Neurosyphilis

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**Neurosyphilis** - part of tertiary syphilis

N.B. *Treponema pallidum* į CNS patenka jau ankstyvose sifilio stadijose (CSF pokyčiai be neurologinės klinikos)

* true incidence unknown (≈ 5000 new cases each year in USA); incidence is higher in HIV-infected population! (frequency of neurosyphilis in HIV-positive population < 2%)
* it is estimated that ≈ 10% of untreated early syphilis will develop neurosyphilis.

Pathology, Clinical Features

Early neurosyphilis

(5-7 yrs after initial infection) – pakenkiami meninges & blood vessels (**meningovascular neurosyphilis**):

1. **Basilar meningitis (luetic meningitis)**
2. **chronic nonsuppurative meningitis**
3. **acute syphilitic meningitis** (typically, more early – 1-2 yrs after initial infection)
	* obstructive or communicating ***hydrocephalus***.
	* ***cranial nerve palsies*** (esp. facial diplegia, hearing loss).
	* ***ophthalmologic findings*** are frequent - acute optic neuritis, slowly progressive optic atrophy, chorioretinitis, oculomotor cranial neuropathy (esp. *Argyll Robertson pupil* – small irregular pupil, reacts to convergence, but not to light).
	* ***partial seizures*** (25%) may be sole manifestation of neurosyphilis!; 30% patients have no interictal clinical findings.

N.B. treponemal serologic test should be obtained in every adult with acquired partial seizures!

Pathology - perivascular infiltration of meninges with lymphocytes & plasma cells; inflammation also involves cranial nerves (→ axonal degeneration); focal meningeal inflammation → proliferation of fibroblasts & capillaries → hypertrophic meninges or **gummata** (avascular granuloma attached to dura - localized form of meningeal syphilis!).

* + gummata in basal cisterns, leptomeninges, parenchyma → headache, focal neurological deficits, cranial nerve palsies.
	+ *spirochetes* are rarely demonstrated.
1. **Ischemic strokes** (patients are younger than those in typical atherosclerotic age range):
2. **brain** (e.g. middle cerebral artery is commonly involved → *luetic hemiplegia*).
3. **spinal cord** (*acute transverse myelitis*) - sensory & motor signs (vs. tabes).

Pathology - inflammatory cells invade blood vessel walls (small-vessel obliterative endarteritis) → luminal occlusion by thrombosis → ischemia, multiple areas of infarction.

***Bilateral lesions in basal ganglia*** (high signal on T2-MRI) - vascular territory of lenticulostriate arteries - are most common abnormality.

**Heubner arteritis** – arteritis of *circle of Willis* due to basal meningitis (syphilis, tbc, fungi).

Late neurosyphilis

(5-30 yrs after initial infection) – pakenkiama CNS parenchima (**parenchymatous neurosyphilis**):

Rarely seen now! (asymptomatic and meningovascular neurosyphilis are much more common nowadays!)

1. **Cerebral cortex** atrophy (esp. frontal) – paretic neurosyphilis (s. dementia paralytica, general paresis of insane, syphilitic meningoencephalitis) – imitates Alzheimer’s disease.
* personality changes → slow deterioration in cognitive functioning, behavioral changes (incl. delusions of grandeur; may suggest psychosis), loss of appendicular strength, tremor of tongue and hands, pupillary abnormalities, loss of bowel-bladder control →→→ severe dementia with quadriparesis.
* if untreated, fatal in 3-5 years.

Pathology - **chronic meningoencephalitis**: mononuclears infiltrate small cortical vessels and extend into cortex itself → neuronal degeneration and loss → gliosis → brain atrophy, thickened cloudy meninges adherent to cortex.

* + *spirochetes* can be demonstrated in tissue sections.
	+ frequent hydrocephalus with damage to ependymal lining and proliferation of subependymal glia (granular ependymitis).
1. **Posterior column of spinal cord** – tabetic neurosyphilis (s. tabes dorsalis) - most common form of neurosyphilis in preantibiotic era:

legs >> arms

* 1. paresthesias / dysesthesias in radicular distribution
	2. proprioceptive and vibratory sensory deficits (tendon reflexes↓↓↓, etc)
	3. progressive sensory ataxia
	4. stabbing (lancinating, lightning) pains in back & legs – may be due to heavy metal therapy used to treat neurosyphilis in preantibiotic era!

**Visceral crises** – pain paroxysms in viscera (esp. ***gastric crises*** – pain & vomiting).

* 1. impotence, urine retention / incontinence
	2. trophic disorders (Charcot’s arthropathy, ulcers, etc).
	3. irregular pupils (94% patients), incl. Argyll-Robertson pupils; may lead to blindness!

Pathology - mononuclears infiltrate posterior columns and preganglionic portion of dorsal roots → atrophy (loss of both axons and myelin).



Degeneration of dorsal columns and dorsal roots:



Congenital neurosyphilis

* now rare.
* spirochete infect fetus between 4th and 7th months of pregnancy.
* clinical types and treatment are *similar to those in adults* (but tabes dorsalis is uncommon).

Diagnosis

**Serum FTA-ABS test** – highly specific test to suspect diagnosis (positive in 95-100% neurosyphilis cases).

N.B. in tertiary syphilis, ***nonspecific tests*** may already be negative, but ***specific tests*** remain positive lifelong! (e.g. only 70% patients with neurosyphilis have positive VDRL)

* negative serum FTA-ABS test makes CSF analysis unnecessary.

Negative FTA-ABS = no neurosyphilis

* false-positive rate < 1% (e.g. collagen vascular disorders).

Positive serum FTA-ABS indicates past infection with syphilis (FTA-ABS remains reactive indefinitely, even after treatment) → **CSF analysis** - used as guide to presence & activity of neurosyphilis.

N.B. always perform CSF analysis before starting treatment of syphilis of > 1 yr. duration! (partial therapy may be insufficient to eradicate organisms in CNS and eye)

1. lymphocytic pleocytosis (up to 2000)
2. protein↑ (up to 100), Ig index↑
3. normal glucose
4. positive serologic tests
	* VDRL is test of choice in CSF (positive VDRL - strong evidence for neurosyphilis, but negative VDRL does not rule out neurosyphilis\*):
5. positive even if serum VDRL is negative.
6. *false-positive are rare* – a)contamination with seropositive blood [e.g. traumatic tap, SAH], b)entry of serum reagin into CSF during meningitis.

\*most clinicians treat for neurosyphilis if positive serum FTA-ABS + CSF lymphocytic pleocytosis + CSF protein↑ (despite CSF VDRL results); jei CSF VDRL negative, AIDS pacientams reikia atlikti CSF FTA-ABS

* + FTA-ABS test is not used in CSF - *false-positive 4-6%* (small amounts of antibodies passively entered from serum).

N.B. positive FTA-ABS does not establish diagnosis of neurosyphilis!

1. **PCR** may have future applications.

Today many patients with late (parenchymal) neurosyphilis have normal CSF – current recommendation:

signs of neurosyphilis + positive serum FTA-ABS → treat (regardless of CSF findings).

* CSF pleocytosis may be provoked after 1 week of therapy.

General rule:

**neurosyphilis** = syndrome consistent with neurosyphilis + positive serum treponemal test + positive CSF nontreponemal test

N.B. at present time, asymptomatic neurosyphilis is quite common!

Treatment

Antibacterial treatment for 10-21 days:

1. aqueous crystalline penicillin G 2-4 million U q4h IV
2. procaine penicillin 2.4 million U / d IM (with probenecid 500 mg orally × 4/d - reduces penicillin renal excretion)

(vs. other forms of syphilis are treated with benzathine penicillin G)

* if penicillin allergy:
1. desensitization.
2. ceftriaxone 2 g/d IM or IV for 10-14 days.
3. doxycycline 300 mg/d (orally in divided doses) for 30 days.
* treatment follow-up (esp. in HIV-infected patients with neurosyphilis!) - quantitative *blood serology* at 3-month intervals (decline in titers) + *CSF* at 6 and 12 months:
	1. **CSF pleocytosis** must resolve in 6 months - best measure of disease activity!
	2. **CSF-VDRL titers** should (but may not) decrease – not reliable.
* extremely rare - **unsuccessful therapy** (progression of clinical disease / persistence of CSF pleocytosis / reactive CSF-VDRL) → re-treatment with 24 million U/d for 10 days.
* tabes dorsalis may be arrested by treatment, but lancinating pains often continue (H: analgetics, carbamazepine).

Gummas:

1. if clinical condition of patient permits → trial of ***conservative treatment*** (penicillin + steroids).
2. if diagnosis is doubtful → ***biopsy*** and ***excision***.