial response only

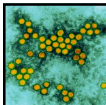
Dependent of thrombocyte infusion

G-CSF therapy

Died due to peracute sepsis of *St. aureus*.

Detection of high HHV-6 DNA quantity is NOT NECESSARY an active infection.

Detection in hair, or nails detects Ci-HHV-6 safely.



Picornaviridae - Coxsackieviruses

- Previously, there were Human coxsackievirus A1 to A24 and B1 to B6 – recently there are part of Enterovirus A, Enterovirus B and Enterovirus C group.
- Coxsackie virus is named after the town Coxsackie (NY, USA), where it was discovered by Gilbert Dalldorf (1948-1949).
- ss (+) RNA virus, délka genomu 7,2-8,5 kb
- Coxsackie A – muscle necrosis and paralysis, conjunctivitis
- Coxsackie B – less severe damage of the organs (susp. T1DM)
 - Both are able to cause meningitis, myocarditis and pericarditis
- Coxsackie A serotype 16 is cause of Hand, Foot and Mouth disease
- Encephalitida/myeloencephalitida

Hand Food & Mouth Disease

Hand, foot, and mouth disease, or HFMD, is a contagious illness that is caused by different viruses. Infants and children younger than 5 years old are more likely to get this disease. However, older children and adults can also get it. In the United States it is more common for people to get HFMD from spring to fall.

Symptoms
By Mayo Clinic Staff

Hand, foot, and mouth disease may cause all of the following signs and symptoms or just some of them. They include:

- Fever
- Sore throat
- Feeling of being unwell (malaise)
- Painful, red, blister-like lesions on the tongue, gums and inside of the cheeks
- A red rash, without itching but sometimes with blistering, on the palms, soles and sometimes the buttocks
- Irritability in infants and toddlers
- Loss of appetite






http://www.nhs.uk/tools/documents/visual_guides_v2/data/baby_rashes/images/slideshow_6.jpg

http://images.slideplayer.com/19/5871386/slides/slide_27.jpg




<http://healthosphere.com/wp-content/uploads/2012/02/Hand-Foot-and-Mouth-Disease-1.jpg>

<http://www.blogger.com/www.parenting.com/slides/2012/02/hand-foot-and-mouth.jpg>

Hand Food & Mouth Disease



Blisters In & Around The Mouth

Blisters On Palms of Hands

<http://healthosphere.com/wp-content/uploads/2012/02/Hand-Foot-and-Mouth-Disease1.jpg>



And now what?



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