Infections in pregnancy. Sexually transmitted diseases (STD)

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Infections in pregnancy (intrauterine transmission)

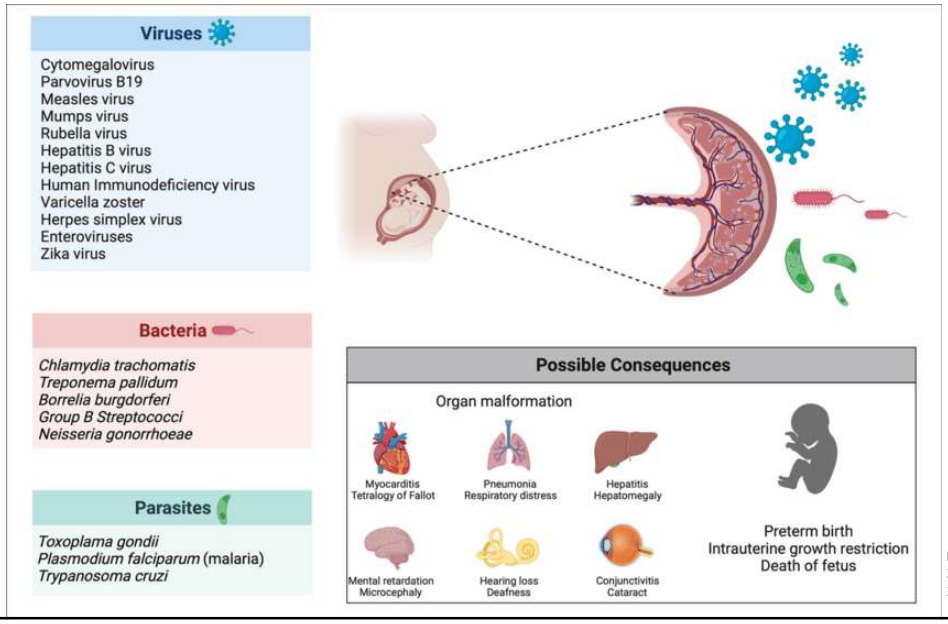
- primoinfection of mother: no immunity - rubella, CMV, parvovirus, toxoplasma
- reactivation of latent infection: immunosupression of mother - CMV, HSV
- chronic infection of mother - HBV, HIV
- neither of above - listeria, syphilis

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 (intrauterine transmission)



Liu et al. Front. Glob. Womens Health 2022 3:756362.

Infections in pregnancy (with the risk to the fetus)

- sexually transmitted

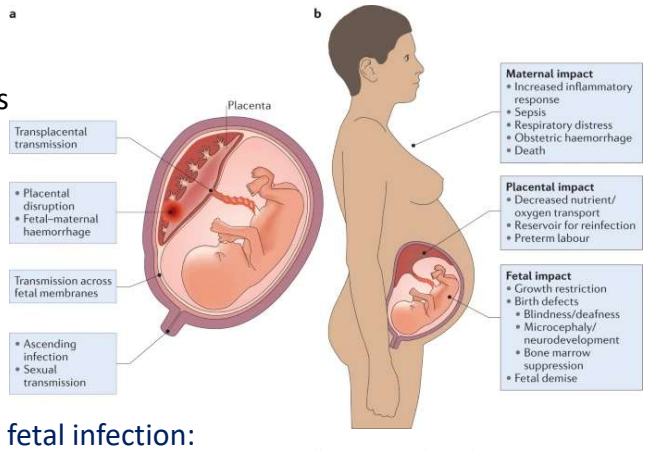
  HIV, herpesviruses (HSV2), syphilis
- not STD

  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

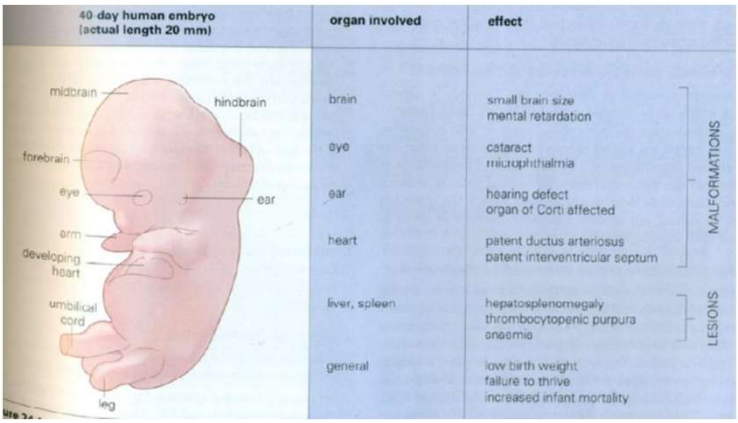
  - gestational age at the time of infection



https://www.nature.com/articles/s41579-021-00610-y

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:

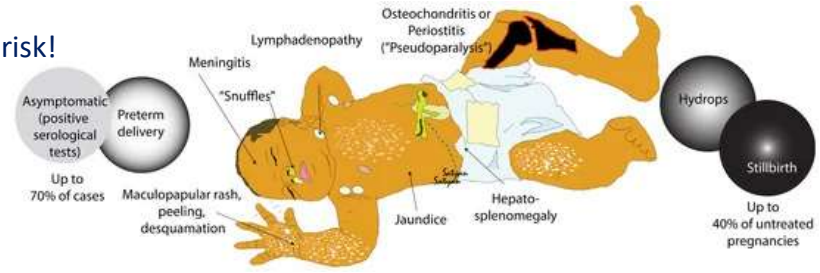
Syphilis Ab
Hepatitis B HBsAg
HIV Ab
(rubella)
(toxoplasma)
GBS culture

Treponema pallidum

Teratogenic

- Afftecting the fetus:
- Primary or secondary stage at the mother = risk of transmission
- almost 100%

... therapy eliminates that risk!



Children 2023, 10, 1310. https://doi.org/10.3390/children10081310

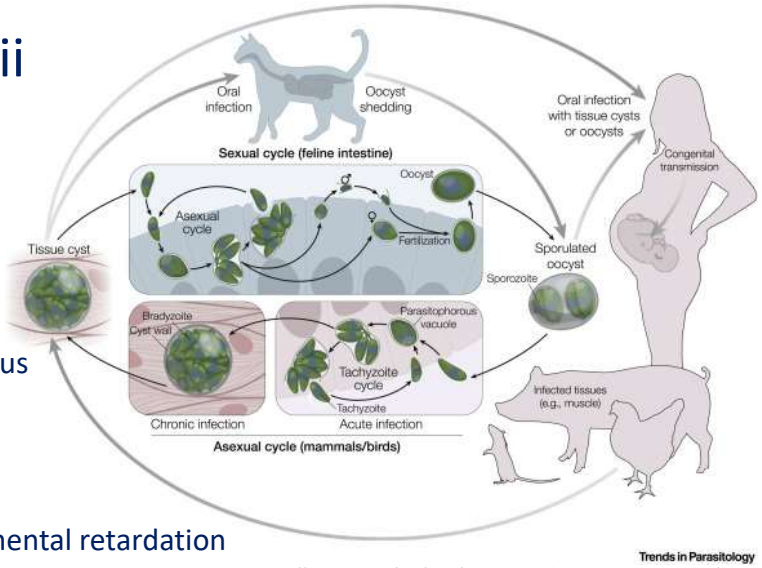
Congenital syphilis:

- 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



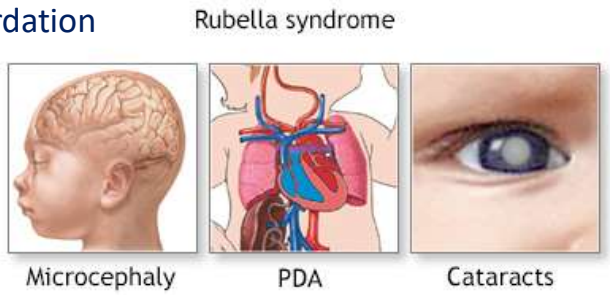
https://www.cell.com/cms/asset/95b90be8-7d6f-4311-8291-289422a7cb53/fx1.jpg

Congenital toxoplasmosis
often late onset of signs
microcephalia, chorioretinitis, mental retardation

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

Rubella

- teratogenic : deafness, mental retardation
  affected
- until week 11: 90% of fetuses
- until week 16: 20% of foetuses
- week 20 and above: 0%



https://ssl.adam.com/graphics/images/en/17253.jpg

Congenital rubella syndrome (CRS):

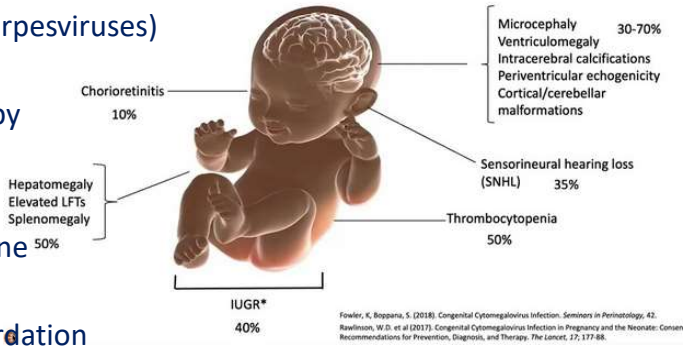
= Gregg's syndrome: eyes (cataract, microphtalmia), heart, deafness

secretion of viruses from saliva, urine as the example of persistent infection after birth

later signs of CRS: deafness, mental retardation

Cytomegalovirus

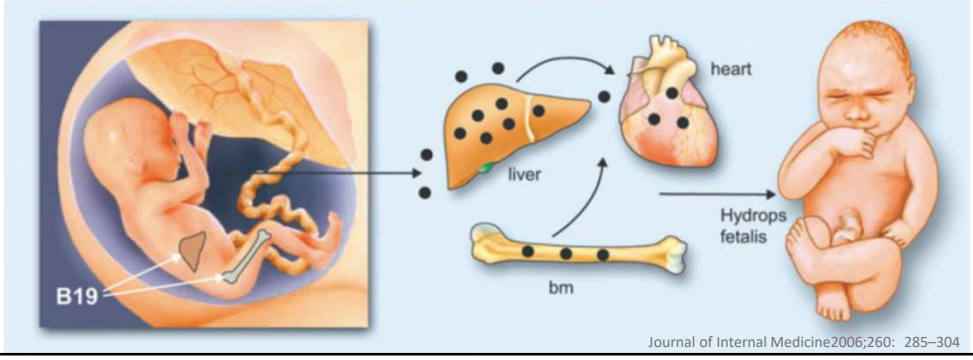
- Congenital CMV = most common congenital disease (in 90% asymptomatic)
  haematopoesis affected: anaemia, thrombocytopenia
  chorioretinitis, hepatitis
- teratogenic (also, VZV, HSV from herpesviruses)
- Symptomatic: Blueberry muffin baby
- secretion of viruses from saliva, urine
- later signs of congenital infection:
  deafness, mental retardation



https://www.youtube.com/watch?app=desktop&v=L1qkpxW5jQw

Parvovirus B19

- affinity to myocard cells, erythroblasts
- non-teratogen
- but serious risk to develop hydrops fetalis
  (due to severe anaemia)
- affinity to myocard cells, erythroblasts



Journal of Internal Medicine2006;260: 285–304

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 of neonatal meningitis[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

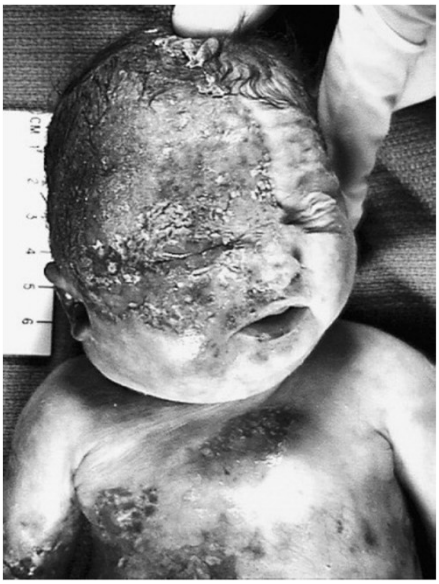
[a]Studies were performed in different time periods, with varying vaccination st

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

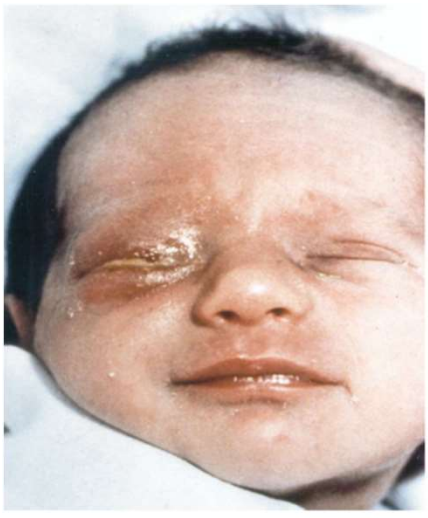


Figure 2 An infant with chlamydial conjunctivitis. Reprinted from Long S, Pickering LK, Prober CG (eds): Principles and Practice of Pediatric Infectious Diseases. New York, Churchill-Livingstone, 2003, p. 904 used with permission. (Color version of figure is available online.)

Darville T. Semin Pediatr Infect Dis. 2005 Oct;16(4):235-44.

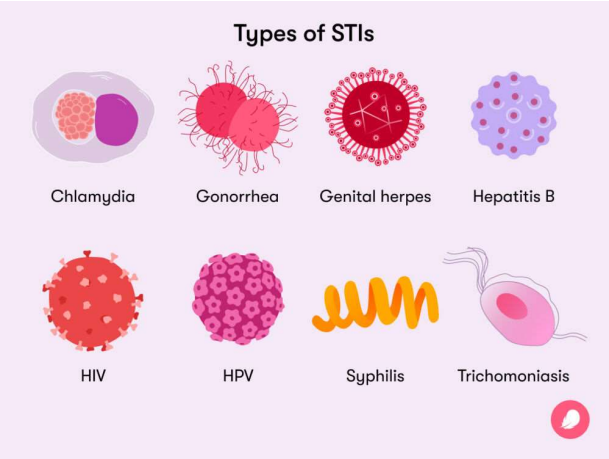
STD

Paradox: controllable diseases

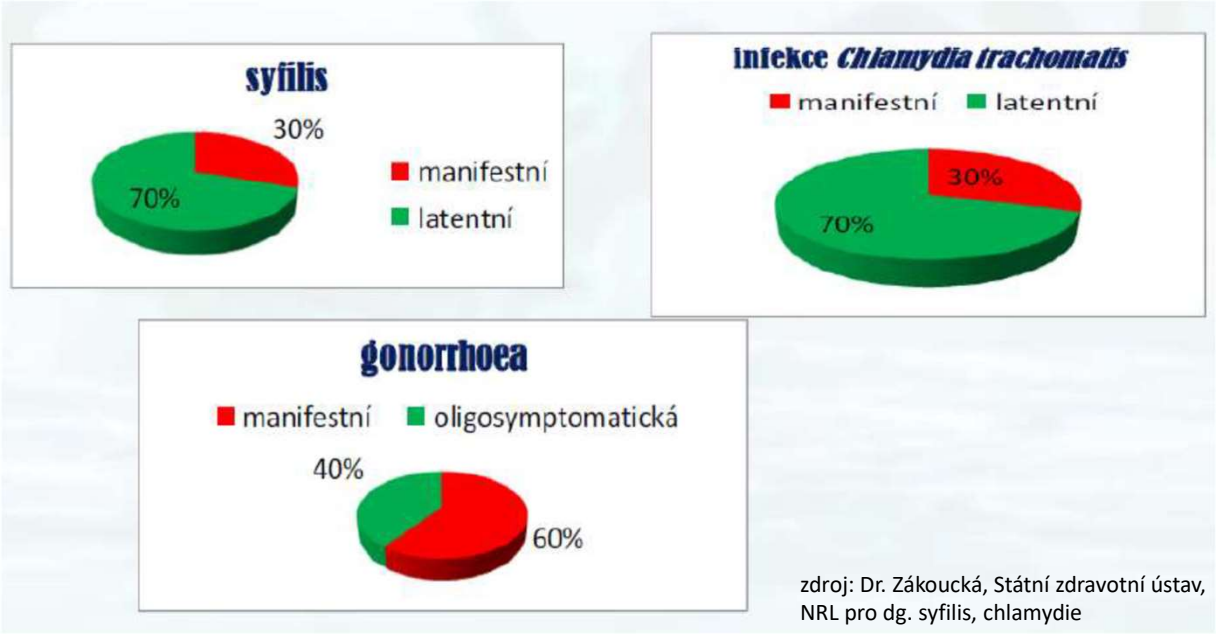
- no reservoir in environment
- mechanisms of transmission is not easy
- sensitive agents

but these are not under control

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



https://flo.health/uploads/media/sulu-1000x-inset/08/7358-sexually-transmitted-infections-types-10_1006x755.jpg?v=1-0



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

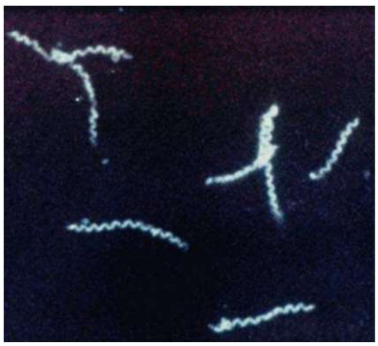
Treponema pallidum subsp. pallidum

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

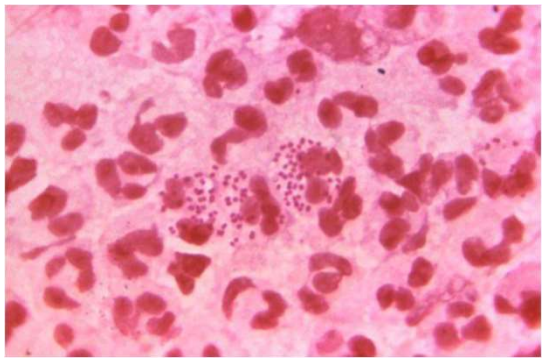
- indirect diagnostics
  - non-specific = VDRL (RPR, BWR)
  - specific - TPHA, TPPA; FTA-ABS, ELISA, WB

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



https://en.wikipedia.org/wiki/Neisseria_gonorrhoeae#/media/File:Gonococcal_urethritis_PHIL_4085_lores.jpg

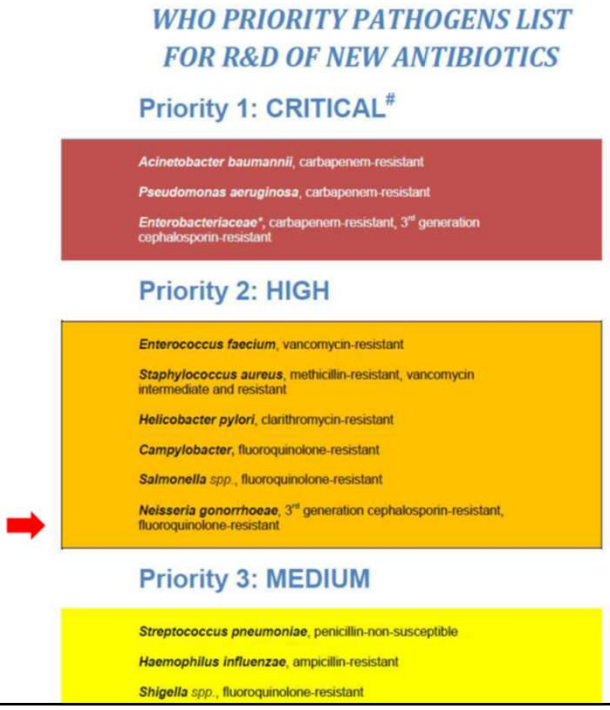
Therapy:

- 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



Chlamydia trachomatis

Serotypes associated with different diseases:

- A,B,C: trachoma (not STD)
- L: lymphogranuloma venereum
- D - K: STD: urethritis, prostatitis

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

cervicitis, salpingitis (also chronic asymptom. -- infertility)

proctitis

reactive arthritis

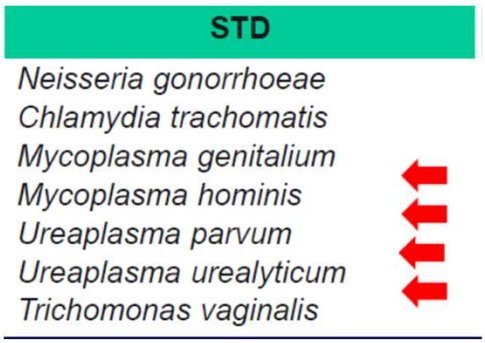
paratrachoma = neonatal conjunctivitis

neonatal pneumonia

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

Therapy:
macrolides
tetracyklins
quinolons

Mycoplasma and ureaplasma



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)

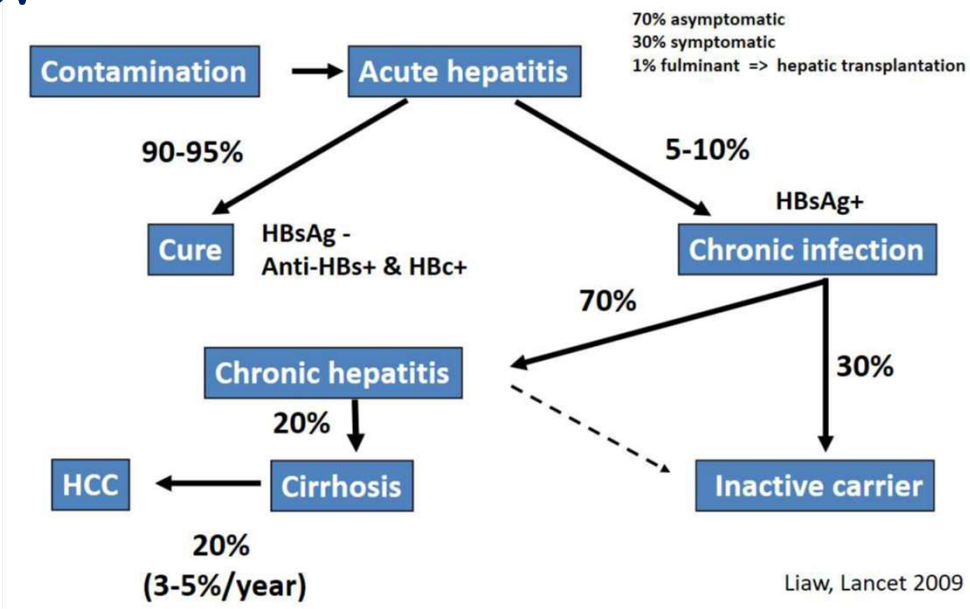
HCV

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

HBV



70% asymptomatic
30% symptomatic
1% fulminant => hepatic transplantation
Contamination
Acute hepatitis
90-95%
5-10%
Cure
HBsAg -
Anti-HBs+ & HBc+
HBsAg+
Chronic infection
70%
30%
Chronic hepatitis
20%
HCC
Cirrhosis
Inactive carrier
20%
(3-5%/year)
Liaw, Lancet 2009

HIV

Today 37 million patients
(2/3 in Africa)
Czech Republic (since 1985):
4,000 (20% developed AIDS)

1981 June 5;30:250–2

Pneumocystis Pneumonia — Los Angeles

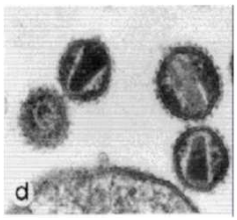
In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV)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

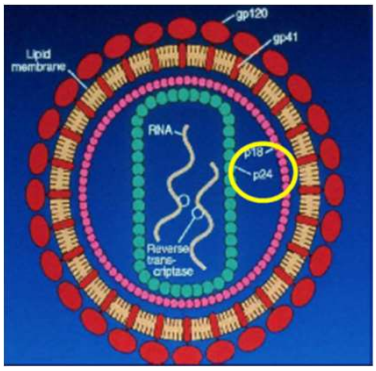
Morbidity nad mortality weekly report. Center for Disease Control (CDC).

Diagnostics:

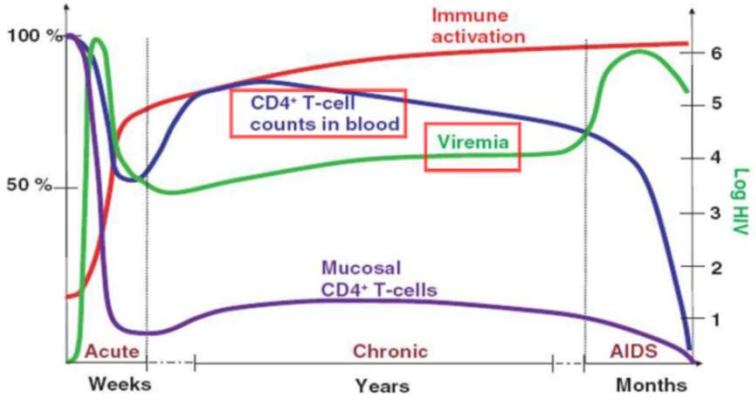
- antibodies (ELISA): in 3 weeks p.i.
  (to confirm with immunoblot)
- Ag p24: in 2 weeks p.i.
- RNA: in 10 days p.i.

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:

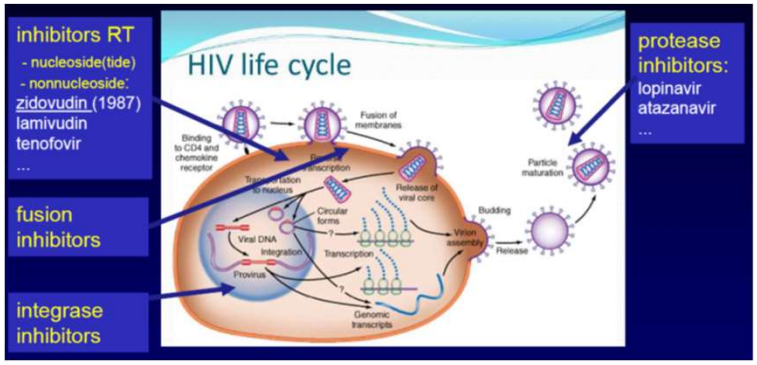
norm: 500-1400/mm3

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)



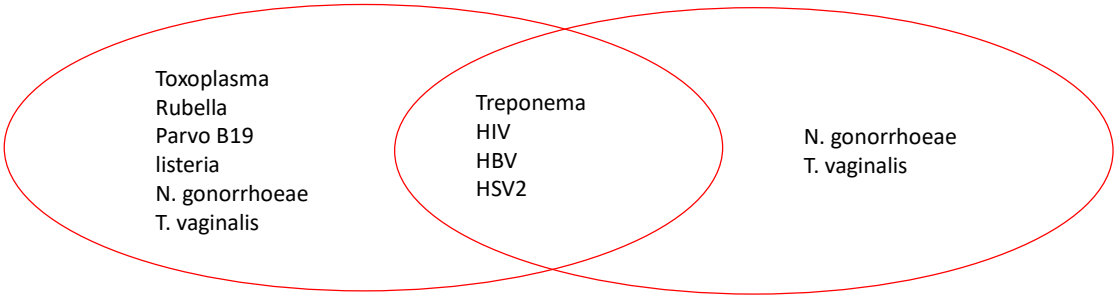
cART (HAART earlier): to administer in two-, three drug combo (two nucleoside inhibitors + third drug)

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