Infections in pregnancy. Sexually transmitted diseases (STD)

Pavel Drevinek

Infections in pregnancy (intrauterine transmission)

- primoinfection of mother: no immunity
  rubella, CMV, parvovirus, toxoplasma
- recurrence of latent infection:
  CMV, HSV
- chronic infection of mother
  hepatitis B, HIV
- neither of above
  listeria, syphilis

perinatal transmission:

HIV, syphilis (more frequently intrauterine)
HSV, *C. trachomatis*, *N. gonorrhoeae*, GBS ....

hepatitis B (via blood)
E. coli (contamination from stool) ...

Infections in pregnancy

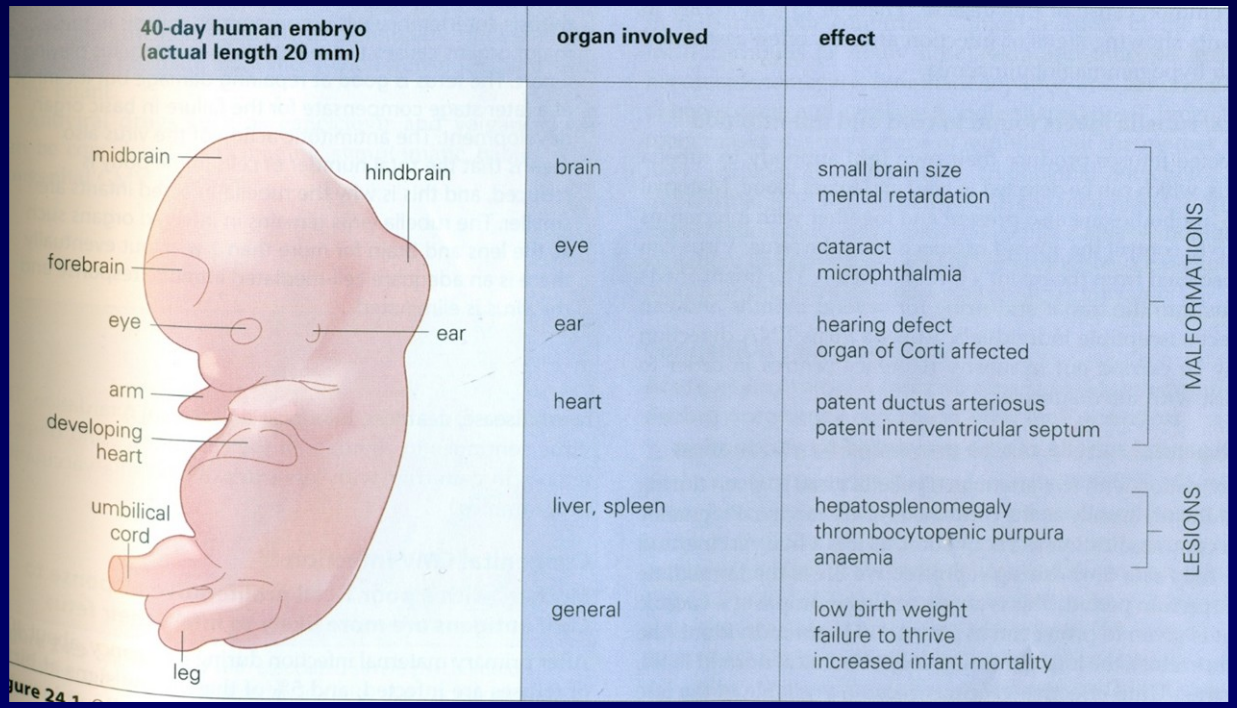
- sexually transmitted
  HIV, herpesviruses (HSV), syphilis
- not STD
  rubella, parvovirus, toxoplasma

Pregnant woman asymptomatic / benign signs of infection
Child severely affected

Infections in pregnancy

- death of the fetus
- malformation of the fetus (teratogenic effect)
- after birth:
  - congenital infection (with persistence of the agent)
    - early with immediate symptomatology
    - late
  - peri(neo)natal infection

Risk factors:
- immunity of mother
- week of pregnancy



Infections in pregnancy

- S Syphilis
- T Toxoplasmosis
- O Other (parvovirus B19, VZV, hepatitis B, E, …)
- R Rubella
- C CMV
- H HSV, HIV

Mikrobiological diagnostics:

serology

PCR of viruses

Treponema pallidum

- teratogenic

- Afftecting the fetus:
  - Primary of secondary stage at the mother = risk of transmission almost 100%
  - ... therapy eliminates that risk!

Congenital syphilis:

early: like II. stage in adults

alteration of cartilages, bones, skin lesions, hepatitis

late: Hutchinson trias: teeth, deafness, keratitis

Toxoplasma gondii

- teratogenic

affected

- first trimester: 10% of fetuses, but more serious
- third trimester: 60%

Congenital toxoplasmosis

often late onset of signs

microcephalia, chorioretinitis, mental retardation

(rarely as Sabin trias: hydrocephalus, calcifications in brain)

problem in dg. in pregnancy: long-term IgM positivity

Rubella

- teratogenic

Congenital rubella syndrome (CRS):
= Gregg's syndrome: eyes (cataract, microphtalmia), heart, deafness

secretion of viruses from saliva, urine as the example of persistent infection after birth
later signs of CRS: deafness, mental retardation

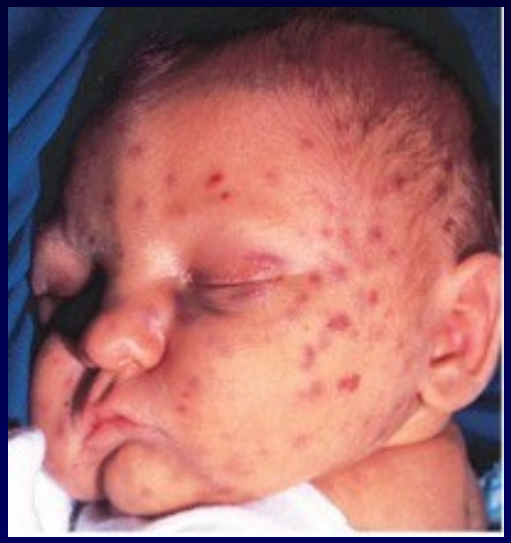
affected
- until week 11: 90% of fetuses
- until week 16: 20% of foetuses
- week 20 and above: 0%

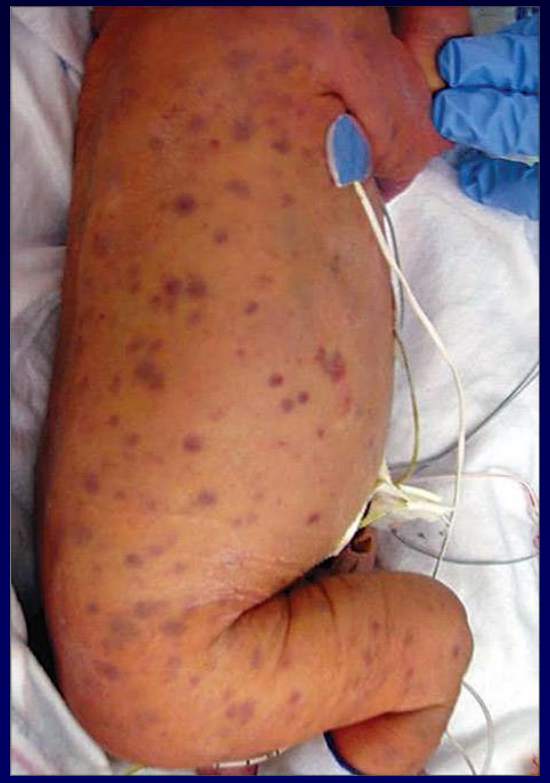
Cytomegalovirus

- teratogenic

Congenital CMV = most common congenital disease (in 90% asympt.)
haematopoesis affected: anemia, thrombocytopenia; chorioretinitis

Blueberry muffin baby





secretion of viruses from saliva, urine
later signs of congenital infection:
deafness, mental retardation

Parvovirus B19

affinity to myocard cells, erythroblasts

non-teratogen,
but serious risk to develop hydrops fetalis

HIV

Congenital infection:
progression to AIDS

25% risk of vertical transmission

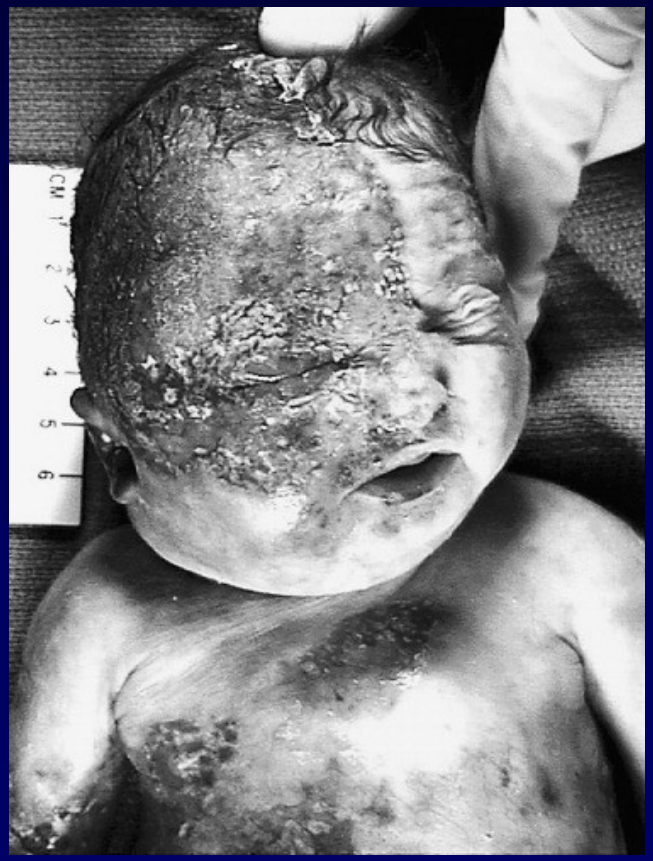
- antiretrovirotic therapy of mother (third trimester) – today with combined therapy (lowering risk to less than 0.5%)
- cessarian section
- no breastfeeding

Listeria monocytogenes

- intrauterine infection:
  premature labour and sepsis, rarely granulomatosis infantiseptica
- perinatal infection:
  meningitis

Streptococcus agalactiae (GBS)

- perinatal infection:
  sepsis, meningitis, pneumonia
- "late" infections in first month of life



HSV

- most often to be perinatal infection:
  disseminated skin infection
  encephalitis
  other organs (lungs, liver)

Hepatitis B

risk of fulminant hepatitis
prophylaxis: vaccine + immunoglobulins

N. gono, *C. trachomatis*

keratoconjunctivitis – eye drops
C. trachomatis - pneumonia

Diagnostics

Screening during pregnancy:

- hepatitis B
- syphilis
  - in I. and III. trimester and in neonates
- HIV
- rubella
- (toxoplasma)

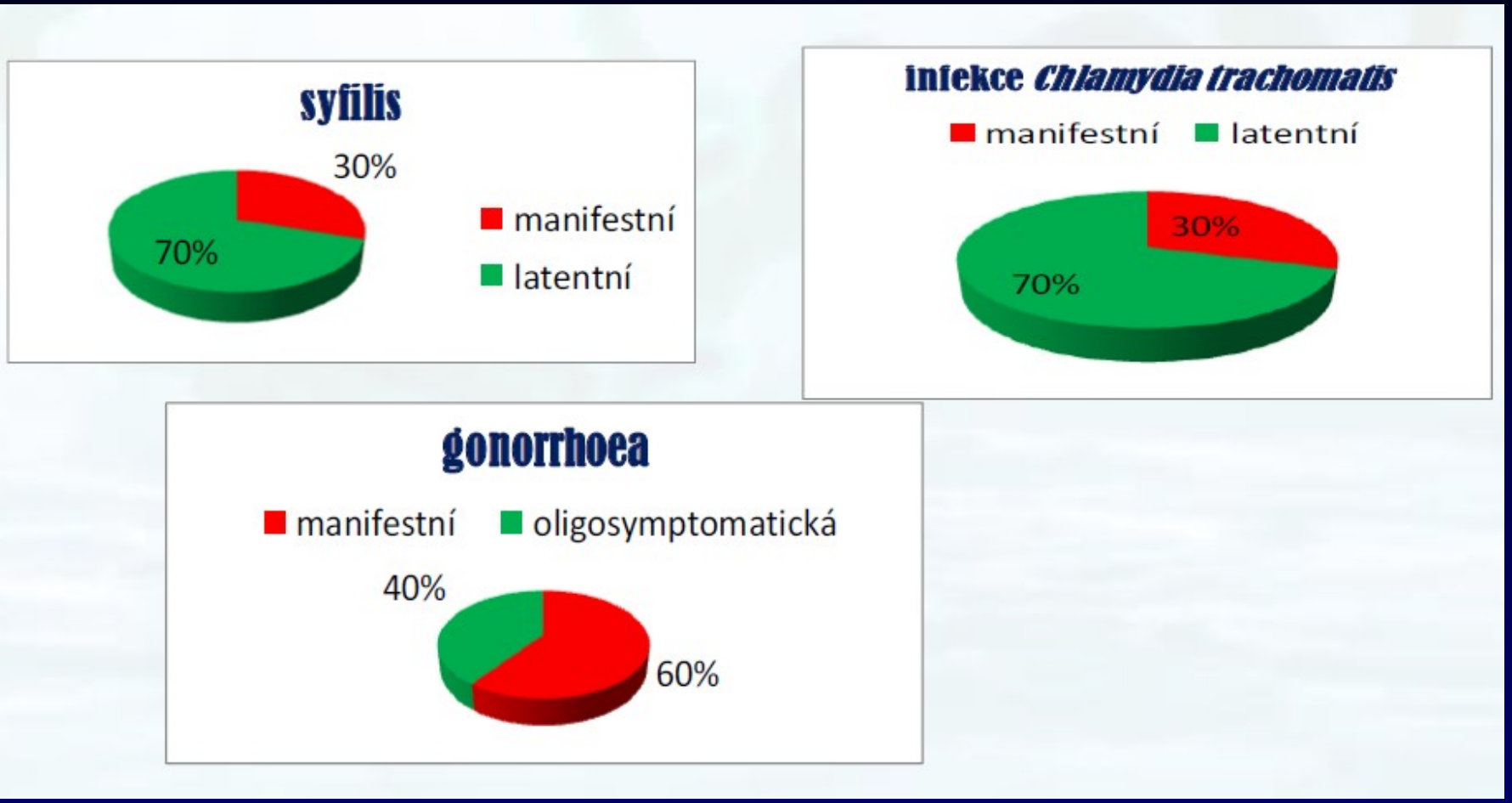
Sexually transmitted diseases

Paradox: controllable diseases

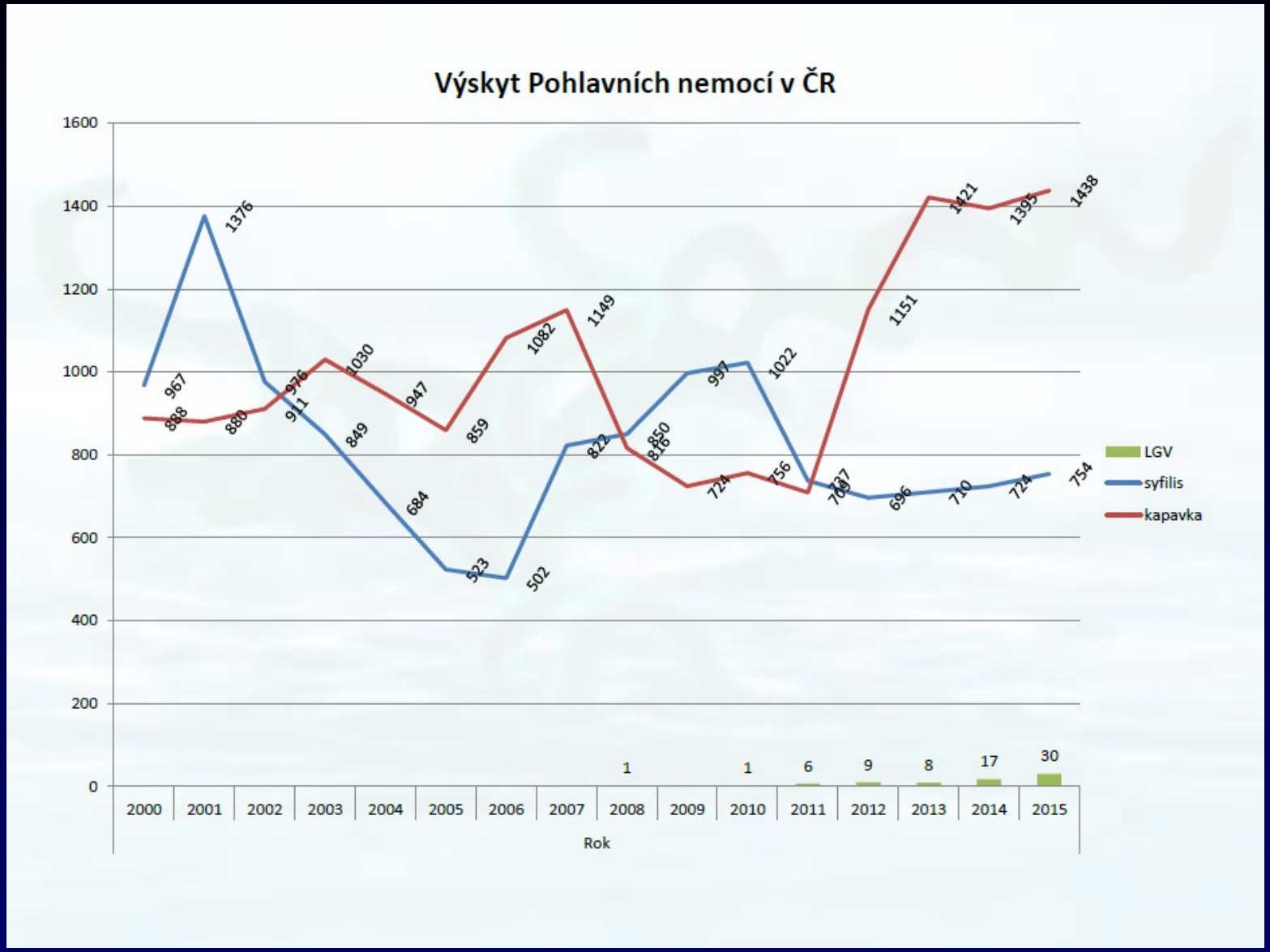
- no reservoir in environment
- mechanisms of transmission is not easy
- sensitive agents

but these are not under control

- no vaccination (except HPV, HBV)
- often asymptomatic
- late diagnostics (not because of labs)
- sexual practices



zdroj: Dr. Zákoucká, Státní zdravotní ústav, NRL pro dg. syfilis, chlamydie



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NRL pro dg. syfilis, chlamydie

Basic signs:

- discharge
- changes on mucosa - ulcers, pustules... (mucosa which were in contact - genital organs, mouth, rectum)

Basic nosological unit = urethritis, cervicitis

THESE ARE NOT urinary tract infections

Eligible material

- urine (first in the morning)

  - PCR (species specific)

- swab from urethra, cervix, vagina

  - microscopy if immediately put on the microscopic slide
  - culture (transport medium)

- swab from skin lesion

  - microscopy
  - culture
  - PCR

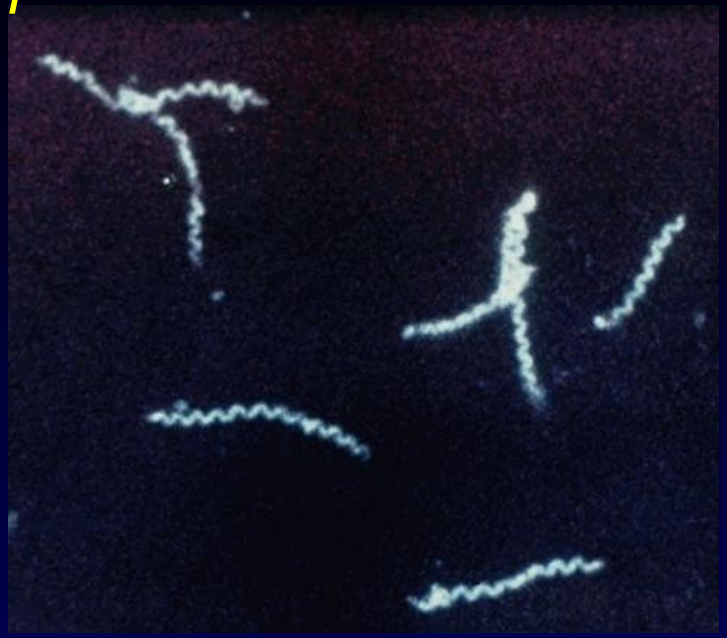
- serum

	Agent	disease
Viral STD		
	HSV2 (HSV1) HBV HCV HIV HPV	Herpes genitalis Viral hepatitis B Viral hepatitis C AIDS Condyloma, verruca, ca of cervix
Bacterial		
	Treponema pallidum	syphilis
	Nesseria gonorhoeae	gonorrhoea
	Chlamydia trachomatis	lymphogranuloma venereum, urethritis…
	Haemophilus ducreyi	ulcus molle
Parasites		
	Trichomonas vaginalis *Phthirus pubis* *Sarcoptes scabiei*	Trichomoniasis Phtiriasis pubis Scabies
Mykotic		
	Candida spp.	Candidosis

Treponema pallidum subsp. *pallidum*

Stage		Time period	manifestation	diagnostics
early	**primary**	weeks	ulcum durum and bubo	microscopy, PCR, antibodies
	secondary	weeks - months	Generalisation: skin, condylomata lata	antibodies
	latent	1 year (2 yrs)	none	antibodies
late		many years	none	antibodies
	tertiary		Organs: neurosyphilis, cardiovascular, gumma	antibodies

Treponema pallidum subsp. *pallidum*



- direct diagnostics

  - microscopy (dark field)
  - PCR

- indirect diagnostics

  - non-specific (non-treponema) = VDRL (RRR, BWR)
    cardiolipin as an antigen
    positive earlier (~ from 4 weeks p.i.), positivity disappears with therapy
    risk of false findings

  - specific (treponema) - TP (hem)agglutination TPHA, TPPA; FTA-ABS, ELISA, WB
    says which isotypes IgG, IgM (important for congenital syphilis)
    IgG positive life long
    confirmation at the reference lab

Treponema pallidum subsp. *pallidum*

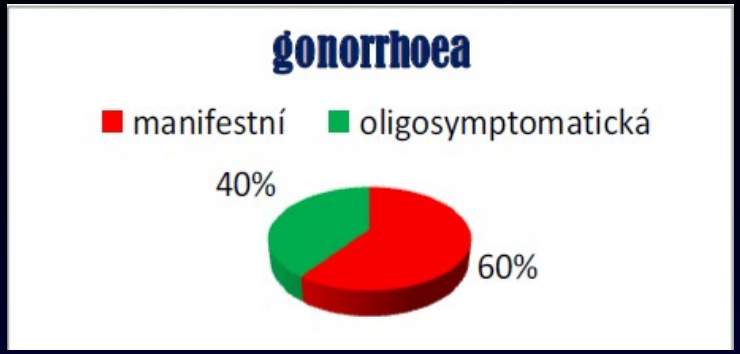
- indirect diagnostics

- non-specific = VDRL (RRR, BWR)

- specific - TPHA, TPPA; FTA-ABS, ELISA, WB

VDRL	specific reaction	interpretation
+	+	active infection
+	-	false positivity ?
-	+	successful therapy

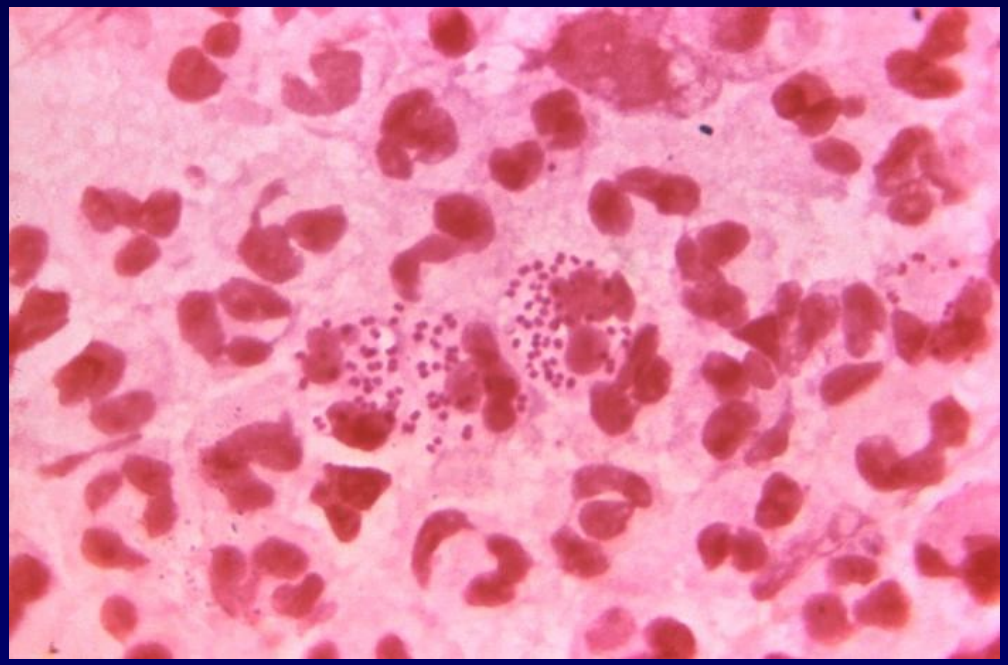
Neisseria gonorrhoeae



high penetration
- urethriti, cervicitis
- complication: disseminated
(peritonitis, sepsis, meningitis)

- tonsilopharyngitis, proctitis
- neonatal conjunctivitis

Diagnostics:
microscopy (urethritis; MOP IV)
culture (special conditions)
PCR



Therapy:
cephalosporins
III. generation
+
macrolides
tetracyklins
quinolons

WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

Priority 1: CRITICAL#

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

Chlamydia trachomatis

Serotypes associated with different diseases:

- A,B,C: trachoma (not STD)
- L: lymphogranuloma venereum
- D - K: STD: urethritis, prostatitis
  cervicitis, salpingitis (also chronic asymptom. -- infertility)
  proctitis
  paratrachoma = neonatal conjunctivitis
  neonatal pneumonia

Diagnostics:
~~microscopy~~
~~culture~~
PCR

STD
Neisseria gonorrhoeae
Chlamydia trachomatis
Mycoplasma genitalium
Mycoplasma hominis
Ureaplasma parvum
Ureaplasma urealyticum
Trichomonas vaginalis

Therapy:
macrolides
tetracyklins
quinolons

male 33 years

pain during urination

18.5.2018:
urine

STD agents	result
Neisseria gonorrhoeae	neg.
Chlamydia trachomatis	**+++**
Mycoplasma genitalium	neg.
Mycoplasma hominis	neg.
Ureaplasma parvum	neg.
Ureaplasma urealyticum	neg.
Trichomonas vaginalis	neg.

↓

azitromycin

25.6.2018:
urine

STD agents	result
Neisseria gonorrhoeae	neg.
Chlamydia trachomatis	neg.
Mycoplasma genitalium	neg.
Mycoplasma hominis	neg.
Ureaplasma parvum	neg.
Ureaplasma urealyticum	neg.
Trichomonas vaginalis	neg.

male 33 years

pain at urination,
whitish discharge

sex partner not treated

22.8.2018:
urine

STD agents	result
Neisseria gonorrhoeae	neg.
Chlamydia trachomatis	++
Mycoplasma genitalium	neg.
Mycoplasma hominis	neg.
Ureaplasma parvum	neg.
Ureaplasma urealyticum	neg.
Trichomonas vaginalis	neg.

↓

azitromycin

5.10.2018:
urine

STD agents	result
Neisseria gonorrhoeae	neg.
Chlamydia trachomatis	neg.
Mycoplasma genitalium	neg.
Mycoplasma hominis	neg.
Ureaplasma parvum	neg.
Ureaplasma urealyticum	neg.
Trichomonas vaginalis	neg.

Mycoplasma and ureaplasma

STD
Neisseria gonorrhoeae
Chlamydia trachomatis
Mycoplasma genitalium
Mycoplasma hominis
Ureaplasma parvum
Ureaplasma urealyticum
Trichomonas vaginalis

Risk factor or a causative agent ?
urethritis, prostatitis
chorioamnionitis and premature labours

female 38 years

- macules and pustules on belly and legs; not itchy
- lesion on tongue

- in patient's history: oral sexual contact with a friend 2 months ago

Findings:

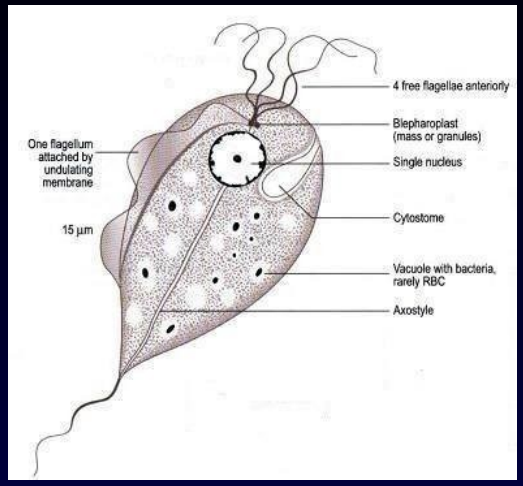
throat swab

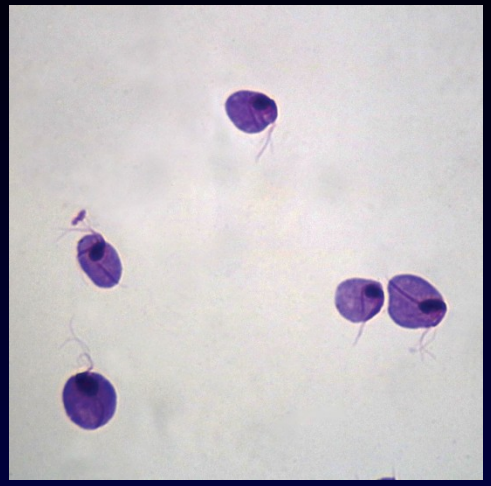
STD agents	result
Neisseria gonorrhoeae	neg.
Chlamydia trachomatis	neg.
Mycoplasma genitalium	neg.
Mycoplasma hominis	**++++**
Ureaplasma parvum	neg.
Ureaplasma urealyticum	neg.
Trichomonas vaginalis	neg.

Serum

RPR	**reactive**
TPPA	**reactive**

Trichomonas vaginalis





vaginitis, urethritis

Diagnostics:
~~microscopy (MOP V)~~
~~culture (Diamond's medium)~~
PCR

Therapy:
metronidazol

Herpes simplex (HSV2, HSV1)

primary, recurrent infections -- vesicles

HPV

Genotypes associated with different diseases:

- warts
- condyloma (condylomata accuminata)
- oncogenic (cervix, oropharyngeal, larynx)

HCV

not only via sexual contact (not the major route)

- high tendency to develop chronic infection (min. 60 %)
- curable thanks to DAA (direct acting antivirals) - specific by HCV genotype
  success of therapy to be monitored by quantification of viral load

HBV

not only via sexual contact

Stages / forms of inection: (susceptible neonates: 90 % vs. 5 % adults)

	Findings:	
- acute infection	HBsAg+	anti-HBc+ (IgM)/-
- chronic hepatitis		
- active	HBsAg+ HBeAg+	anti-HBc+ anti-HBe-
- carriage	HBsAg+ HBeAg-	anti-HBc+ anti-HBe+
- hepatocellular carcinoma		
- "recovery" (latent infection)		anti-HBc+, anti-HBs+

Diagnostics:

with antigens and antibodies

HBsAg	anti-HBs
---	anti-HBc (life-long evidence of infection)
HBeAg	anti-HBe

HIV

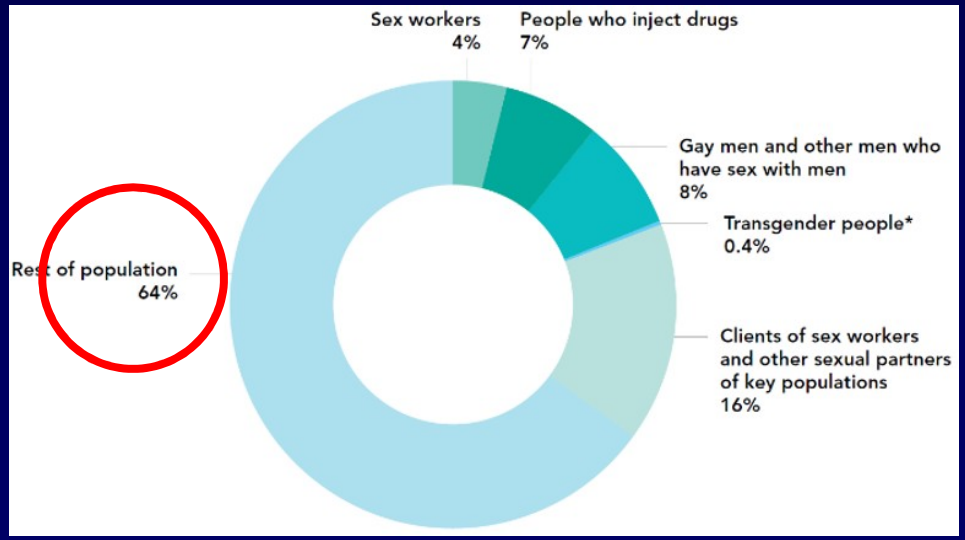
1981 June 5;30:250–2

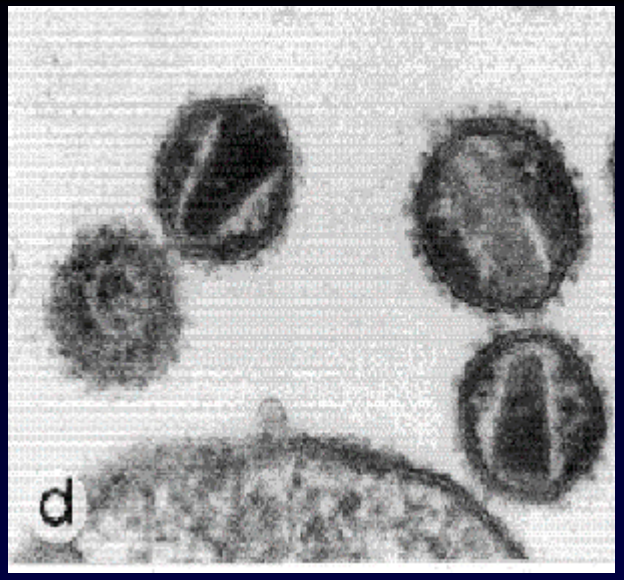
Pneumocystis Pneumonia – Los Angeles

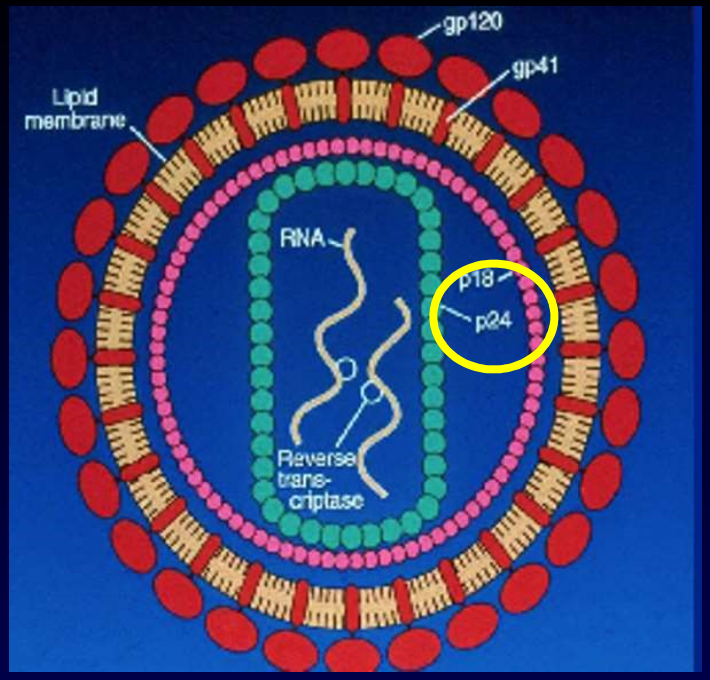
In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Today 37 million of patients (2/3 in Africa)

Morbidity nad mortality weekly report. Center for Disease Control (CDC).



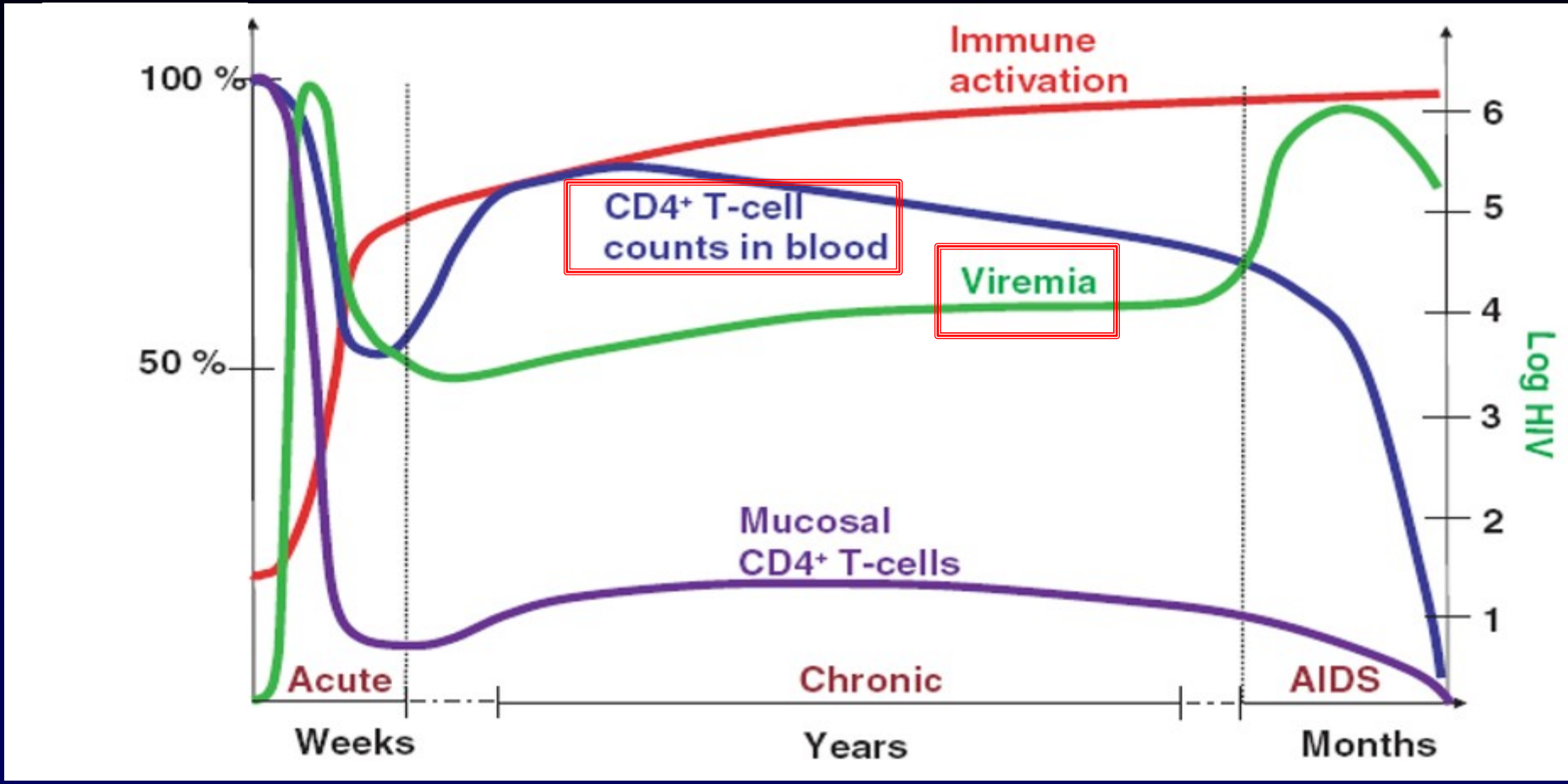




Diagnostics:

- antibodies (ELISA): in 3 weeks (to confirm with immunoblot)
- Ag p24: in 2 weeks
- RNA: in 10 days

Course in untreated individual:



zdroj: Grossman et al. Pathogenesis of HIV infection: what the virus spares is as important as what it destroys. Nat Medicine 2006.

CD4 positive T cells:

norm: 1400/mm^3

AIDS: < 200

(speed of progression depends on viral load)

Therapy:

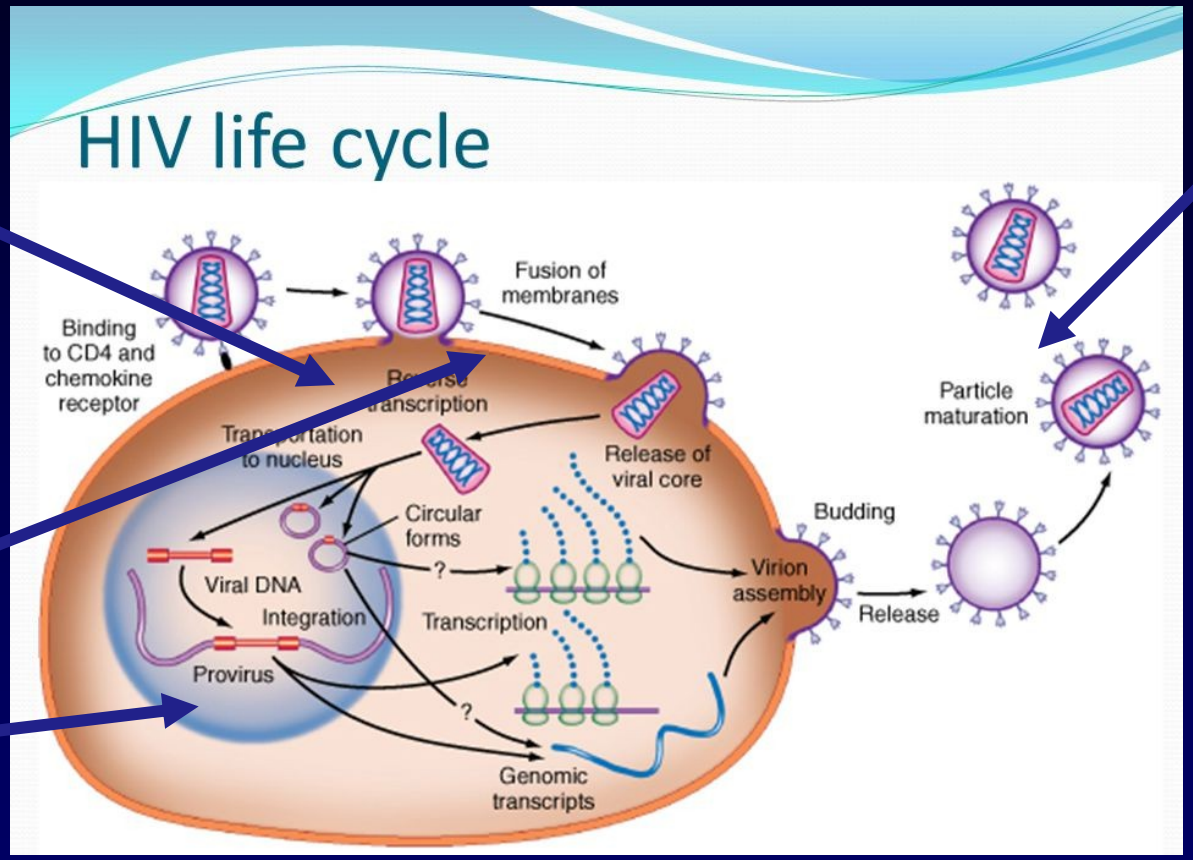
Goal: to suppress replication of HIV, viral load in blood
When to start: immediately (regardless the CD4+ count)

inhibitors RT
- nucleoside(tide)
- nonnucleoside:

zidovudin (1987)
lamivudin
tenofovir
...

fusion inhibitors

integrase inhibitors



protease inhibitors:
lopinavir
atazanavir
...

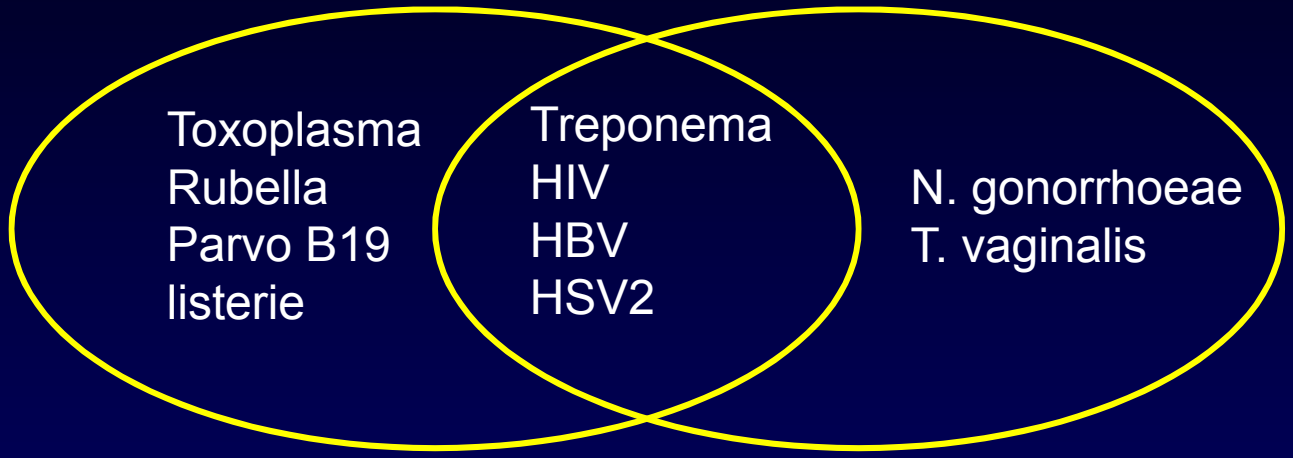
HAART: to administer in two-, three drug combo (two nucleoside inhibitors + third drug)

Opportunistic pathogens at the stage of AIDS:

Pneumocystis jiroveci
CMV (retinitis, oesophagitis)
Toxoplasma gondii
NTM (*M. avium* complex) and *M. tuberculosis* (developing countries)
Cryptococcus neoformans (meningitis)

Conclusion:

Infections in pregnancy and STD agens overlap, but not completely



… no overlap with UTI