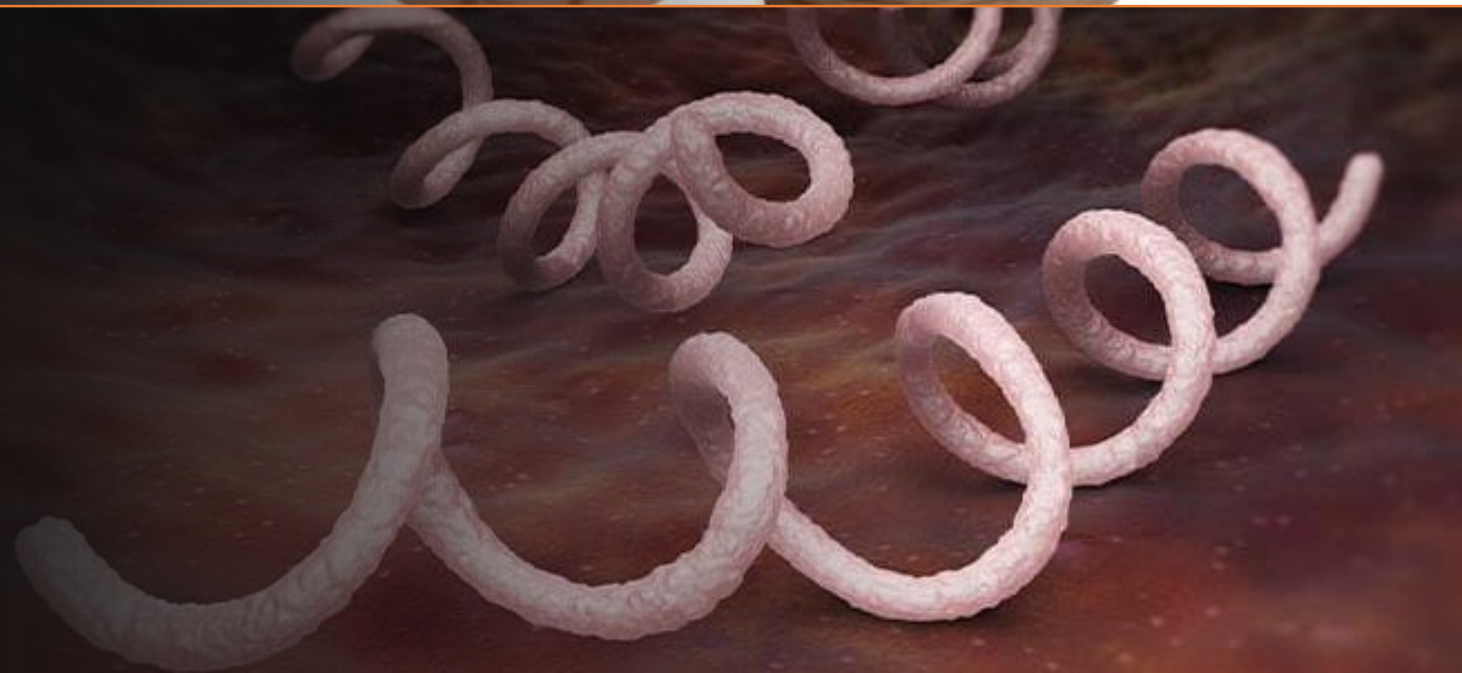
Nevrosifilis

Barbara Kokošar Ulčar, dr.med.

KIBVS

Klinični seminar, 23.1.2024

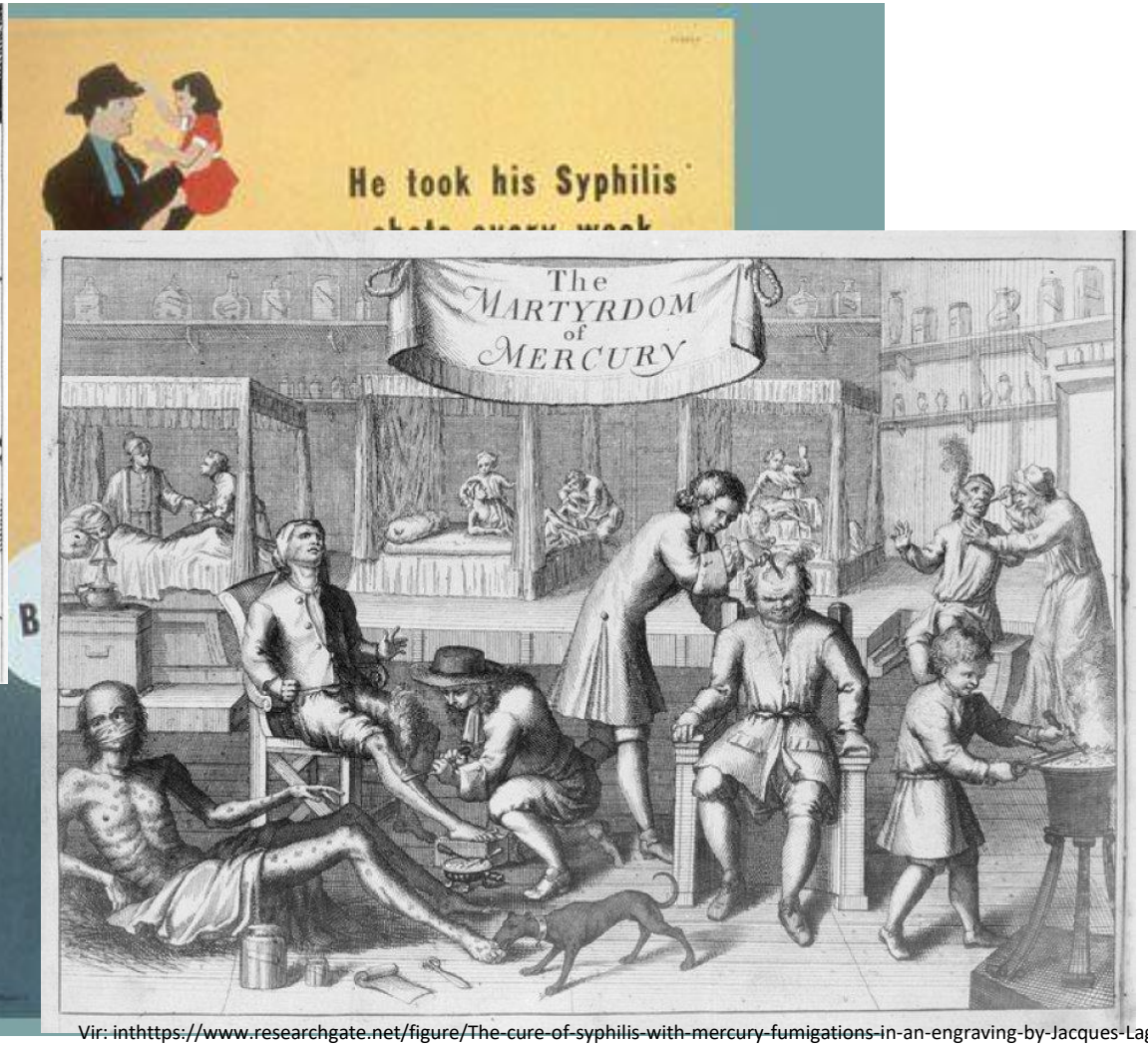


“The physician who knows syphilis, knows medicine”

(sir William Osler)

- Ligue Nationale Française contre le Peril Vénérién, Francija, ca. 1926.

Zdravljenje v preteklosti

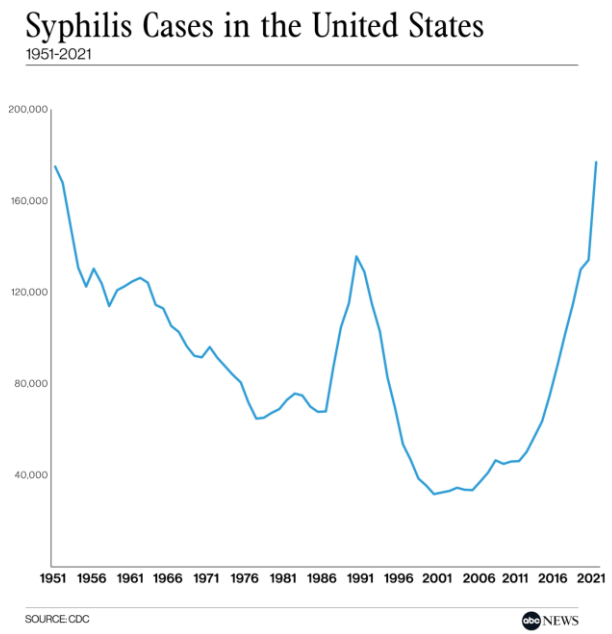


Predantibiotično obdobje:

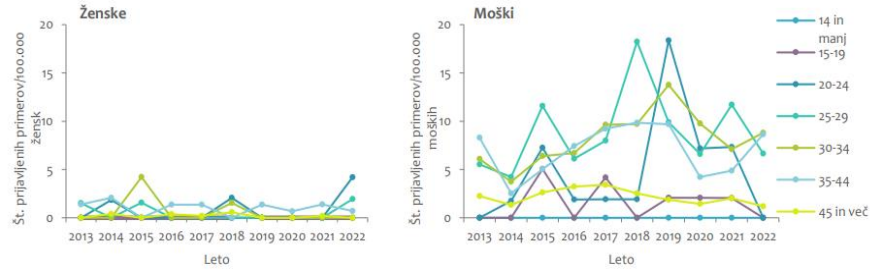
- Nevrosifilis pri 25-35% osebah s sifilisom
  - 1/3 asimptomatski sifilis
  - 1/3 tabes dorsalis
  - 10% pareza
  - 10% meningovaskularni sifilis

Vir: inthttps://www.researchgate.net/figure/The-cure-of-syphilis-with-mercury-fumigations-in-an-engraving-by-Jacques-Lagnier_fig4_358884045ernet;
https://www.sciencemuseum.org.uk/objects-and-stories/history-syphilis-part-two-treatments-cures-and-legislation
https://www.everydayhealth.com/syphilis/painful-history-odd-bug/

Kaj pa danes?

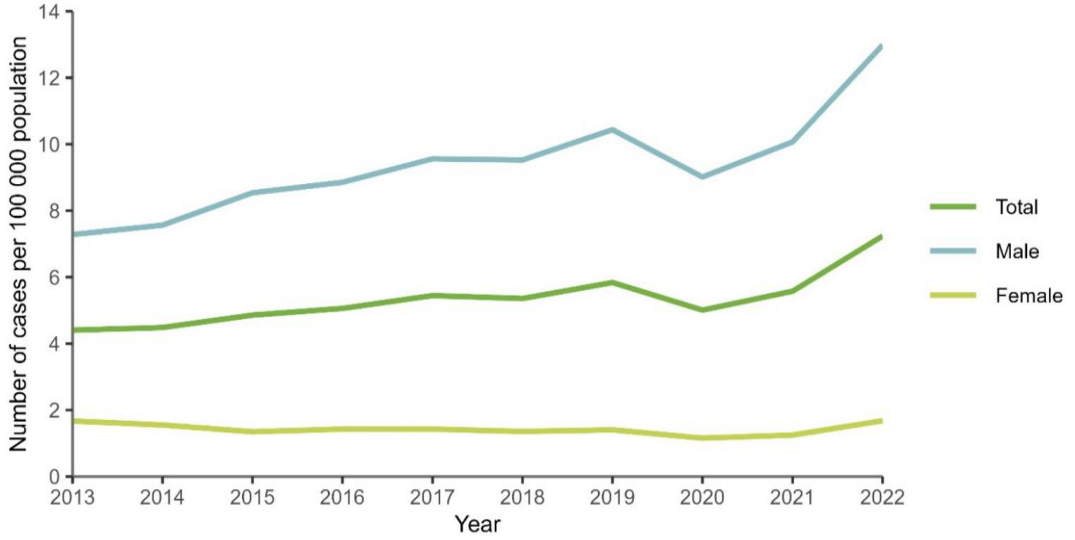


Slika 12: Prijavne incidence zgodnjega sifilisa po spolu in starostnih skupinah, Slovenija, 2013–2022



Vir: Evidenca pojavnosti spolno prenesenih bolezni (NIJZ 53), 12. 12. 2023.

Figure 4. Rate of confirmed syphilis cases per 100 000 population, total and by gender for cases with available data, EU/EEA countries reporting consistently, 2013–2022



Source: country reports from Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, and Sweden.

L. 2022 (29 EU/EEA držav): **35.391 potrjenih primerov sifilisa** (34% porast glede na l. 2021, 74% MSM, tudi porast primerov pri heteroseksualnih osebah!)

ECDC (https://www.ecdc.europa.eu/en/publications-data/syphilis-annual-epidemiological-report-2022)
https://abcnews.go.com/Health/stis-including-syphilis-rose-2nd-year-pandemic-cdc/story?id=98478883
https://nijz.si/wp-content/uploads/2024/04/Spolno-prenesene-okuzbe-v-Sloveniji-v-letu-2022.pdf

Tudi v pozni obliki…

Primer iz leta 2017

Klinični primer bolnice z nevrosifilisom na sprejemnem oddelku psihiatrične bolnišnice

Clinical case of a patient with neurosyphilis in the admitting department of a psychiatric hospital

Nace Žgavec, dr. med.
Psihiatrična bolnišnica Idrija, Pot sv. Antona 49, 5280 Idrija

Dr. Marko Pišljar, dr. med., spec. psih.
Psihiatrična bolnišnica Idrija, Pot sv. Antona 49, 5280 Idrija

Korespondenca:
nace.zgavec@gmail.com
marko.pisljar@pb-idrija.si

Izvleček
Nevrosifilis je končni stadij poznega, nezdravljenega ali slabo zdravljenega sifilisa. Zaradi dobrega obvladovanja in kontrole bolnikov z zgodnjo obliko bolezni je nevrosifilis postal tako redek, da ga v zadnjih 50 letih videvamo le sporadično. Majhno število bolnikov z nevrosifilisom je seveda pomemben uspeh medicine, zastavlja pa nove diagnostične probleme – na bolezen redkeje pomislimo, saj jo v množici drugih prav lahko spregledamo. Zaradi ponovnega porasta primerov bolezni ter variabilne in neznačilne klinične slike nevrosifilisa potekajo diskusije o ponovni uvedbi rutinskega serološkega testiranja za sifilis ob sprejemih na psihiatrične oddelke. V prispevku predstavljamo klinični primer 50-letne bolnice, pri kateri je bila po pojavu spoznavnih in razpoloženjskih motenj postavljena diagnoza nevrosifilisa.

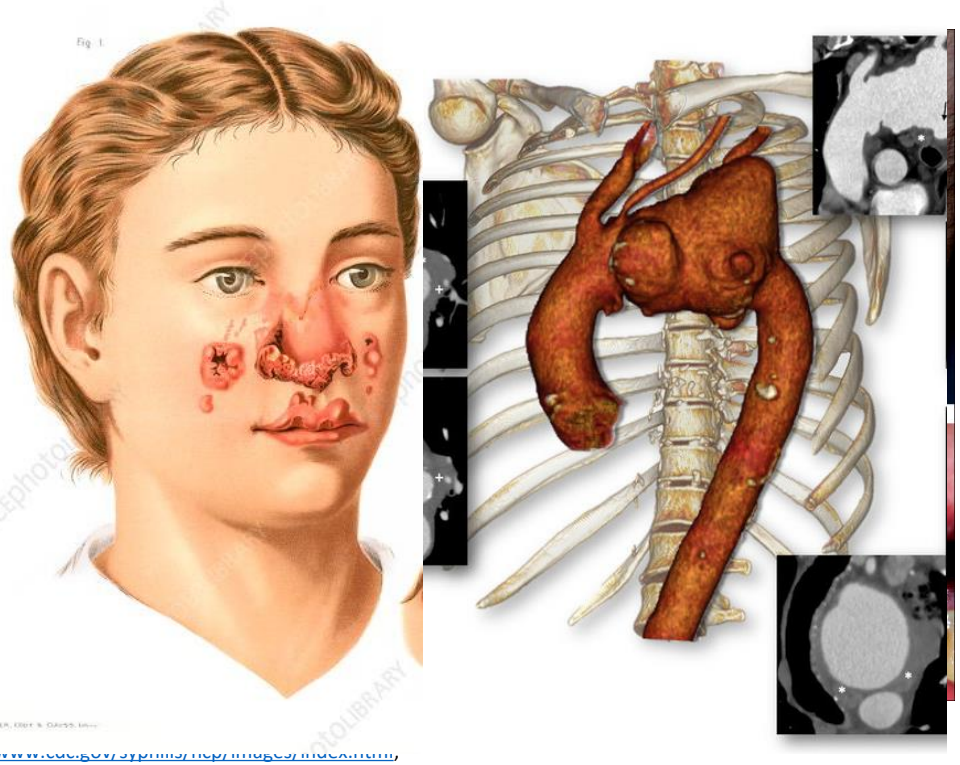
Ključne besede: nevrosifilis, demenca, depresija, elektroencefalografija

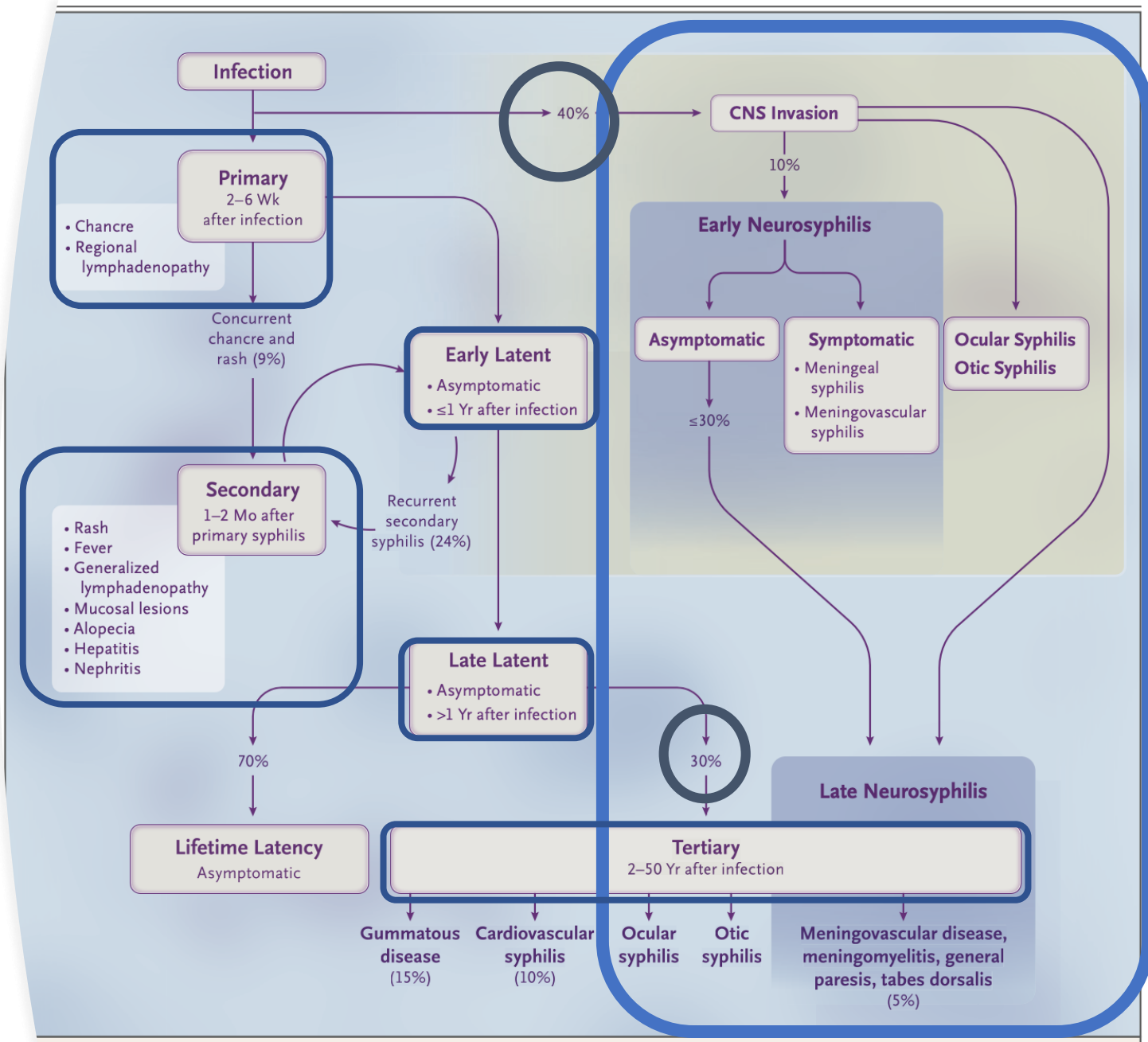
Abstract
Neurosyphilis is the final stage of late, poorly treated syphilis. Because of we patients with early forms of the disease lis has become extremely rare, over the only sporadic cases have been reported. ber of patients with neurosyphilis is a m ment of medicine, but it sets new diag lems – we rarely think of neurosyphilis a of other diseases, can easily overlook incidence of primary syphilis has beer and taking into account the variable ar teristical presentation of neurosyphilis, cussions in place about the potential re of routine serological testing for syphilis sion to psychiatric treatment. The pap a clinical case of a 50-year-old woman th with cognitive and behavioural disord later diagnosed with neurosyphilis.

Key words: neurosyphilis, dementia, electroencephalography

Naravni potek okužbe s *T. pallidum*

- INKUBACIJA: 10 – 90 dni (povpr. 3 t)





ure 2. Natural History of Untreated Syphilis.

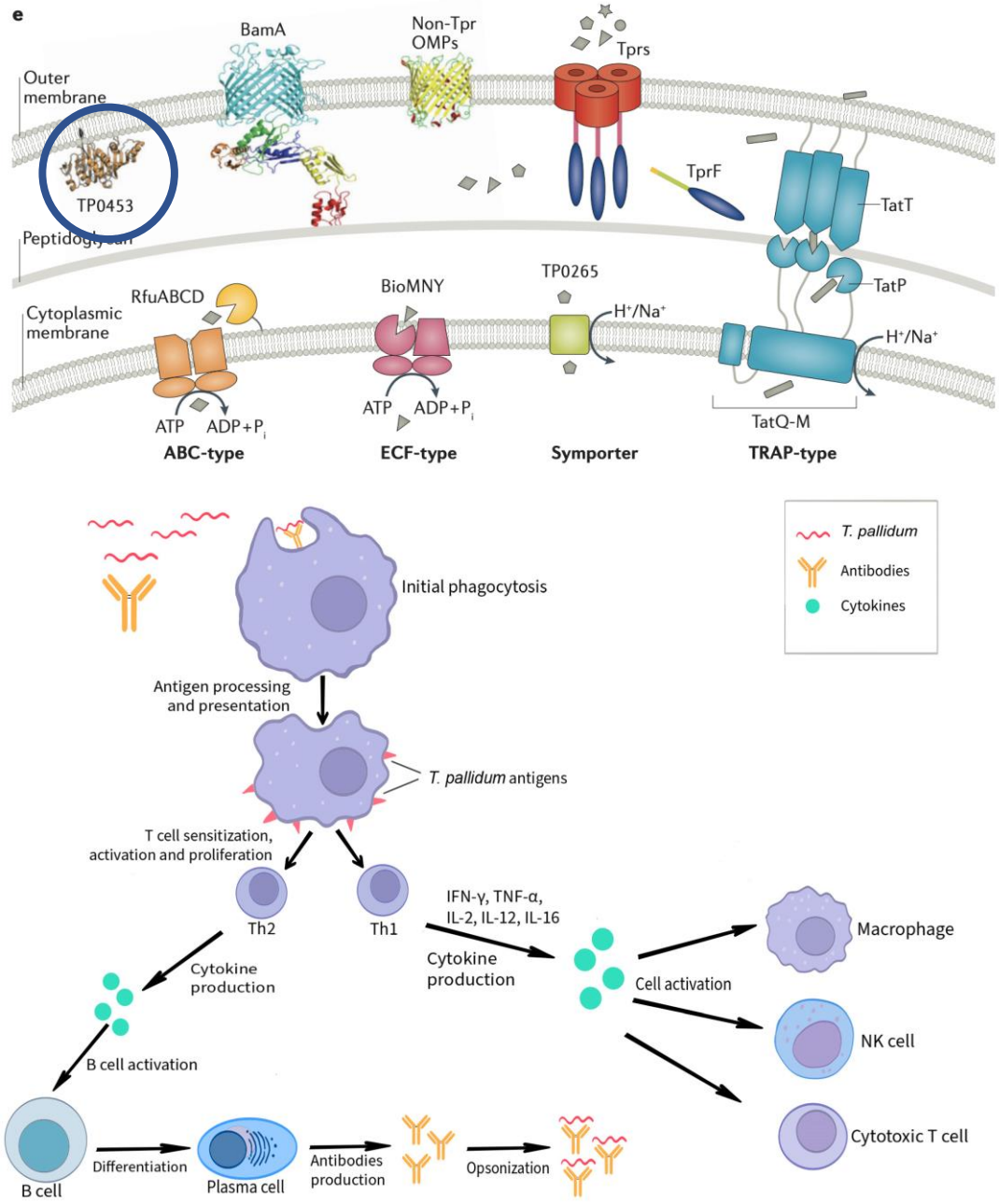
e time intervals between stages of syphilis are shown, along with the approximate percentages of persons progressing to the indicated es. Invasion of the central nervous system (CNS) by treponemes may not be a necessary prerequisite for the development of certain s of ocular syphilis. Adapted from Ho and Lukehart.[10]

https://www.cdc.gov/syphilis/hcp/images/index.htm,
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(16)30129-3/abstract
https://www.researchgate.net/publication/357665067_Contained_rupture_of_an_aortic_arch_aneurysm_in_a_patient_with_syphilitic_aortitis_A_case_report
Ghanem KG, et al. N Engl J Med. 2020

Patogeneza okužbe s *T. pallidum*

- *T. pallidum* brez LPS
- Lipoproteini (PAMPs) skriti, TLR ne zaznajo – **slab odziv naravnega imunskega sistema**
- Hitra **diseminacija**/metastaziranje – tudi v CŽS!
- Pomembna vloga **tkivnih dendritičnih celi**c in **CELIČNE IMUNOSTI**
- Protitelesa slabo zaznajo submembranske lipoproteine + hiter razvoj antigenskih variant – izogibanje opsonofagocitozi!
- Celični odgovor + opsonizacija > T. pallidum = latentna faza

perivaskularni infiltrati (limfociti, makrofagi, plazmatke)
+
obliterativni endarteritis



Ávila-Nieto C, et al. Front Immunol. 2023
Radolf, J. D., et al. Nature Reviews Microbiology, 2016.

Sifilis – serološki odgovor

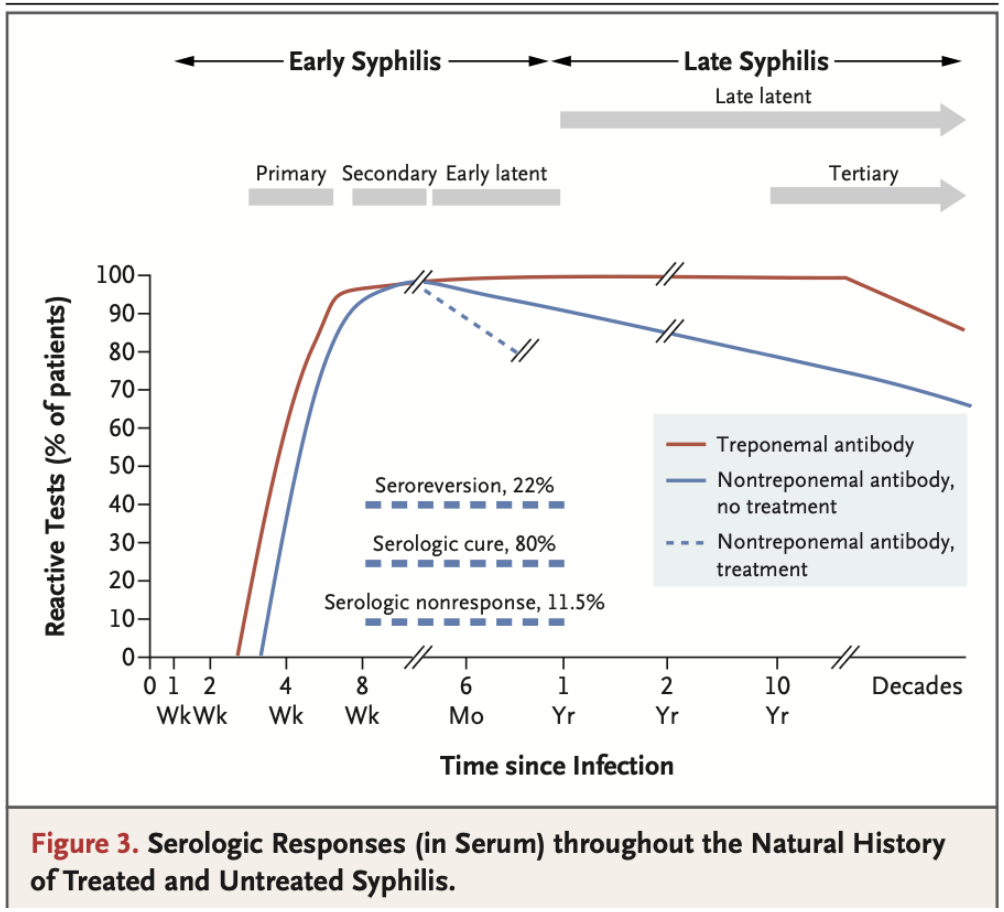


Figure 3. Serologic Responses (in Serum) throughout the Natural History of Treated and Untreated Syphilis.

Table 1. Sensitivity and Specificity of Serologic Tests for Syphilis

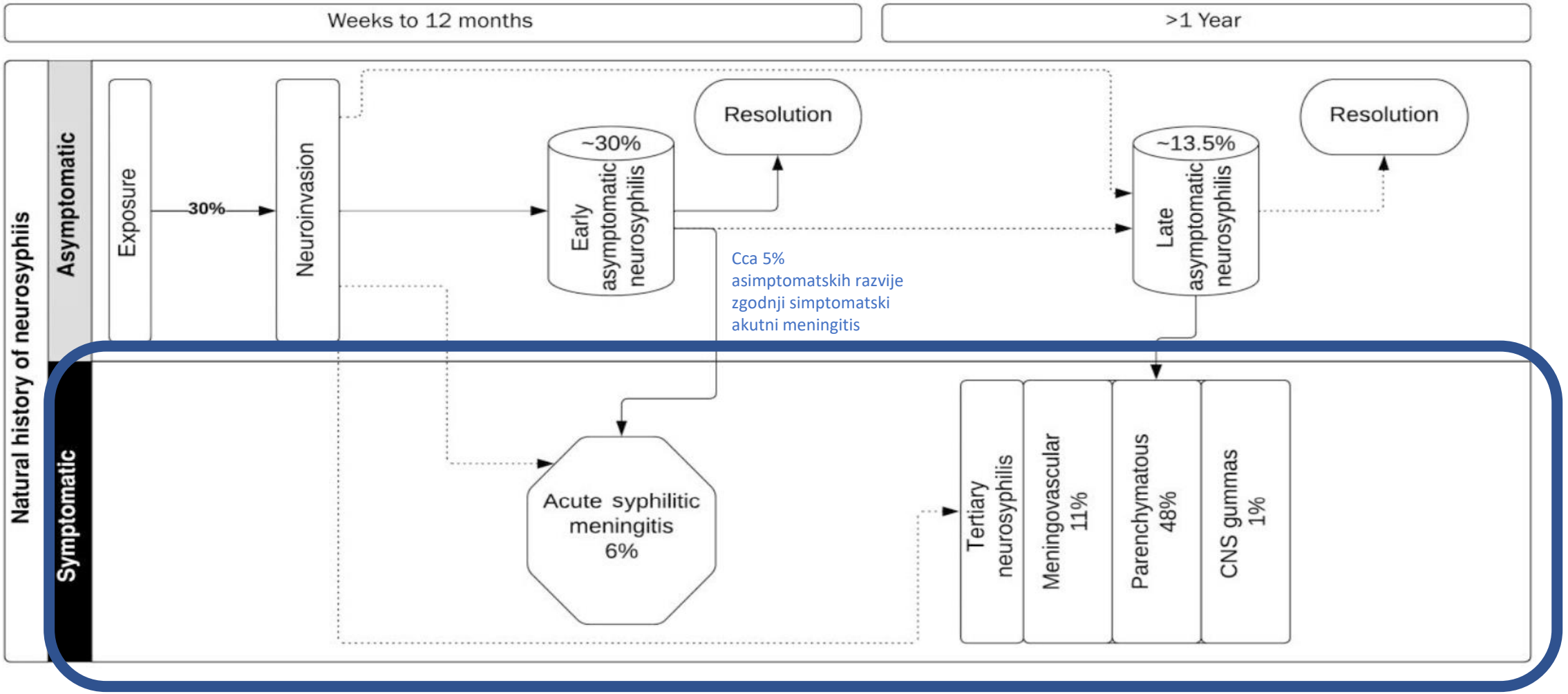
Test	Sensitivity during stage of infection, % (range)				Specificity, % (range)
	Primary	Secondary	Latent	Late	
Nontreponemal tests					
VDRL [14]	78 (74–87)	100	96 (88–100)	71 (37–94)	98 (96–99)
TRUST [14]	85 (77–86)	100	98 (95–100)	NA	99 (98–99)
RPR [14]	86 (77–99)	100	98 (95–100)	73	98 (93–99)
Early treponemal tests					
MHA-TP [15]	76 (69–90)	100	97 (97–100)	94	99 (98–100)
TPPA [16]	88 (86–100)	100	100	NA	96 (95–100)
TPHA [17]	86	100	100	99	96
FTA-ABS [14]	84 (70–100)	100	100	96	97 (94–100)
Enzyme immunoassays					
IgG-ELISA [18]	100	100	100	NA	100
IgM-EIA [19]	93	85	64	NA	NA
ICE [20]	77	100	100	100	99
Immunochemiluminescence assays					
CLIA [21]	98	100	100	100	99

NOTE. CLIA, chemiluminescence assay; ELISA, enzyme-linked immunosorbent assay; EIA, enzyme immunoassay; FTA-ABS, fluorescent treponemal antibody absorption assay; ICE, immune-capture EIA; MHA-TP, microhemagglutination assay for *Treponema pallidum;* NA, not available; TPHA, *T. pallidum* hemagglutination assay; TPPA, *T. pallidum* particle agglutination; TRUST, toluidine red unheated serum test.

Dober serološki odgovor, če vsaj 4x upad titra RPR/VDRL (vsaj 2 razredčini).

Seña AC, et al. Clin Infect Dis. 2010
Ghanem KG, et al. N Engl J Med. 2020

Nevrosifilis



Hamill MM, et al. Clin Infect Dis. 2024

Oblike nevrosifilisa

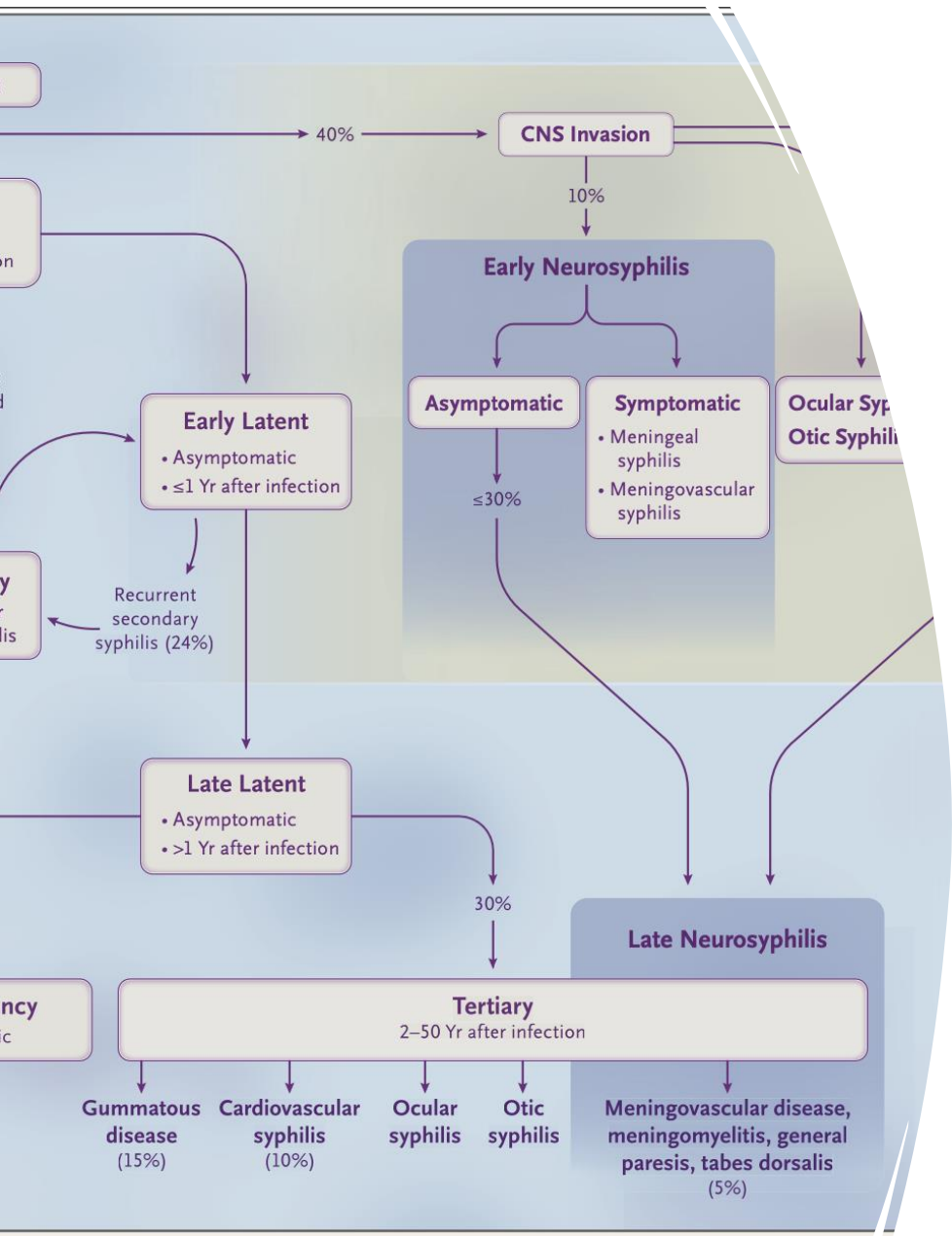
TIP	Časovni interval po okužbi	Možni klinični sindromi	Možni simptomi in znaki
Akutni meningitis	**Do 12 mesecev** (lahko tudi kasneje)	**meningitis** (pogosto bazilarni**),** **okvara MŽ** (3,6,7,8), **hidrocefalus**	Glavobol, fotofobija, slabost, zmedenost, krči, simptomi in znaki prizadetosti MŽ, znaki meningitisa/hidrocefalusa
Meningovaskularna oblika	**5-12 let** lahko že prej (0-7 let po okužbi)	Cerebralna: **možganska kap** (endarteritis, infarkt) Spinalna: **meningomielitis/kronični spinalni meningitis z endarteritisom/infarktom spinalnega žilja**	Simptomi in znaki možganske kapi (**MLADI, lahko prodromi -** glavobol, omotičnost, motnje osebnosti ali prizadetosti hrbtenjače (parestezije, parapareza, bolečina, paraplegija, inkontinenca)
Parenhimska oblika - napredujoča paraliza	**5– 12 let**	**kronični napredujoči meningoencefalitis**, lahko pridružen **komunikantni hidrocefalus**	Izguba spomina, spremembe osebnosti, glavoboli, nespečnost, motnje koncentracije, težave pri govoru/pisanju, tremor, motnje refleksov, zmedenost, dezorientacija, labilnost, paranoja, krči; simptomi in znaki hidrocefalusa, hemipareza
Parenhimska oblika - tabes dorsalis	**20 – 25 let**	**degeneracija zadnjih stebrov in korenin hrbtenjače**	Ataksija, parestezije, napadi žgoče bolečine v sp. okončinah, visceralni napadi, zmanjšan občutek za dotik/bolečino/ vibracije, širokotirna hoja, poz. Romberg, Charco sklepi
Gume v CŽS	**2 – 40 let**	**benigni cerebralni ali spinalni tumorji**	Asimptomatski/simptomi pritiska na strukture CŽS
Očesni sifilis	**Kadarkoli**	**anteriorni/posteriorni uveitis, optični nevritis, atrofija/nevropatija optičnega živca, horioretinitis, intersticijski keratitis, vaskulitis mrežnice**	Izguba/prizadetost vida, bolečina, motnjave, bliskanje, pritisk v očesu, fotofobija, Argyll Robertsonova zenica, znaki uveitisa
Otogeni sifilis	**Kadarkoli**	**Senzorinevralna ali prevodna izguba sluha**	Izguba sluha, vrtoglavica, tinitus, motnje ravnotežja

Hamill MM, et al. Clin Infect Dis. 2024

Zgleda enostavno….pa je res?

- Kdaj pomisliti na nevrosifilis?
- Asimptomatski nevrosifilis – ga iščemo? Kaj pa pri bolnikih, okuženih s HIV?
- Kako diagnosticiramo nevrosifilis?
- Je pri očesnem/otogenem sifilisu potrebna LP?
- Zdravljenje nevrosifilisa – je kaj novega?
- Ali je po zdravljenju potrebna kontrolna LP?
- Kortikosteroidi pri očesnem sifilisu – DA ali NE?
- Kortikosteroidi za preprečevanje Jarisch-Herzheimerjeve reakcije – DA ali NE in KDAJ?

"I said, was it Manet or Monet who had syphilis?"



eated Syphilis.

s of syphilis are shown, along with the approximate percentages of persons progressing to h
rvous system (CNS) by treponemes may not be a necessary prerequisite for the develop
from Ho and Lukehart.[10]

Kdaj pomislimo na nevrosifilis (in potrebo po LP)?

1. **Nevrološki simptomi in znaki ob dokazanem sifilisu**
2. **Okularni/otogeni sifilis**
3. **Asimptomatski nevrosifilis, če:**
   - ***a.*** ***Terciarni sifilis*** (gume, KVS sifilis)
     - do 30% bolnikov ima konkomitantni asimptomatski nevrosifilis
   - ***b.*** ***Neustrezen (< 4x) upad titra RPR/VDRL protiteles po 12 mesecih*** (primarni in sekundarni) ***oz. 24 mesecih*** (latentni/HIV bolniki) *(CDC 2021, IUSTI 2020)*
   - ***c.*** ***Kljub ustreznemu 4x upadu titer RPR/VDRL vztraja >1:32*** *(CDC 2021)*; **≥ 1:8**? *(IUSTI 2020)*
   - ***d.*** ***Ponovni porast RPR/VDRL (> 4x) brez ponovnega rizičnega spolnega stika (sum na neuspeh/relaps***) *(CDC 2021)*
   - ***e.*** ***Pozni sifilis pri HIV+, ki imajo CD4 ≤350/mm3 in/ali titer VDRL/RPR > 1:32*** (IUSTI 2020); (CDC 2021 in EACS 2024 ne priporočata več)

Janier M, et al. J Eur Acad Dermatol Venereol. 2021
https://www.cdc.gov/std/treatment-guidelines/neurosyphilis.htm
https://www.bashh.org/resources/25/updated_guideline_syphilis_2024/
Klein M, et al. Neurol Res Pract. 2020

Diagnostika nevrosifilisa

Lumbalna punkcija

a. **pleocitoza** (>5/microL;)
   - **Osebe s HIV - PAZI:** možna pleocitoza 6 – 20/microL, če brez ART, CD4 >200 celic/microL ali HIV RNA v plazmi > 50 kopij/mL)
   - **Parenhimska prizadetost**: lahko brez pleocitoze

b. **proteini (> 0,45 g/L)**

c. **reaktiven likvorski VDRL/RPR**
   - Atravmatska punkcija!

d. **PCR *T. Pallidum***
   - Senzitivnost: 40 - 70%
   - Specifičnost: 60 – 100%

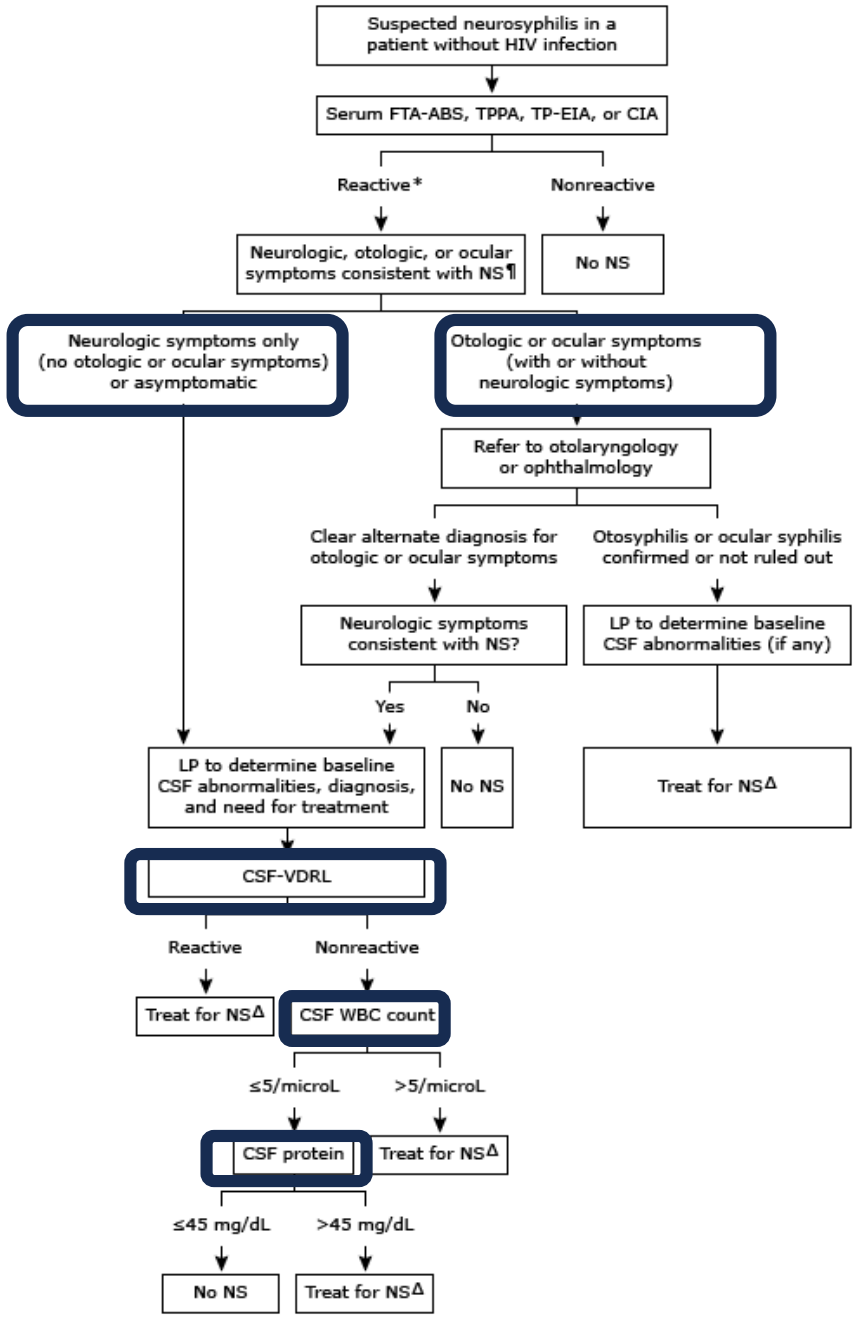
e. **TPHA/TPPA > 1:320 (≥ 1:640) v likvorju?** *(BASHH 2024; CDC 2021)*
   - **Negativna TPPA/TPHA izključuje diagnozo**

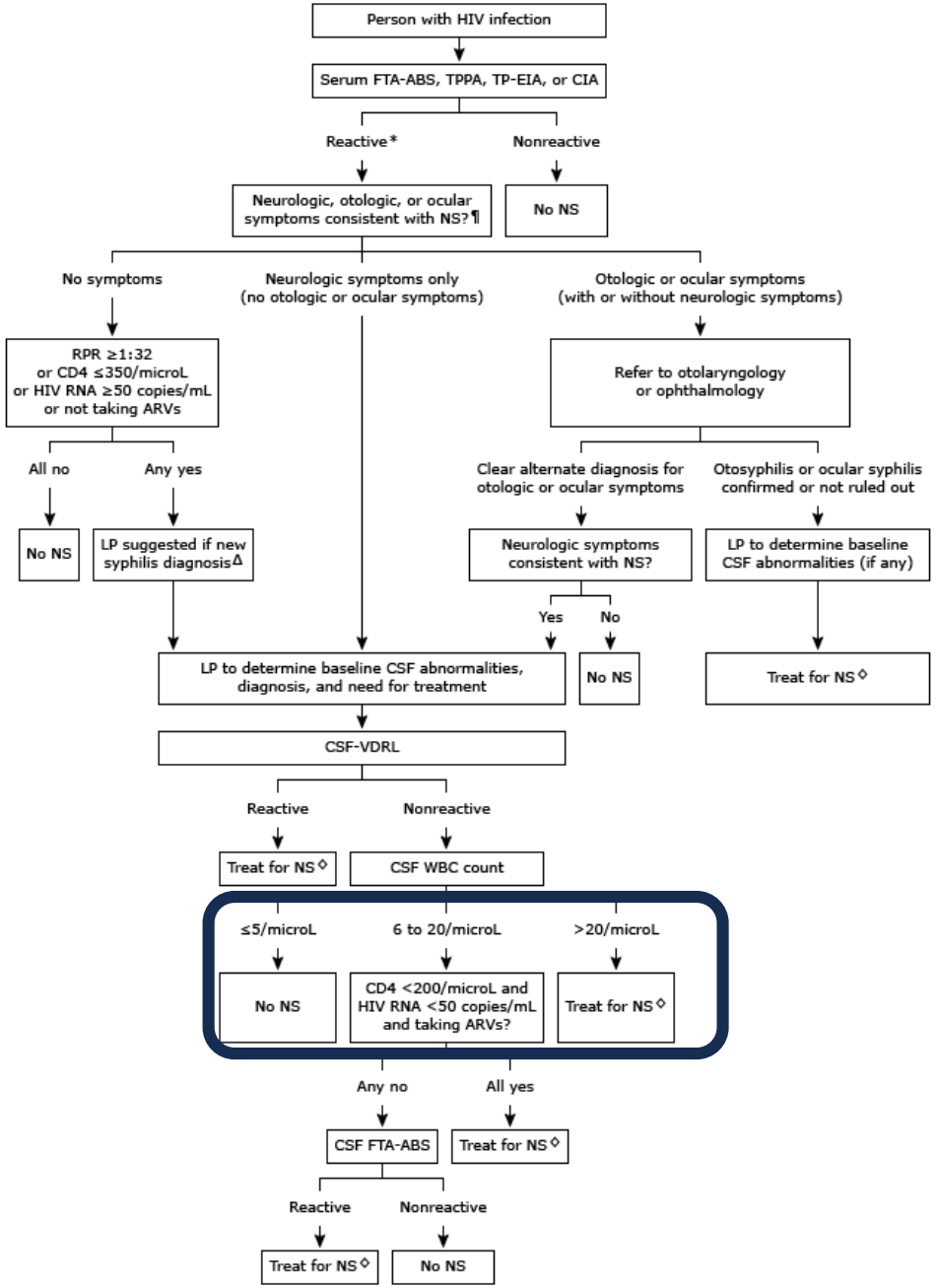
Table 2. Summary: Nontreponemal Antibodies for Various Stages of Syphilis

Stage of Syphilis	Nontreponemal Test	Sensitivity	Specificity	Quality of Studies
Primary	Serum RPR	62.5–76.1%[a]	N/A	High
	Serum VDRL	62.5–78.4%[b]	N/A	High
Secondary	Serum RPR	100%[c]	N/A	High
	Serum VDRL	100%	N/A	High
Early latent	Serum VDRL	85–100%	N/A	High
Late latent or unknown duration	Serum RPR	61%	N/A	High (1 study)
	Serum VDRL	64%	N/A	High (1 study)
Tertiary	Serum VDRL	47–64%	N/A	Lower (2 studies)
Neurosyphilis	CSF RPR	51.5–81.8%	81.8–100%	High
	CSF VDRL	49–87.5%	74–100%	High
Ocular	CSF VDRL	0–50%	N/A	Lower
Otic	CSF VDRL	5.5–5.6%	N/A	Lower (2 studies)

Janier M, et al. J Eur Acad Dermatol Venereol. 2021
https://www.cdc.gov/std/treatment-guidelines/neurosyphilis.htm
https://www.bashh.org/resources/25/updated_guideline_syphilis_2024/
Klein M, et al. Neurol Res Pract. 2020

Diagnostika nevrosifilisa





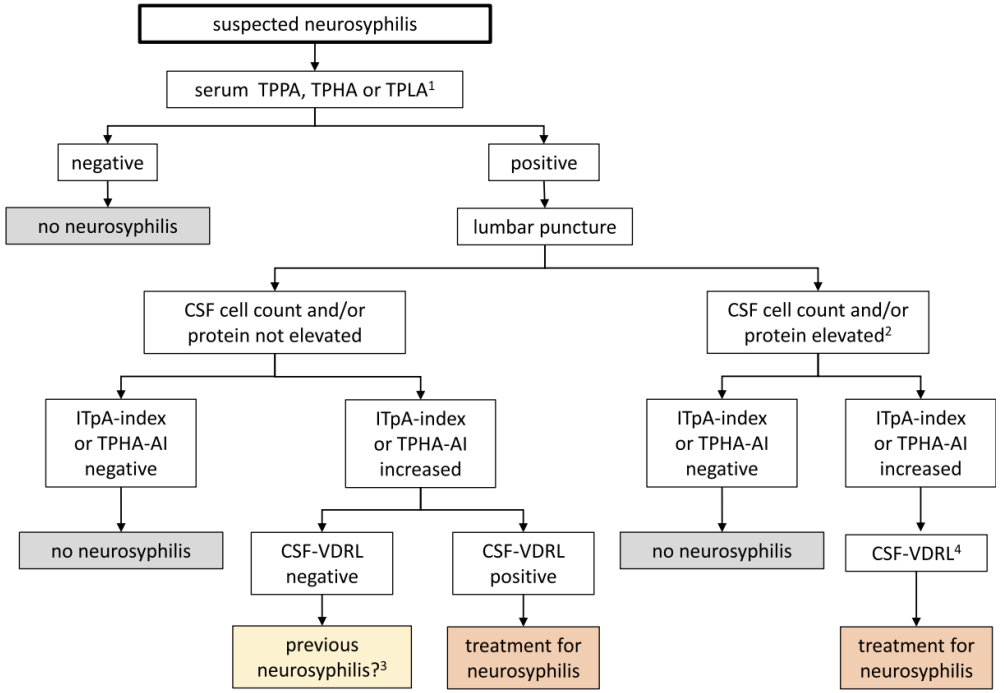
UpToDate, 2024

Diagnostika nevrosifilisa

Table 2. CSF criteria supporting a diagnosis of neurosyphilis.[12,69,74]

CSF parameters	In HIV-negative individuals	In people living with HIV
Protein	>0.45 g/L	>0.45 g/L
White cell count	>5/μl	>20/μl untreated or 6–20/μl on ART/plasma HIV viral load undetectable, or blood CD4 count <200 cells/mm^3
RPR	+	+
TPHA	>1:320	>1:320

BASSH guidelines, 2024



German guidelines on the diagnosis and treatment of neurosyphilis, 2020

Zdravljenje nevrosifilisa

Zdravljenje izbora:

- **benzilpenicilin 18–24 miljonov enot IV (3-4 miljone enot/4h) 10-14 dni**

Alternativno:

- ceftriakson 1–2 g IV/24h 10–14 dni ALI
- prokain penicilin 1.2–2.4 miljonov enot IM/dan 10-14 dni + probenecid 500 mg/6h 10–14 dni

Alergija na penicilin - desenzibilizacija!

Janier M, et al. J Eur Acad Dermatol Venereol. 2021

Zdravljenje s ceftriaksonom?

- **premalo podatkov**

> Trials. 2022 Oct 1;23(1):835. doi: 10.1186/s13063-022-06769-w.

Ceftriaxone compared with penicillin G for the treatment of neurosyphilis: study protocol for a multicenter randomized controlled trial

Fang-Zhi Du [1], Min-Zhi Wu [2], Xu Zhang [1], Rui-Li Zhang [3], Qian-Qiu Wang [4]

Affiliations + expand

PMID: 36183101 PMCID: PMC9526986 DOI: 10.1186/s13063-022-06769-w

Abstract

Background: Neurosyphilis may cause irreversible neurological sequelae. First-line treatment consists of penicillin G, with ceftriaxone being an alternative treatment in patients allergic to penicillin. The lack of clinical data comparing the efficacy of these two drugs indicated the need for comparative clinical trials to improve national treatment guidelines in China.

Methods/design: In this multicenter randomized controlled clinical trial, 290 patients newly diagnosed with neurosyphilis will be randomized 1:1 to treatment with aqueous crystalline penicillin G (ACPG) or ceftriaxone. Patients will be treated with standard regimens of ACPG or ceftriaxone according to Chinese National Guidelines and will be followed up for 12 months. All clinical parameters will be assessed at baseline and at follow-up 3, 6, 9, and 12 months later. The primary outcomes will include cerebrospinal fluid (CSF) white blood cell (WBC) count, serological efficacy, and clinical efficacy. The secondary outcomes will include CSF protein concentrations, Mini-Mental State Examination (MMSE) scores, imaging results, recurrence, and time to recovery from neurosyphilis. Adverse events will be monitored and recorded during the trial.

Discussion: This trial will provide clinical data to determine whether ceftriaxone is non inferior to ACPG in treating neurosyphilis and will provide evidence for the improvement of treatment guidelines.

Multicenter Study > Lancet Infect Dis. 2021 Oct;21(10):1441-1447.
doi: 10.1016/S1473-3099(20)30857-4. Epub 2021 May 26.

Ceftriaxone compared with benzylpenicillin in the treatment of neurosyphilis in France: a retrospective multicentre study

Thomas Bettuzzi [1], Aurélie Jourdes [2], Olivier Robineau [3], Isabelle Alcaraz [3], Victoria Manda [4],

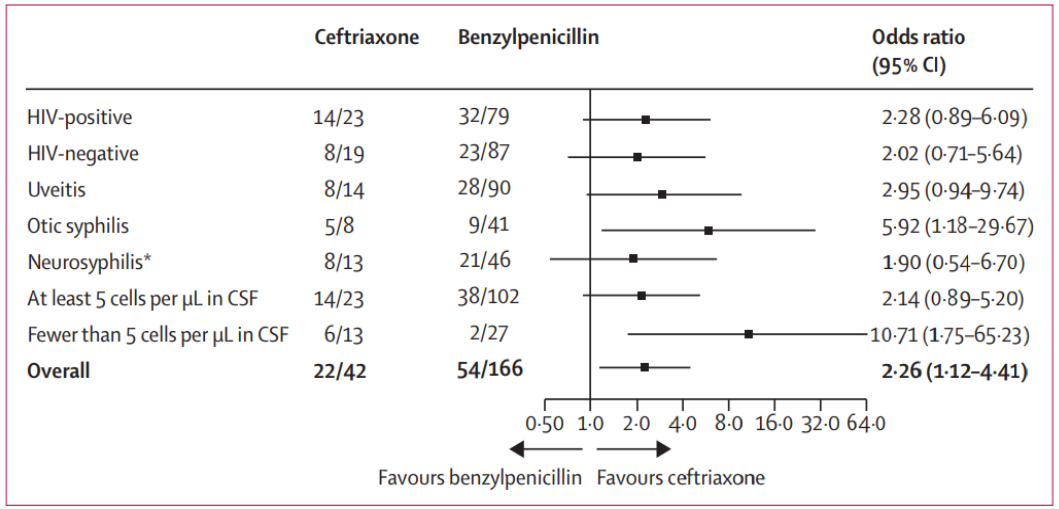


Figure 2: **Complete response rates in patients treated with ceftriaxone or benzylpenicillin, by HIV status, subtype of neurosyphilis, and CSF cellularity**
Odds ratios and their 95% CIs are presented with a log-linear scale. Vasculitis and facial palsy were grouped with meningitis because there were too few events. *Includes neurovascular syphilis, facial palsy, and meningitis.

Clinical Trial > Clin Infect Dis. 2000 Mar;30(3):540-4. doi: 10.1086/313725.

A pilot study evaluating ceftriaxone and penicillin G as treatment agents for neurosyphilis in human immunodeficiency virus–infected individuals

C M Marra [1], P Boutin, J C McArthur, S Hurwitz, P A Simpson, J A Haslett, C van der Horst, T Nevin, E W Hook 3rd

Kontrolna lumbalna punkcija ?

- ***IUSTI guidelines 2020:***
  - Kontrolna LP 6 tednov – 6 mesecev po koncu zdravljenja (ocena pleocitoze, proteinov); lahko se izognemo, če normalizacija RPR titrov;
- ***CDC guidelines 2021:***
  - Kontrolna LP ni potrebna, če je bolnik imunokompetenten (tudi oseba s HIV na ART) in je prisoten dober klinični in serološki odgovor;
- ***BASSH UK guidelines 2024:***
  - Kontrolna LP 6 tednov - 6 mesecev po koncu zdravljenja.
- ***Nemške smernice diagnostike in zdravljenja nevrosifilisa, 2020:***
  - Kontrolna LP vsakih 6 mesecev do normalizacije likvorja.

› Sci Rep. 2017 Aug 30;7(1):9911. doi: 10.1038/s41598-017-10387-x.

Serological Response Predicts Normalization of Cerebrospinal Fluid Abnormalities at Six Months after Treatment in HIV-Negative Neurosyphilis Patients

Yao Xiao [1 2 3], Man-Li Tong [1 4], Li-Rong Lin [1 4], Li-Li Liu [1 4], Kun Gao [1], Mei-Jun Chen [1], Hui-Lin Zhang [1], Wei-Hong Zheng [1], Shu-Lian Li [5], Hui-Ling Lin [5], Zhi-Feng Lin [5], Tian-Ci Yang [6 7], Jian-Jun Niu [8 9 10]

› Clin Infect Dis. 2008 Oct 1;47(7):893-9. doi: 10.1086/591534.

Normalization of serum rapid plasma reagin titer predicts normalization of cerebrospinal fluid and clinical abnormalities after treatment of neurosyphilis

Christina M Marra [1], Clare L Maxwell, Lauren C Tantalo, Sharon K Sahi, Sheila A Lukehart

Janier M, et al. J Eur Acad Dermatol Venereol. 2021
https://www.cdc.gov/std/treatment-guidelines/neurosyphilis.htm
https://www.bashh.org/resources/25/updated_guideline_syphilis_2024/
Klein M, et al. Neurol Res Pract. 2020

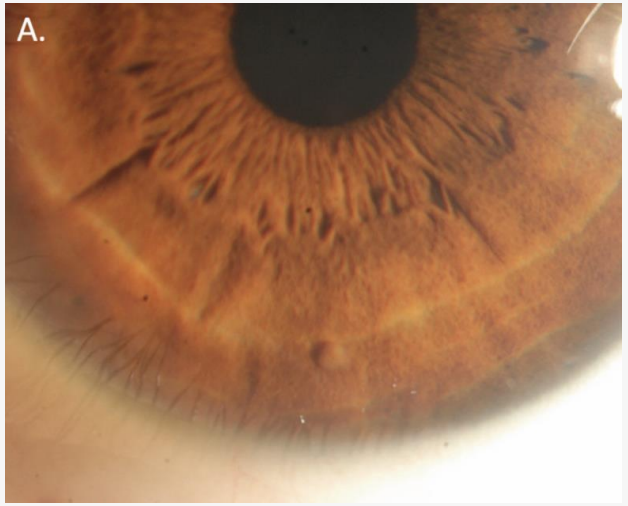
Očesni sifilis

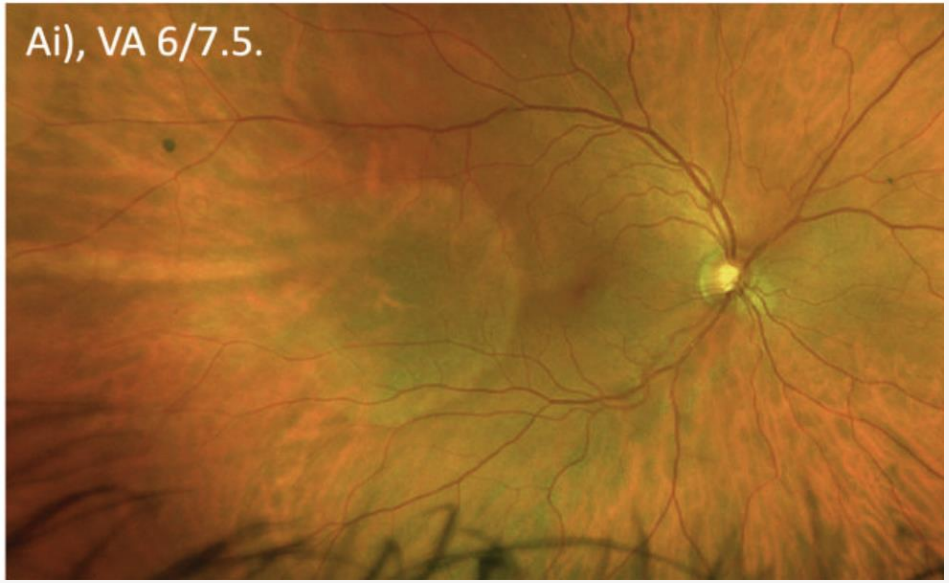
- Manifestacija **kadarkoli po okužbi** (najpogosteje v pozni latentni in terciarni fazi)
- Lahko prizadene **katerokoli očesno strukturo**
- Najpogosteje **uveitis**
  - anteriorni/intermediarni/posteriorni/panuveitis
  - Vsi pacienti z uveitisom testirani na sifilis!
  - Akutni sifilitični posteriorni plakoidni horioretinitis (ASPPC) – neboleča izguba vida
- lahko optični nevritis (pogosteje pri okuženih s HIV)

Table 1. Classification Criteria for Syphilitic Uveitis, SUN working group 2021.

Criteria
1. Uveitis with a compatible uveitic presentation, including
Anterior uveitis OR
Intermediate uveitis or anterior/intermediate uveitis OR
Posterior or panuveitis with one of the following presentations
Placoid inflammation of the retinal pigment epithelium or
Multifocal inflammation of the retina/retinal pigment epithelium or
Necrotising retinitis or
Retinal vasculitis
AND
2. Evidence of infection with *Treponema pallidum*, either
Positive treponemal test and non-treponemal test
Positive treponemal test with two different treponemal tests
Exclusions
History of adequate treatment for syphilitic uveitis*

*See also: Reverse Sequence Syphilis Screening Algorithm.





Reid GA, et al. Eye (Lond). 2024

Lumbalna punkcija pri otogenem/očesnem sifilisu

- ***IUSTI guidelines 2020:***
  - LP kontroverzna (zdravljenje enako). Lahko v pomoč pri izključevanju drugih patologij.
- ***CDC guidelines 2021:***
  - LP ni potrebna, če so očesni simptomi izolirani (brez CŽS simptomatike) in potrjeni pri oftalmološkem pregledu.
- ***BASSH UK guidelines 2024:***
  - LP pri okularnem in otogenem sifilisu redko uporabna, ne glede na stopnjo bolezni
- ***Nemške smernice diagnostike in zdravljenja nevrosifilisa, 2020:***
  - LP je indicirana.

- Pri 1/3 oseb z očesnim/otogenim sifilisom je LP negativna.
- CSF VDRL/RPR imajo nizko senzitivnost tako pri očesnem (<50%) kot otogenem sifilisu (<10%) (CDC lab).

Table 2. Summary: Nontreponemal Antibodies for Various Stages of Syphilis

Stage of Syphilis	Nontreponemal Test	Sensitivity	Specificity	Quality of Studies
Primary	Serum RPR	62.5–76.1%[a]	N/A	High
	Serum VDRL	62.5–78.4%[b]	N/A	High
Secondary	Serum RPR	100%[c]	N/A	High
	Serum VDRL	100%	N/A	High
Early latent	Serum VDRL	85–100%	N/A	High
Late latent or unknown duration	Serum RPR	61%	N/A	High (1 study)
	Serum VDRL	64%	N/A	High (1 study)
Tertiary	Serum VDRL	47–64%	N/A	Lower (2 studies)
Neurosyphilis	CSF RPR	51.5–81.8%	81.8–100%	High
	CSF VDRL	49–87.5%	74–100%	High
Ocular	CSF VDRL	0–50%	N/A	Lower
Otic	CSF VDRL	5.5–5.6%	N/A	Lower (2 studies)

Janier M, et al. J Eur Acad Dermatol Venereol. 2021
https://www.cdc.gov/std/treatment-guidelines/neurosyphilis.htm
https://www.bashh.org/resources/25/updated_guideline_syphilis_2024/
Klein M, et al. Neurol Res Pract. 2020
Tuddenham S, et al. Clin Infect Dis 2020

Očesni sifilis in kortikosteroidi

Ni nadzorovanih študij, ki bi poročale o koristih adjuvantnega sistemskega zdravljenja s kortikosteroidi.

CDC guidelines 2021:

Čeprav se sistemski steroidi pogosto uporabljajo kot adjuvantna terapija pri otosifilisu in očesnem sifilisu, ni dokazano, da je zdravljenje koristno.

Priporočila oftalmologov:

Anteriorni uveitis:

- topikalno kortikosteroidno zdravljenje

Posteriorni uveitis, panuveitis in optični nevritis:

- sistemski KS (prednizon 1 mg/kg in počasno nižanje 6-8 t)
- preprečevanje paradoksnega poslabšanja

Review > Eye (Lond). 2024 Aug;38(12):2337-2349. doi: 10.1038/s41433-024-03150-w. Epub 2024 Jun 24.

Ocular vs neurosyphilis. are they the same? A guide to investigation and management

Gerard A Reid [1 2], Gabor Michael Halmagyi [3 4], Claudia Whyte [5 6], Peter J McCluskey [7 6 8]

Multicenter Study > Br J Ophthalmol. 2019 Nov;103(11):1645-1649. doi: 10.1136/bjophthalmol-2018-313207. Epub 2019 Jan 30.

Current ophthalmology practice patterns for syphilitic uveitis

Genevieve F Oliver [# 1], Roy M Stathis [# 1], João M Furtado [2], Tiago E Arantes [3], Peter J McCluskey [4], Janet M Matthews [1]; International Ocular Syphilis Study Group; Justine R Smith [5]

Review > Surv Ophthalmol. 2022 Mar-Apr;67(2):440-462. doi: 10.1016/j.survophthal.2021.06.003. Epub 2021 Jun 18.

Ocular syphilis

João M Furtado [1], Milena Simões [2], Daniel Vasconcelos-Santos [3], Genevieve F Oliver [4], Mudit Tyagi [5], Heloisa Nascimento [6], David L Gordon [7], Justine R Smith [4]

Jarisch-Herxheimerjeva reakcija in steroidi

- Jarisch–Herxheimerjeva reakcija lahko **potencialno življenjsko nevarna, če prizadeta kritična področja** (npr. koronarno ustje, grlo, CŽS)
- **Ni kliničnih študij** (korist steroidov, časovni okvir)
- Namen preprečiti poslabšanje simptomov optičnega nevritis, uveitisa, nevroretinitisa, disfunkcije kohleovestibularnega sistema.

- ***IUSTI guidelines 2020:***
  - KS, če prizadetost CŽS (vključno z optičnim nevritisom) ali KVS
  - prednizon 20-60 mg/dan 3 dni (z začetkom 24h pred uvedbo KP)
- ***CDC guidelines 2021: /***
- ***BASHH UK guidelines 2024:***
  - Prednizon 40–60 mg/dan 3 dni (z začetkom 24h pred uvedbo antibiotika)
- ***German guidelines 2020:***
  - Ni študij, ki bi podpirale zdravljenje s KS, zato se ga rutinsko ne priporoča.

Janier M, et al. J Eur Acad Dermatol Venereol. 2021
https://www.cdc.gov/std/treatment-guidelines/neurosyphilis.htm
https://www.bashh.org/resources/25/updated_guideline_syphilis_2024/
Klein M, et al. Neurol Res Pract. 2020

Zaključek

- Diagnoza nevrosifilisa je redka, a nevarna.
- Diagnostika je včasih težavna.
- Pri očesnem/otogenem sifilisu LP ni nujna, je pa zaželena.
  - Pomembna je natančna anamneza možnih pridruženih nevroloških težav!
- Zdravljenje s ceftriaksonom – zaenkrat le alternativa, premalo podatkov
- Kortikosteroidi pri očesnem sifilisu – individualna presoja
- Preprečevanje Jarisch-Herxheimerjeva reakcije (3 dnevna terapija s steroidi)
- Bolniki z nevrosifilisom so vodeni na KIBVS.
- Bolnike je potrebno testirati na ostale SPO.

The Course of Syphilis
(neznani avtor, l. 1920)

There was a young man from Back Bay
Who thought syphilis just went away.
He believed that a chancre
Was only a canker
That healed in a week and a day.

But now he has "acne vulgaris"
(Or whatever they call it in Paris);
On his skin it has spread
From his feet to his head,
And his friends asking where his hair is!

There's more to his terrible plight:
His pupils won't close in the light
His heart is cavorting,
His wife is aborting,
And he squints through his gun-barrel sight.

Arthralgia cuts into his slumber;
His aorta's in need of a plumber;
But now he has tabes,
And saber-shinned babies,
While of gummas he has quite a number.

He's been treated in every known way,
But his spirochetes grow day by day;
He's developed paresis,
Has long talks with Jesus,
And thinks he's the Queen of the May