Infections in pregnancy.
Sexually transmitted diseases (STD)

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Infections in pregnancy (intrauterine transmission)

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

perinatal transmission:

- but more frequently intrauterine: syphilis, listeria
- and more frequent than intrauterine: HIV, HSV, HBV
- only perinatal: *C. trachomatis*, *N. gonorrhoeae*, GBS

maternal blood
vagina
stool

Infections in pregnancy (with the risk to the fetus)

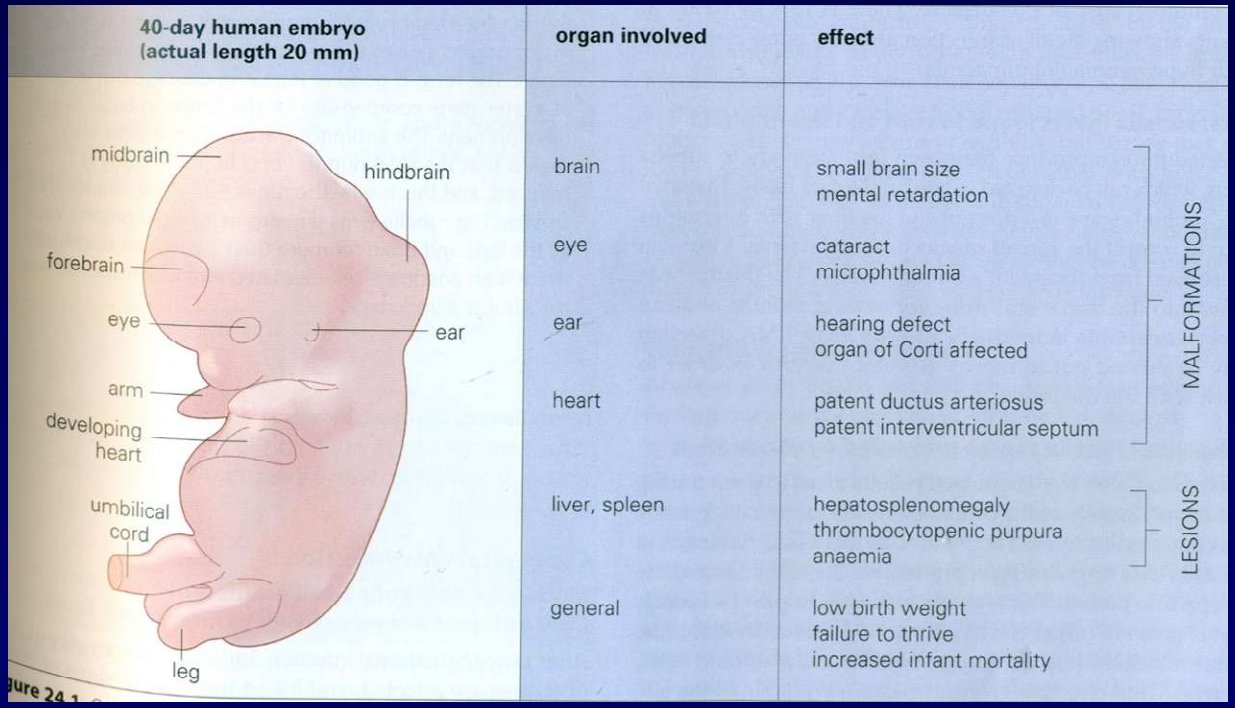
- sexually transmitted
  HIV, herpesviruses (HSV2), syphilis
- not STD
  rubella, parvovirus, toxoplasma

Pregnant woman asymptomatic / benign signs of infection
Child severely affected

Risk factors for the development of the fetal infection:
- primary infection vs. re-infection/recurrence
- gestational age at the time of infection

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 (silent at birth)
  - peri(neo)natal infection



Infections in pregnancy

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

Microbiological diagnostics:
serology
PCR of viruses

Screening at pregnancy:
Syphilis Ab
Hepatitis B HBsAg
HIV Ab
(rubella)
(toxoplasma)

GBS culture

Treponema pallidum

- teratogenic

- Afftecting the fetus:
  - Primary or 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%, less serious

Congenital toxoplasmosis

often late onset of signs

microcephalia, chorioretinitis, mental retardation

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

Rubella

- teratogenic

affected

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

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

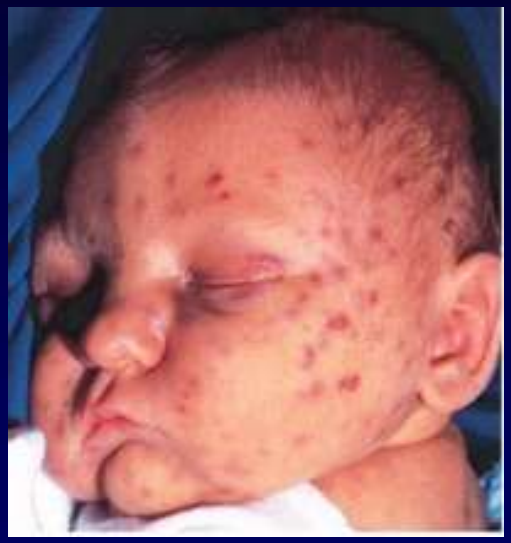
later signs of CRS: deafness, mental retardation

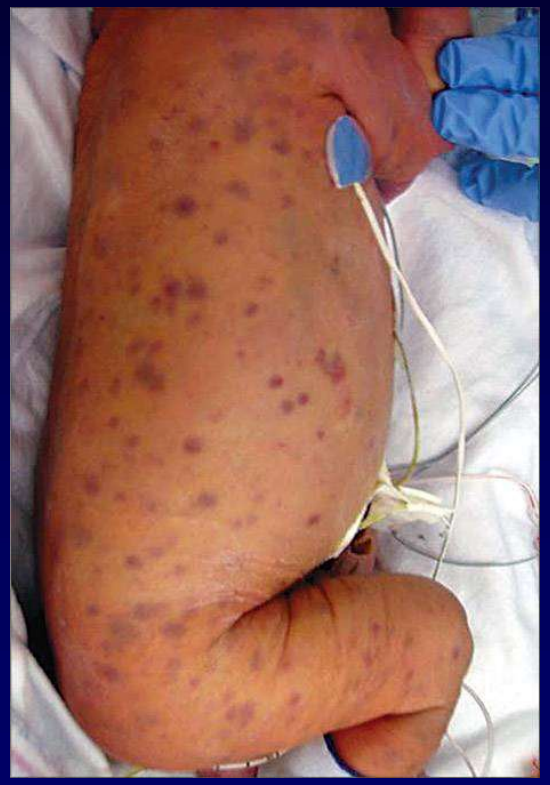
Cytomegalovirus

- teratogenic (also, VZV, HSV from herpesviruses)

Congenital CMV = most common congenital disease (in 90% asymptomatic)
haematopoesis affected: anaemia, 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 (due to severe anaemia)

Perinatal transmission:

- but more frequently intrauterine: syphilis, listeria
- and more frequent than intrauterine: HIV, HSV, HBV
- only perinatal: *C. trachomatis*, *N. gonorrhoeae*, GBS

Listeria monocytogenes

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

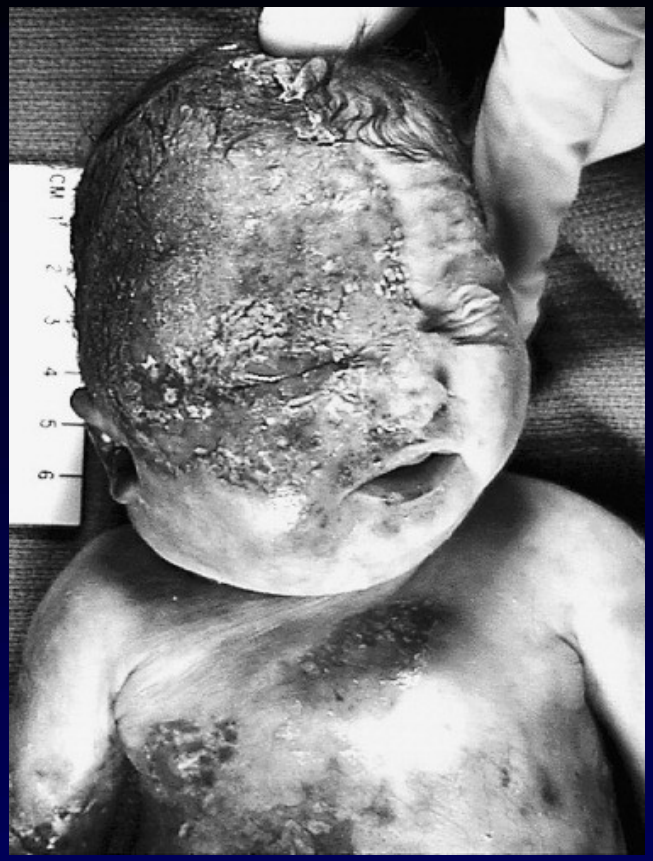
TABLE 2.1. Causative organisms o neonatal neningitis[a]

Country	United Kingdom [12]	Total
Observation period	2010–2011	
Streptococcus agalactiae	150	565 (58%)
Escherichia coli	41	203 (21%)
Listeria monocytogenes	11	19 (2%)
Streptococcus pneumoniae	28	39 (4%)
Other	72	156 (16%)
Total	302	982

[a]Studies were performed in different time periods, with varying vaccination st

HSV

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



Hepatitis B

risk of acute, fulminant hepatitis
prophylaxis: vaccine + immunoglobulins

HIV

Congenital infection:
progression to AIDS

25% risk of vertical transmission

- antiretroviral therapy of mother (third trimester) – today with combined therapy (lowering risk to less than 0.5%)

N. gonorrhoae, *C. trachomatis*

neonatal conjunctivitis – eye drops
C. trachomatis - pneumonia

Streptococcus agalactiae (GBS)

perinatal infection:
sepsis, meningitis, pneumonia

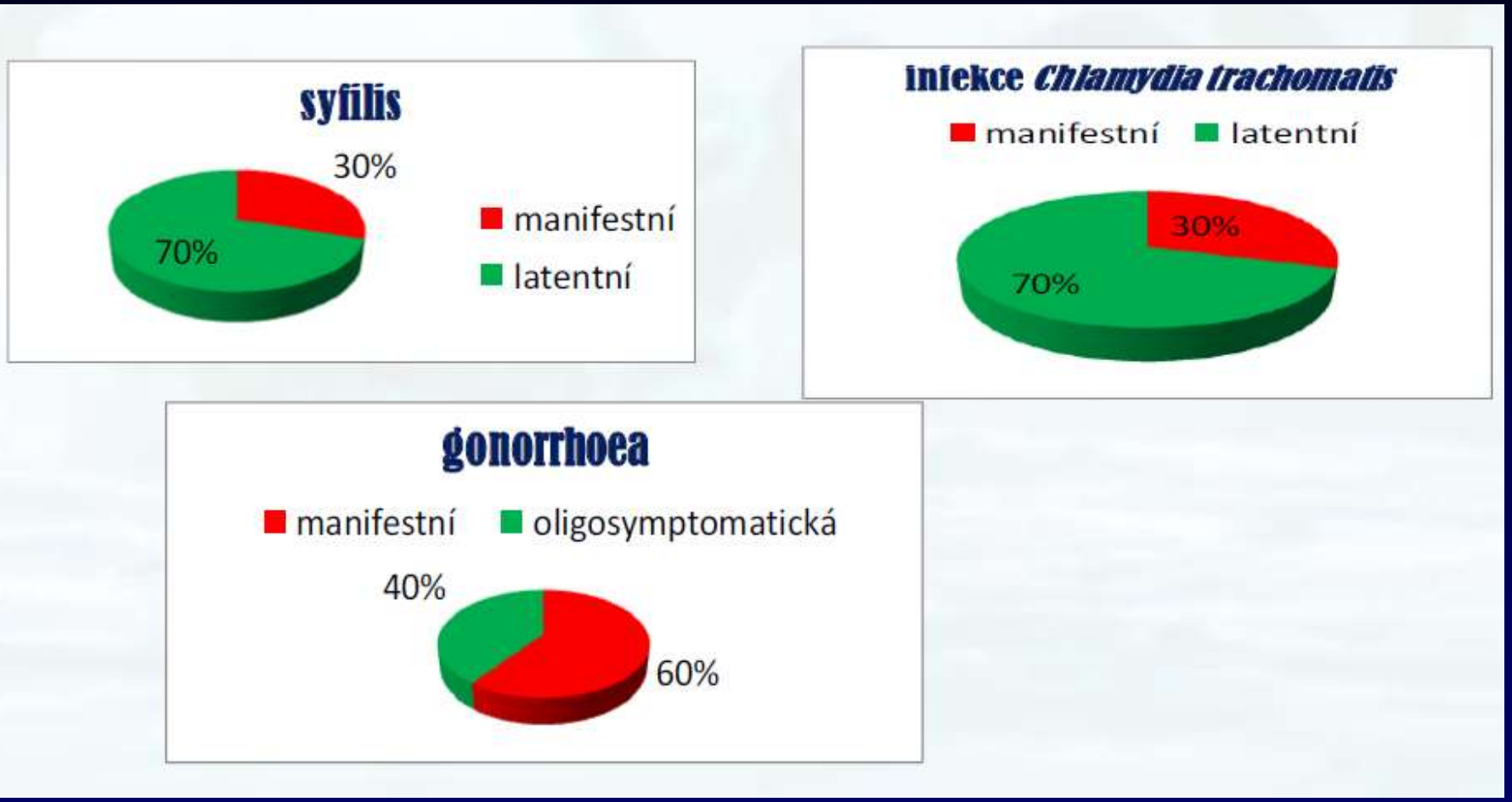
Sexually transmitted diseases

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)



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

Basic signs:

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

the diagnosis cannot be made without microbiology

Basic nosological unit = urethritis, cervicitis

THESE ARE NOT urinary tract infections

Eligible material

- urine (first in the morning)

  - PCR (species specific)

- swab from urethra (discharge), cervix, vagina

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

- 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
Fungal		
	Candida spp.	Candidosis

Treponema pallidum subsp. *pallidum*

Stage		Time period	manifestation	diagnostics
early	**primary**	weeks	ulcum durum (primary chancre) and bubo	microscopy, PCR, antibodies
	secondary	weeks - months	Generalisation: skin rash, 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-treponemal) = VDRL (RPR, BWR)
    cardiolipin as an antigen
    positive earlier (~ from 4 weeks p.i.), positivity disappears with therapy
    risk of false findings

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

Treponema pallidum subsp. *pallidum*

- indirect diagnostics

- non-specific = VDRL (RPR, BWR)

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

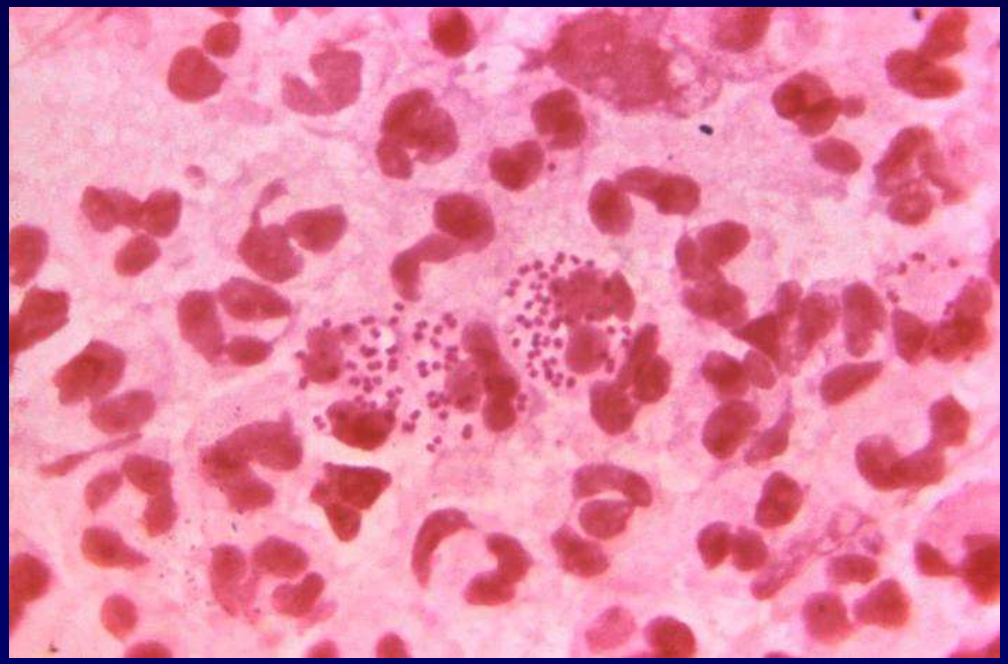
VDRL	specific reaction	interpretation
+	+	active infection
+	-	false positivity ?
-	+	successful therapy

Neisseria gonorrhoeae

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

- tonsilopharyngitis, proctitis
- neonatal conjunctivitis

Diagnostics:
microscopy
culture (special conditions)
PCR



Therapy:

no longer valid that it is susceptible to PNC, tetracycline or quinolones
(N. gono is competent for the DNA uptake, mostly in oropharynx)

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
  reactive arthritis
  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

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

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 of transmission)

- 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

Diagnostics:

antigens and antibodies

HBsAg — anti-HBs

anti-HBc (life-long evidence of infection)

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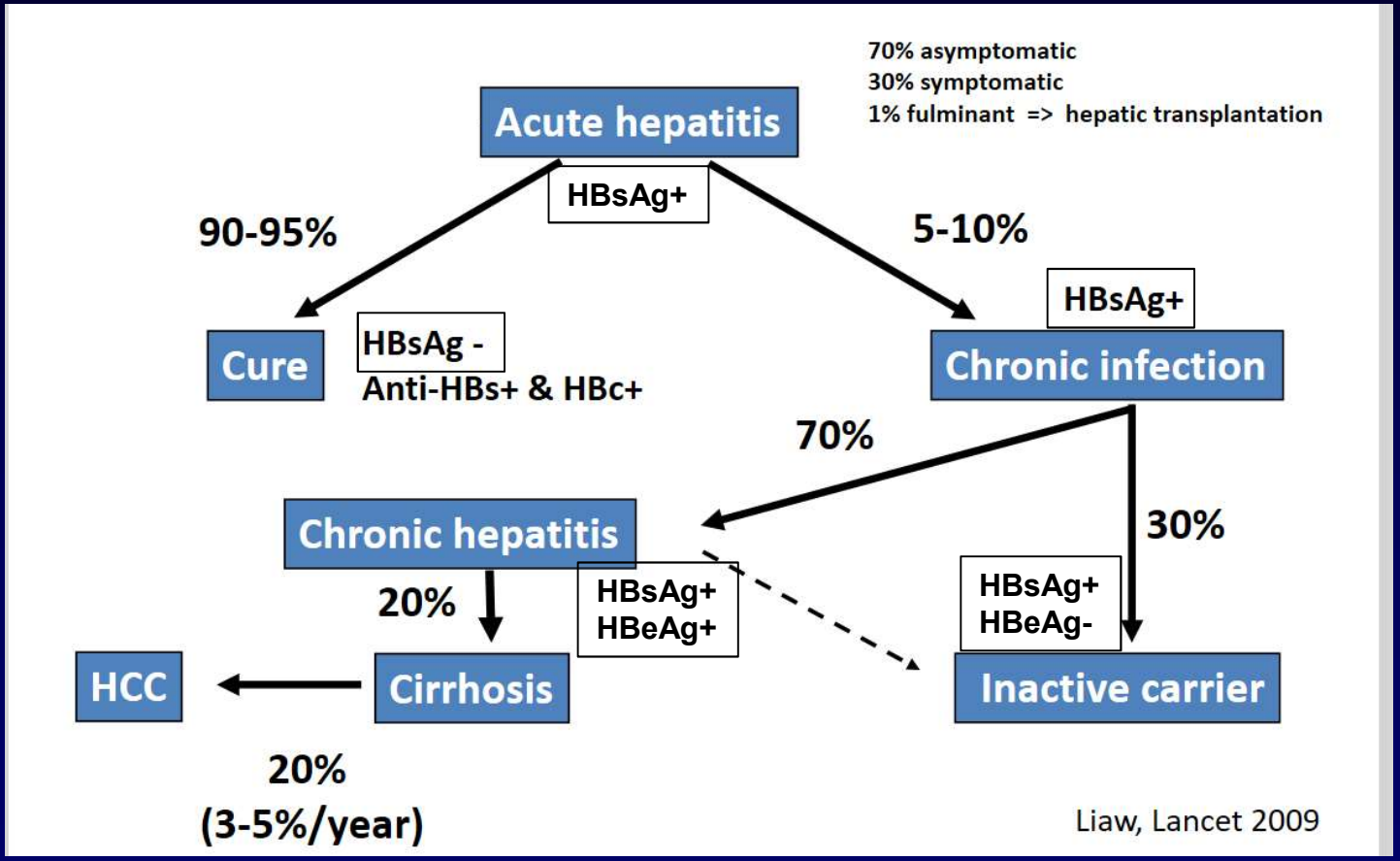
HBeAg — anti-HBe

... and HBV DNA

Infectivity: HBeAg > HBsAg



Diagnostics:

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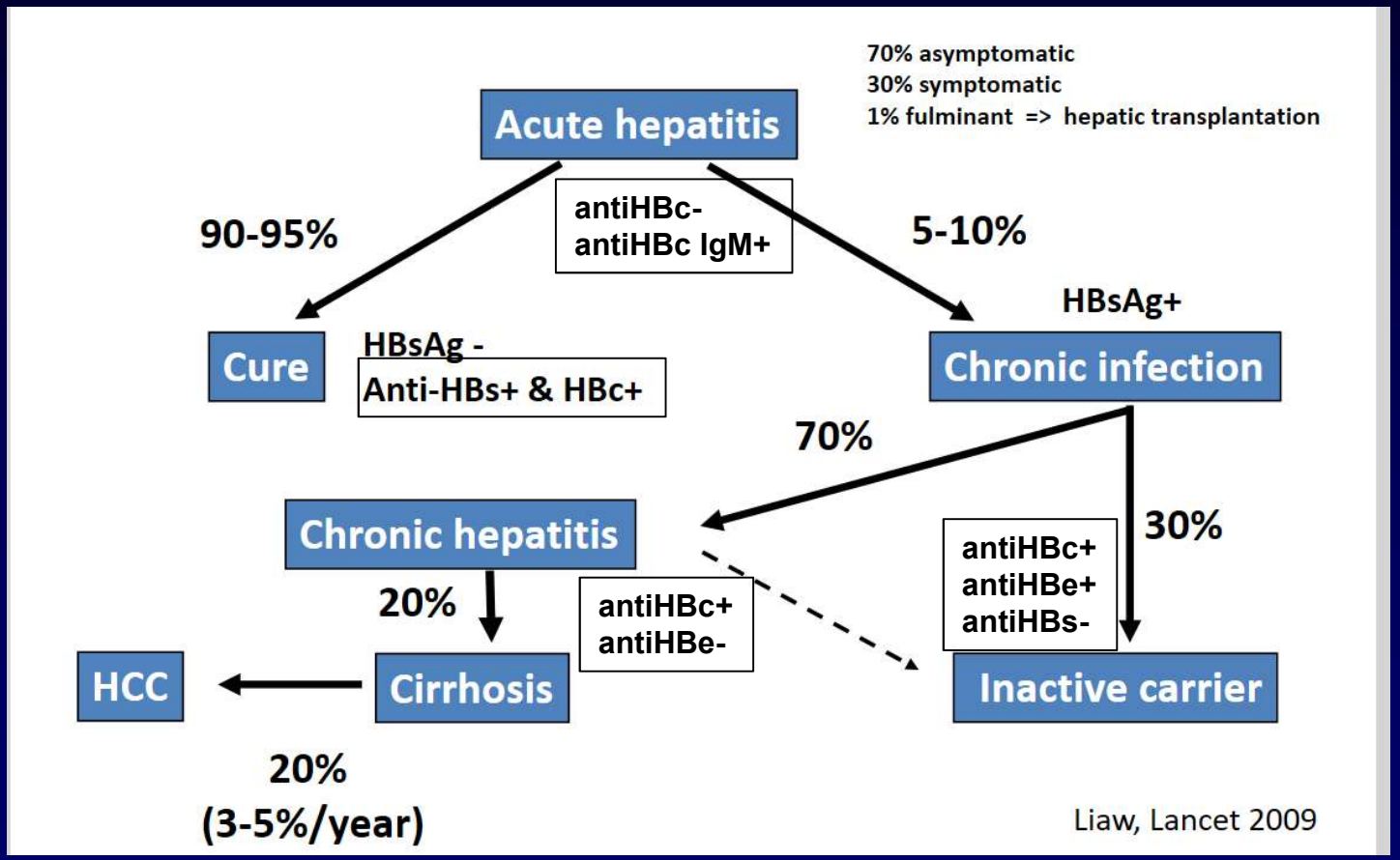
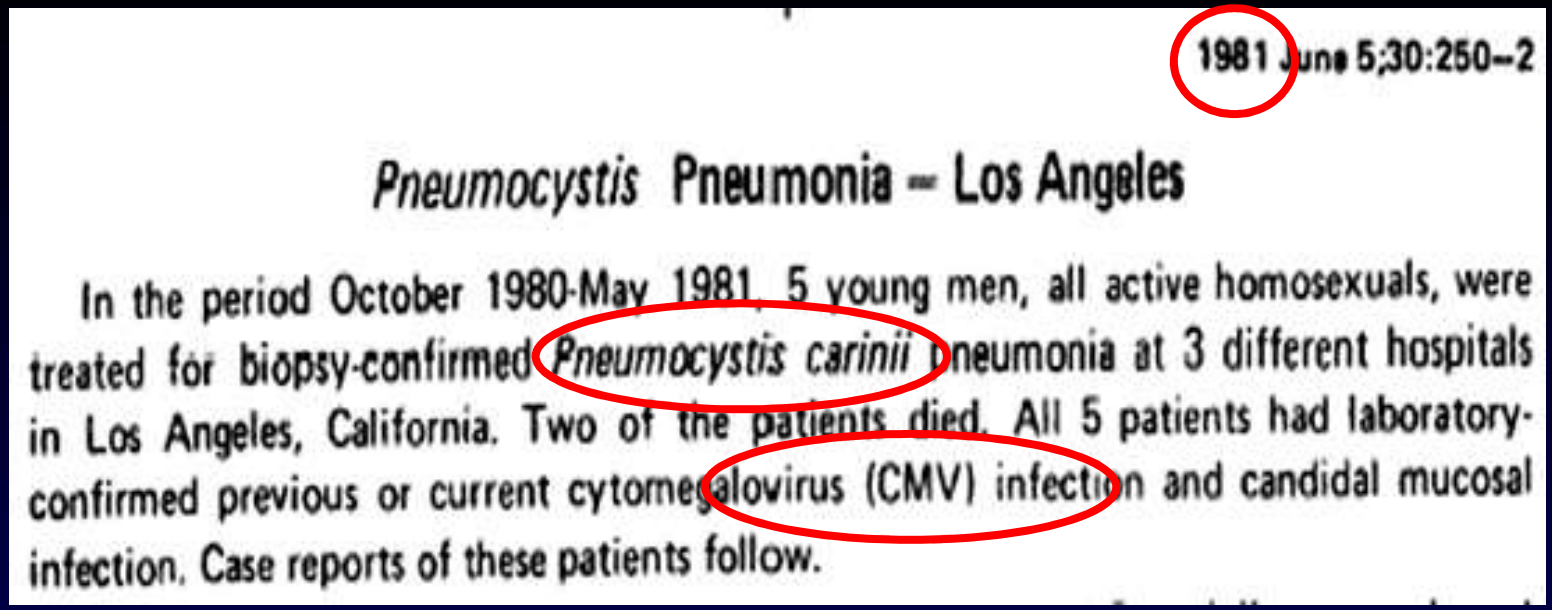


HIV



1981 June 5;30:250–2

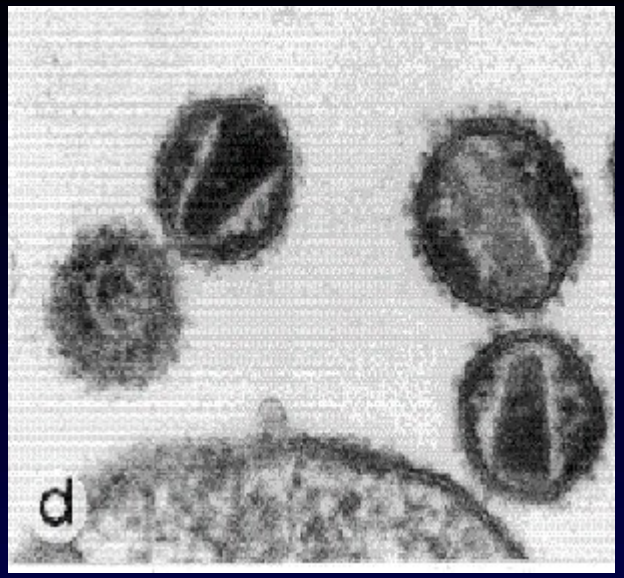
Pneumocystis Pneumonia – Los Angeles

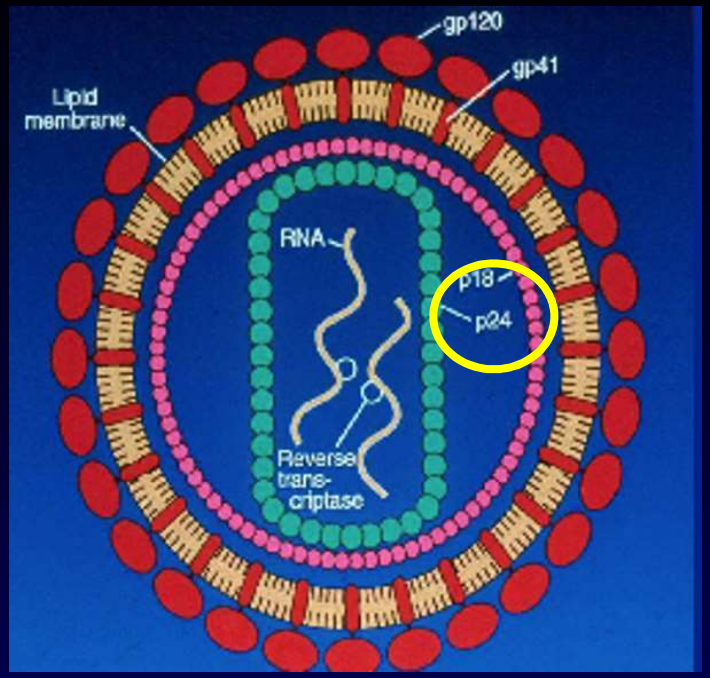
In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV)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

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

Today 37 million patients
(2/3 in Africa)

Czech Republic (since 1985): 4,000 (20% developed AIDS)



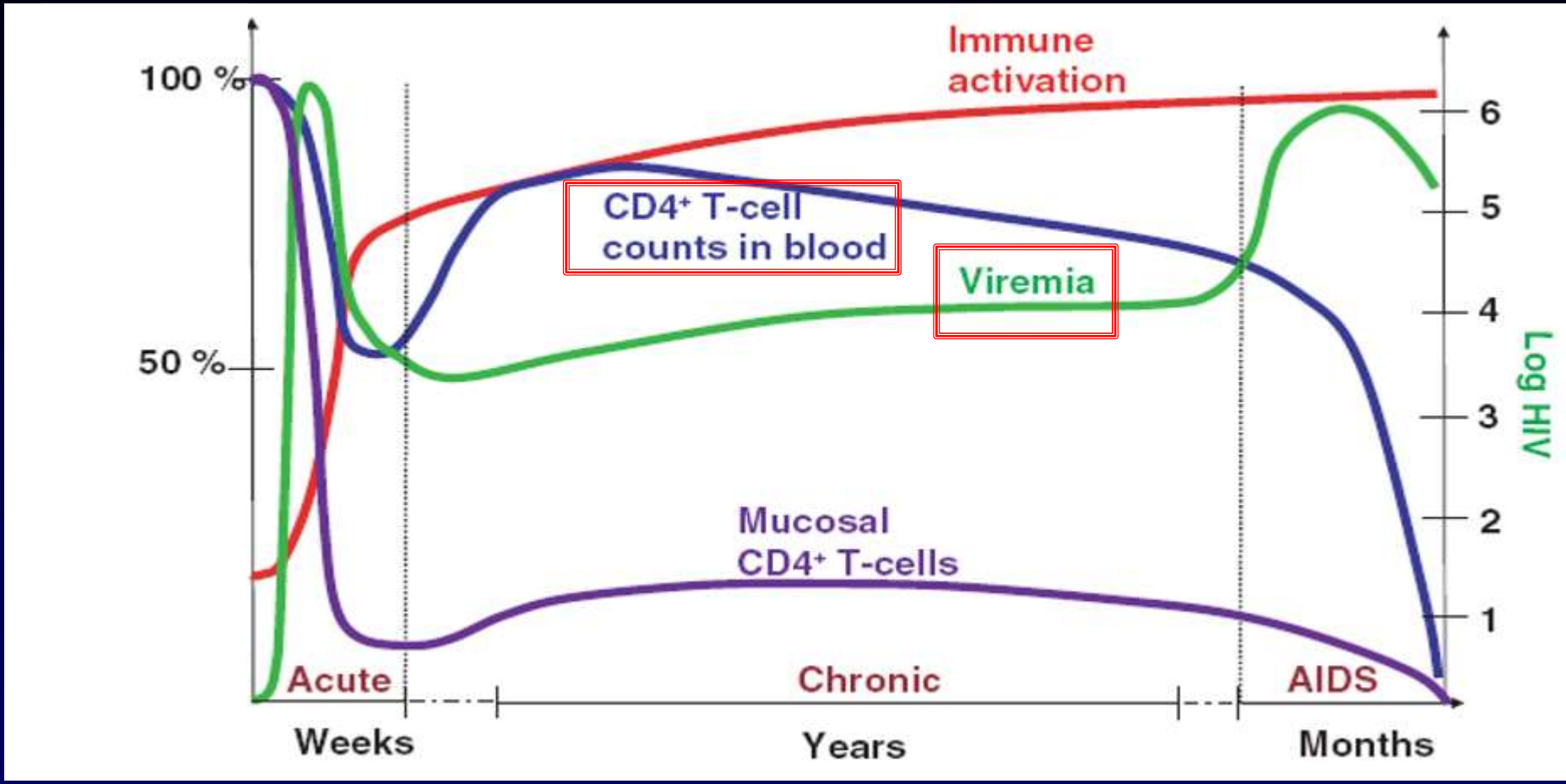


Diagnostics:

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

still many cases diagnosed late (1/5 in the CR)

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: 500-1400/mm^3

AIDS: < 200

(speed of progression depends on viral load and CD4 counts)

Therapy:

Goal: to suppress replication of HIV, viral load in blood: as low as possible, as long as possible

When to start: immediately (regardless the CD4+ count)

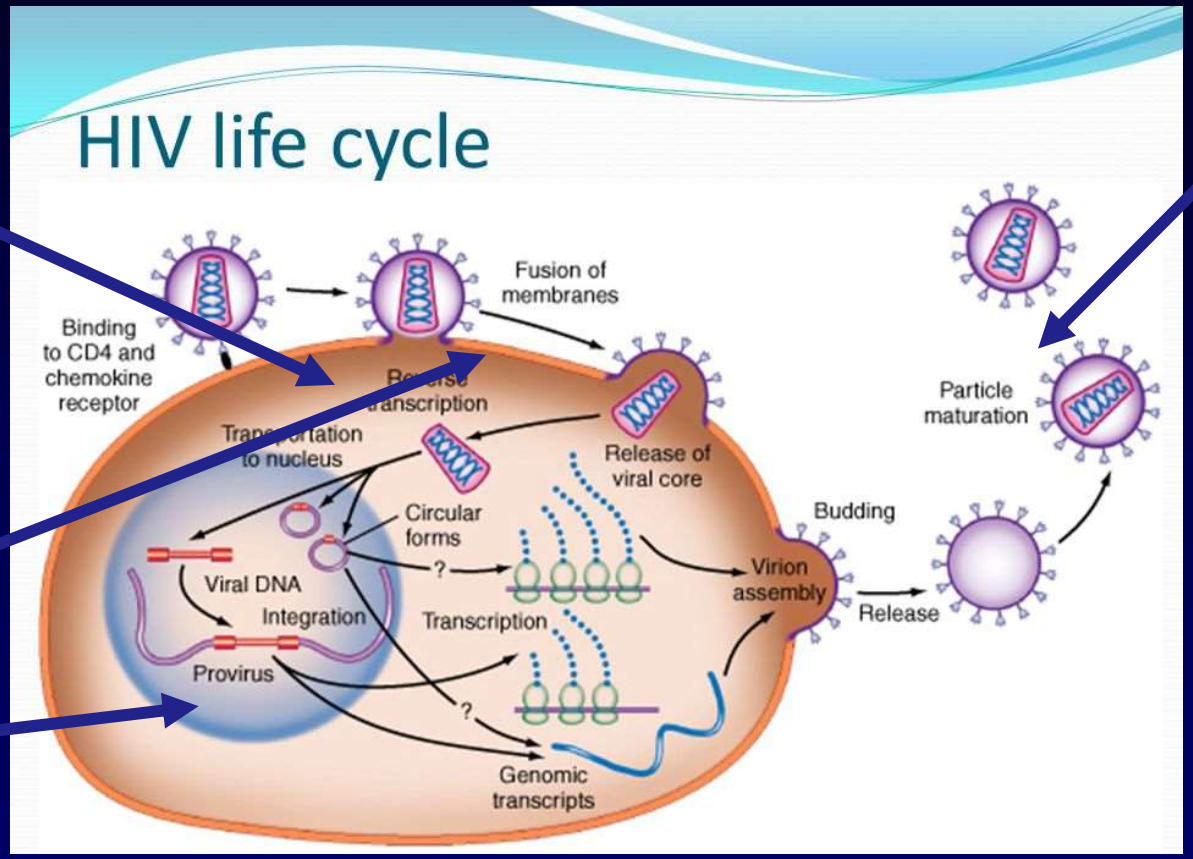
inhibitors RT

- nucleoside(tide)
- nonnucleoside:

zidovudin (1987)
lamivudin
tenofovir
...

fusion inhibitors

integrase inhibitors



protease inhibitors:

lopinavir
atazanavir
...

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

Opportunistic pathogens at the stage of AIDS:

Pneumocystis jiroveci (CD4+ below 200)
NTM (*M. avium* complex) and *M. tuberculosis* (developing countries)
recurrent pneumonia

CMV (retinitis, oesophagitis), (CD4+ below 50)

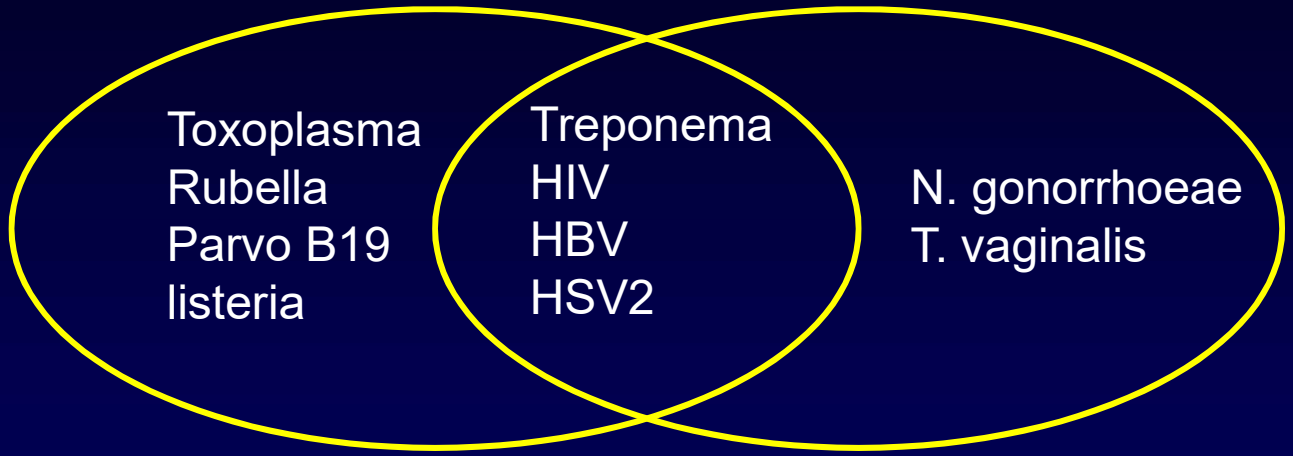
Toxoplasma gondii (CD4+ below 100)
Cryptosporidium

Cryptococcus neoformans (meningitis)

Salmonella septicaemia
HBV
...

Conclusion:

Infections in pregnancy and STD agens overlap, but not completely



… no overlap with UTI