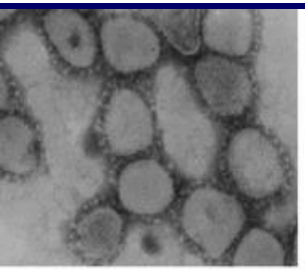
RNA VIRUSES

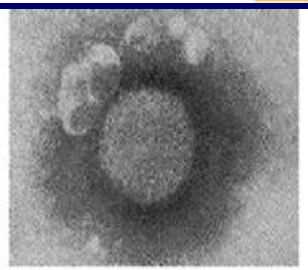
Paramyxoviridae	ss, -,	spheric, lipid capsule
Orthomyxoviridae	ss, -, seg.,	spheric lipid capsule,
Coronaviridae	ss, +,	,,
Arenaviridae	ss, -, seg.,	,,
Rhabdoviridae	ss, -,	projectil, lipid capsule
Filoviridae	ss, -,	filamentous, lipid
Bunyaviridae	ss, -,	spheric, l.capsule,
Retroviridae	ss, +	spheric, l. capsule,
Reoviridae	ds, seg.,	icosahedral, no capsule
Picornaviridae	ss, +,	icosahedral, no capsule
Togaviridae	ss, +,	spheric, l. capsule,
Flaviviridae	ss, +,	spheric, l. capsule,
Caliciviridae	ss, +,	icosahedral, no capsule,

RNA VIRUSES

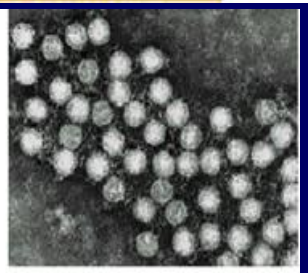
- **Single strand positive**
  - Enveloped
    - Togaviridae
    - Coronaviridae
    - Retroviridae
  - Non-enveloped
    - Picornaviridae
    - Calciviridae
- **Single strand negative**
  - Enveloped
    - Orthomyxoviridae
    - Paramyxoviridae
    - Rhabdoviridae
    - Bunyaviridae
    - Arenaviridae
    - Filoviridae
- **Double strand**
  - Non-enveloped
    - Reoviridae



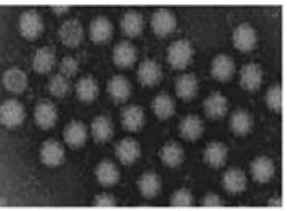
Coronaviridae (NS+)



Arenaviridae (S, ambi)



Picornaviridae (NS+)

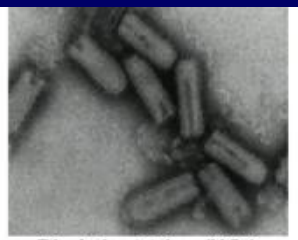


Calciviridae (NS+)

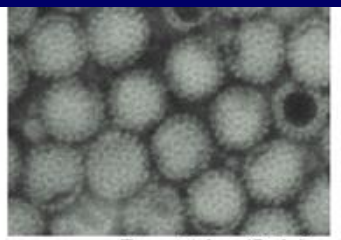
RNA viruses Positive strand (+)
S=segmented NS=non-segmented
Ambi: part + and part -

100nm

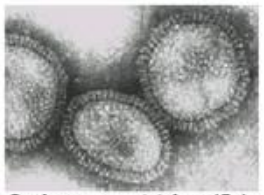
Paramyxoviridae (NS-)



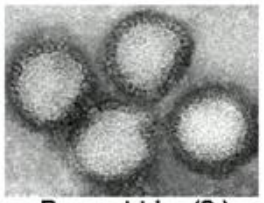
Rhabdoviridae (NS-)



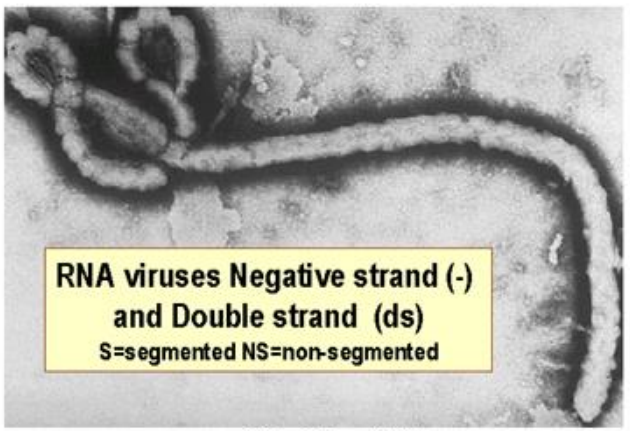
Reoviridae (S,ds)



Orthomyxoviridae (S-)



Bunyaviridae (S-)



RNA viruses Negative strand (-) and Double strand (ds)
S=segmented NS=non-segmented

Filoviridae (NS-)

100nm

Properties of RNA viruses

* Lability

* Replication in cytoplasma

* Cell cannot replicate RNA – virus must have or code the RNA dependent RNA polymerase

* Frequent mutations

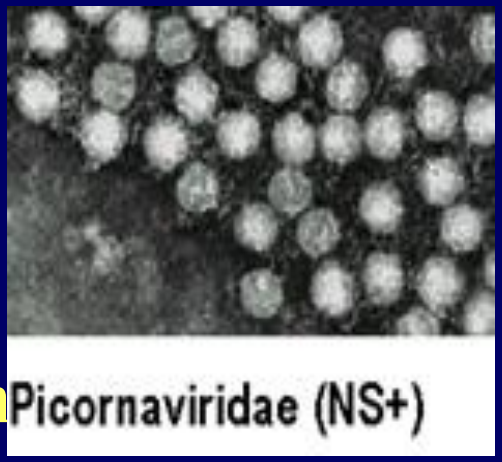
* Retroviruses - RNA dependent DNA polymerase – genom is not replicatings, but it incorporates to the host chromatin

Paramyxoviridae – v.morbilli, v.mumps, RSV, v. parainfluensae
Orthomyxoviridae – v.influenza A, B, C
Coronaviridae – coronavírus, astrovírus
Arenaviridae – v.lymfocytic choriomeningitis (LCM)
Rhabdoviridae – v.rabies
Filoviridae – v. hemorhagic fevers, v. Marburg, v. Ebola
Bunyaviridae – v.hemorhagic feversy
Retroviridae – HIV I, II, HTLV I, II
Reoviridae – rotavirus
Picornaviridae – rhinovirus, poliovirus, ECHO, coxsackie, VHA
Togaviridae – v. rubeolla,
Flaviviridae – v. yellow fever, v. dengue, v. St.Louis encefalitis
Caliciviridae – Norwalk agens

Arbovírusy – artropodborne and zoonoses – toga, flavi, bunya, reo, arena viruses

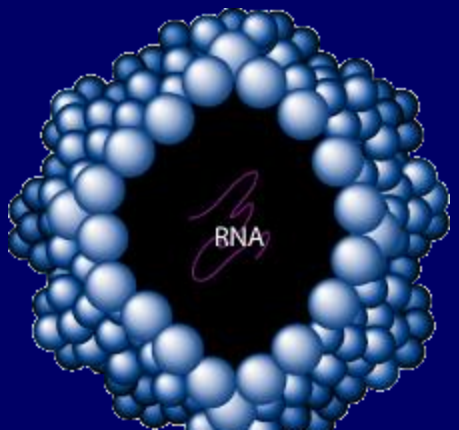
GIT – norwalk, calici, astro
Hepatitis – v.yellow fever, VHA, VHB, VHC, delta antigen, VHE, Prions

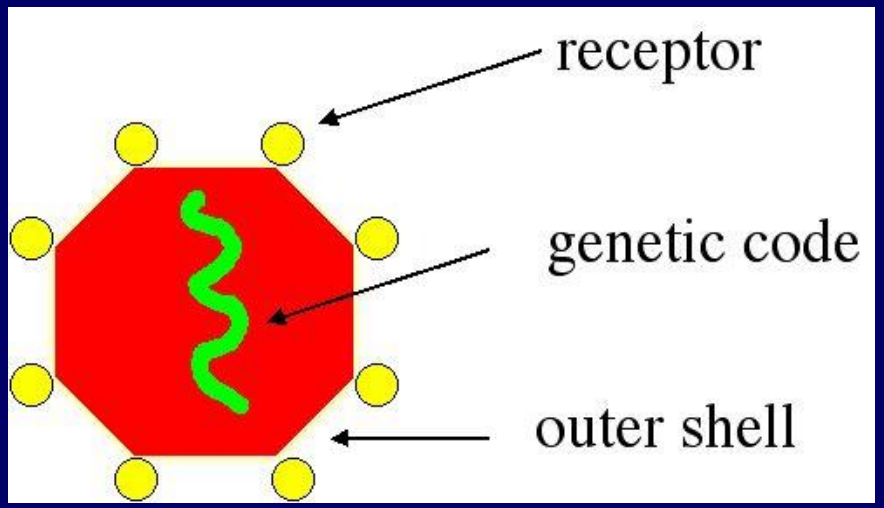
PICO*RNA*VIRIDAE
small,
no lipid capsule,
ss RNA + capsid with VAP
replication in cytoplasma produce cytolytic in


Picornaviridae (NS+)

***RHIN*OVIRUSESs**

1-100 types
lability in acid environment,
optimum 33*C,
releasing histamin,
local infection: rhinitis





RHINOVIRUSES

Characteristic: Lability in acid,
grow at 33*C – nose, URT,
infected cells release *bradykin and histamin* – serouse secretions,
short term immunity - local infection
many times in life - 100 serotypes

Transmission: hands, contaminated material, aerosol, sesonality, mild climat, allergy like

Disease: Infection of URT, rhinorrhoe, headache, cough,

Diagnostic: – usually not needed
– experimental isolation on cell lines – at 33*C – CPE.
Serology – not practical value – many serotypes, local immunity

Therapy: symptomatic

Prevention: vaccination is not available – many serotypes

Hand washing, desinfection

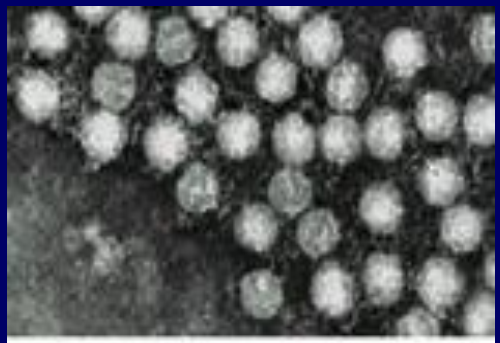
PICORNAVIRIDAE

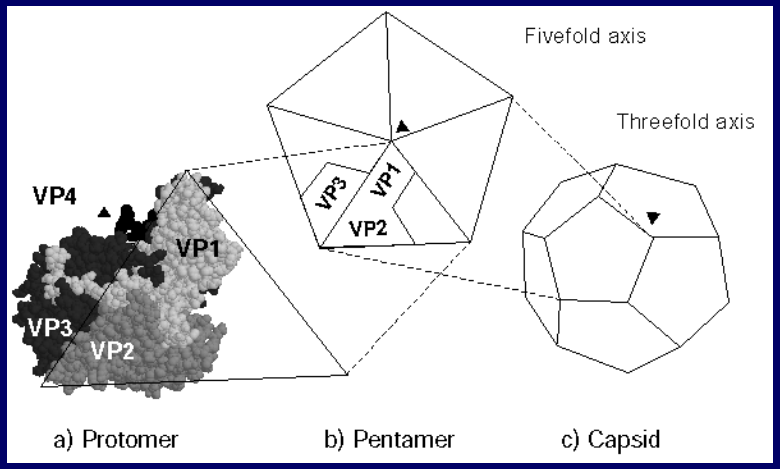
ENTEROVIRUSES

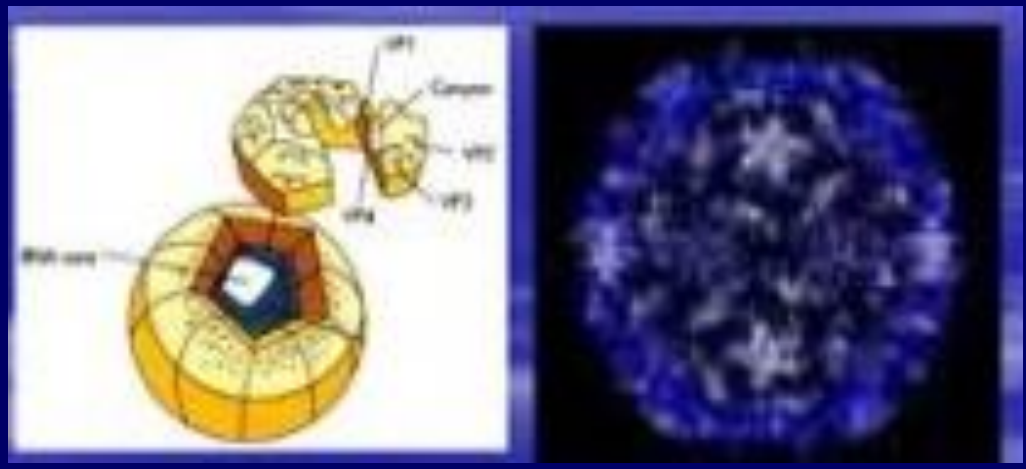
– 72 serotypes

- resistent to pH 3-9,(gastric acid)

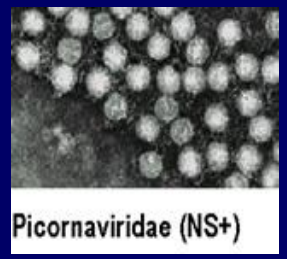
- surviving in water – water borne infections







PICORNAVIRIDAE - Enteroviruses


Picornaviridae (NS+)

Symptoms:

asymptomatic – inluenza like symptoms–paralytic diseasen

Viruses:

Poliovirus typ 1,2,3 – infection of cells of anterior corns of spine tissue and dorsal ganglia, motoric neurones, skeletal muscles, lymfoid tissue

Coxackie A 1-22, 24., Coxackie B 1-6 – almost all organs, in summer Food Mouth Hand infection

ECHO 1-9, 11-27, 29-34 – Enteric Cytopathic Human Orphan

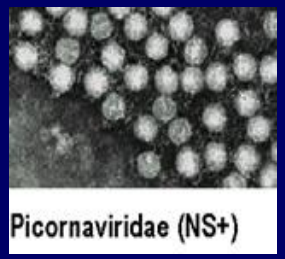
Enteroviruses 68-72 (72 = VHA) – hepatocytes

Immunity – antibodies, secretoric and circulating IgA, IgG,

Prevention - poliovaccination

Transmission fecal oral, sesonality, social conditions

PICORNAVIRIDAE – Enteroviruses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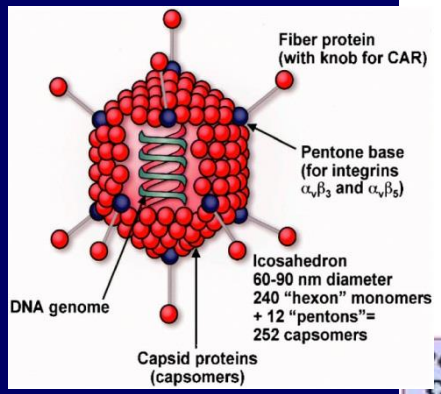
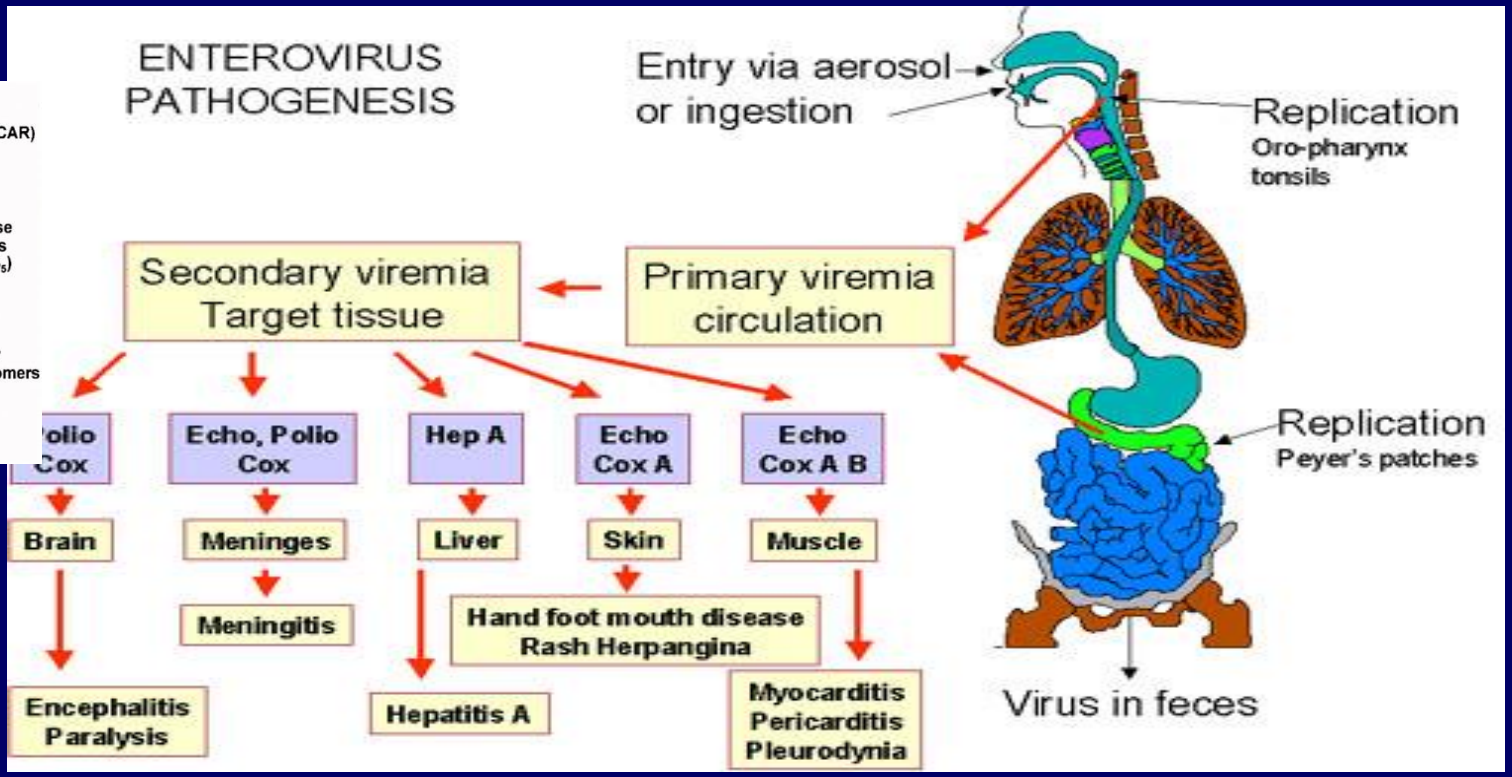
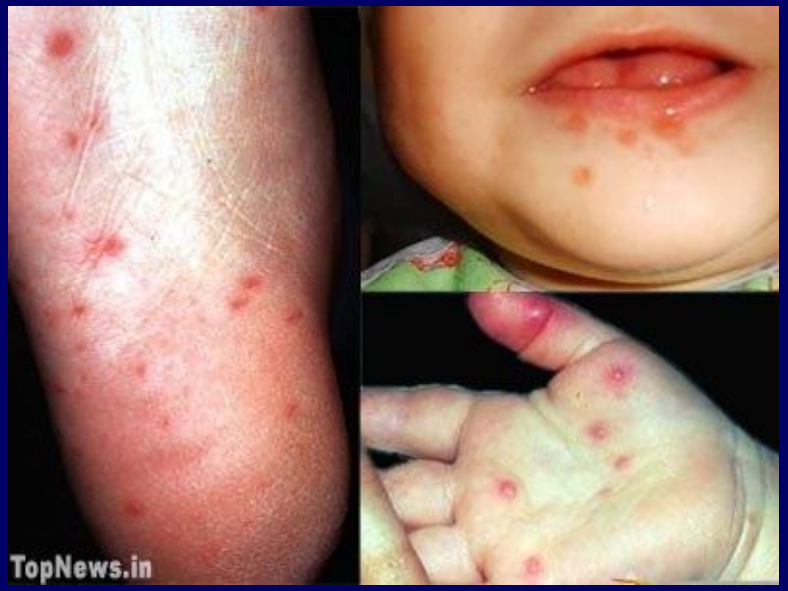
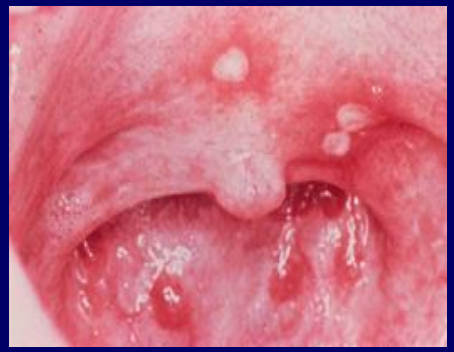




Coxackie- a Echovirus – different symtomes and syndromes : asymptomatic – polio-like, aseptic meningitiss,

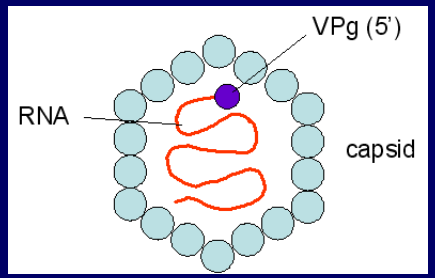


Foot, mouth hand disease,



Coxackie A – **herpangina – herpetic-like**
Coxackie B – myocarditis , pleurodynia, pancreatitis

Eneroviruses – 70, cox A-24 – acute hemorhagic conjunctivitis
Enteroviruses – 72 VHA



Poliovirus– poliomyelitis – wild virus

vaccination - **VAP –** vaccination associated polio – after vaccination with live vaccine and in non immune

Clinical picture:

asymptomatic – infection of orofarynx and intestin (90%)

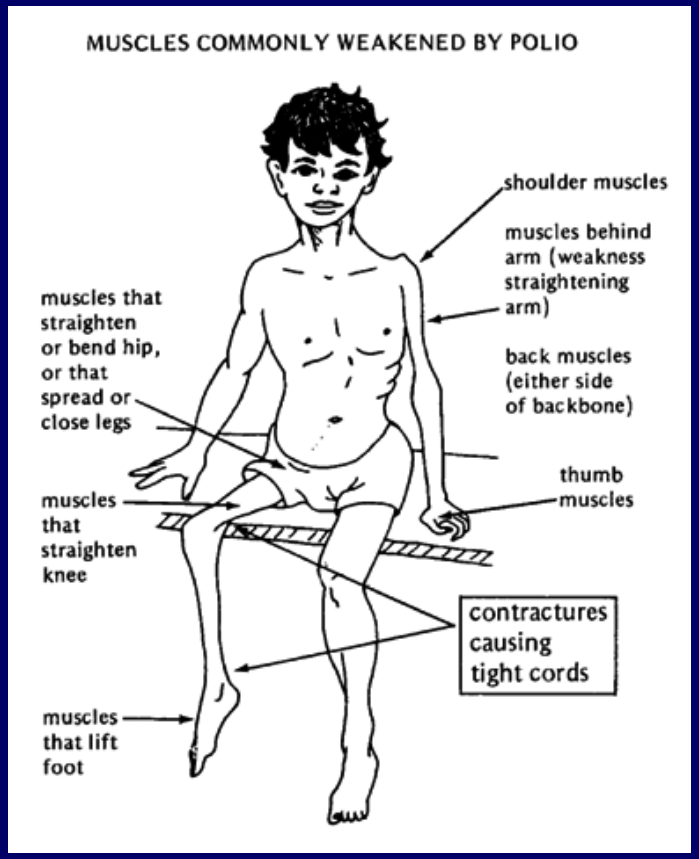
abortive – *polio minor* – nonspecific febrile disease, fever, headache, pharyngitis, vomiting

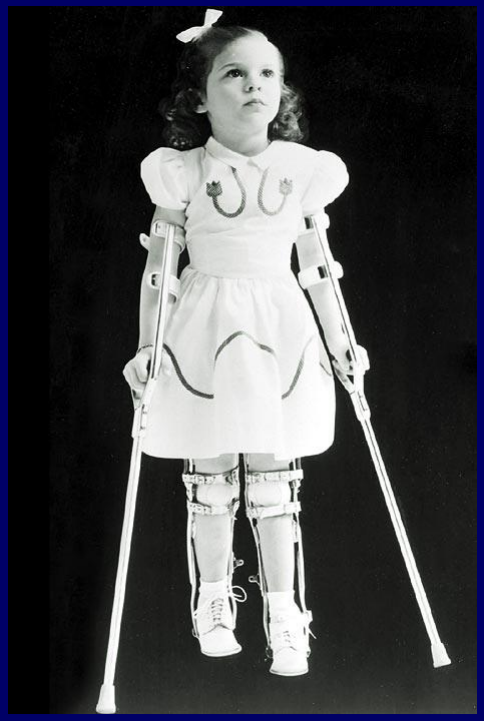
nonparalytic – *aseptic meningitis* – 1-2% - progression to CNS, aches and musles spasmus

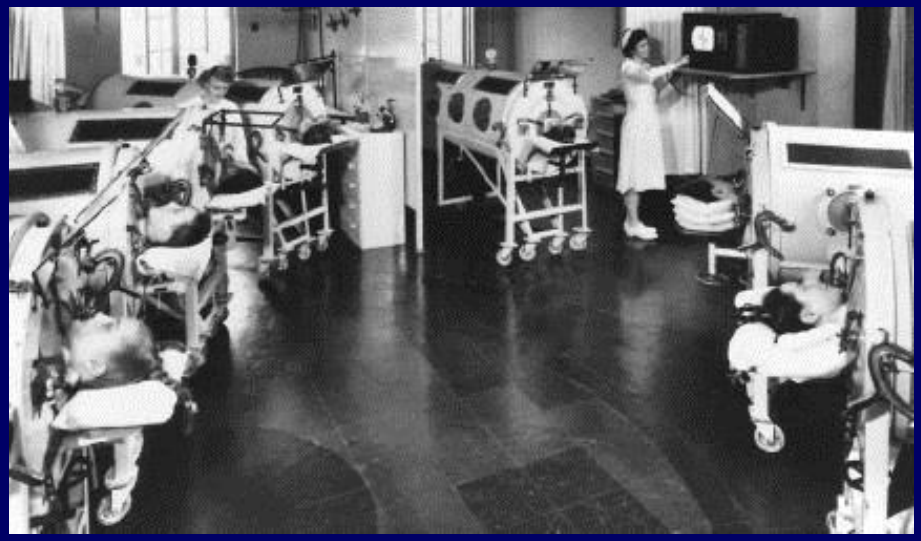
paralytic – *polio major* – 0,1 – 2% - bifasic course after signs of polio minor spread to blood and to the anterior cornes of spine nerve tissue and brain – different spinal paralysis – extremities, cranial, bulbar paralyses, center of respiration - asymetric faible paresis without the loss of sensoric sensitivity, typ 1 in 85%, Different severity– lethal.

Bulbare poliomyelitis– sever, muscles of pharynx and respiration 75% letality Iron lung

Post-polio sy – several years after clinical polio – palsy of the same muscles







Laboratory dg

CSM –lymfocytosis

isolation. – from stool

serology, – IgM, CF

Th

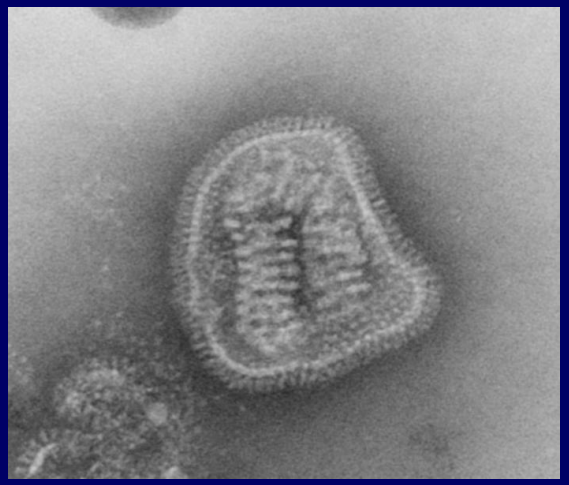
suportive, symptomatic

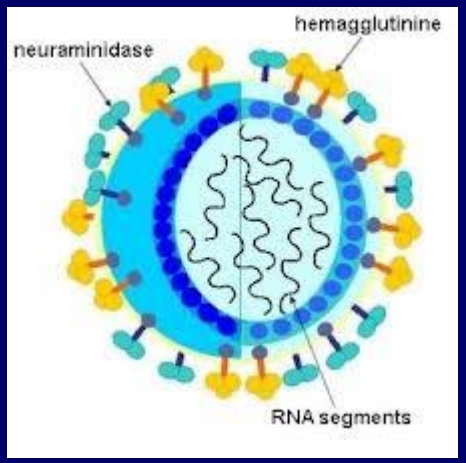
Prevencion

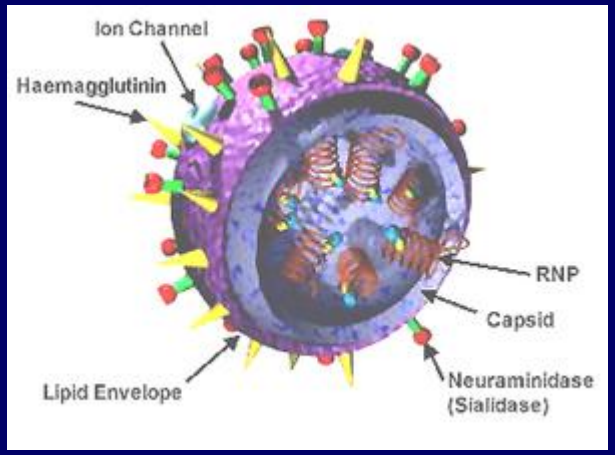
OPV, IPV

ORTHOMYXOVIRIDAE – **infuenza virus A**, B, (C not in men), lipid envelope, segmented genom – prone to mutations and recombination between human and annimal viruses

STRUCKTURE: lipid layer and 2 glykoproteins
hemaglutinín HA(trimér) – bindning to sialic acid od epitelial cells, hemaglutination of chicken ery, drift and shift (only in A) – H1, H2...
neuraminidase NA (tetramér) – enzymatic activity, changes N1, N2







ORTHOMYXOVIRIDAE – **infuenza virus A**, B, (C not in men), lipid envelope, segmented genom – prone to mutations and recombination between human and annimal viruses

Antigenic drift –mutation – epidemic – every 2-3 years
Antigenic shift – recombination – pandemic – every 10 years

Recombination of segmented genom and possibility to infect annimal and bird – coinfection

Type/locality/date/(antigenic structure) A/Bangkok/1/79(H3N2)

Influenza B – mostly in human, not prone to antigenic shift

Target organ – epitelial cells, NA cleaves sialic acid in mucus –naked tissue of m. membrane. In bronchi and lung - desquamation. Inflamation reaction with monocytes and lymfocytes, oedema of submucosis, alveolar emphysema and necrosis

Interferon production(influenza like symptoms) and **T bb imunity** (type specific). Protection – **antibodies against** HA (specific)

Influenza – generalised respiratory infection with influensa like symptomes –fever, malaise, headaches, mylgia, artralgia + complication

Acute disease in adult – abruptly – influenza lide sy, cough

Acute disease in children – + higher temperature, GIT symptomes, otitis**,** laryngitis

Complications – primary viral pneumonia, secundary bacterial pneumonia, myositis, neurological sy,– Guillain-Barré sy, encefalitis,

Disease: Influenza – new antigenic structure and antigenically naive population – children - epidemie.
Transmission: Droplet infection. Virus persists on surfaces Children, immunosuprimated, geriatric, polymorbid, smokers.

Therpay : amantadin and rimantadin – efficacy if applied 48 hrs after exposition to virus A

Prevention: respiratory infection – rapid spread

Vaccination: inactivated vaccine
whole cell vaccine – most reactogenic
split vaccine - RNA +HA +NA – antibodie – humoral immunity + stimulation of immunity via dendritic APC
subunite – safe – only humoral immunity
Every year vaccination pandemic plan,

Diagnostic. during epidémic spread, isolation of virus from nasal secretions

PARAMYXOVIRISES

– lipid envelope -

RNA + proteins for adhesione and glycoproteins for fussion of cell – multinucleated giant cells,

Transmission via respiratory tract

Cell immunty responsible for symptoms and protection

Morbillivirus – v.of rubella

Paramyxovvirus – parainfluenza vírus 1-4 , v. mumps

Pneumovirus – Respiratory syncycial virus RSV

Family: **Paramyxoviridae**

Subfamily: Paramyxovirinae

Genus: Avulavirus
Henipavirus - Hendra, Nipah
Morbilivirus - measles
Respirovirus - parainfluenza virus 1,3, Sendai virus
Rubulavirus - parainfluenza 2,4, parotitis virus, Newcastle virus

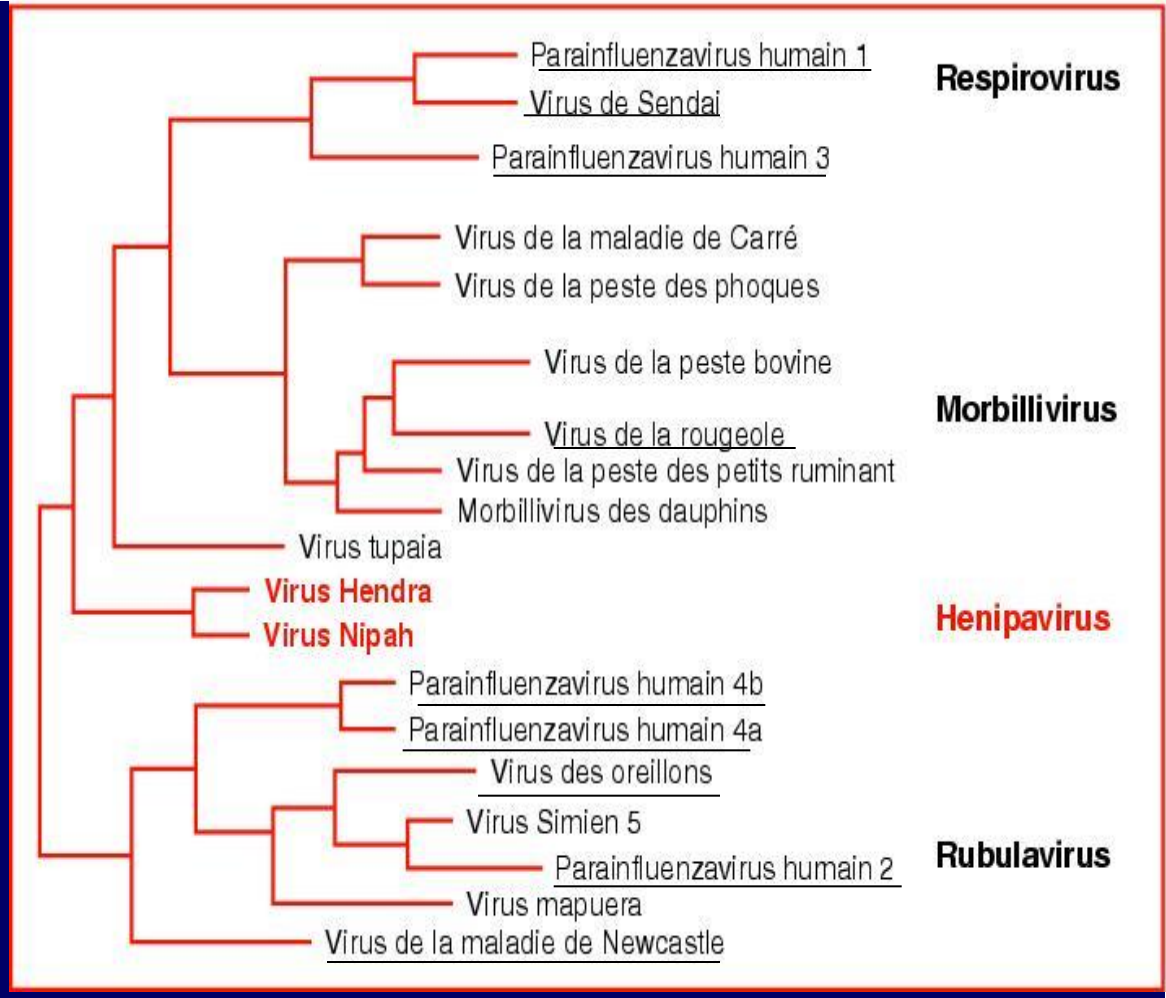
Genus: Metapneumovirus
Pneumovirus - RSV

Family: **Paramyxoviridae**

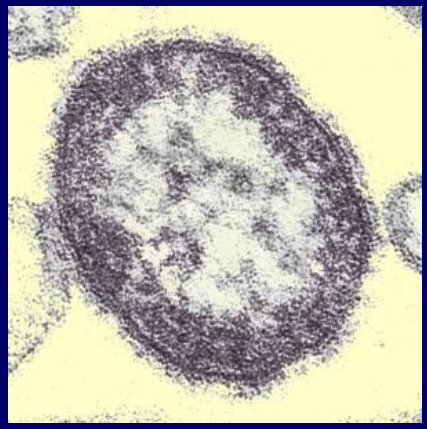
Subfamily: Paramyxovirinae

Genus: Avulavirus
Henipavirus -
Morbilivirus -
Respirovirus -
Rubulavirus -

Genus: Metapneumovirus
Pneumovirus -



Genus: Avulavirus
Henipavirus - Hendra, Nipah
Morbilivirus - measles
Respirovirus - parainfluenza virus 1,3, Sendai virus
Rubulavirus - parainfluenza 4, parotitis virus, Newcastle virus

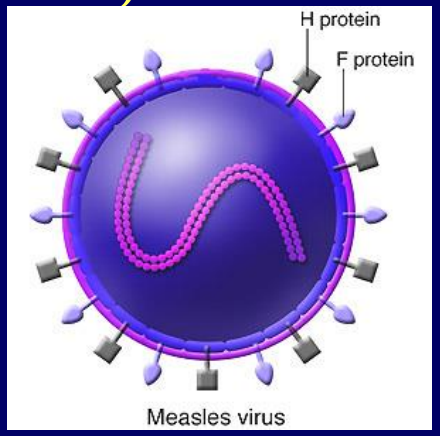


Virus of morbilli, measles, rubella - Morbillivirus

infection of epitelial cells of respiration ways
– lymfocytes – viraemia
– replication in cells of conjunctiva, GIT, urinary tract, lymphatic system and CNS

Spread intercellular – avoid antibodíes
Can cause lysis of cells or persistant infection of cells (CNS) without lysis

1 serotype – 1-3years epidemic cycles - vaccination



Clincal sy

Sever febril infection with exantema

P**rodromal stage:** cough, rhinitis, conjunctivities + photophobia Koplik signs on buccal mucousa – Ílike grains of salts with red halo, maculopapular exantema, confluent rash, starting behind ear – from head downwards

Complications: encefalitis 0,5%, pneumonia (60% lethality), pneumonia with giant cells – without exantema in T bb deficiency

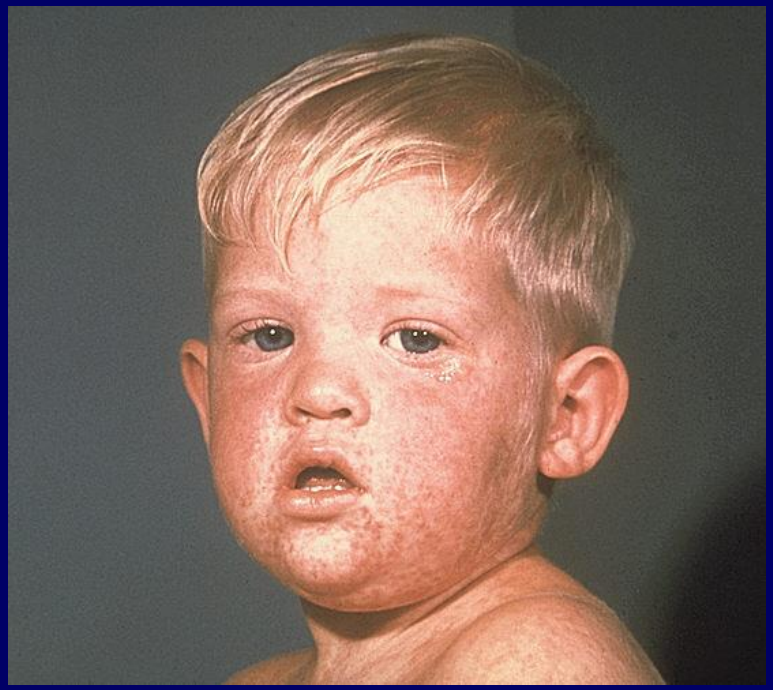
Atypical measels: after the contact of person vaccinated with the older type of vaccine with a wild virus – exagerated immunopathological reaction after sensibilisation with vacinal ags

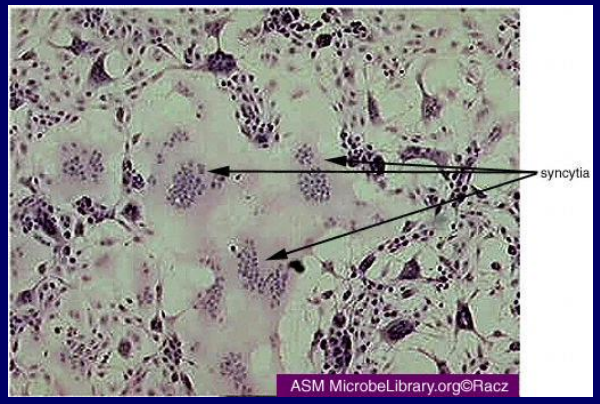
SPE – subacute sclerotising panencefalitis – sever neurologic sequelae of measels – defective virus can persist and replicate in CNS cells – symptoms after many years

Laboratory diagnosis : **Antigen** – IF in cells from pharynx, urine sediment Isolation of virus – CPE – multinucleated giant cell. + inclusions **Antibodies:** IgM acute, IgG persistent

Th: symptomatic

Prevenion – vaccination – live atenuated strain - in present combined vaccine MMR





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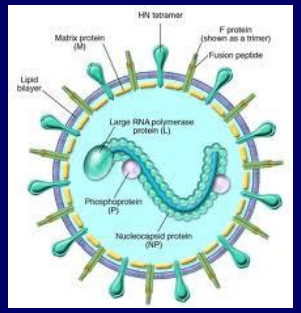


– lipid envelope - RNA + proteins for adhesione and glycoproteins for fussion of cell – multinucleated giant cells,

Infection of respiratory tract – repliction –viraemia – systemic signs
– gl. parotis – multiplication in epitelial cells, oedema
- testes, ovaria, periferal nerves, eye, inner ear, CNS
- pancreas – iuvenil DM

Involvement of organs also without clinical signs

Virus in CNS in 50% infected –10% aseptic meningitis, e
cerebelitis – problems with walking

Laboratory diagnosis. Isolation of virus from saliva, urine, farynx, CSM – CPE on cells lines, – multinuckear giant cells

Antibodies: IgG, IgM – hemaglutination inhibition test

Genus: Avulavirus
Henipavirus - Hendra, Nipah
Morbilivirus - measles
Respirovirus - parainfluenza virus 1,3, Sendai virus
Rubulavirus - parainfluenza 4, parotitis virus, Newcastle virus

Parainfluenza virus – paramyxoviridae - respiroviridae

– 1-3 sever infection of LRT in children,
4 not sever URTI – without viraemia and systemic invovement, shortterm immunity.

Clinical signs : respiratory infection – brochitis, brochiolitis, laryngotracheobronchitis– croup

Seasonality, Symptomatic therapy, Lab. Dg serologic

Vaccination is not efficient – no local immunity

Family: **Paramyxoviridae** *Subfamily:* Paramyxovirinae
Genus: Avulavirus
Henipavirus - Hendra, Nipah
Morbilivirus - measles
Respirovirus - parainfluenza virus 1,3, Sendai virus
Rubulavirus - parainfluenza 2,4, parotitis virus, Newcastle virus

Genus: Metapneumovirus
Pneumovirus – RSV

Respiratory syncytial virus

– localised infection of LRT without viraemia – direct cytopatic efect on cells – syncitia a necrosis (immunological)

Maternal antibodies do not protect newborns,

natural immunty does not protect against reinfection,

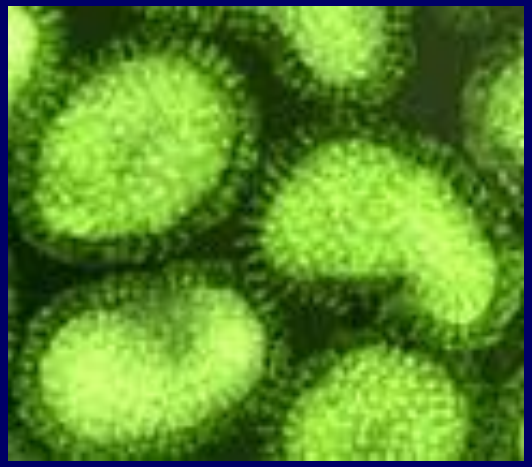
vaccination did not protect, but worstened course of infection

Family: ***Rhabdoviridae***

Genera

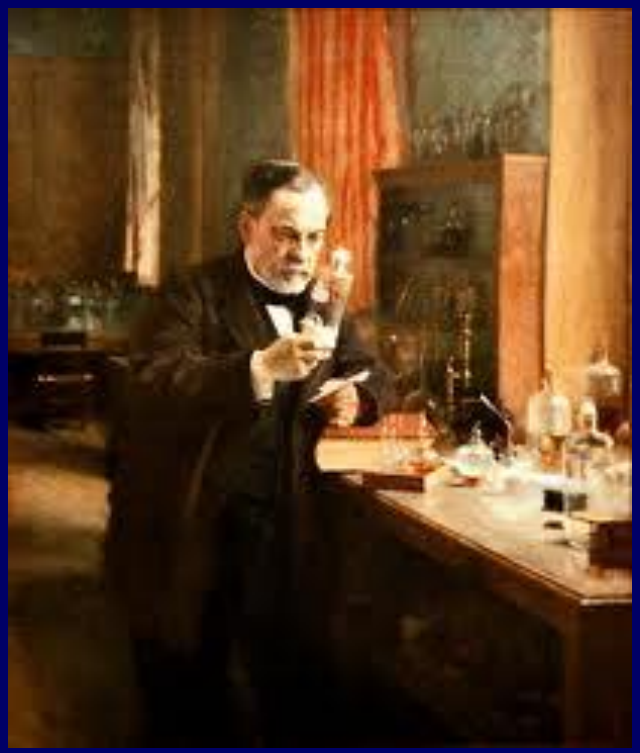
Cytorhabdovirus Dichorhabdovirus Ephemerovirus
Lyssavirus Novirhabdovirus
Nucleorhabdovirus
Vesiculovirus

- Rhabdoviridae - ssRNA lipid envelop
- Lyssavirus - rabies virus
- - Lagos bat virus
- -Mokola virus
  - Duvenhage
  - European bat virus 1,2
  - Australian bat virus



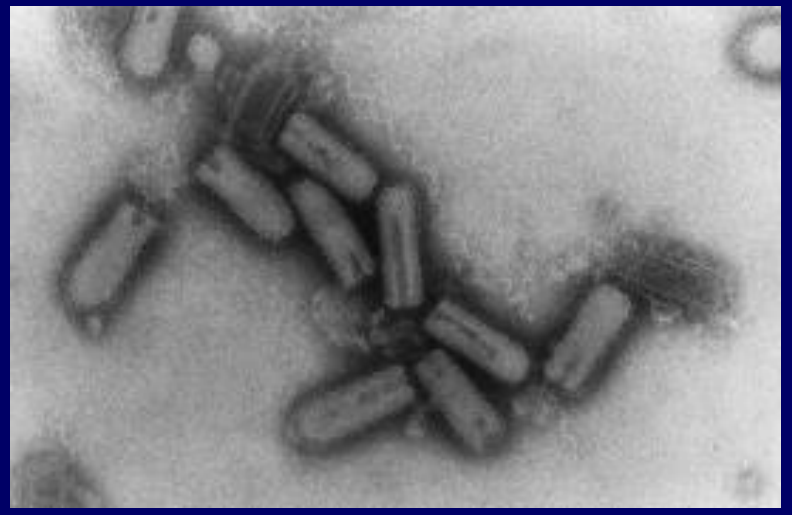
RABIES - Pasteur

- Predicted the structure
- Attenueted the virus by several subcultures on rabbit brain
- Fixed virus
- Development of the vaccine
- Use of it



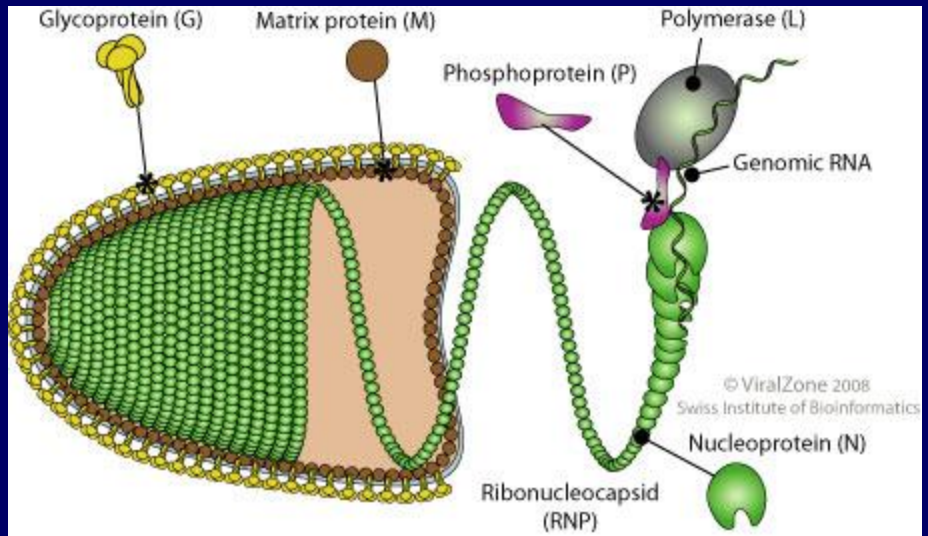
RABIES - history

- 1804, 1821- experimental transmission
- 1881 Pasteur
- 1961 elektronmicroscopy



ViRUS - morphology

- Gun projectil 180x65 nm
- 3% - nonsegmented, negative ssRNA
- 74% - proteins N (l, NS) helical structure
- 20% - lipids - enveloped – physical properties,

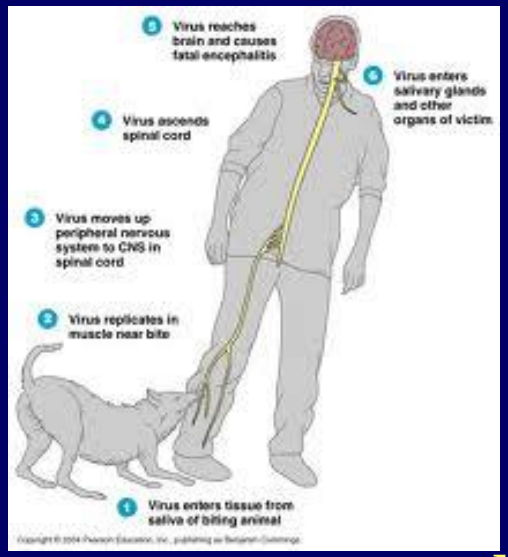


ViRUS - properties

- Termolability half time of surviving 4h/40st.C
  35s/60st.C)
  0-4 st.C – several days, -70 st.C - longterm
- saliva - 24 hrs.
- Inactivation: pH less 4, more than 10, oxidation, org. solutions, detergents, amonium salts, proteolytical ensymes, soaps, UV, X-rays

RABIES - Infection-ethiology

- Nature infection – street strain, wild, Pasteur
- Intracranial subcultures – modified properties-incubation time was short „fixed“ 5-8 days
- Fixed virus - neurotropic, changed virulence to CNS, paralytic form, lower virulence in perif. innoculation. Inclusions in CNS



RABIES - Pathogenesis

- Replication of virus in cell of muscles and skin epitelium
- Invasion to neurons
- Pasive transport in axoplasma of neurons (3mm/hrs) centripetal
- specific symptoms in different stages-virus induced dysfunction of specific area of CNS (agresivity-limbic system,)
- After proliferation in brain – spread to perifery (mouth, nose, retina, cornea, skin)

RABIES – infection in dog

- Change of atttitude (agresivity, quietness)
- Without hydrophobia
- Salivation 3-4 days before clinical disease
- Direct transmission with ill annimal (saliva, bite, urine)
- Non fatality in annimal only (oulou fato – mild paralytic, W Africa, rabies-like vírusy

RABIES – infection in human

- Zoonosis (biting, sctatches, inhalationof inf.dust in bat caves, laboratory transmission, corneal transplantation
- Not every exposition mean disease
- Risk rate (15%): 0,1% small periferic wound, 60% sever biting of the face
- Interhuman very seldom
- Practicaly 100% fatality

RABIES – infection in human

- INTime 1-2 months (9days - 1 year)
- children - adults, head - extremities
- Nonspecific symptoms - (hever, malais, anorexia, headaches, cought, myalgia, anxiety, depression, agresivity, hyperactivity, delirium)
- Local - (aches, paresthesia)

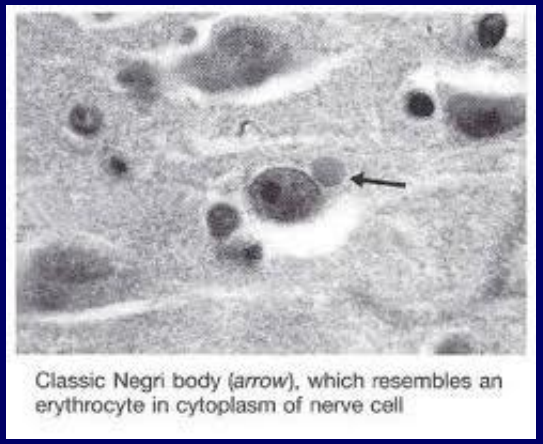
RABIES – clinical signs

- Specific: spontaneously or provocated (aerofagia, hydrophobia)
- Rage forme – anxiety, rage /- apathia

  Neurological signs, coma, death in 3-7 days after first signs
- Paralytic forme - ascendent paralysis, without fydrophobia, prolonged, fatality

RABIES - epidemiology

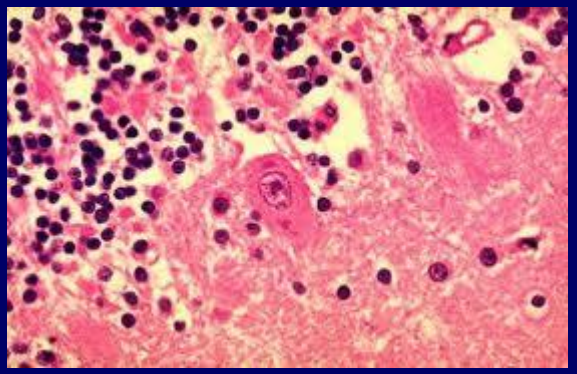
- Home annimal, cattle
- Wildly living – abortive and latent infection do not exist (virus kill rapidly)
- Bats (4 serotypes, inhalation)



Classic Negri body (*arrow*), which resembles an erythrocyte in cytoplasm of nerve cell

RABIES – diagnostic in human

- Postmortem – Negri bodies – intracellular inclusions in CNS



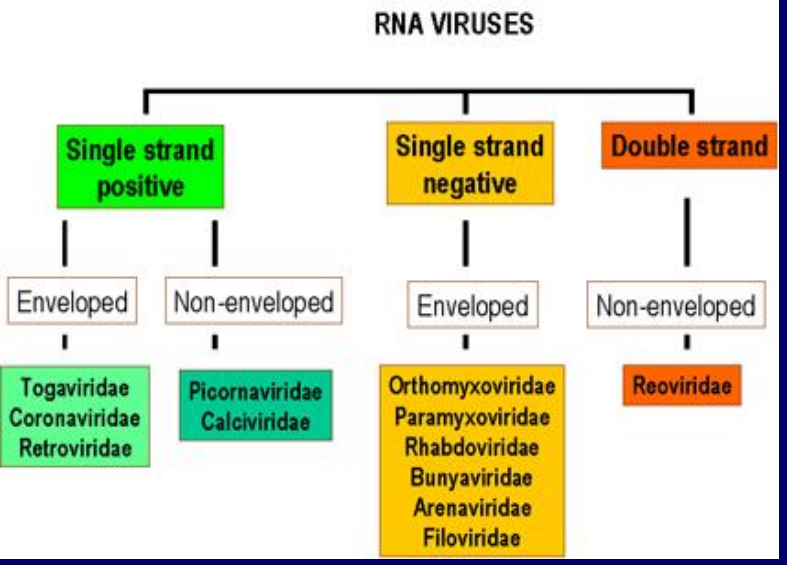
- dot blot, PCR
- inoculation to suckling mouses
- isolation on cell lines

- Antemortem – isolation of virus, saliva, nose,CNS
- - detection of antigen - fluorescence

PCR – sample from cornea. skin

RABIES – diagnostic in annimal

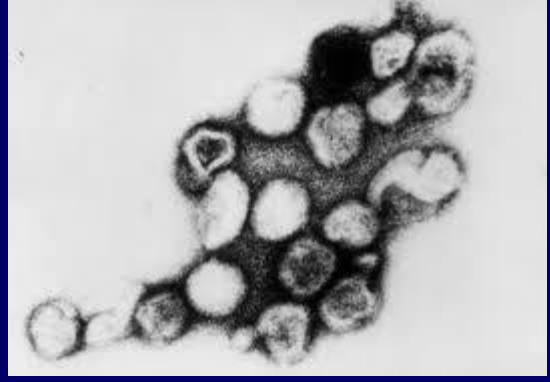
- Post mortem
- Direct detection in brain by fluorescence
- The most rapid detection for routine detection
- Rapid dg is essential for further procedure and can save the traumatisation from vaccination



Togaviruses, flaviviruses (arboviruses)

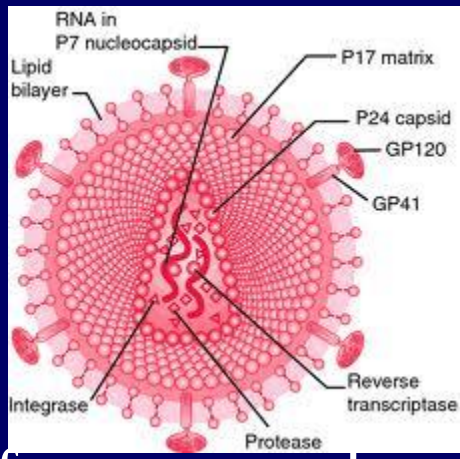
- Togaviruses
  - alfavirus (arbovirus)
  - virus VEE venesuel equine encefalitis, virus EEE – Eastern equine encephalitis, WEE
  - rubivirus (rubella virus)
- Flaviviruses (arboviruses) – v. of central Europ encefalitis, virus Dengue, yellow fever virus, Japnese encefalitis…….

Togavíruses and flaviviruses



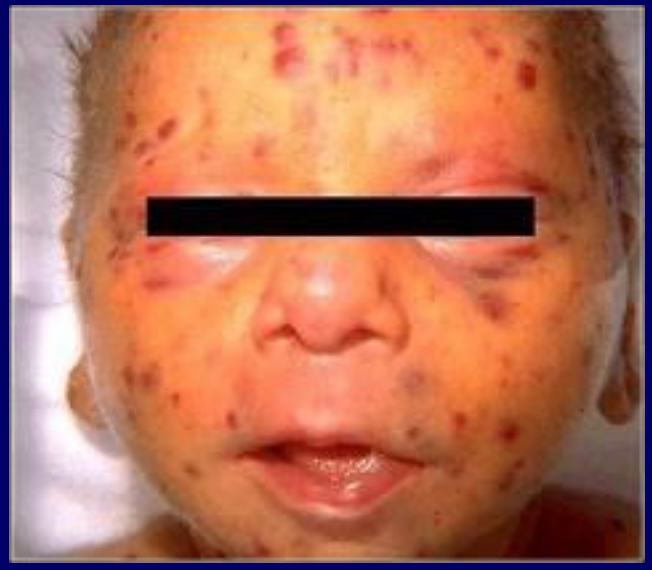
- Envelope ss+RNA
- Togaviruses replicated in cytoplasma, leaving the cell via plasm.membrane – envelope
- Flaviviruses replication in cytoplasma – leaving the cell by budding
- They produce lytical or pesistent infection of other cells
- Some of them are Arbovirueses : artropod - borne

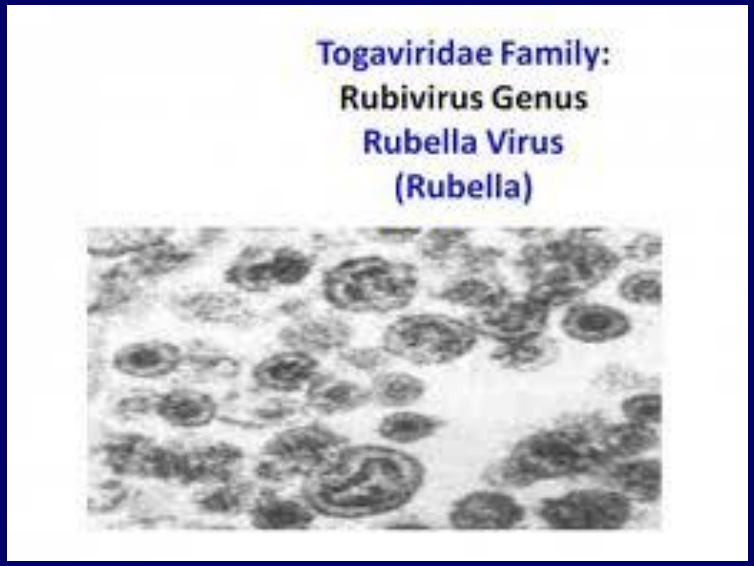
Virus rubeolla – rugeolle – German measles



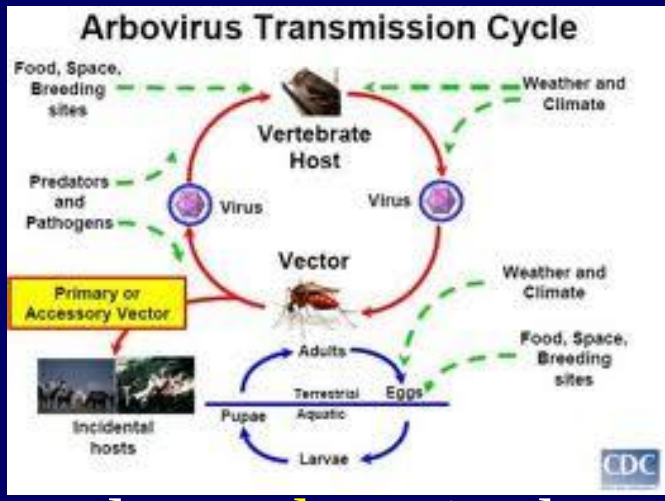
- Inhalation trasmission, URTI, lymphdenopatia, viraemia + rash
- Mild disease with exantemae – differentiated form measels by german doctors – „German measels“
- Trasmission in primary infection of a pregnant intrauteinally - terratogenic – in borne infection cytolytical infection, persistence of the virus in the tissue and spread as long as 4 yrs. Norman McAlister Gregg - Greggov sy – cataracta, hydrcephalus, heart vicium
- Th: symptomatic, vacination
- Lab.dg: serological IgM, isolation of the virus from urine on tissue cultures, - identification - interference with picorna víruses

Virus rubeolla – rugeolle – German measles





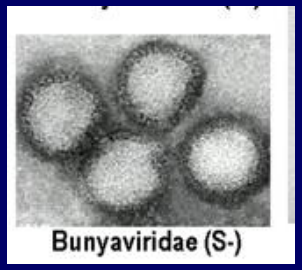
- Arbovirueses
- Togaviruses
- Flaviviruses
- Bunyaviruses,
- some haemorhagic fever viruses



- Insect female suckles viruses from infected vertebrae in the stage of viraemia. Virus invade epitelial cells of the intestin of the insect and spread to the circulation and invade cells of saliva glands, where it produce persistant infection, replicates and spread to saliva. During biting the host the female is suckling and regurgitate saliva contaminated with virus. Virus circulate in the host blood – first viraemia and invade cells of RES , where it replicates and spread to target organs – sec.viraemia followed by typical clinical signs.
- - encephalitis (TBE), hemorhagic fever, ...

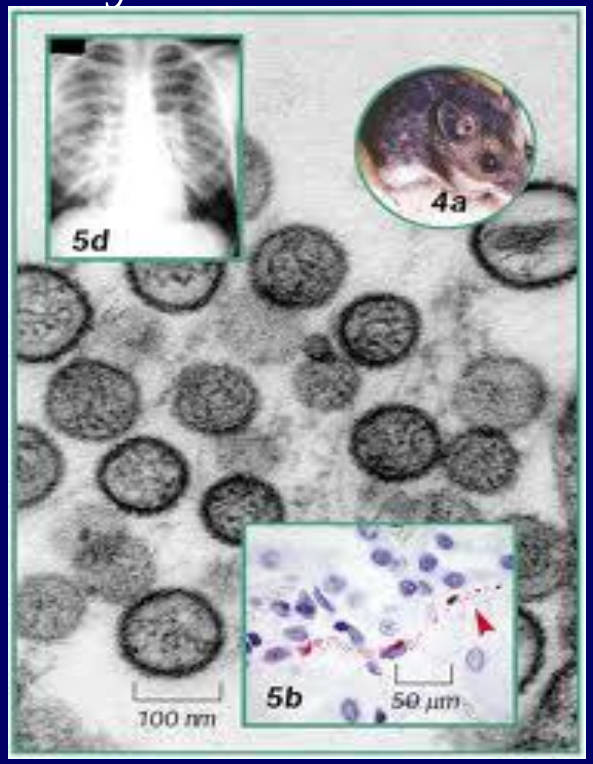
Hemorhagic fever virusesH

- Bunyaviruses - arbo
- Arenaviruses - arbo
- Filoviruses – not arbo
- Hantaviruses – not arbo



Bunyaviruses

- 200 enveloped -RNA viruses with segmented genom
- arboviruses endemic acc.insect vector (Rift valley fever v., LaCross vírus)
- Systemic disease after sec. Viraemia, usually with involvement of brain, hemorhagy and kidney necrosis – haemorhagic fever, haemorhagic encephalitis, haemolytic uremic sy

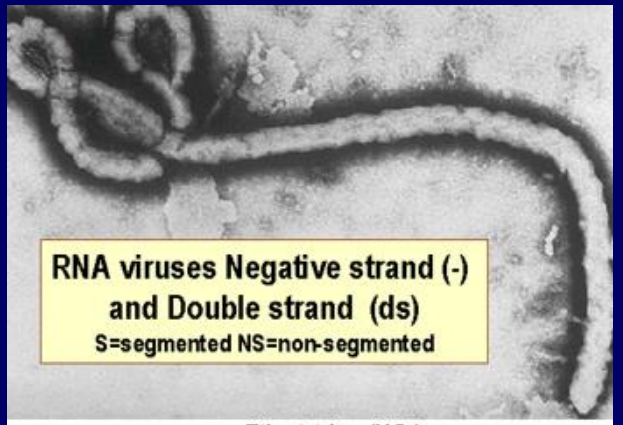


Hantaaviruses

– not arbo – spread via aerosol,

Filoviruses

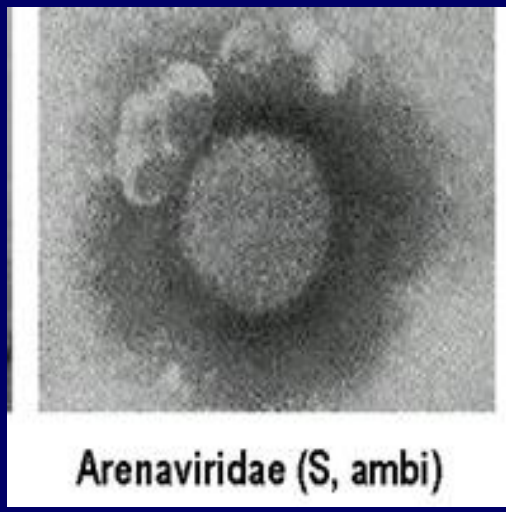
- Filamentous enveloped, -RNA, sever and fatal haemorhagic fevers with oedema and hypovolemia (influenza like sy, myalgia, aches headache, malaise diarrhoe, haemorhagies, deathe in 90% pf clinical imf), endemic .
- Marburg v., Ebola v., (previously grouped to rhabdoviridae) – transmissible via aerosol, laboratory infections from infected monkeys(Marburg), infections in Zaire, Sudane : presence of antibodies in 18% - inaparentné infections possible (Ebola)
- eosinofilic cytoplasmatic inclusions of infected cells with necrosis of the tissue of parenchymatouse organs
- Dg Marburg – isolation on tissue cultures of Vero bb, Ebola innoculation of annimals, Imunofluorescence, ELISA,
- Th: serotherapy, interferon, isolation
- Safety precautions 4th dg



Filoviridae (NS-)

Arenaviruses

- Vírus of lymfocytare choriomeningitis LCM - meningitis (at 25% of infected, or subacute persistent for several months, perivascular mononuclear infiltration of neurons and menings) or fever disease with myalgia
- Hemorhagic fevers viruses - Lassa: zoonoses - peszistente infections or rat - reservoirs, endemic (tropical Africa, S. America) – fever, coagulopaty, petechiae, visceral haemorhagies, necrosis, šock
- Lethality 50%
- Biological safety dg.4
  *Enveloped RNA vírus – shape - persistent – infection of macrophages, releasing cytokíns against cell and vessels Tissue damage is produced by T lymfo immunity
  *Infection transmitted via aerosol, contaminated food by saliva, urine from inf. annimals
- *Dg epidemiologically, clinically, serologically


Arenaviridae (S, ambi)

agensies as biological weapons

- **Cathegory A**. High priotrity, easily disseminatable with high lethality, causing panics, needs special public health approches
- - Antrax (*Bacillus antracis*)
- - Botulismus (toxin *Clostridium botulinum*)
- - Plague (*Yersinia pestis*)
- - Small pox (variola major)
- - tularemia (*Francisella tularensis*)
- - viral haemorhagic fevers (filoviruses – Ebola, Marburg., arenavírusy – Lassa, Machupo)

B

easily disseminated, medium lethality and morbidity, specific dg in CDC

- - Brucelosis (*Brucella* sp.)
- - Epsilon toxin (*Clostridium perfringens*)
- - Food borne, (*Salmonella* sp., *Escherichia coli* O 157:H7, *Shigella* sp.) - water borne (*Vibrio cholerae*, *Cryptosporidium parvum*)
- - Maleus, Melioidóza (*Burkholderia mallei*, *pseudomallei*)
- - Psitakosis (*Chlamydophila psittaci*) - Q horúčka (*Coxiella burnetii*)
- - Ricine intoxication (*Ricinus communis - mushrooms*)
- - *Staphylococcus aureus* toxin B
- - Spotted fever (*Rickettsia prowazekii*)
- - Viral encephalitis (alfaviruses – VEE, EEE, WEE)

C

Agensies with third priority, emerging and reemerging, availability, potential of high morbidity and mortality

- Nipah vírus a hantaavírusy
- H5N1, pandemic flu strain

Rotaviruses

REOVIRIDAE – orthoreovíruses – gastroenteritís, URTI, biliar.atresia, asymptomatic, in stool of children
- orbivíruses – febril infection with headache
- **rotaviruses – gastroenteritis in children**

Proteolytical activity of GIT – virus change to – **infectious subviral bodiy –(ISVP) –** infiecting cells., replication , agregation lysis of cells

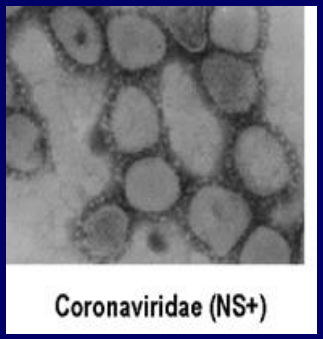
Resist acid environment – flattness of microvilli, mononuclear infiltration of lamina propria – water disbalances - dehydratation. Selflimiting – or sever dehydratation

Diagnosis - detection of ag from the stool latexaglutination

Therapy. - hydratation, mild free diet

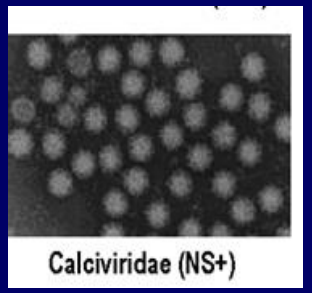
Vacccination – the original vaccine was not successful – intususception, new vaccine form infant

Coronaviruses



- Coronaviruses –
- name acc.to electron microscopic picture - sun corona
- 2nd most common ethiology of rhinitis
- Enveloped virus with helical capsid + RNA nonsegmented
- URTI, SARS
- Optimal temperrature for the growth 33-35*C.
- Antibodies present in 10-15% of adult, reinfections.
- Lab.dg routinelly not performed.

Caliciviruses and others



- Caliciviruses
- astroviruses,
- Non classified viruses: Norwalk agens

SRGV (small round gastroenteritis viruses –

In jejunum – flat villi , vacuolisation of cytoplasma of enterocytes, infiltration of mononuclear leucocytes,interference with absorbtion of water,

prolonged evacuation on stomach,

fecal-oral transmission

short term immunity

Children,

INT 24 hrs malaise, nausea, vomiting (not in astro)

Hepatitis viruses

– virus infect liver during viraemia or by mononuclears.

The liver is the source of sec.viraemia and hepatocytes are damaged by infection.

Similar clinical signs

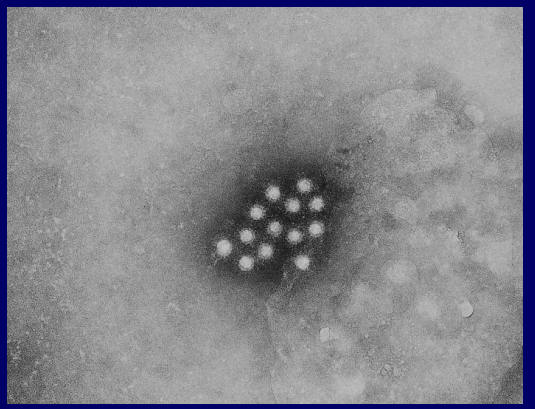
Hepatitis = inflamation of the liver – (disease)
I***cterus*** = symptom – yellow color of skin caused by hemolysis, or cholestasis.

Hepatitis A, B, C, D, E, G viruses, TTV
Hepatitis in EBV infection
Yellow fever

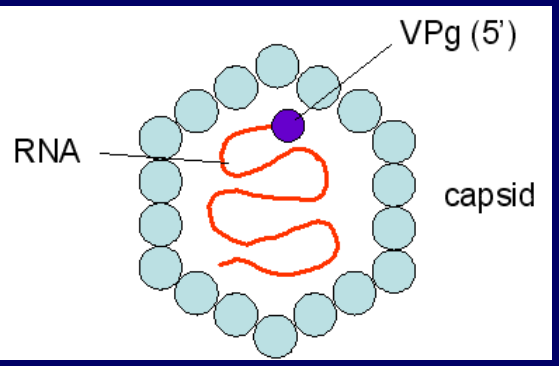
In imunocompromised during CMV infection
in newborne - HSV, varicella, inborne rubeola,

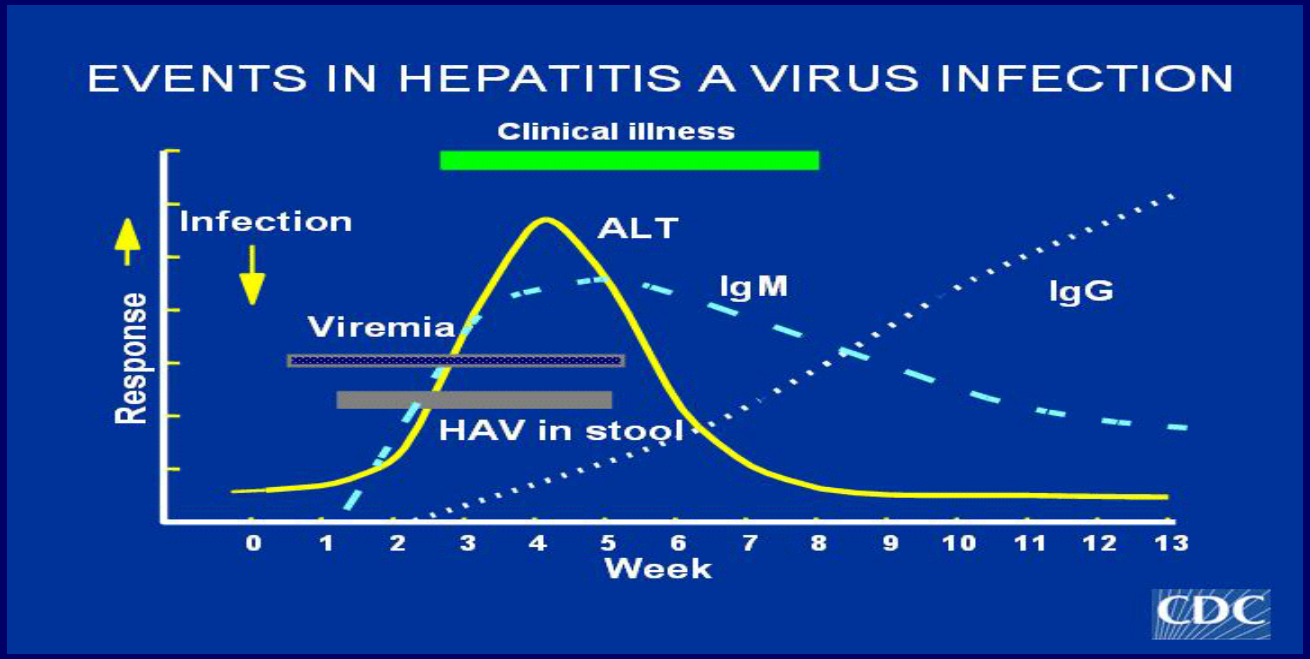
	Hepatitída A	Hepatitída B	Hepatitída C	Hepatitída D	Hepatitída E
Name	Infectiouse	Serum	nonAnonB postransfúzna	Delta Ag	Enteric nonAnonB
Vírus	Pico**rna**,	Hepa**dna**, enveloped	Flavi, RNA	Viroid, RNA circular	Calicivirus-like, RNA
transmission	Fecal oral	Blood borne	Blood borne	Blood borne	Fecal-oral
start	Abrupt	Slow	Slow	Abrupt	Abrupt
Incubation time	15-50 d	45-160	14-180	15-64	15-50
Letality	0.5%	1-2%	0.5-1%	High	1-2% pregnant20%
Chronicity	No	Yes	Yes	Yes	No
Comorbidity	No	Ci, Ca	Ci, Ca	Ci, fulminant	No
Lab. Dg	antiHAV	HBsAg	antiHCV	antiHDV	Anti HEV
severity	mild	Mild to sever	Subclinical	Koinfection superinf.HB	mild, pregnant sever

Hepatitis A virus - enterovirus, picornavirus



Stability in pH 3
resists ether, chloroform, detergent
drying, - 20 to –70 *C (years) /ice/,
56*C 30 min,
61*C 20min – partial inactivation
present in water (sea water) months
Inactivated – chlorin, formaldehyd, UV rays
Fecal- oral transmission, socioeconomic conditions, MX autumn,
Vaccination,
inaparent infections



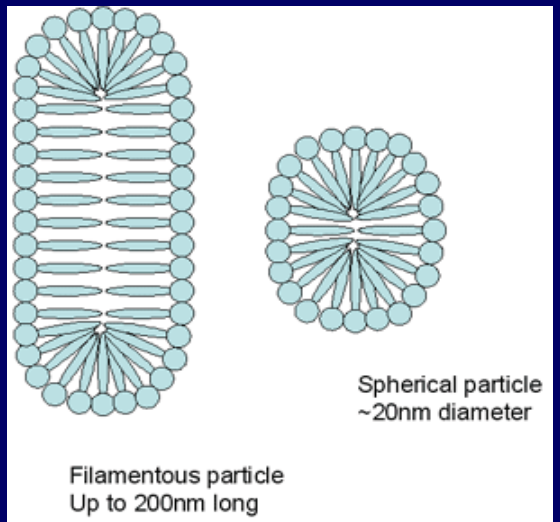


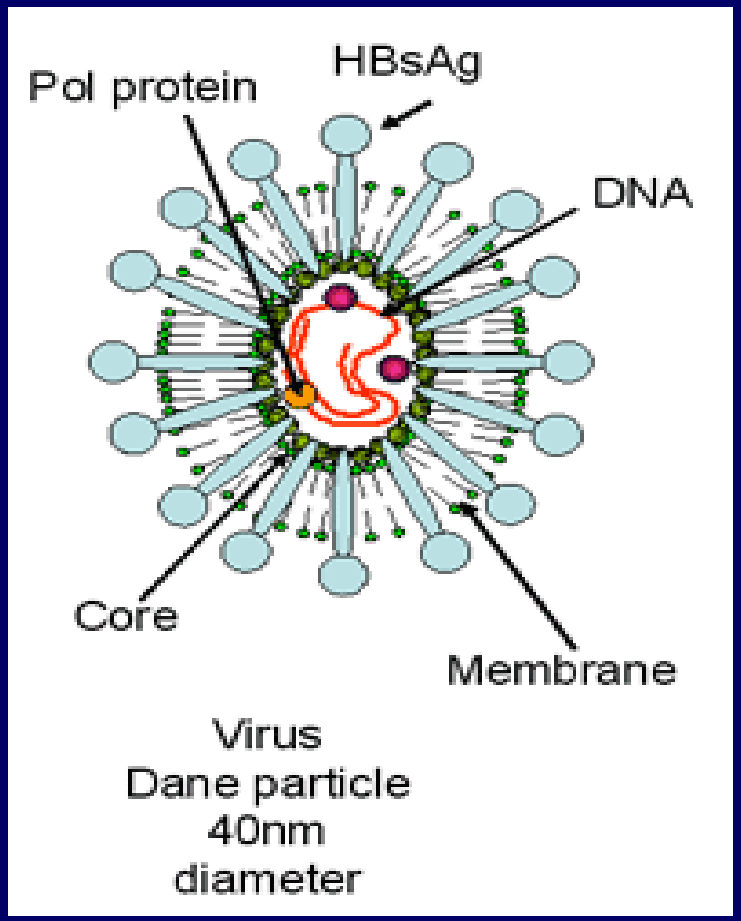
Hepatitis B virus - hepadnavirus

Virion (contain HBeAg) is surrounded by HBcAg (core) and glykoprotein HBsAg (surface). Has 3 more glykoproteins L,M,S which contain group (a) and type specific determinants d, y, w or r. Their combination is the base for 8 subtypes HBV (ady, adw..)

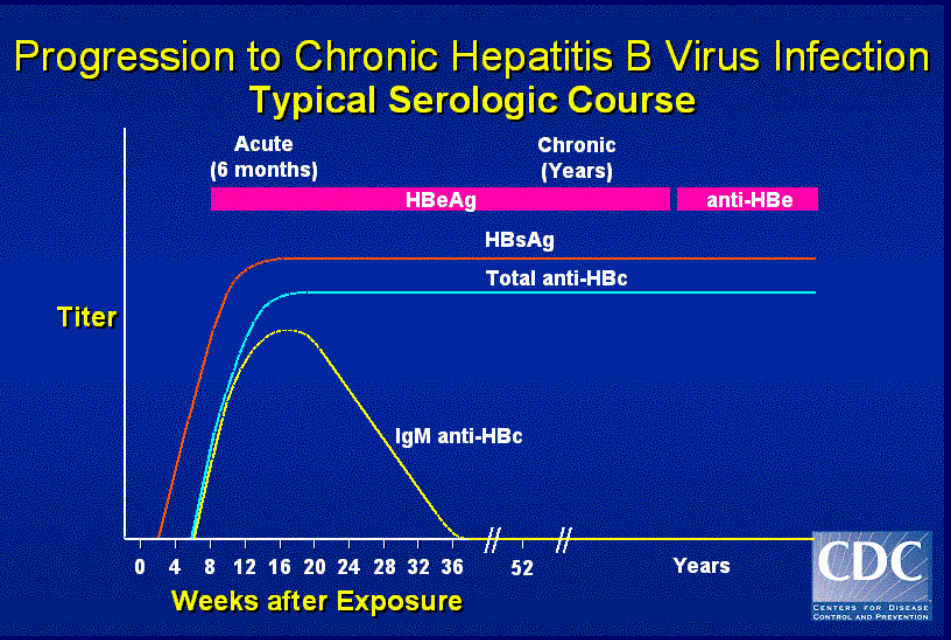
VHB does no infect the liver
– does not produce the direct damages
– it is based on the cell immunity reaction
= lysis of the cells, symptoms,healing

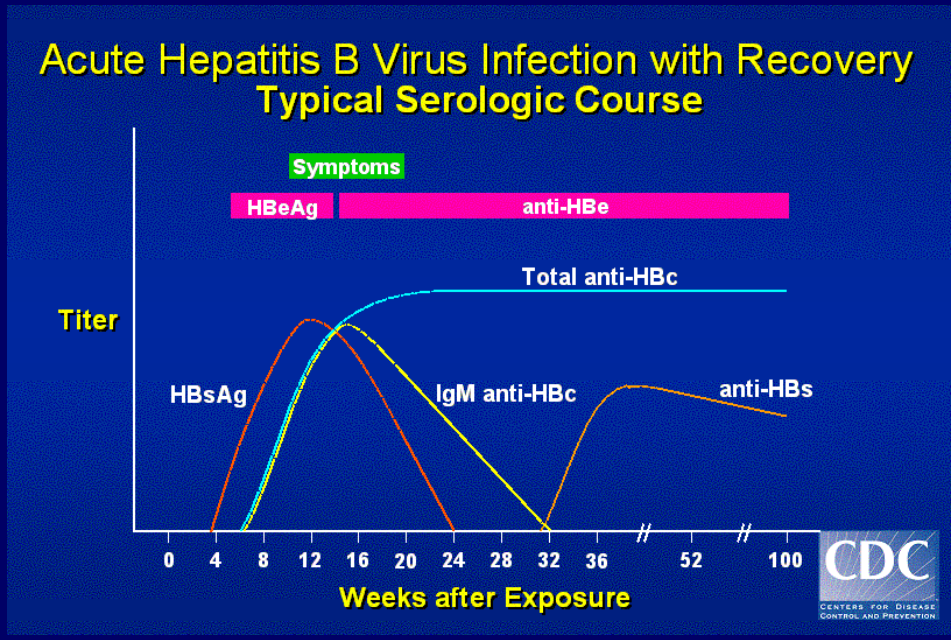
In faible immune reaction = chronicity

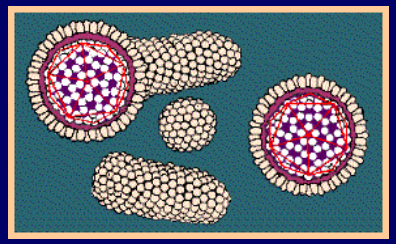


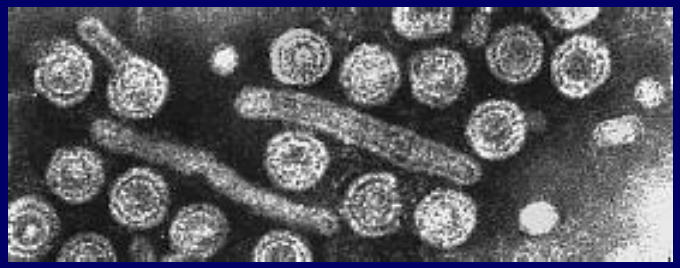


Hepatitis B virus









Infction starts – injection, innoculation.
Spread of the virus – via blood to the liver, replication – viraemia – HBV in all secretions and blood .
Symptomes – cell mediated immunity + CIk

<u>Symptomes of acute viral hepatitis type B</u>:

expozícia

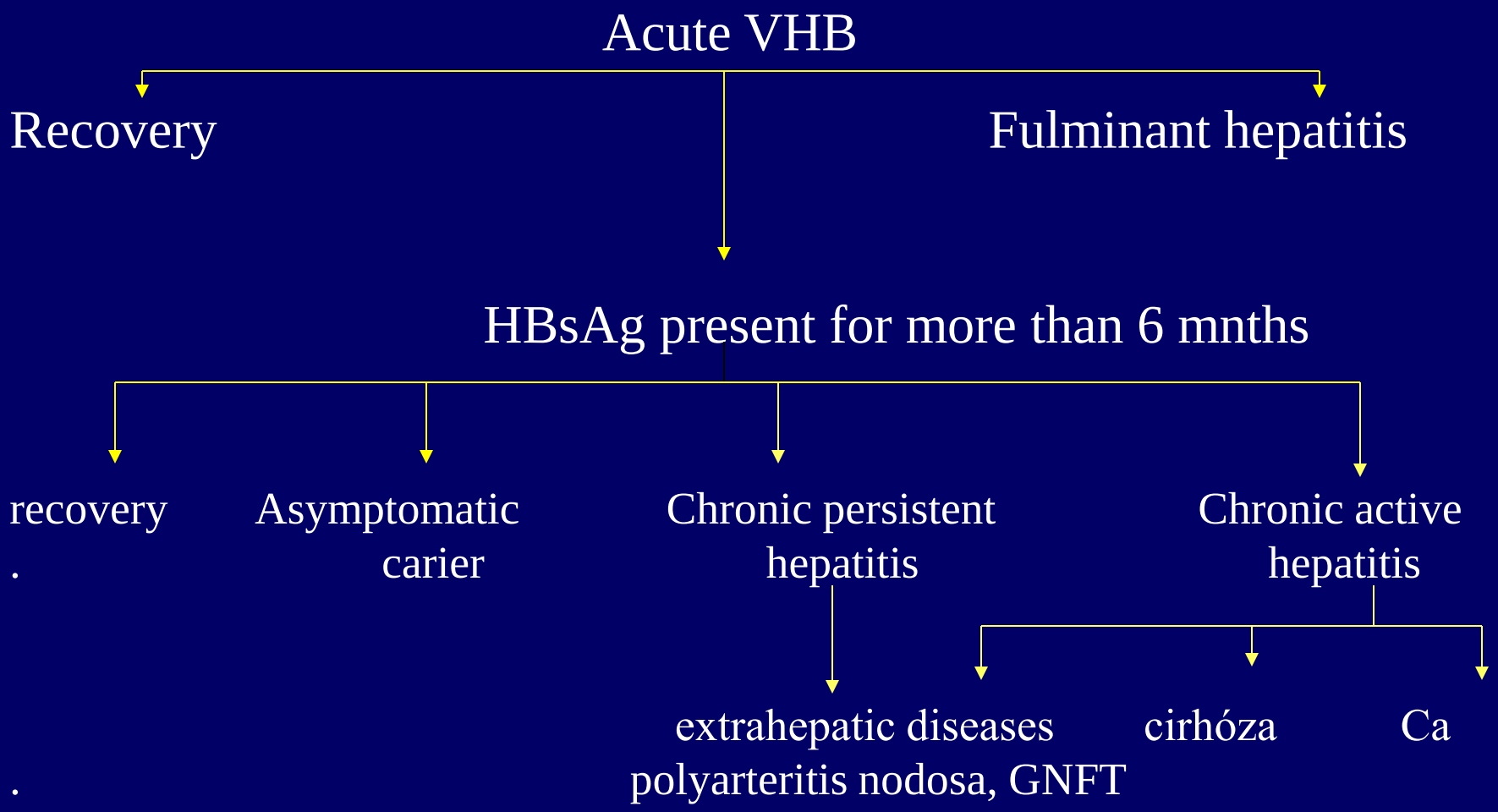
fever, rash, artritis, malaise, anorexia

nausea, aches

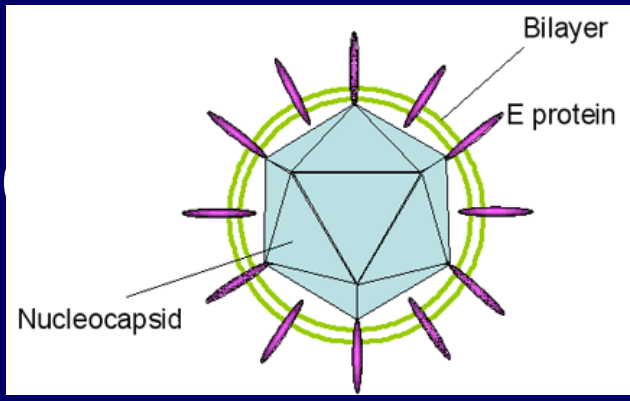
icterus, dark urine

pruritus

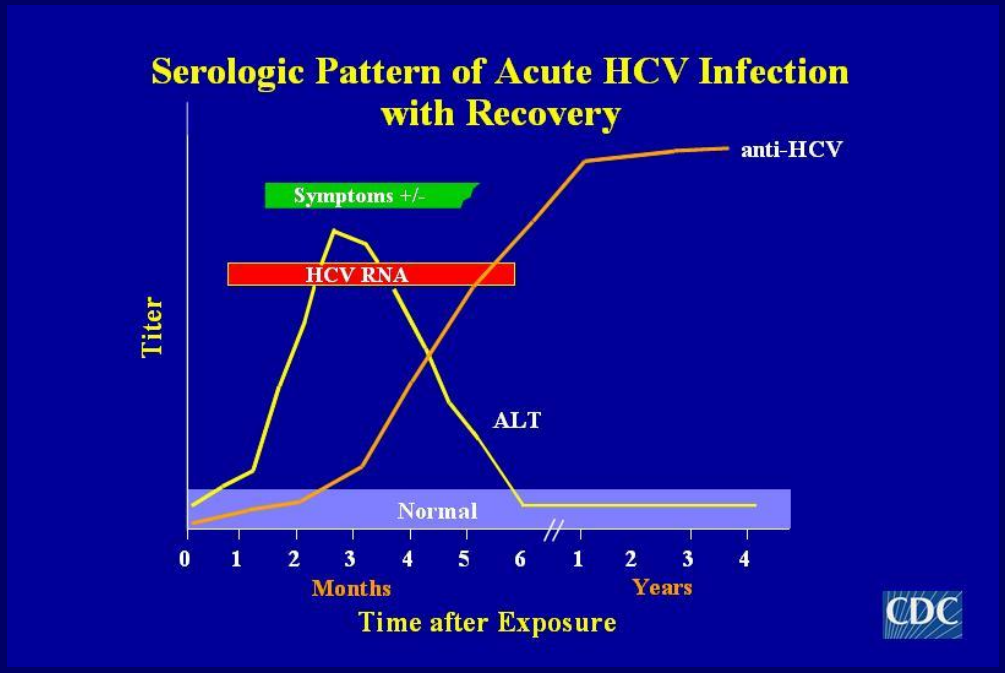
Incubation periode, preicteric, icteric, reconvalescence

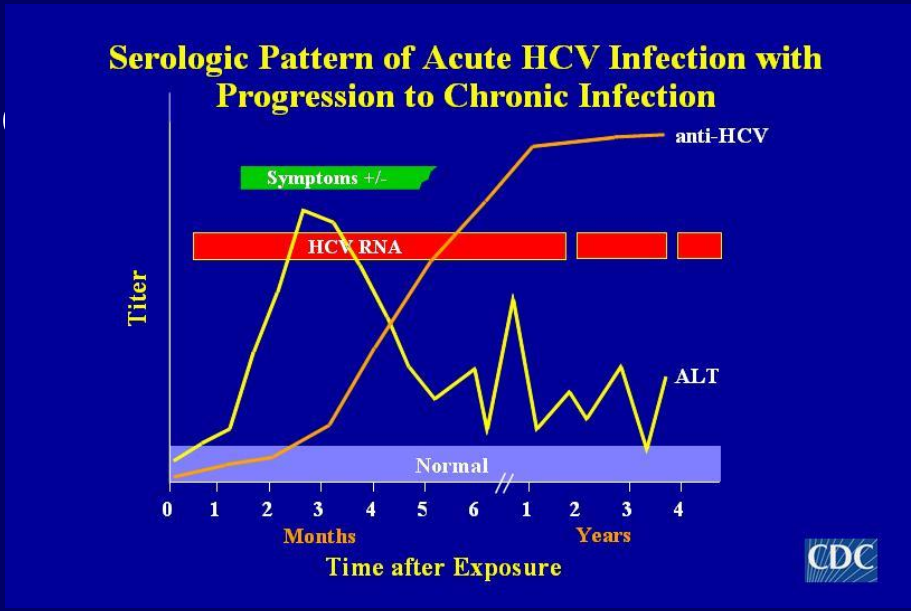

Acute VHB
Recovery
Fulminant hepatitis
HBsAg present for more than 6 mnths
recovery
.
Asymptomatic carier
Chronic persistent hepatitis
Chronic active hepatitis
extrahepatic diseases polyarteritis nodosa, GNFT
cirhóza
Ca
.

Hepatitis C virus – flaviviurs
in 90% potransfussion, dialysed, i.v drug abusers
chronic at 50% and cirhosis in 20%



Acute or chronic disease
acute – milder, chronic more frequent than VHB, Ca, Ci,
coexistence of anti VHC and VHC
the immunity is not necessary always l



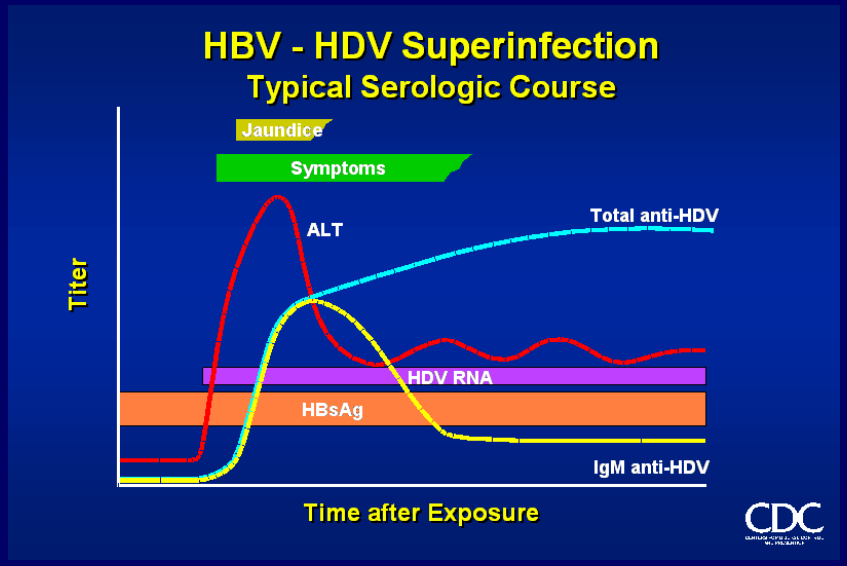


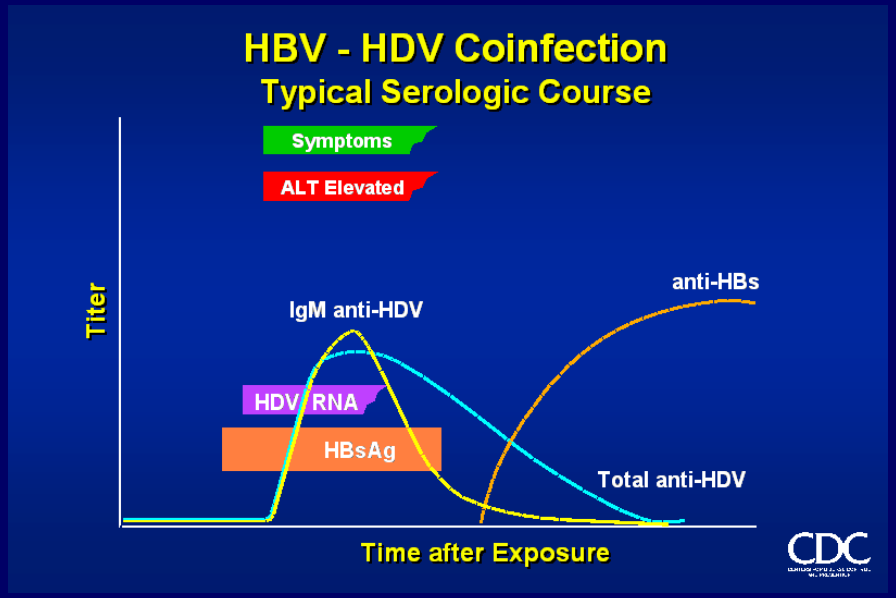
Hepatitis D virus – it is not a complete virus – just a agens of NA delta virus, delta agens

Replication only in cells infected by VHB (persons with active hepatitis B).

Transmission and spread – as VHB – blood borne = coinfection or superinfection in carrier (abrupt begining and severity

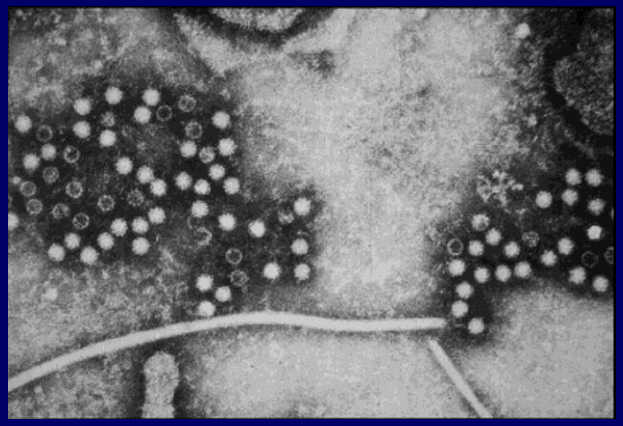
Endemic in – S-Italy, Amasonia,
iv drug abusers

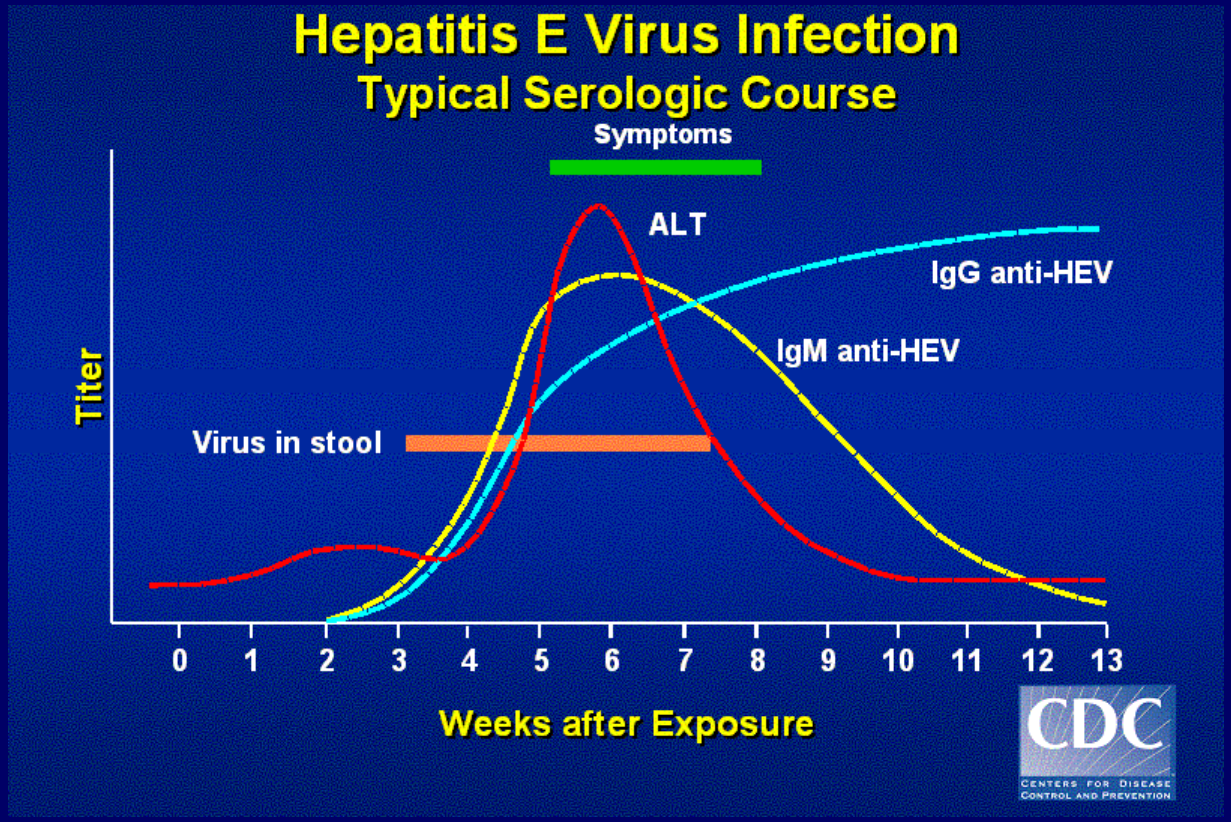




Hepatitis E – virus

endemic – S Italy,
fecal oral transmission, contaminated water
acute mild, mortality 1-2%,
in pregnant – sever infection





HIV a AIDS

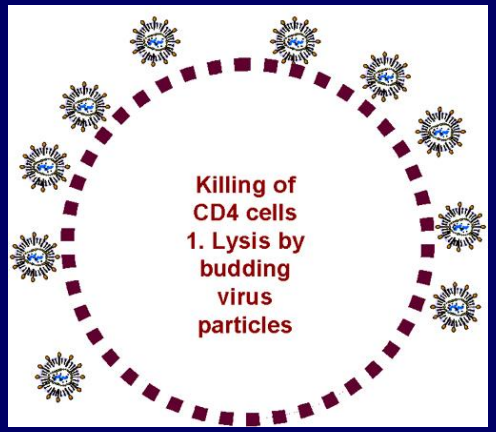
HIV – retrovirus – RNA virus

RNA dependent DNA polymerase – able to produce the DNA variant of its RNA, that will be incorporated to DNA of host cells (CD 4 T lymfocytes, macrophages).

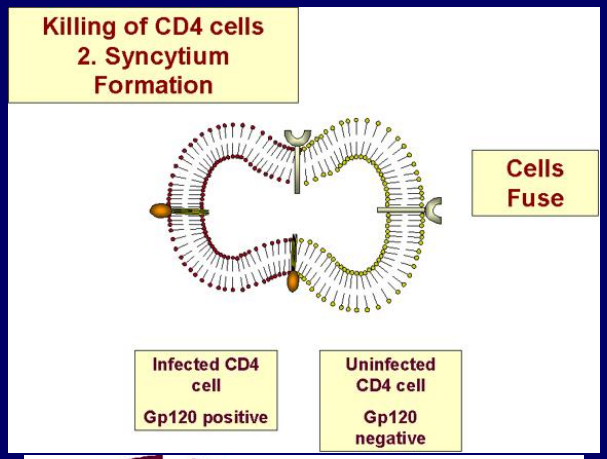
Makrophages do not end with lysis – spread of HIV to different organs (horse of Troia)

after activation HIV is produced and released form the infected cell (lysis) – T lymfocyte – defect of immunity – oportunistic infection from insufficient immunity – **AIDS – disease.**

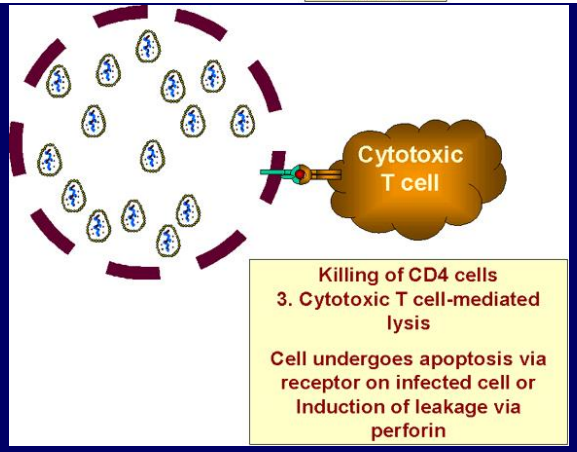
Vírus is latent – avoid immunity and produce mild chronic infection



1.HIV kills infected lymfocyte, because after replication it is released by budding and lysis of the host cell

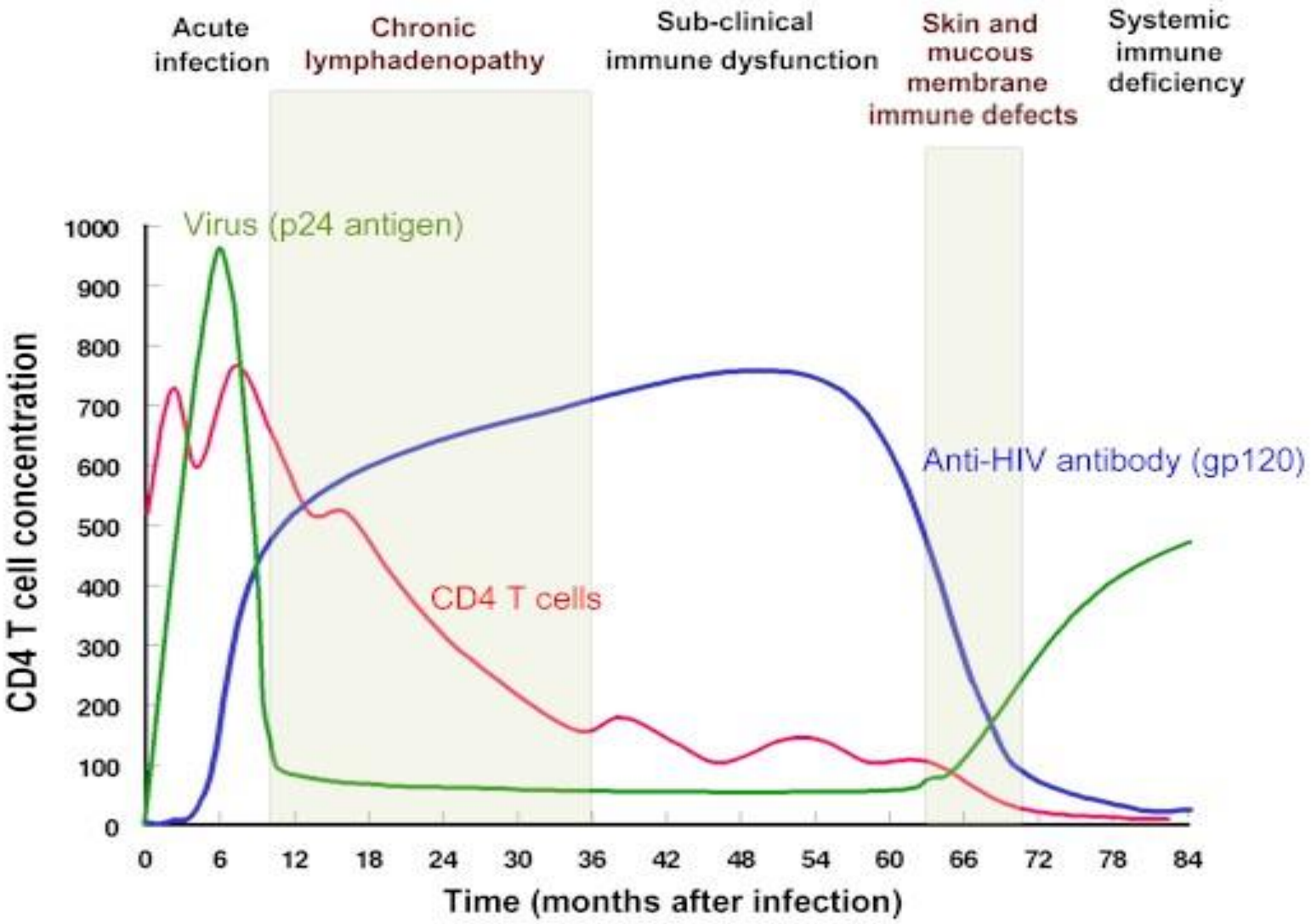


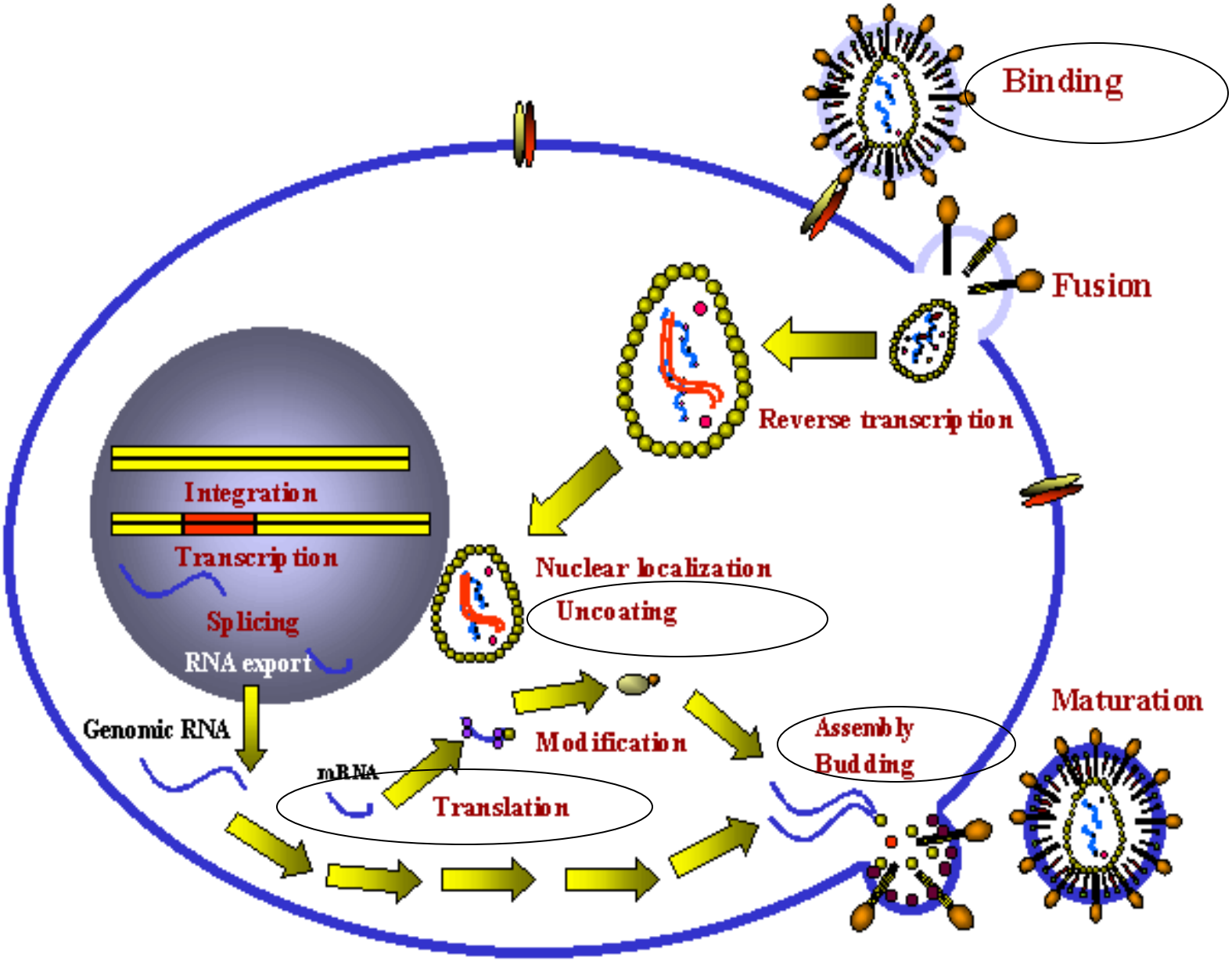
2.Infected and noninfected cell unify and form nets and syncytia of non functionnal lymfocytes



3 Immunocompetent cells do not recognise infected cells, which are foreign for them and they kill them

Depression of T cell quantity


Acute infection
Chronic lymphadenopathy
Sub-clinical immune dysfunction
Skin and mucous membrane immune defects
Systemic immune deficiency
Virus (p24 antigen)
Anti-HIV antibody (gp120)
CD4 T cells
CD4 T cell concentration
1000
900
800
700
600
500
400
300
200
100
0
0
6
12
18
24
30
36
42
48
54
60
66
72
78
84
Time (months after infection)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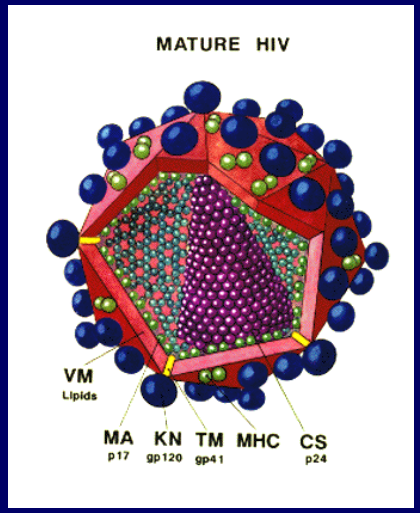
Budding
Maturation

HIV

RNA virus, that contains ensyme *reverse transkriptase - RT*

RT enable, that after infection of T lymphocyte the viral NA is incorporated to the host genome where it survives for several months or years

After a periode of chronical mild persistent infection the number of T lymphocytes gain the critical level, the imunity is compromised and the replication of HIV in the infected T lymfocytes starts, that damage completly the rest of immunity – what finishes clinically with the disease - AIDS.



Desinfection – 70% etanol, 2% glutaraldehyd, 6% H2O2

Imunisation – antigenic variations, not protective antibodies

Virus is situated intracellularly, evade the ab, The principal cell of immunity (T lymfocyte is infected)

Therapy – tricombination, resistnence

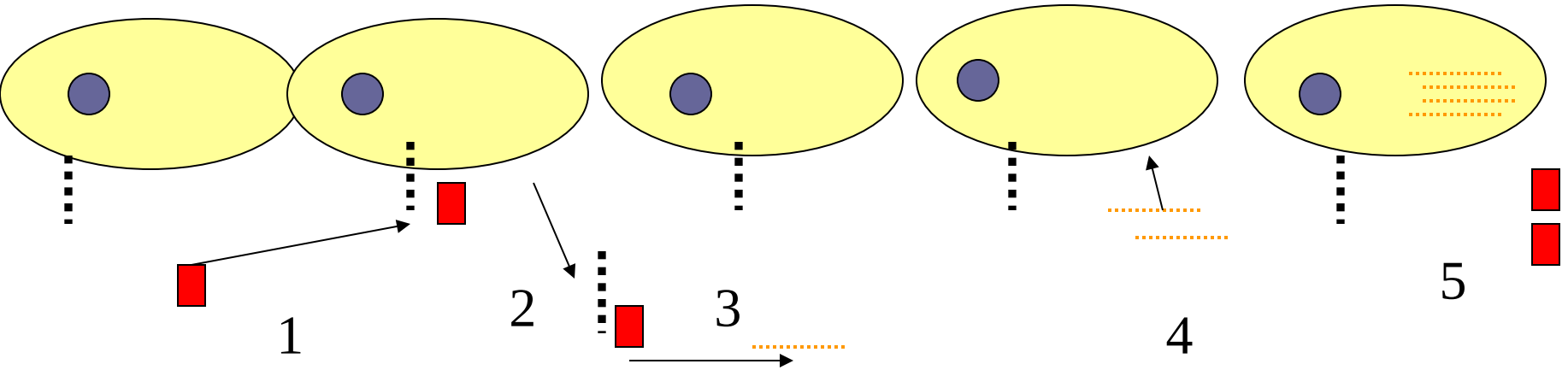
Transmission

Innoculation to blood – transfusion, common needles in drug abusers, injuries with contaminated needle, ooen wound, exposition of mucous membrane in health care workers, tatoo needles
Sexual transmissions – heterosexual
Perinatal – intrauterin, delivery, breast feeding

AIDS – oportunistic infections (*toxoplasmosis of brain, candidosis, of oesophagus, lung, infection with Pneumocystis carini, perzistent or disseminated HSV infection,, disseminated mycobacteriosis)* oportunistic neoplasiae,(*Kaposhi sarcoma, primary lymfoma of brain*

Non convetial viruses Prions

- **Patogenesis:** Normal cell protein PrPc on the surface of cell membrane. PrPsc aggregates(1) with PrPc what allowes its release (2) from the surface of the cell and its change (3) to PrPsc. This new PrPsc is accepted (4) by the cell as own, accumulate (5) in neural cells that make them look like sponge - spongiforme



PrPsc – protease resistent hydrophobic glycoprotein - scrapie prion – nenconvential virus, aggregates to amyloid fibrils in cytoplasmatic vesicules and is secreated out of the cell

Slow viral infections

- **Classical viruses – morbilli virus - SSPE, HIV….**
- **Prions** – not convential viruses – procuces typical pathologically distinct diseases **spongiforme encephalitis** – slowly progreeding neurodegenerative disease: kuru, Creutzfeldt Jakobova disease, Gerstmann-Straussler-Scheinkerova disease. (mad cow disease, scrapie – in annimal). Human variant

Spongiforme encephalopathy

- **dg:** clinical, histological,
- Full blood to EDTA transport on ice – specialised laboratory
- **Clinical signs**: lost of muscle control, tremor, lost of coordination, of memory, demention
- **Transmission:** parenteral

  transplantation - cornea

  contaminated instruments – intra brain probes

  ritual canibalismus

- **Characteristics of prions**:

filtratable inf.agens

Without NA,

Without define shape

Modified host protein

Persistant to common desinfection (formaldehyd, proteases, 80*C, ionisation, UV),

Long lasting generation time, replication every 5 day

Not antigenic, do not induce interferon production, do not induce inflamation or immunity answer or cytopathic effects

Prion diseases are

1. lethal,

2. not curable – the only tool is the prevention

3. transmissible – former PD is resistent to standard means of desinfection and sterilisation

Most important prion diseases

HUMAN

ANNIMAL

CREUTZFELDTOVA-JAKOBOVA

BSE

Bovinná spongiformná

Encefalopátia

Classical VARIANT

New VARIANT

FORM:

1. SPORADIC (Pôvod neznámy)
2. GENETIC (Mutácia PRNP)

3. IATROGÉN (Lekársky zákrok)

Specific incidence

- World: 1-1.5/mil.inhab./year
- Slovakia: 1.6 /mil/inhab./year

  Orava 11.4/ mil./ rok „

New circumstances of CJD

- Genetic risk group with mutation
- Presence of CDJ in elderly patients – escape from statistics
- Transfer of nwCJD by transfusion

Known ways of transmission

SPORADIC CJch

PACIENT

GENETIC

PACIENT + „healthy"

ASYMPTOMATIC

Cornea

Dura mater

Growth hormon

IATROGÉN CJch

Transfúzia

PACIENT + also in incubation time

New VARIANT CJch

Antiviral treatement

Antivirotics

Main problem in antiviral therapy

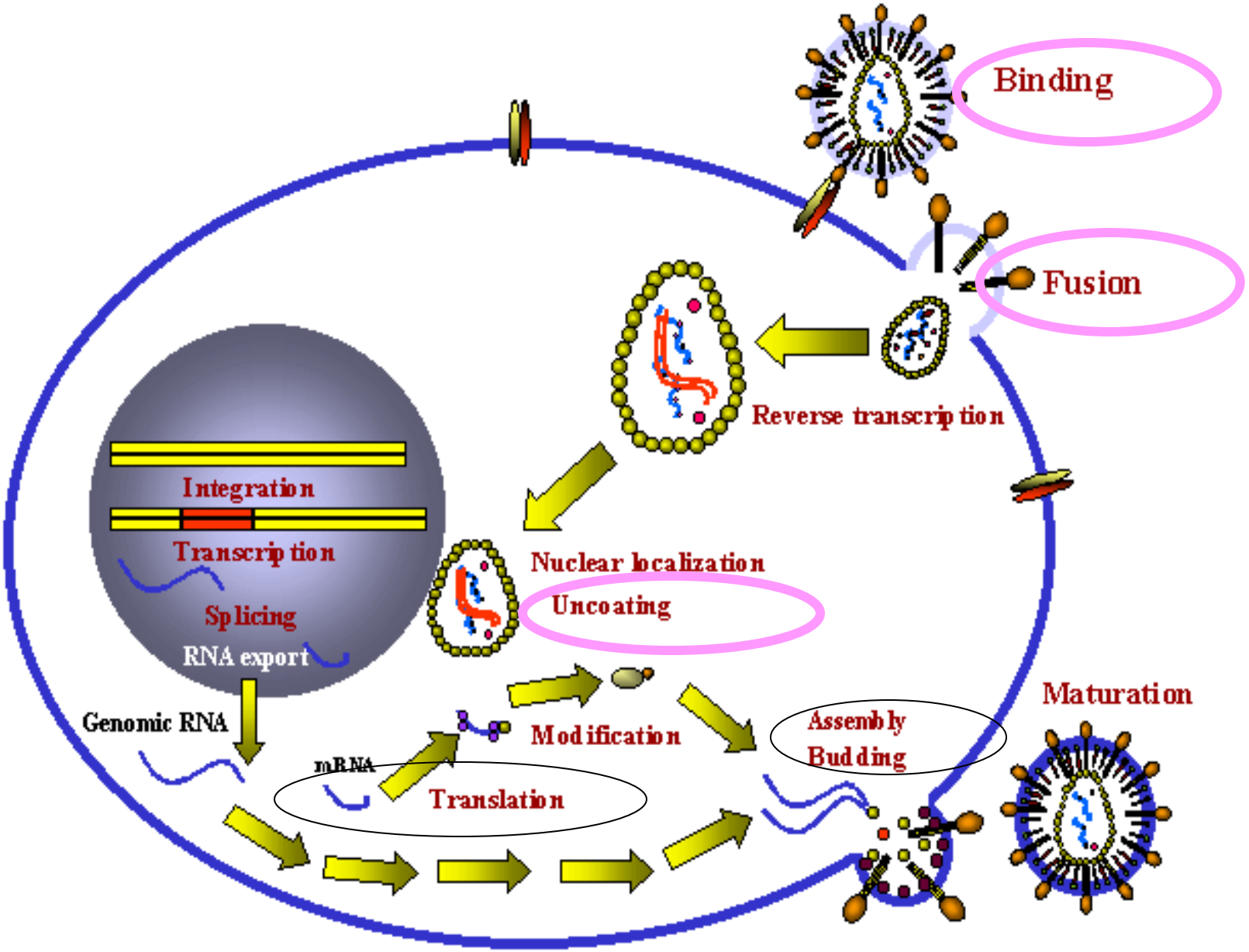
- intracelular localisation of viruses
- use of host structures for replication
- any approch to kill virus in the host cell is toxic for the host

Approaches in antiviral therapy

- they copies the replication cycle
- The best therapy is to increase the existing and functionnal immunity

Antivirotics are not broad spectrum because of different replication pathways of viruses

They are the most efficient if used in prophylaxis or in very early stages of infections.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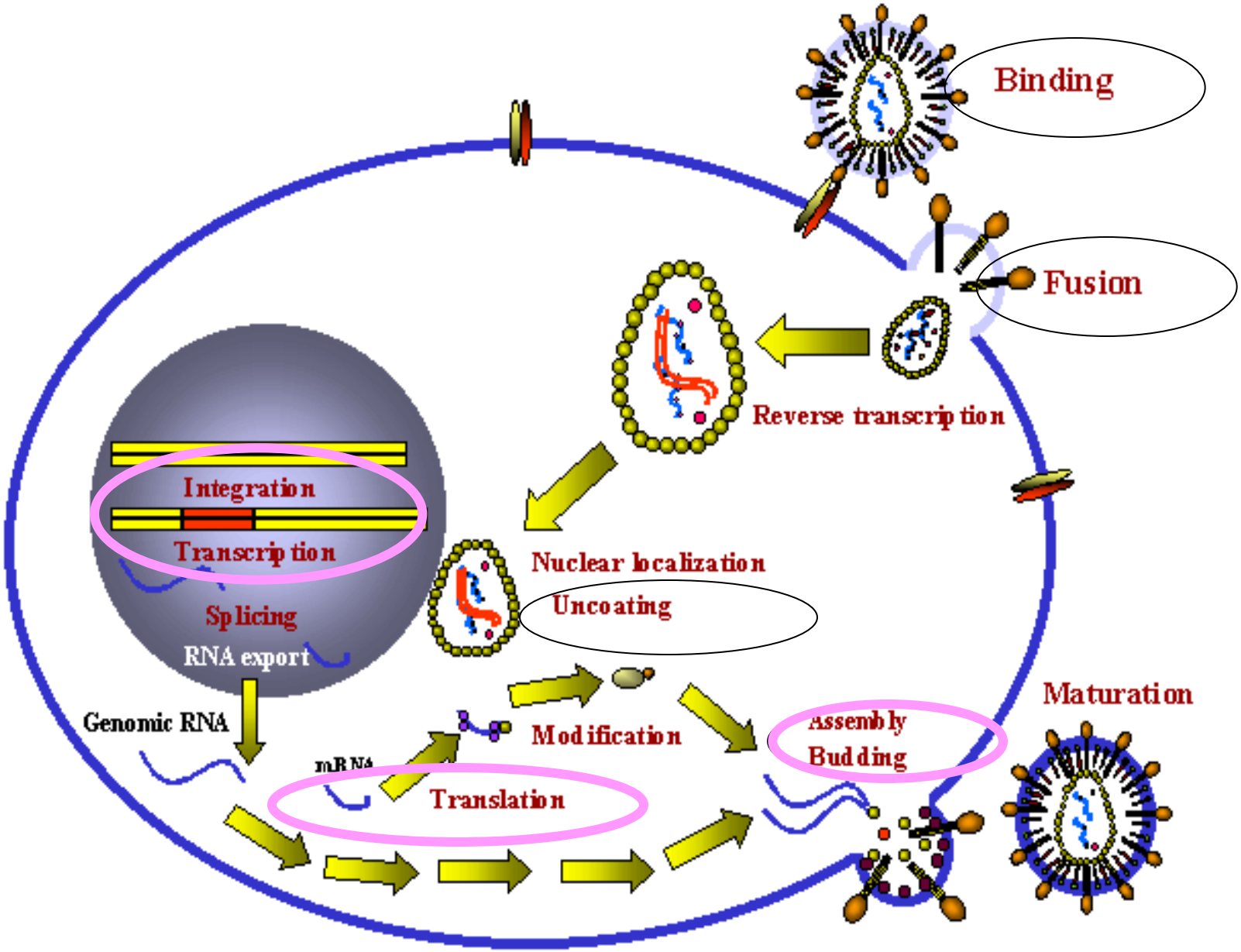
- Recognition and attachment – one of the way is the neutralisation of surface viral antigens with antibodies
  passive immunisation
  antagonists of host cell receptors for viral antigens are peptide analogues, heparin or dextransulfate

- Penetration and uncoating - entry of viruse to cytoplasma and acidic environment of endocytic vacuoles can be neutralised by faible organic bases (amantadin, ribavirin)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- Synthesis of mRNA – is the key point of replication, it cannot be inhibited without host cell mRNA damage.

- Drug targeted to ensymes transcriptase (interferón), polymerase. – This is also the way how works antibacterial ATB Rifampicin, (efficient against adenoviruses and poxvirus.
- anticomplementary nucleotides that block binding of nucleotides to ribosomes and interrupt elongation of peptide chain of RNA (acyclovir, gancyclovir, adeninarabinosid, ziduvidin) or incorporation produces error in new synthetised chain (Idoxuridin).
- Thimidin kináza is ensyme preparing nucleotid substrate by its activity. Its inhibitors cause lack of essential construction units for proteosynthesis

- Assembley of synthetised proteins - inhibited by the help of protease., elimination of lipid envelope by help of detergent-like molecules

- Antivirotics increasing immunity – interferon, interferon inducing drugs, nonspecific immunity support, vaccines.

- Attachment
- – peptide analogue of host cell receptors – HIV gp120
- – neutralising ab –vaccination, passive immunisation
- – dextran sulfate, heparin – HIV, HSV
- Penetration and uncoating
- - amantadin, rimantadin – influenza A virus
- - tromantadin – HSV
- - disoxaril – picornaviruses
- Transcriptions, synthesis of proteins
- - interferon – VHA, VHB, VHC, papilomaviruses
- DNA replication
- - polymerase, nucleotide analogues – herpesviruses, HIV
- - fosfonofumaratet – herpesviruses
- Synthesis of nucleoside
- - ribavirin – RSV
- Thymidin kinse inhibitions
- - nukleotide analogues – HSV, VZV
- Maturation
- - proteases against assembley of subunits – HIV

Best target viruses for antivirotics are
herpesviruses (HSV, VZV, CMV),
HIV,
Influenza A virus, RSV,
Viruses of hepatitis A, B, C. papilomaviruses.

HSV – Acyclovir (Zovirax), Adeninarabinoside (Vidarabin), Iododeoxyuridin, Trifluorothymidin – local th

CMV – gancyclovir, fosfonoformat (Foscarnet)

HIV– azidothymidin (Retrovir, Zidovudine), dideoxyinosine (DDI), dideosycytidine

Influenza A virus – amantadin

VHC – interferon (Intron, Roferon)

Papilomaviruses – interferon alfa

RSV, Lassa virus – ribavirin (Virazol)