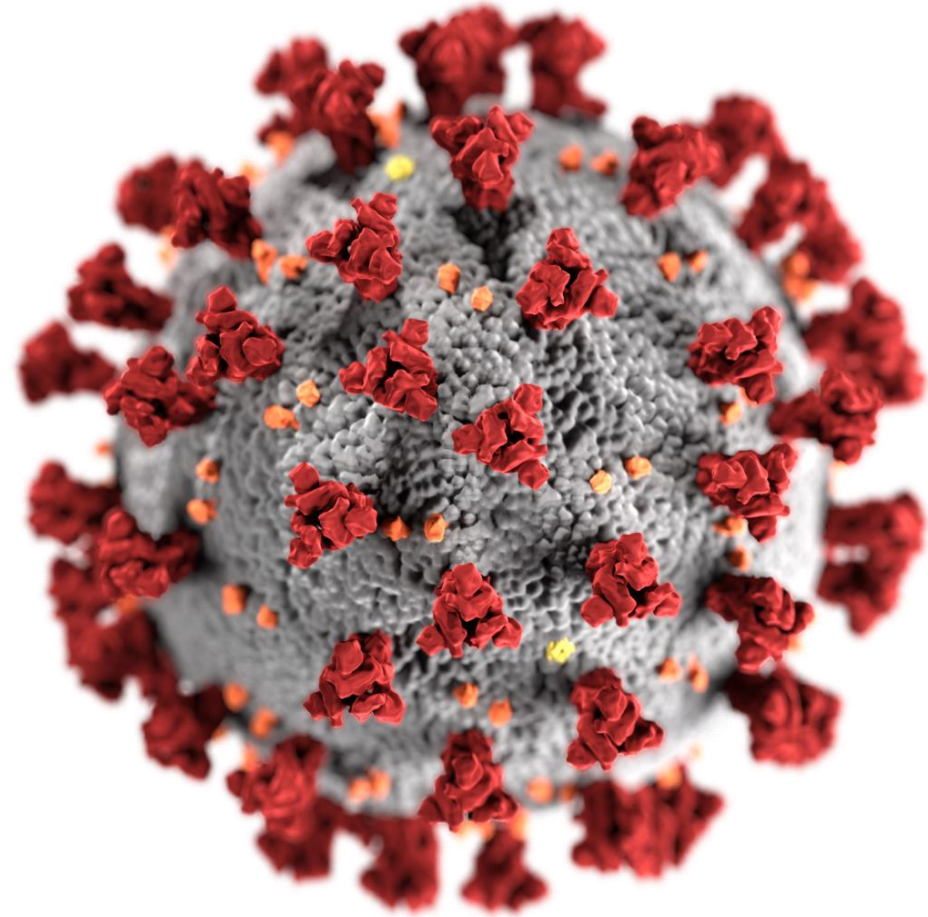


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# Virology

PharmDr. Jakub Treml, Ph.D.



# Types of microorganisms

Parasites:

Fungi:

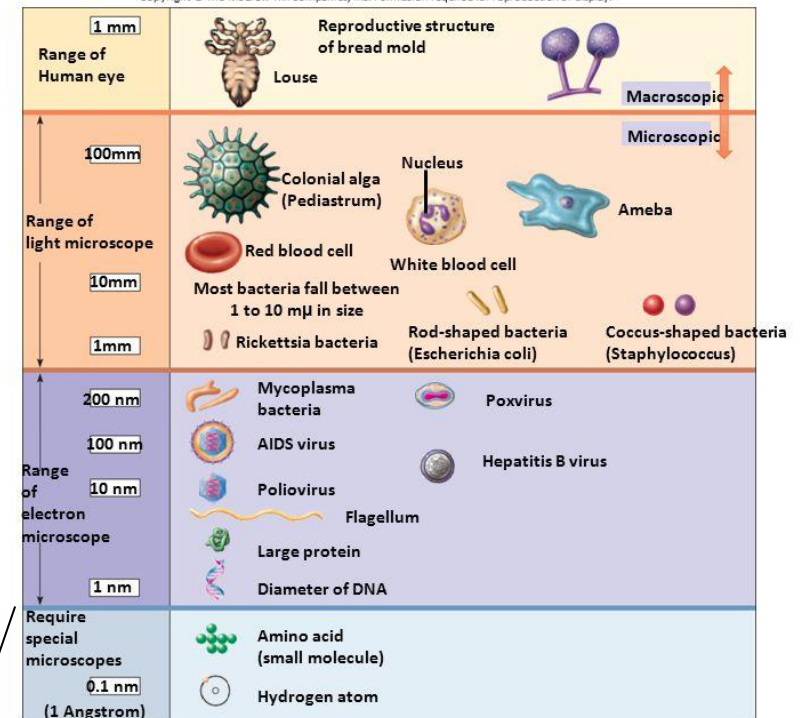
Bacteria:

**Viruses:**  
intro into virology;  
subcellular

Prions:

## Size Range of Microbes

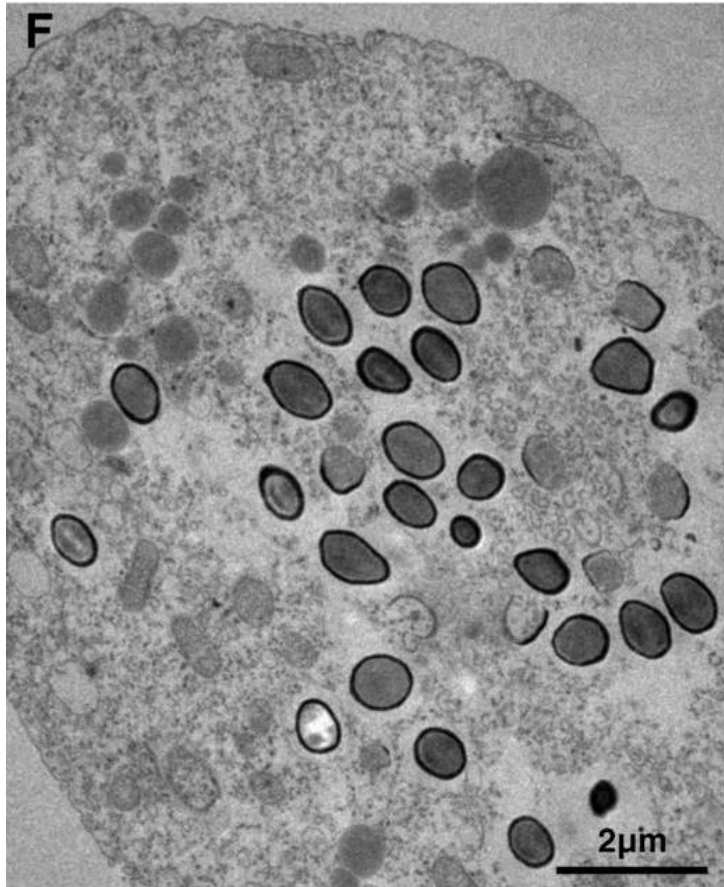
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# Definitions and concepts

- *virus* = lat. poison, venom
- *virion* = 1 viral particle [NA (RNA; DNA) + proteins]
- **noncellular** organisms (dependent on host proteosynthesis)
- intracellular parasites
- high **species** and organ **specificity** (infectious and oncogenic)
- size: 20 nm (parvoviruses) – largest: 300 nm (poxviruses)
- mimivirus (750 nm); 2013 pandoravirus, 2014 pithovirus (1500 nm)

# *Pandoravirus salinus*



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HOME > SCIENCE > VOL. 341, NO. 6143 > PANDORAVIRUSES: AMOEBIA VIRUSES WITH GENOMES UP TO 2.5 MB REACHING THAT OF PARASITIC EUKARYOTES

REPORT f t in g+ vk e

## Pandoraviruses: Amoeba Viruses with Genomes Up to 2.5 Mb Reaching That of Parasitic Eukaryotes

[NADÈGE PHILIPPE](#), [MATTHIEU LEGENDRE](#), [GABRIEL DOUTRE](#), [YOHANN COUTÉ](#), [OLIVIER POIROT](#), [MAGALI LESCOT](#), [DEFNE ARSLAN](#), [VIRGINIE SELTZER](#), [LIONEL BERTAU](#), [...] [CHANTAL ABERGEL](#)

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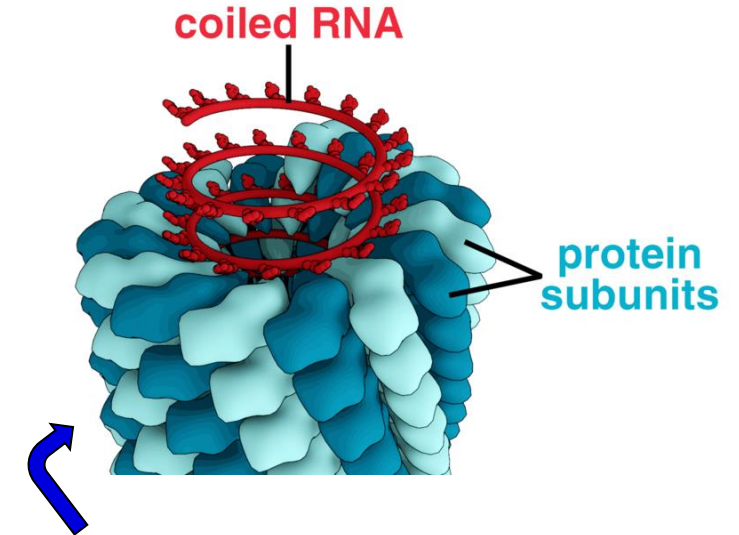
# Morphology

– *virion* = 1 viral particle (NA = **nukleoid**;  
proteins = **capsid**)

– capsid: subunits = capsomers; symmetry **spiral (helical)** or **cubic (icosaedral)**

– some viruses have **envelopes**:

- lipoprotein complex (double layer from cell + viral glycoproteins)
- inner M-protein (anchoring to nucleocapsid)
- influenza virus, HIV, SARS-CoV2



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# Where do viruses come from?

3 main theories:

- 1. „virus-first“** hypothesis: complex NA+protein before cells (or in the same time; RNA world)
- 2. regressive** hypothesis: cells parasitizing on bigger cc. (loss of unnecessary parts) – like chlamydia e.g. (poxviruses)
- 3. cellular origin (escape** hypothesis): parts of NA „escaping“ – plasmids, mobile genetic elements, etc.

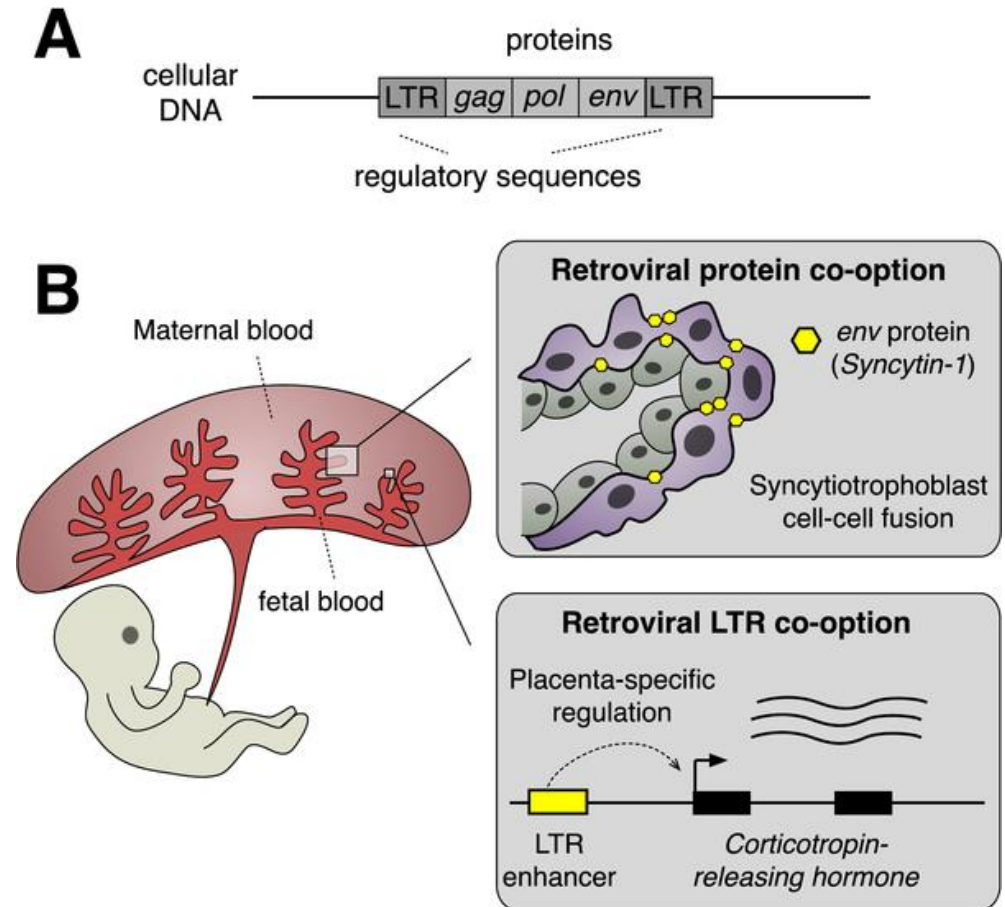
# Reproduction – viral cycle

1. **adsorption** (receptor)
2. **penetration** (fusion of membranes - enveloped; endocytosis – non-enveloped)
3. **uncoating + replication** of NA + viral **proteosynthesis** (provirus; cca 8 % of human genom consisting of endogenous retroviruses)
4. **maturation** (autoagregation of capsid, cell lysis; budding – HIV; enveloped viruses get the envelope and are released)



# Syncytin-1 (gene ERVW-1)

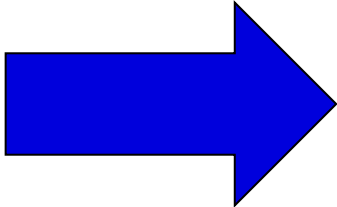
- endogenous retroviral element
- integrated 25 mil. years ago
- humans, primates



zdroj: <https://doi.org/10.1371/journal.pbio.3000028>



# Classification of viruses - criterion

- |                              |  |   |
|------------------------------|--|---|
| 1. nucleic acid              |  | 1. DNA × RNA  |
| 2. symmetry of capsid        |  | 2. helical × icosaedric   |
| 3. enveloped                 |  | 3. enveloped × non-env.   |
| 4. size                      |  | 4. small × large  |
| 5. infection (+ specificity) |  | 5. respiratory × neurotropic ×<br>arboviruses × intestinal,<br>etc. |

# International Committee on Taxonomy of Viruses (ICTV)

**Realm:** *Riboviria* —————

highest taxon is not kingdom (*Plantae*)

**Kingdom:** *Orthornavirae*

**Phylum:** *Pisuviricota*

**Class:** *Pisoniviricetes*

**Order:** *Nidovirales*

**Family:** *Coronaviridae*

not typical binomical nomenclature:  
*[disease]virus*

**Genus:** *Betacoronavirus*

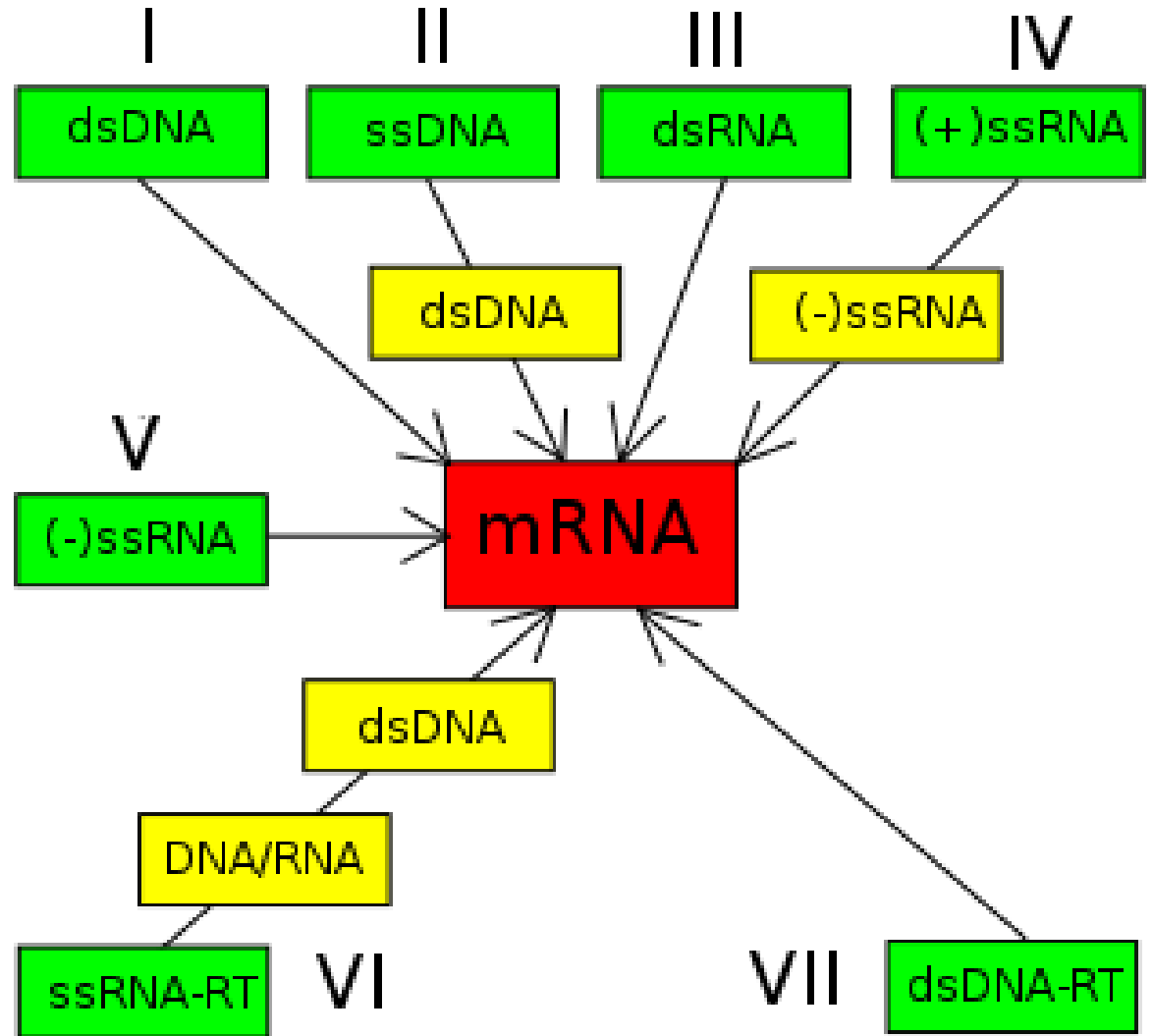
10 **Species:** *Severe acute respiratory syndrome-related coronavirus*

# Baltimore classification

David Baltimore (1971) –  
according to genetic flow –  
originally 6 groups – easier  
than ICTV

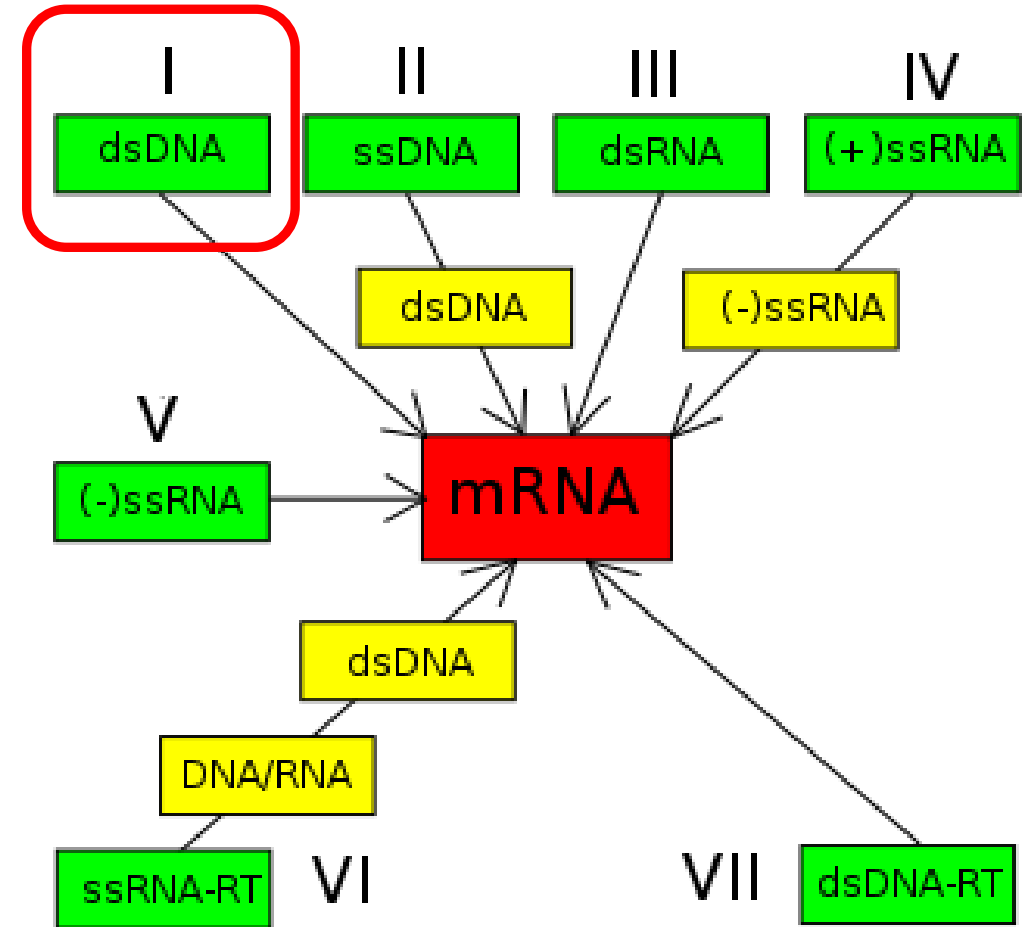
mRNA = template

5' → 3' (+)string



# Class I – dsDNA viruses

- double stranded DNA – to RNA – replication from DNA
- **enveloped**: Herpesviridae, Poxviridae
- **non-enveloped**: Adenoviridae, Papillomaviridae



# Herpesviruses

- capsid with **lipid membrane** ⇒ **sensitive** to drought, acid pH, nonpolar solvents and detergents ⇒ transmission via **direct contact**
- mainly cause of **latent infections** of animals and humans (virus present in body, but not replicating..)

# Herpes simplex virus (HSV)



- two types **HSV-1** (via saliva, orophar. infections) and **HSV-2** (STD, mother → child)
- latent phase in ganglia of dorsal roots
- infections: *herpes labialis*, *genitalis*; life-threatening encefalitis, non-treated inf. of eyes may lead to loss of sight (dangerous for children and immunosuppressed)

## Other herpesviruses

- **varicella zoster virus (VZV):** *chickenpox*

(hematogenous spread, blisters, higher t.; reactivation: *shingles*);

complications if first inf. as adult – incub. time 2w

- **cytomegalovirus (CMV):** severe *congenital infections* (blindness, microcephalia); fever and lymphadenitis; *infectious mononucleosis syndrome* (like IM, lymphadenopathy, atyp. lymphocytes, norm. LDH)





## Other herpesviruses

- **Epstein-Barr virus** (EBV, HHV 4): *inf. mononucleosis* (kissing disease, 15 – 20 yrs. mostly; sore throat, swollen tonsils, fever, swollen liver and spleen (inf. of mucosa and then B-lymph.); KI aminoPNC - rash)
- **HHV 6** (febrilia +/- rash in children (even cramps) = *sixth disease*)

# Poxviruses

- enveloped, but **very resistant** to disinf.
- cause of **variola** (*smallpox*): eradicated since 1979 (WHO) – droplets – fever, skin lesions and blisters, full of pus – deformity, blindness, death



CC: [Otis Historical Archives Nat'l Museum of Health & Medicine](#)



prof. MUDr. Karel Raška, DrSc.  
(1909 - 1987)

In 1967 started eradication  
program in WHO

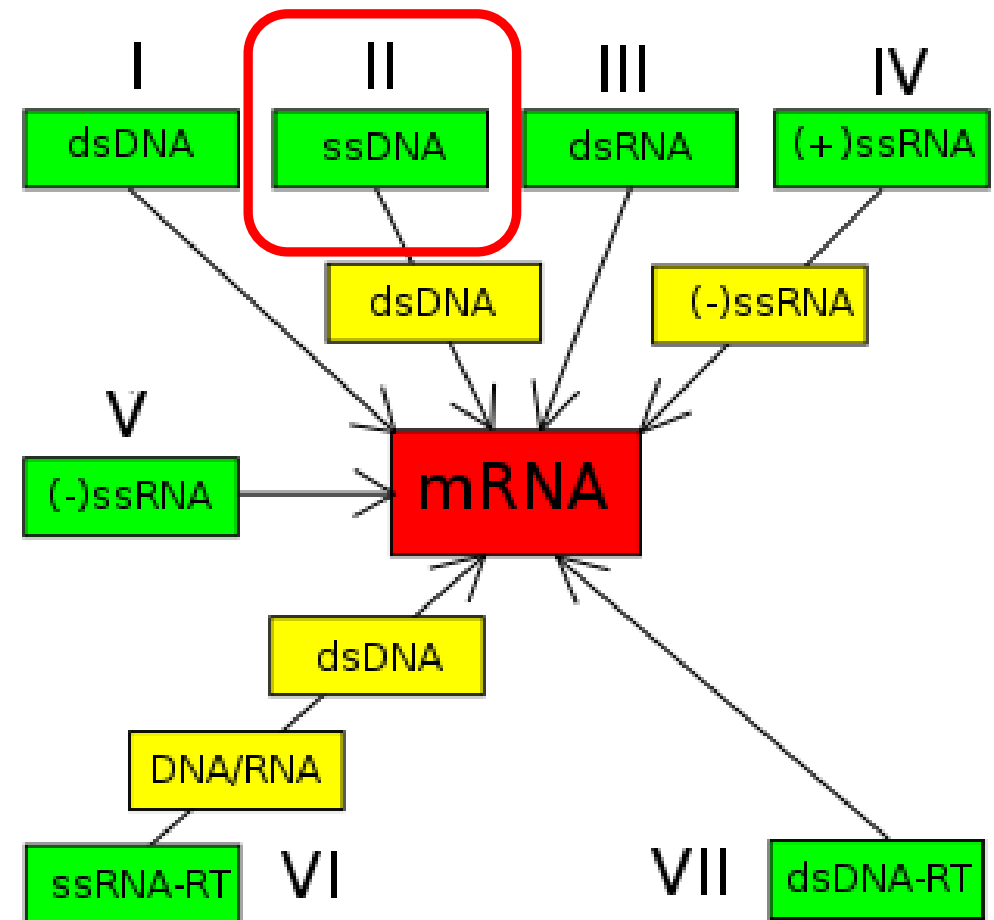
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# Human papillomavirus (HPV)

- main cause of **cervical cancer** – vaccination
- STD (not always prevented with condom)
- several types (HPV 16 and 18, high risk – lead to cancer; 80 – 90% of women spontaneous elimination, thanks to immunity; 20% cancer during 5 years) – in case of screening, 1 % leads to ca.
- other types lead to non-oncogenous *condylomata accuminata*

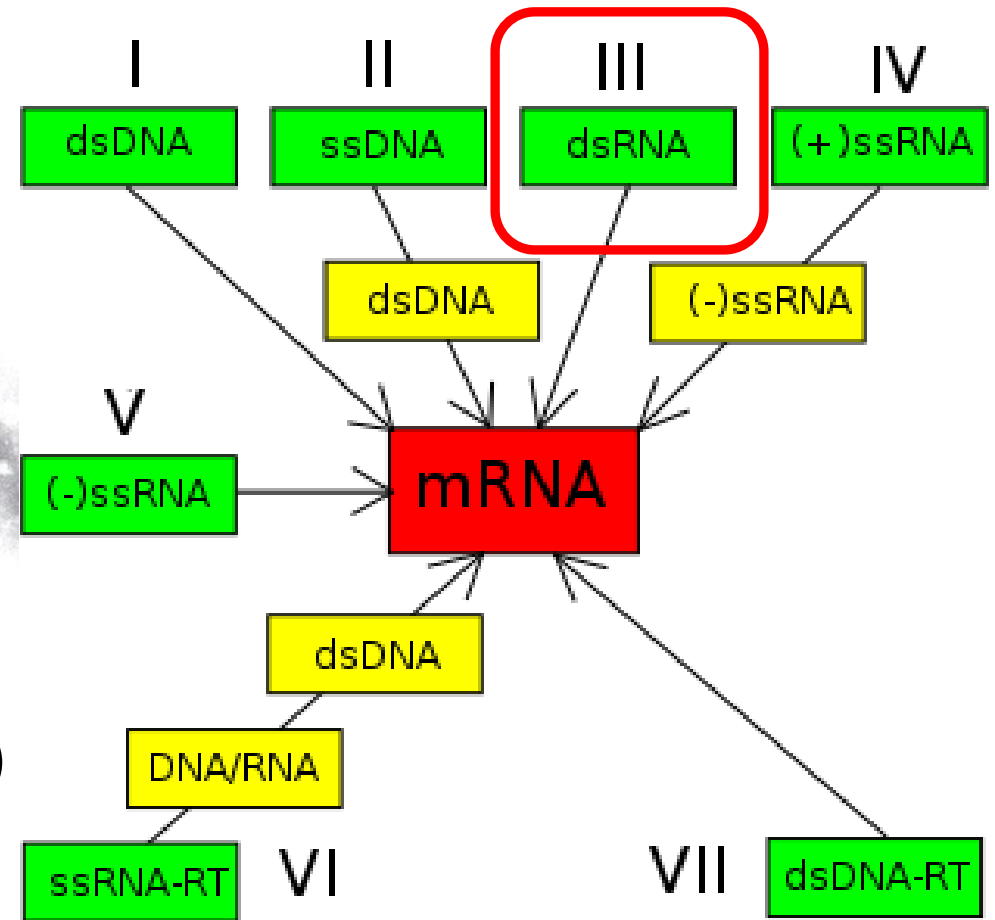
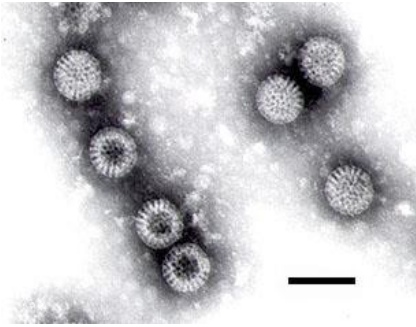
## Class II – ssDNA viruses

- Parvoviridae: non-enveloped, small
- most important: **parvovirus B19**
- childhood rash with fever (face, body) – *fifth disease*



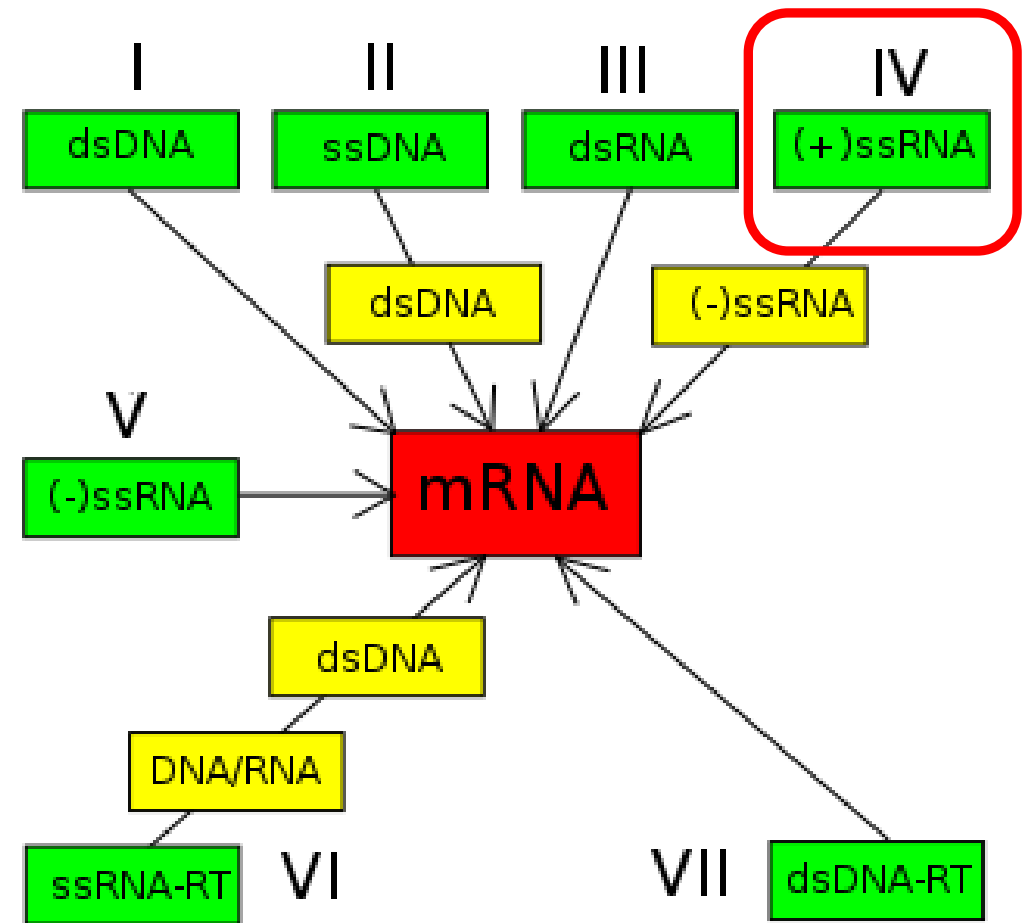
## Class III – dsRNA viruses

- Reoviridae: non-enveloped cubic
- important: **rotavirus**
- causes *enteritis*
- fecal-oral transmission –  
dehydration (risc: 4 month – 3 yrs)
  - 2 deaths/yr
- incub. time: 1 – 3 days
- voluntary vaccination!



## Class IV – (+)ssRNA viruses

- divided into **enveloped** (families Flaviviridae, Coronaviridae and Matonaviridae) and **non-enveloped** (Picornaviridae)



# Flaviviruses

- small (40 – 50 nm) – repl. in CP, budding through vacuolar memb.
- cubic capsid and **lipid envelope** with glycoprotein protusions ⇒ **sensitive** to nonpolar solvents and temp. above 56 °C
- **arboviruses** – transmitted by arthropods (vectors), reservoir in vertebrates – natural focus
- e.g.: tick-borne encephalitis complex virus, dengue virus, yellow fever virus, hepatitis C virus and Zika virus



# Tick-borne encephalitis complex virus

- viruses are antigenically related – Europe, Asia and No. Am.
- reservoir: **wild mammals**; vectors: different species of **ticks**
- *Central European tick-borne encephalitis* (east. France - Ural):  
TBE – tick-borne encefalitis – *Ixodes ricinus* – salivary glands; IT:  
7 – 14 days; **1<sup>st</sup> phase „flu-like“**: viremia, headache, fever – then  
2 – 7 days **apparent healing** (afebrilia) – then **2<sup>nd</sup> phase**  
**meningeal symptoms** (somnolence, limb paresis, vomiting, sleep disorders)

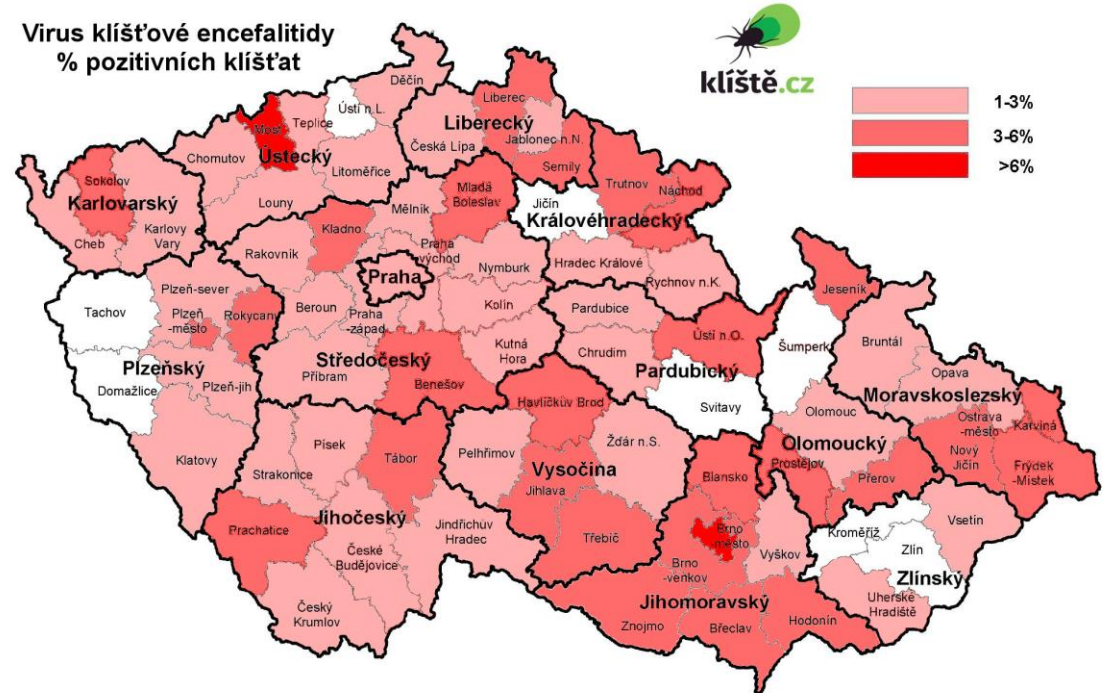
# Central European tick-borne encephalitis

– vaccination rate in CZ (23%) – y. 2019 total 774 cases (7,3 cases/100 000 inh.)

Graf 2: Klíšťová encefalitida v ČR v roce 2019 – podle kraje hlášení, incidence na 100 000 obyvatel



Incidence na 100 000 obyvatel



# Central European tick-borne encephalitis

- during 2<sup>nd</sup> phase if spinal cord is affected then even death
- diagnosis: antibodies in serum (early IgM)
- examination of CSF (aseptic inflammation; leu 100 – 200/ $\mu$ l)
- th.: symptomatic, sleep mode, rehabilitation (in severe cases takes months) – 10% of patients have persistent paresis and impaired concentration

# Dengue fever virus

- cause of **dengue** fever („breakbone fever“) – transmitted by mosquito (*Aedes aegypti*) – tropical Asia, Africa and Latin America
  - span. „dengue“ = cautious (patient walking?)
- high fever, myalgia and arthralgia – rash; hemorrhagic form (w/o treatment 1 - 5% of patients die; most recover)
- 2016: 84 cases in CZ (from travels); symptomatic treatment

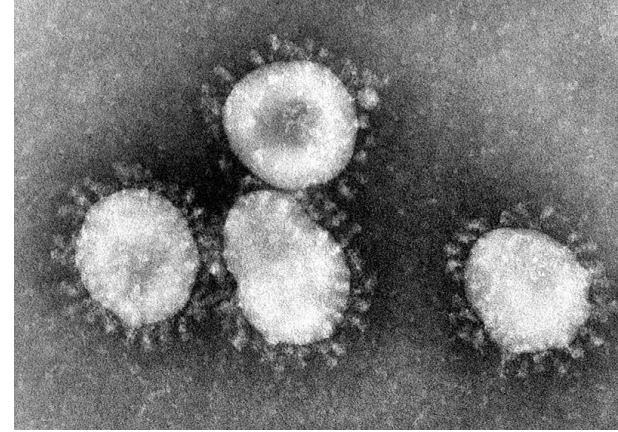
# Yellow fever virus

- cause of **hemorrhagic fever** - mosquito (*Aedes aegypti*) – tropical Asia, Africa and Latin America
- high fever, shivers, pains, during fever bradykardia (Faget's sign), redness (1<sup>st</sup> stadium - red)
- 2<sup>nd</sup> std. (yellow): bleeding from mucosa, vomito negro, liver damage – jaundice; lethality: 25 – 50 %
- vaccination; 2018: 1<sup>st</sup> case in CZ

# Hepatitis C virus (HCV)

- virus is very **variabile** (mutations – no vaccination)
- transm. **parenteral** (blood, i.v. drug addiction, hemodialysis, sex, from mother to child)
- IT 50 days – acute infection (asympto, jaundice; 15% spontaneous elimination; 85 – 90% lead to chronic) – may show as hepatocel. carcinoma after several years
- diagnostics: serology (anti-HCV); there is treatment

# Coronaviruses



- coronaviruses were object of interest of eccentric scientists...
- enveloped (glycoprotein spikes) (+)ssRNA viruses – common cold, inf. of URT – droplets (solar corona)
- **SARS-CoV**: 2003-2004 epidemics (8000 cases; 774 deaths)
- **MERS-CoV**: 2012; camels, 136 patients, 58 deaths
- **SARS-CoV-2**: Covid-19 (fever, cough, stuffiness, aches of muscles)

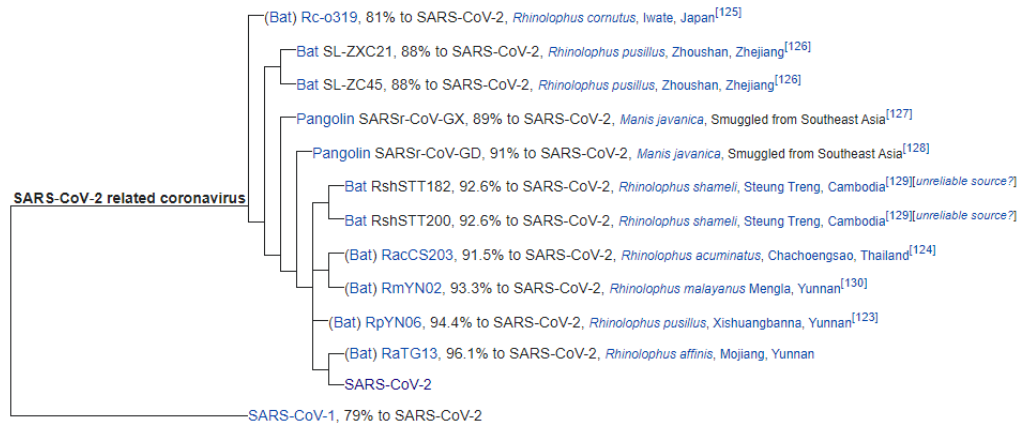


# SARS-CoV-2



## Phylogenetic tree

A phylogenetic tree based on whole-genome sequences of SARS-CoV-2 and related coronaviruses is:<sup>[123][124]</sup>



BBC

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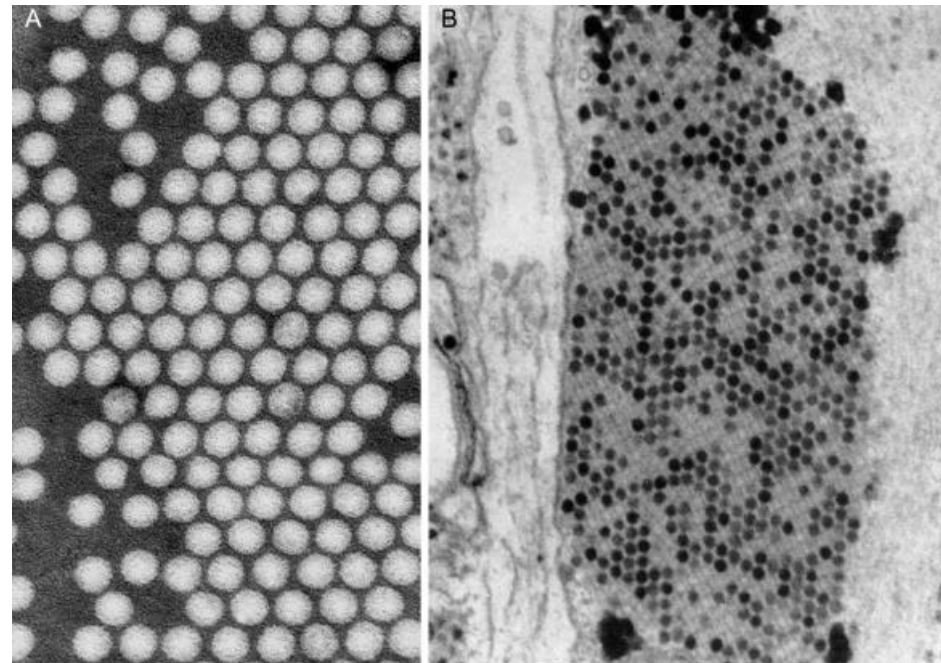
## Matonaviridae

- ***Rubivirus***: cause of rubella (lat. *rubeola*, third disease)
- droplets; it: 17 days – rash, swelled lymph nodes
- vaccination MMR; 2014 – CZ: 1 case
- inf. during first 4 months of pregnancy – abortion, defects (Gregg syn. – deafness, heart defects)



# Picornaviruses

- non-enveloped (+)ssRNA – small (30 nm) – icosahedral capsid
- poliovirus, insensitivity to ether, coxsackievirus, orphan virus, rhinovirus, and ribonucleic acid
- prefix *pico*  $10^{-12}$
- enteroviruses, aphtoviruses
- rinoviruses (80% common cold)



# Enteroviruses

- fecal-oral transmission; often summer and preschool children
- multiplication in nasopharynx to intestines – lymph nodes – prim. viremia – to organs – multiplication – secondary viremia
- examples: **poliovirus** (poliomyelitis – neurotropism; 90% asymptp, other cases fever, body pains – later weakness for whole life; eradicated – 1961 Cs.; Afg. 53/2020); **coxackievirus** A16 (hand, foot, mouth disease – fever, red spots)



# Enteroviruses

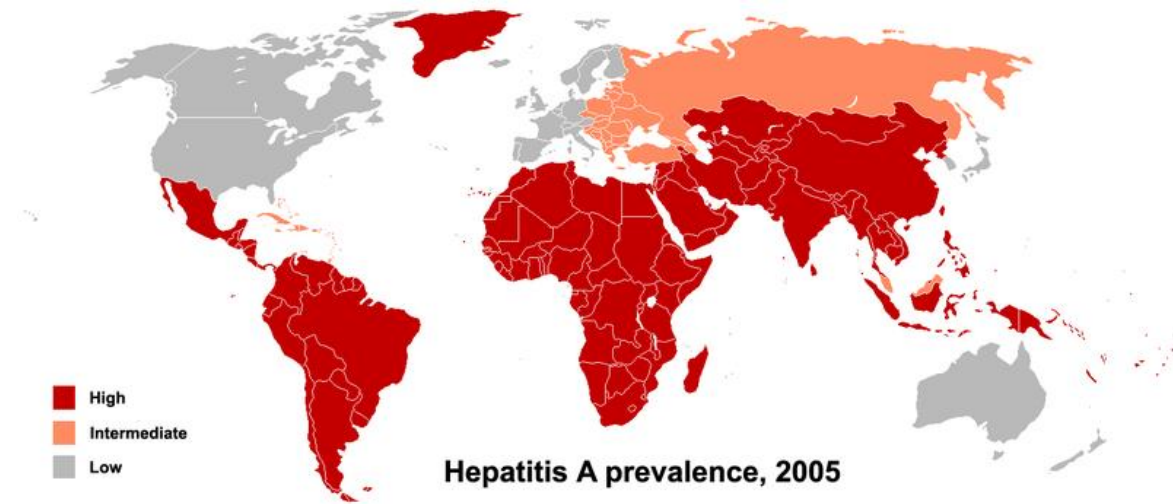


CC: MidgleyDJ at en.wikipedia



KlatschmohnAcker

# Enteroviruses

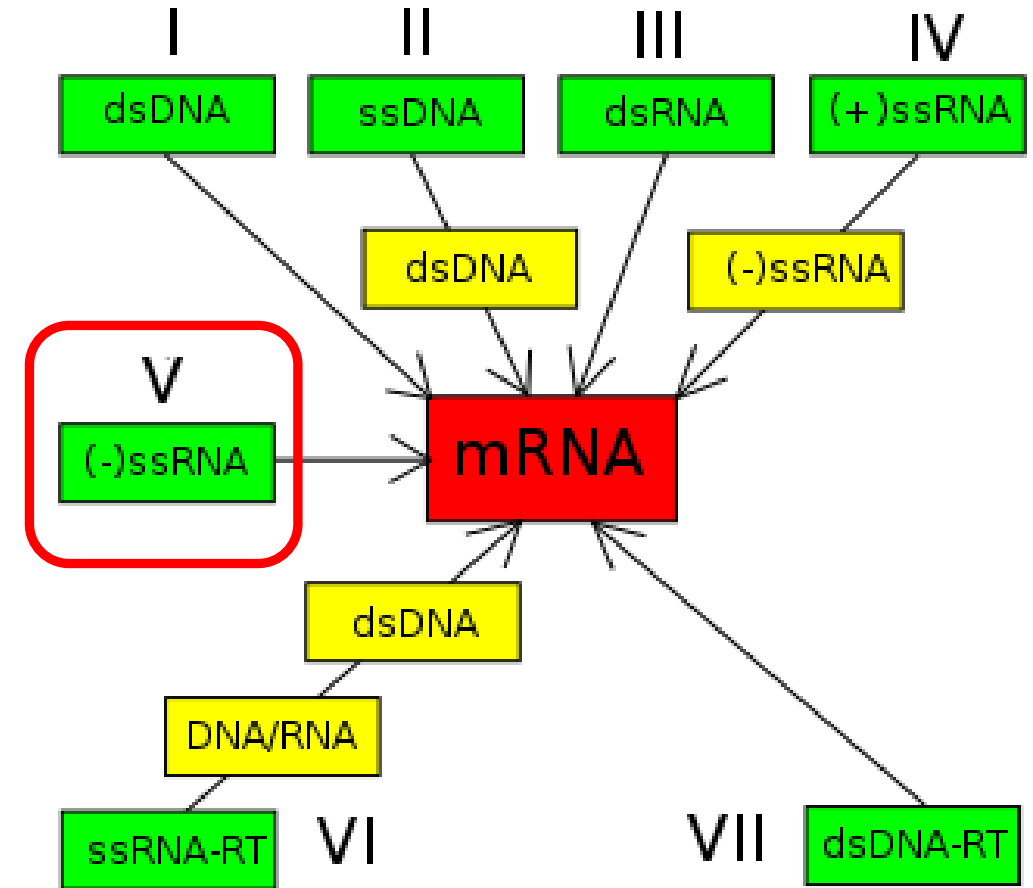


CC: PhilippN

- **hepatitis A virus (HAV)** – „disease of dirty hands“, contaminated food, very resistant
- it: 15 – 48 days – preicteric stage (fatigue, dyspepsia) – icteric stage (antibodies, elevation of bilirubin, ALT, AST)
- symptomatic treatment, rest, restriction of fats, no alcohol

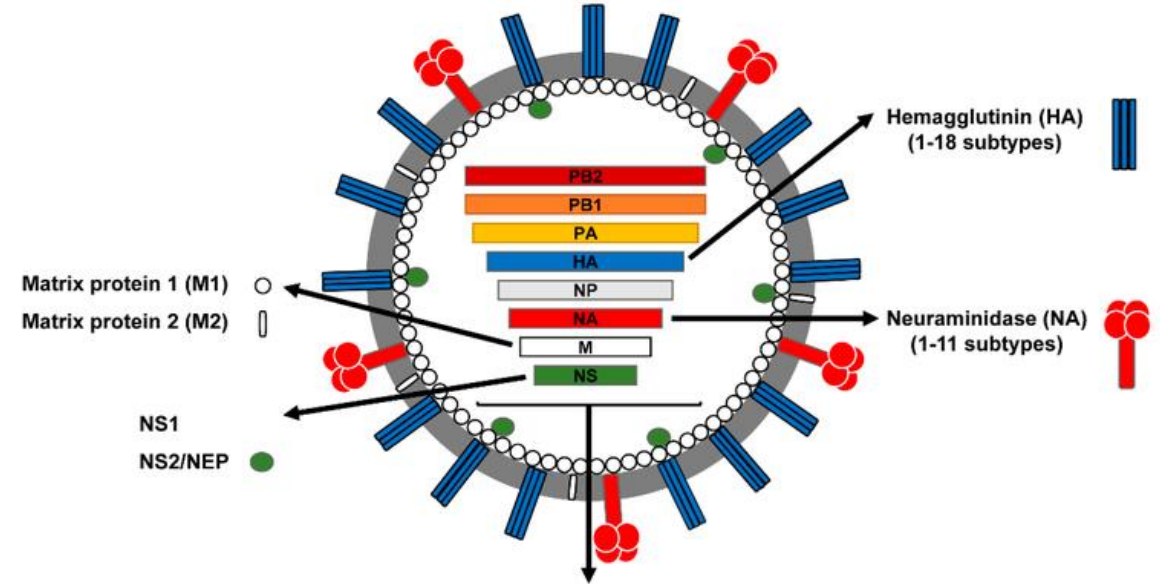
# Class V – (-)ssRNA viruses

- **enveloped** viruses
- orthomyxoviruses
- paramyxoviruses
- rhabdoviruses



# Orthomyxoviruses

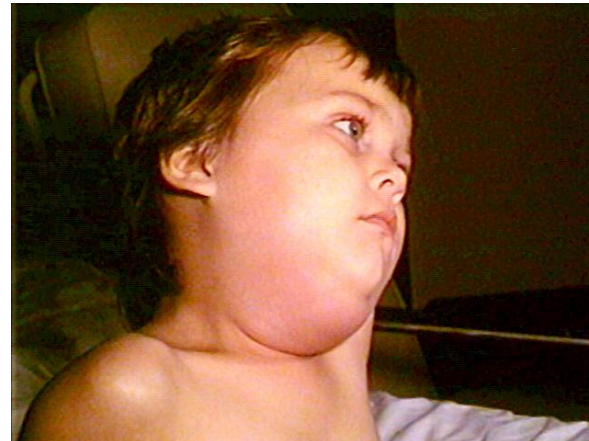
- gr. *mýxa* = slime, phlegma; **flu**
- RNA virus, replication in nucleus;
- genetic **drift** (mutation of surface proteins, no proofreading), **shift** (only A, combination of strains)
- most important **influenzavirus A** (human, pig, bird, etc.) – classification H and N (H1N1 – Spanish 1918, swine 2009)
- **influenzavirus B** (mainly humans, less common than A)





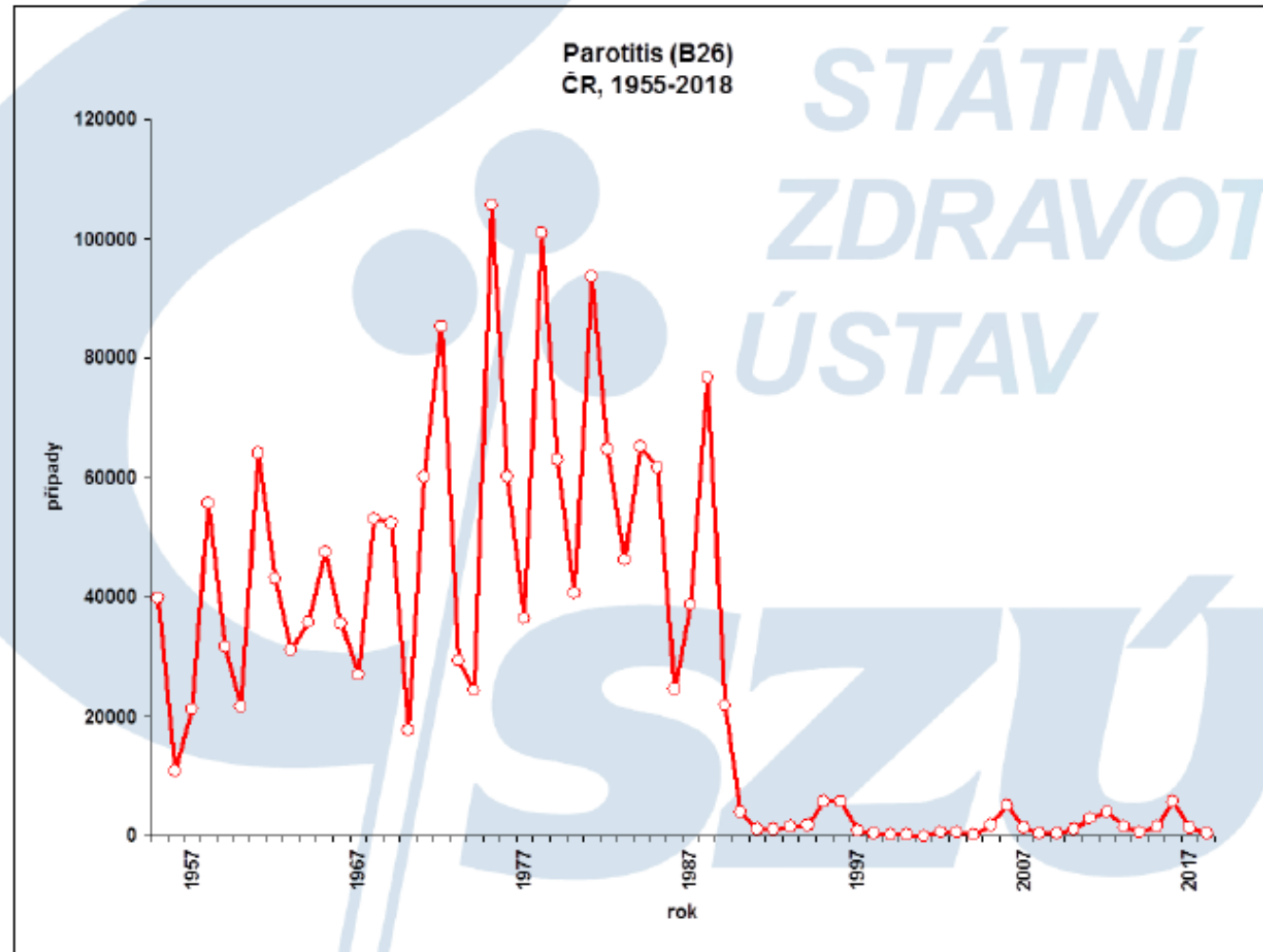
# Paramyxoviruses

- **parainfluenzavirus**: droplets, it 2-3 days; 40% of resp. inf. preschoolers – fever, running nose, pharyngitis – no vacc.
- **mumps virus** (parotitis epidemica): droplets; nasopharynx – lymph nodes – swelling of the parotid glands (70% both sides) + high temp. – vaccination MMR



# Paramyxoviruses

– mumps virus:



# Paramyxoviruses

- ***Morbillivirus***: cause of measles (lat. morbilli)
- droplets; it: 10 – 12 days; high temp., cough, Koplik's spots (white lesions in mouth); exanthema (from head to face, body and limbs; elevated, dark red)
- vacc. MMR; 2,1/100 000 (CZ, 2014) – infectivity 100%, preschool children, spring

# Paramyxoviruses



# Paramyxoviruses

- **human respiratory syncytial virus (RSV)**: cause of respiratory inf. of children – during multip. there are polynucleated *syncytia*
- droplets; it: 2 - 8 days; fever, edema, hypersecretion, even obstruction of airways; complication: otitis media
- no vacc., inf. often mild, th. in severe cases (ribavirin, palivizumab for newborns)

# Rhabdoviruses

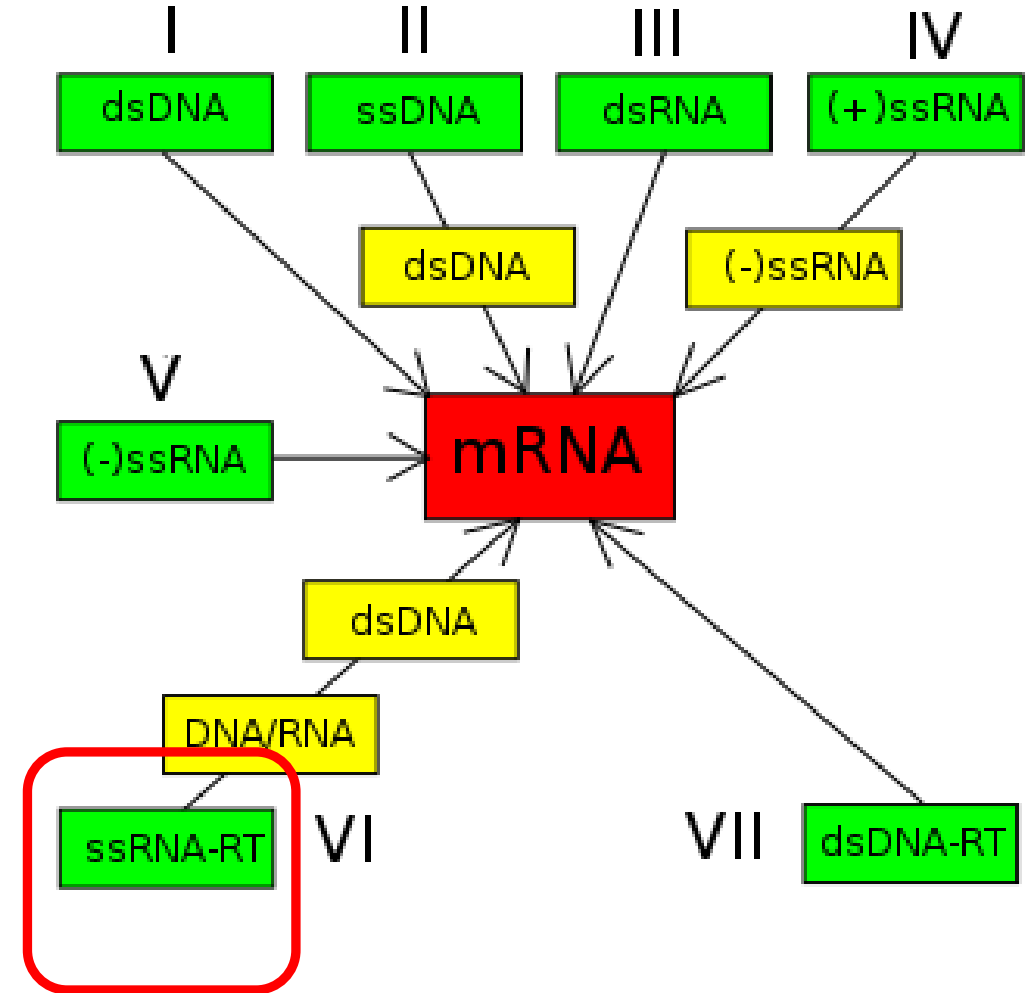
- **lyssavirus** (rabies, lyssa): projectile shape – akute encephalitis, when symptoms appear 100% mortality
- among wild animals (in Europe foxes) – CZ since 2002 rabies-free (import from PL or SK, or after a bat bite)
- transmission by biting by a sick animal (saliva) – it 3 – 8 weeks – neurotropic virus (Negri bodies) – via nerves into CNS – fatigue, disorientation, unrest, headaches – anorexia, salivation

# Rhabdoviruses

- followed by muscleaches (swallowing) – hydrophobia (look on water) – anxiety, nervousness, cramps – death (heart failure)
- most important is to avoid unknown animals – **prophylaxis:**
  - preexposure** (preventive, vet doctors - 3 doses 0 – 7 – 28 days)
  - or **postexposure** (ASAP!; 4 doses: 0 – 3 – 7 – 14 and 30 days) – i.m. or s.c. application (not i.v.) – in case of unknown animal or positive samples after inspection

# Class VI – (+)ssRNA-RT viruses

- **enveloped – retroviruses** (RT = reverse transcriptase)
- NA into (-)ssDNA – hybrid of RNA-DNA – cDNA – provirus
- deltaretrovirus: HTLV-1
- lentivirus: HIV





## genus *Deltaretrovirus*

- HTLV-1 (**human T-lymphotrophic virus**): discovered in 1980 (R. Gallo et al.)
- transm.: sexual, blood, breastfe. – inf. cca 5 – 10 mil. worldwide
- disease: adult T-cell leukemia/lymphoma (**ATL**) - cca 4 – 5% of infected get the disease – similar to non-Hodgkin lymphoma – most patients die

## genus *Lentivirus*

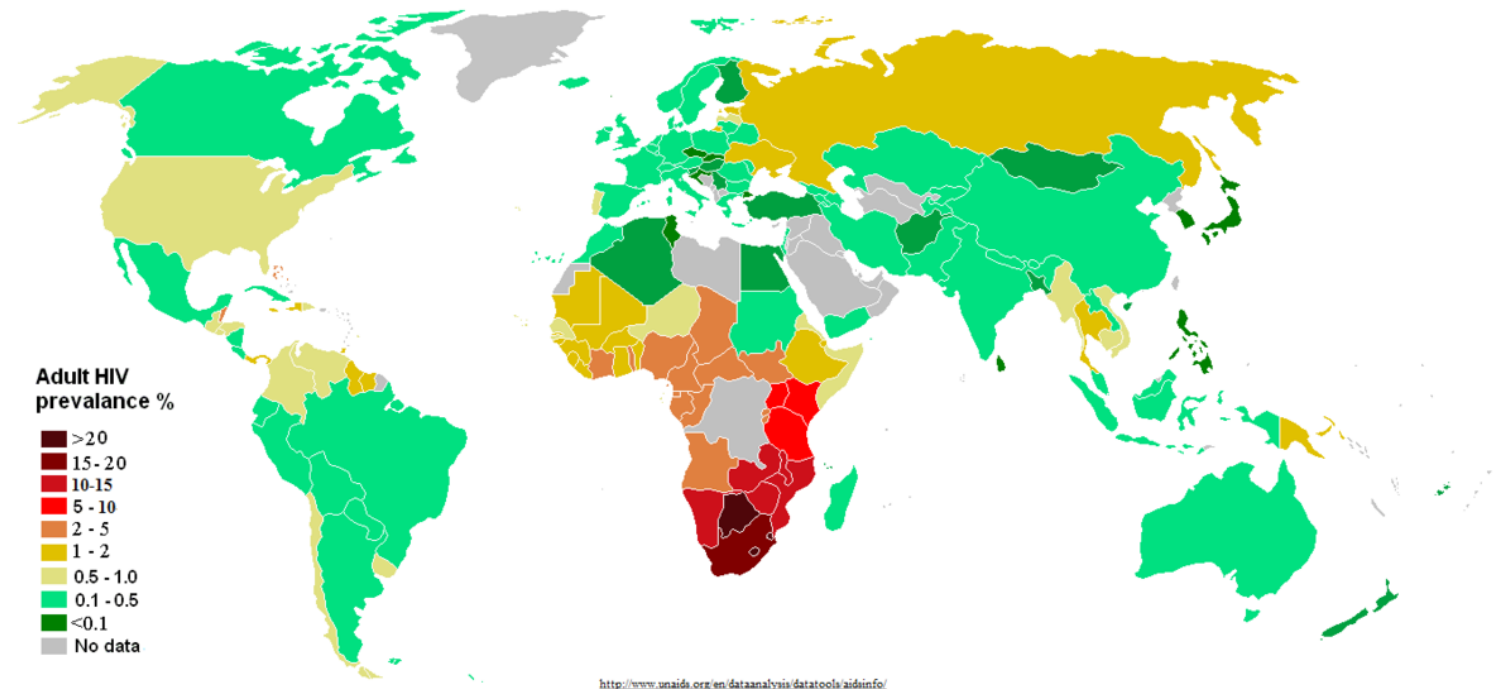
- HIV (**human immunodeficiency virus**): attacks mainly CD4+ helper T-lymphocytes -> failure of immunity (at  $<200 \text{ bb/mm}^3$  AIDS development); HIV-1 (centr. Africa – worldwide)
- transm.: sexual, blood and derivatives, from mother to child
- it: 2 – 6 weeks, without treatment death in 10 yrs, with AIDS in 2 y.
  - 1. HIV primoinfection** (replication, decline of CD4+Th; symptoms like IM or flu)

# HIV virus

- 2. asymptomatic st.:** without subj. prob., swol. nodes., 18m – 15y
- 3. early symptom. st.:** fever, opportunistic infections (candidosis oropharyng. vulvovag., recurr. herpes zoster), skin damage (psoriasis, condylomata, etc.)
- 4. late sympt.:** pneumocyst. pneumonia, toxoplasmic encephalitis, cytomegaloviral inf., tumors (Kaposi's sarc.) - death

# HIV

- diagnostics: antib., 3 months after inf. (ELISA); PCR; CD4+ lymphocyte count (norm 1000/ $\mu$ l)



# HIV

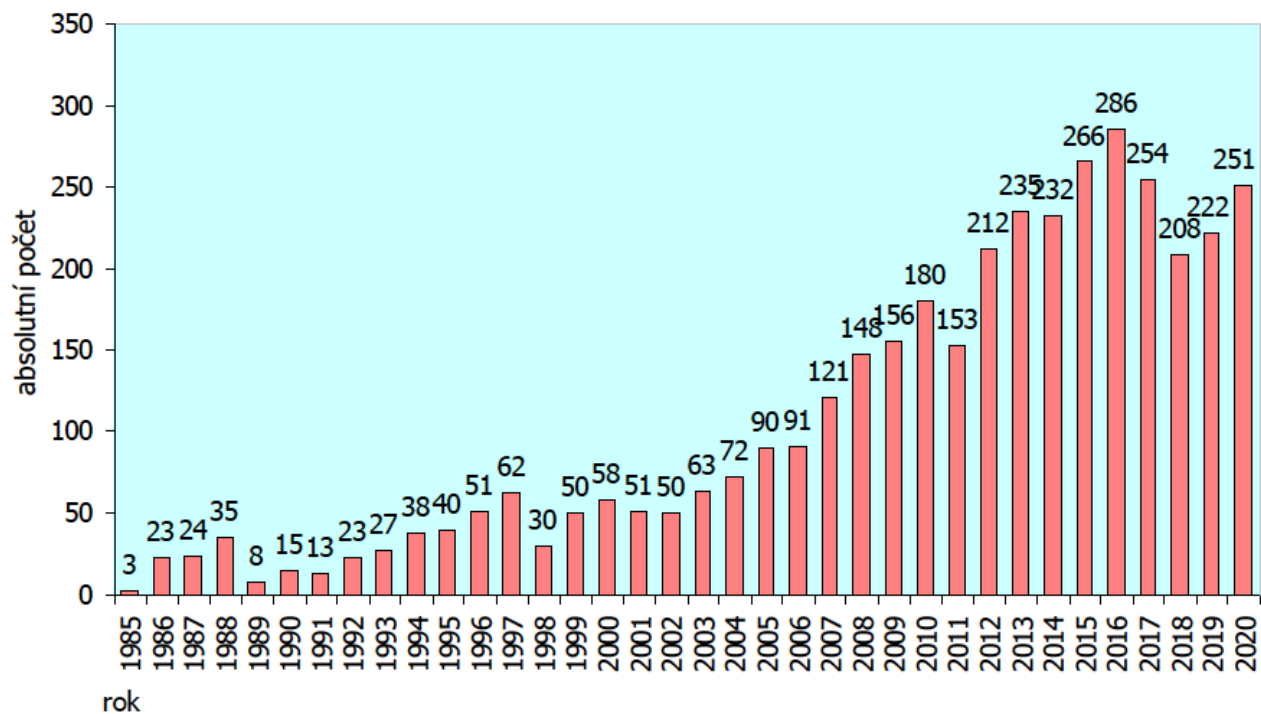
## NOVÉ PŘÍPADY INFEKCE HIV V ČESKÉ REPUBLICE

V JEDNOTLIVÝCH LETECH

(občané ČR a cizinci s dlouhodobým pobytem)

Absolutní údaje ke dni

31.12.2020



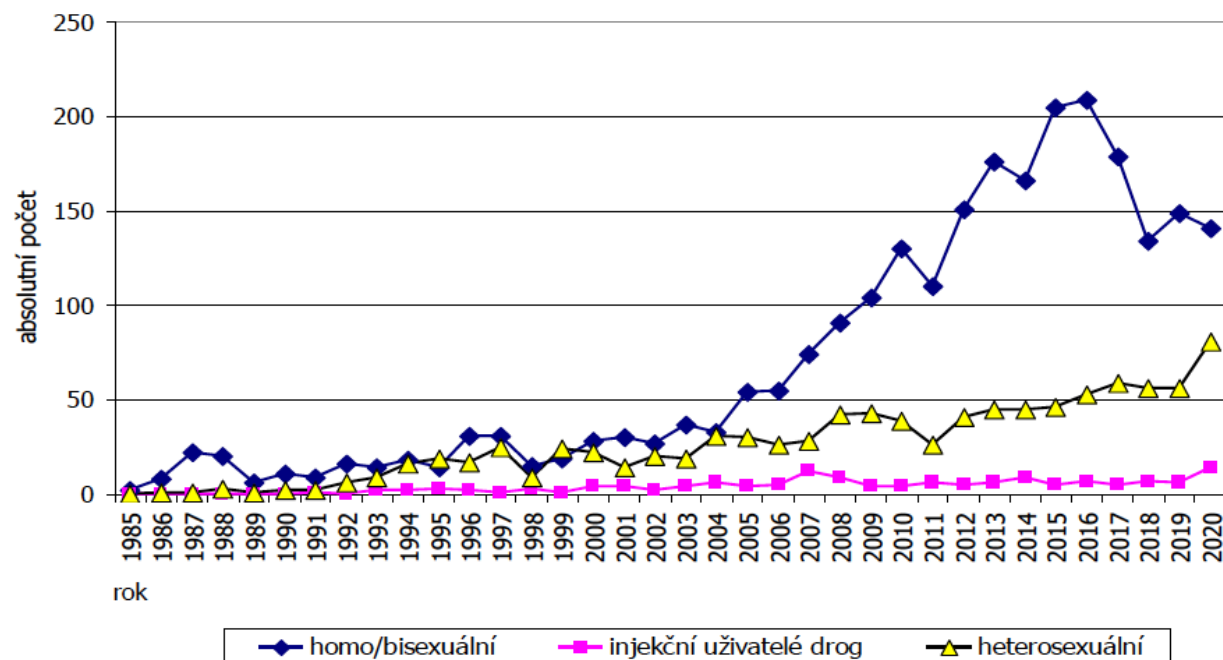
## VYBRANÉ KATEGORIE PŘENOSU HIV V ČESKÉ REPUBLICE

podle roku diagnózy

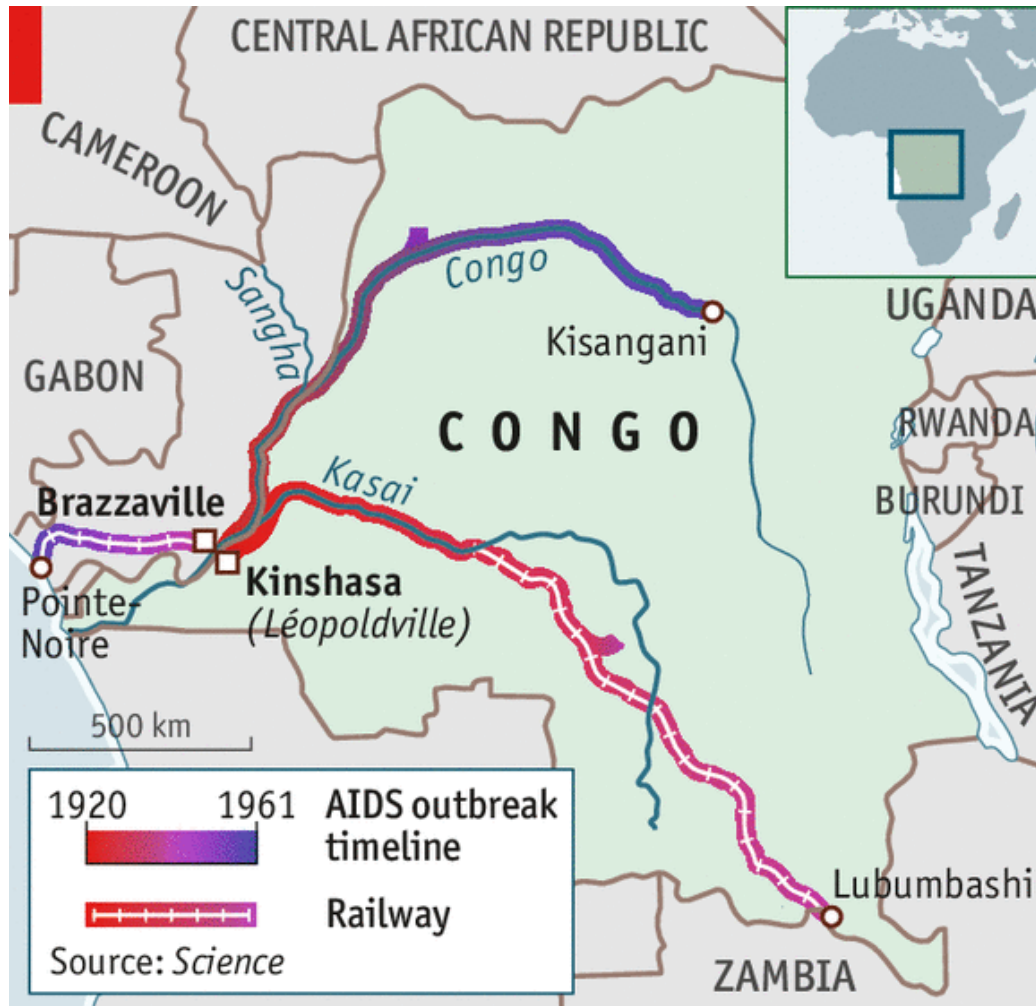
(občané ČR a cizinci s dlouhodobým pobytem)

Absolutní údaje ke dni

31.12.2020



# Origin of HIV?

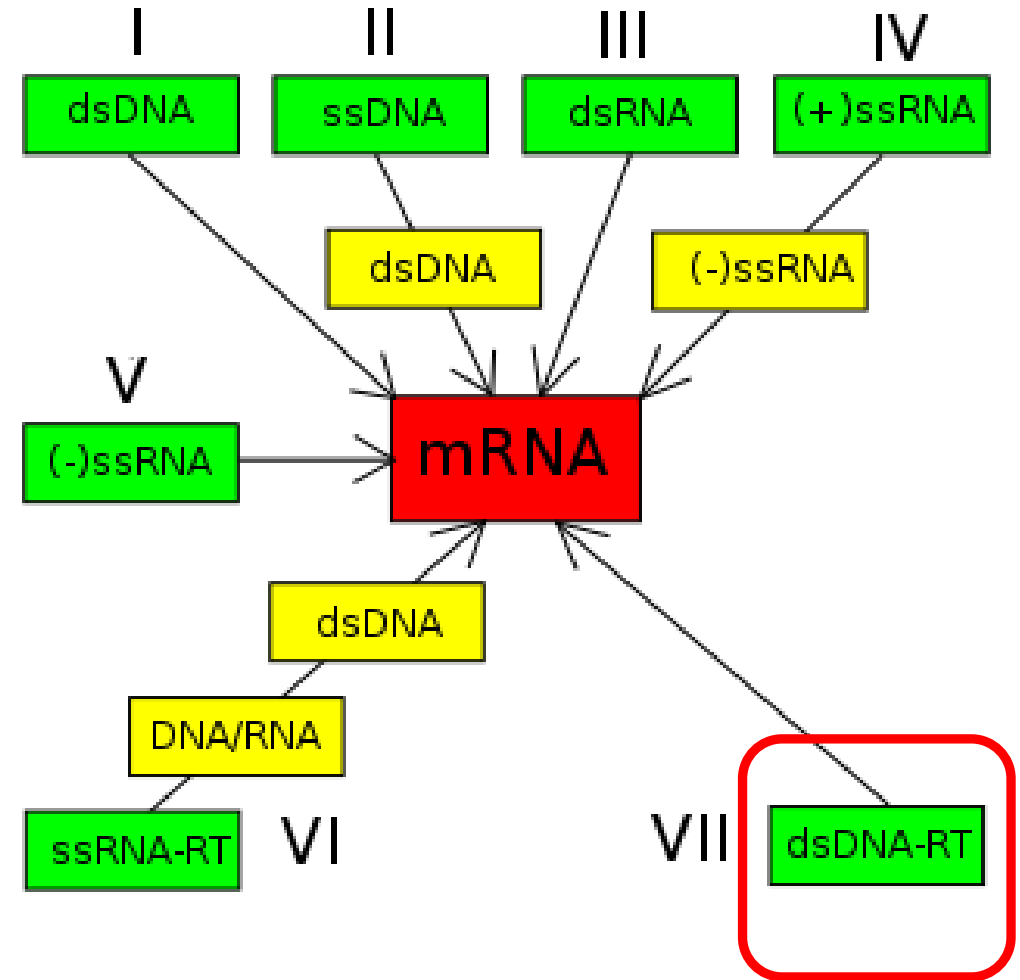


1. SIV: chimpanzee -> hunter (S Cameroon) – begin. 20th cent.
2. prostitution
3. 1959: Congolese patient
4. '70: western hemisphere
5. '81-'84 GRID -> AIDS

<https://www.economist.com/science-and-technology/2014/10/02/journey-into-night>

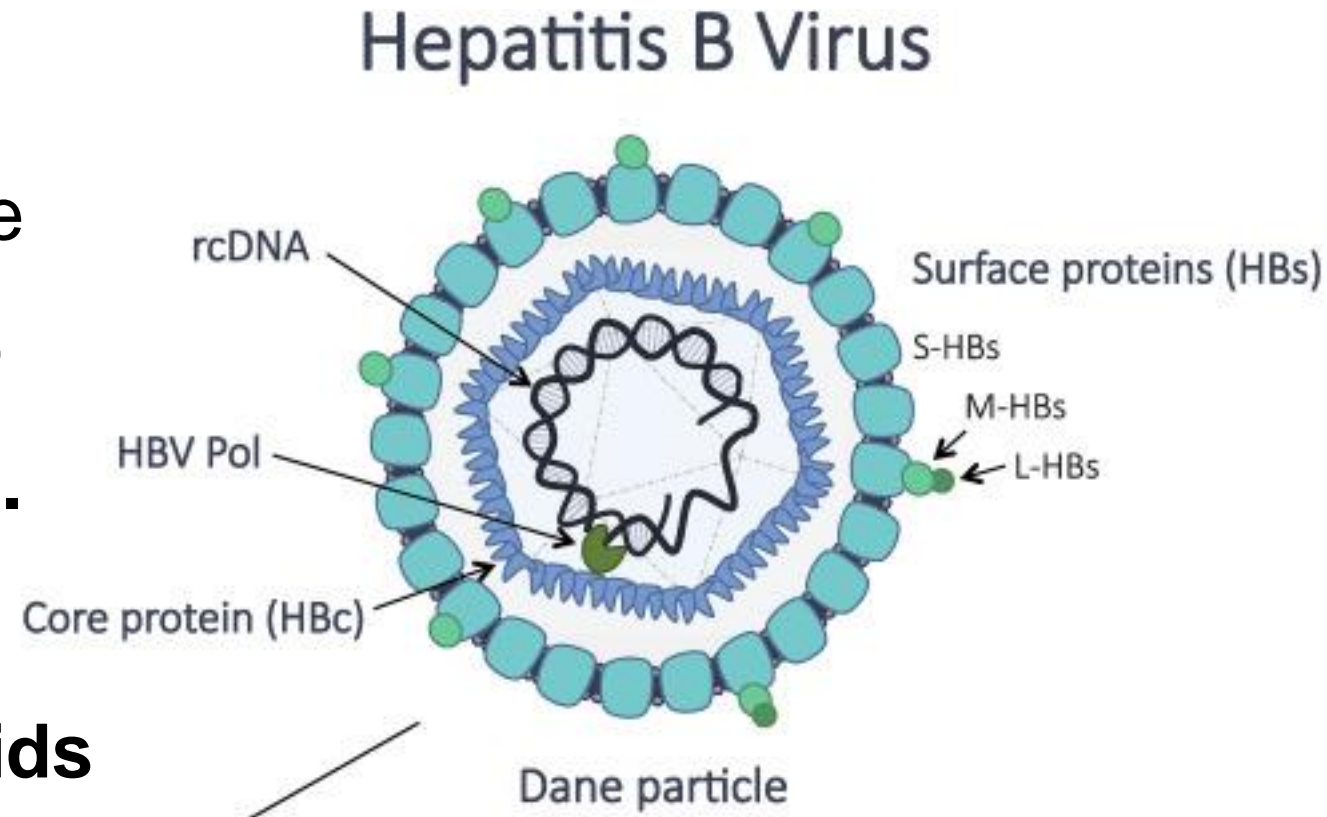
## Class VII – dsDNA-RT viruses

- **enveloped** viruses with **partial pdsDNA** (RNA as intermediate in replication cycle)
- contain RT, but NOT retroviruses
- *Hepadnaviridae* (HBV)



# Hepadnaviridae - Hepatitis B virus (HBV)

- one of the **most serious** vir. human dis. (**5%** of population are **carriers**) – every 5th dies due to **cirrhosis**, every 10th **hepatocel. carcinoma**
- transm.: **blood** and **body fluids**
- it: 60 – 90 days





## ***Hepadnaviridae - Hepatitis B virus (HBV)***

- **acute** infection: elimination by IS 85 - 90% - HBsAg enter into hepatocytes – increase of ALT and AST, hyperbilirubinemia, jaundice – if massive IS response – fulimant hep., acute failure
- **chronic** stage: after acute phase or without 10 - 15% (higher for newborns) – 2 options: **replication** (permanent inflammation – cirrhosis and carcinoma) or **integration** (integration into hepatocytes, carriers)

# ***Hepadnaviridae* - Hepatitis B virus (HBV)**

- diagnostics: ELISA HBsAg, increased levels of hepatic enzymes, jaundice, PCR
- immunisation: active (fragment of HBsAg), pasive (postexposure)
- th.: (INF- $\alpha$ ; lamivudin; adefovir dipivoxil)

# Types of microorganisms

Parasites:

Fungi:

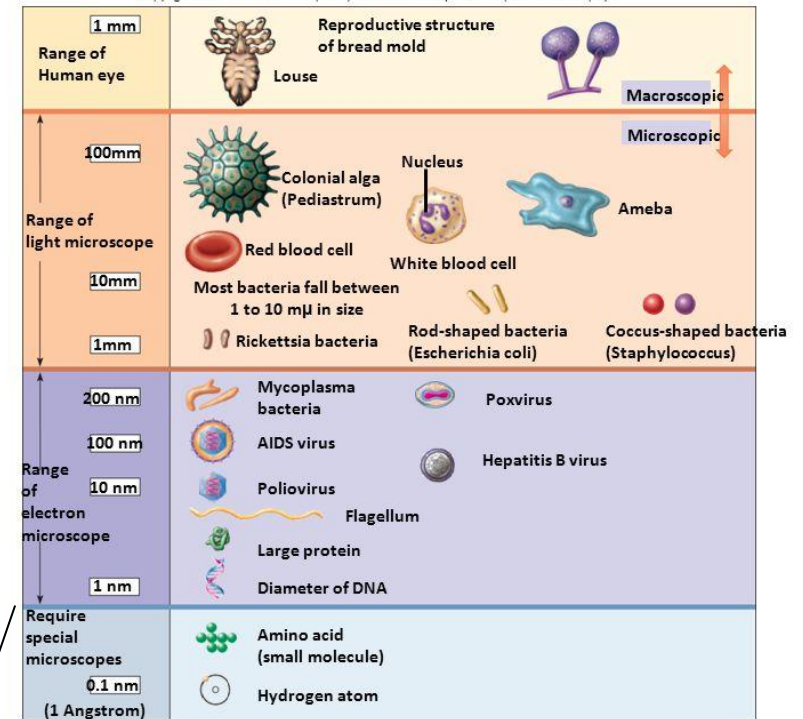
Bacteria:

Viruses:

**Prions:**  
infectious proteins

## Size Range of Microbes

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# Human prion diseases

- PrP protein (normal) is expressed in brain – function unknown (synaptic transmission? differentiation?)
- change to **PrP<sup>Sc</sup>** (aberrant) – primary sequence kept, more  $\beta$ -sheets than normal – WHY? **role of RNA viruses**, **multicomponent** theory (bond of polyanions and lipids), **heavy metal poisoning** (too much or too little copper)

# Human prion diseases

- sterilization according to WHO: 1N NaOH @ autocl. 121°C 30 min. + normal cycle
- cause of **spongiform encephalopathies** (degenerative dis.)
- causal therapy not available
- diagnostics: clinical and histopathological proof (immunohistochemistry, Western blot)

# Creutzfeldt-Jacob disease (CJD)

- symptoms: memory loss, behavioral changes, impairment in coordination and sight
- 70% of patients die in 1 year after dg.
- first described in '20: „spongy“ brains – „pseudosclerosis“
- types: **sporadic** CJD (cca 87% cases; change of PrP; incidence 1-2/1 000 000; in CZ cca 10 people die/yr; onset around 65th year; rapid onset dementia; death in 12 months)

# Creutzfeldt-Jacob disease (CJD)

- **iatrogenic** CJD (occured after application of growth hormone from cadaverous hypophyses, today recombinant prod.); **familiar** CJD (mutation in PRNP gene; 5 – 10% cases); **variant** CJD (psychiatric sympt. – anxiety, depression; neurological symptoms; slower progression and younger patients; probably consumption of meat with BSE; it: 10 let; worldwide deaths: 200)