Infections of Nervous System

Last updated: April 17, 2019

[Pathogenesis 1](#_Toc3082284)

[Classification 1](#_Toc3082285)

[Viruses 1](#_Toc3082286)

[Fungi 2](#_Toc3082287)

[Predisposing Factors 2](#_Toc3082288)

[Diagnosis 2](#_Toc3082289)

[Treatment 2](#_Toc3082290)

[Antibiotics 2](#_Toc3082291)

[Antivirals 3](#_Toc3082292)

[Antifungals 3](#_Toc3082293)

[Candida 3](#_Toc3082294)

**Postoperative Infection** – see [p. Op120 >>](http://www.neurosurgeryresident.net/Op.%20Operative%20Techniques\Op120.%20General%20Principles%20of%20Perioperative%20Neurosurgery.pdf)

Pathogenesis

* CNS is normally sterile.
* parenchyma, coverings, and blood vessels of nervous system may be invaded by ***virtually any pathogenic microorganism***.

Principal routes of entry:

* 1. **hematogenous spread** (bacteria, viruses) via septicemia, septic emboli - most common!
* ordinarily through ***arterial*** circulation, but retrograde ***venous*** spread can occur (e.g. via anastomotic connections between veins of face and cerebral circulation).
* most common sources: pneumonia, bronchiectases, bacterial endocarditis.
  1. **direct implantation** (bacteria) - invariably traumatic (rarely – iatrogenic\*); associated with congenital malformations (e.g. meningomyelocele).

\*esp. LP, ventriculo-peritoneal shunts

* 1. **local extension** (bacteria) from established infection – ***paranasal sinus*** (most often frontal), ***middle air***, ***tooth***, ***surgical site*** in cranium or spine (osteomyelitis → bone erosion → propagation into CNS).
  2. **retrograde transport through PNS** (certain viruses - rabies, herpes simplex, poliovirus).

Infection becomes rapidly disseminated once organisms reach CSF.

* *CSF is area of impaired host defense* - lack of sufficient numbers of complement components and immunoglobulins for opsonization, contains no phagocytic cells; fluid medium impairs phagocytosis.

Damage to nervous tissue:

* + 1. direct invasion by infectious agent
    2. microbial toxins
    3. destructive inflammatory / immune-mediated response - recently recognized as very important (even in bacterial meningitis).

Inflammatory reaction in confined intracranial space can cause **ICP**↑

Classification

- according to **major site of involvement**:

N.B. process frequently involves more than one of these structures (e.g. meningoencephalitis, encephalomyelitis)

1. **Osteomyelitis** – inflammation of bones.
2. **Meningitis** – inflammation of meninges.
3. **Encephalitis** – **viral** invasion of brain parenchyma; often *diffuse*.
4. **Cerebritis** – *focal* **bacterial** invasion of brain parenchyma; no capsule or pus.
5. **Myelitis** – inflammation of spinal cord parenchyma; no capsule or pus.
6. **Abscess** – *focal*, encapsulated, pus-containing cavity in brain parenchyma (rarely, in spinal cord parenchyma).
7. **Empyema** – abscess in enclosed or potential space:
   1. subdural
   2. extradural
8. **Granuloma** – *focal*, more or less encapsulated, chronic inflammatory lesion without pus (e.g. sarcoidosis, syphilis, tuberculosis, fungi, larvae of intestinal parasites).

Infections of spine:

1. vertebral osteomyelitis/discitis
2. epidural abscess
3. subdural abscess\*
4. meningitis
5. spinal cord abscess\*

\*exceedingly rare.

Viruses

***Neuroinvasive*** - virus has ability to enter nervous system.

***Neurotropic*** - virus infects nervous cells.

***Neurovirulent*** - virus causes clinically recognizable neurologic symptoms.

Acute viral infections:

1. viral (aseptic) meningitis
2. encephalitis
3. myelitis

Delayed complications of acute infection - postinfectious polyneuritis, acute disseminated encephalomyelitis (ADEM), acute cerebellar ataxia.

Latent infections with recurrences from time to time: *herpesviruses* (HSV, VZV).

Slowly progressive disorders (slow viral infections):

1. **conventional** viruses:
   1. subacute sclerosing panencephalitis (SSPE) (measles virus)
   2. progressive rubella panencephalitis (PRP) (rubella virus)
   3. progressive multifocal leukoencephalopathy (PML) (JC virus)
   4. human T-lymphotrophic virus (HTLV)-associated myelopathy (HAM) / tropical spastic paraparesis (TSP) (HTLV-I)
   5. acquired immunodeficiency syndrome (AIDS) (HIV)
2. **unconventional** transmissible spongiform encephalopathy agents (prions).

Fungi

– opportunistic organisms – infect only ***immunosuppressed*** individuals.

(except few pathogenic fungi – *Histoplasma*\*, *Blastomyces*\*, *Coccidioides*\*, *Paracoccidioides*\*\* – may infect ***normal*** hosts).

\*endemic to some areas of North America

\*\*endemic to some areas of Central-South America

* most fungi **invade brain** by *hematogenous dissemination* (but *direct extension* by *Mucor*).
* lungs / skin / hair are usual **primary sites**.

Cryptococcosis\* is most common mycotic CNS infection!

\*may be primary infection and occur in ***normal*** individuals!

1. meningitis
2. intraparenchymal abscess / granuloma
3. vasculitis → thrombosis → infarction (often strikingly hemorrhagic) - *Mucor*, *Aspergillus*

Predisposing Factors

1. **Recent infection** that may progress to meningitis (e.g. upper respiratory infection, pneumonia, otitis media leading to pneumococcal meningitis; mumps, chickenpox).
2. **Exposure to** others with **infectious illness** (e.g. meningococcus or *Haemophilus influenzae*).
3. Recent **travel** (e.g. mosquitoes → arbovirus encephalitis; Central America → cysticercosis).
4. **Occupation** (e.g. painter exposed to *Cryptococcus* in pigeon droppings)
5. **Underlying disease**:
6. lymphoma, leukemia, other malignancy
7. renal failure
8. AIDS and other immunodeficiency states
9. alcoholism
10. diabetes
11. **Drugs** (chemotherapy, immunosuppressant, steroids)
12. Recent **head injury** (precedes 10% of pneumococcal meningitis), penetrating skull trauma.
13. Recent **neurosurgical procedure**. [see p. Op120 >>](http://www.neurosurgeryresident.net/Op.%20Operative%20Techniques\Op120.%20General%20Principles%20of%20Perioperative%20Neurosurgery.pdf)
14. Recent **insect bite** (e.g. Lyme disease, rickettsial infection).
15. History of **positive PPD**.

Diagnosis

* **CT / MRI** is indicated in any patient with syndrome compatible with CNS infection!
* **CSF** is indicated in any patient (after exclusion of intracranial mass).
* **brain biopsy** (→ immunostaining techniques, electron microscopy, injection into susceptible animals and tissue culture cell lines) is still standard of diagnosis in some specific CNS infections.
* **CBC with differential** is nonspecific adjunct in diagnostic evaluation.

CBC may be normal in elderly or immunosuppressed patients!

* 2-3 **blood cultures** should be obtained from all patients (even when antimicrobial therapy has already been administered).
* in suspected *any viral CNS infection*, draw ***serum specimen*** acutely and save to compare with convalescent sera (3-5 weeks after onset of illness) – ≥ 4-fold rise in **IgG titers**?
* **search of infection source** – chest X-ray (!), echocardiography, cultures of other body fluids, bone scans.
* serum electrolytes, glucose\*, urea nitrogen, creatinine.

\*for interpretation of CSF glucose level.

Treatment

With exception of viral meningitis, all but most chronic CNS infections require initial inpatient evaluation and treatment:

1. Bed rest
2. Analgesics
3. IV antimicrobials
4. Fluid balance

Antibiotics

|  |  |  |  |
| --- | --- | --- | --- |
| **Dru****g IV** | **Neonates**  (0-7 days → 8-28 days) | **Children** | **Adults** |
| penicillin G | 100,000-150,000 U/kg/d (divided every 12 hr) → 150,000-200,000 U/kg/d (divided every 6-8 hr) | 250,000-400,000 U/kg/d (divided every 4 hr) | 20-24 million U/d\* (divided every 4 hr) |
| ampicillin | 50-75 mg/kg q12h →  50-100 mg/kg q6-8h | 50-100 mg/kg q6h | 2 g q4h |
| methicillin |  | 50 mg/kg q6h |  |
| oxacillin | 50-75 mg/kg q12h →  50 mg/kg q6-8h | 33 mg/kg q4h or 50 mg/kg q6h | 2 g q4h |
| nafcillin |  | 33 mg/kg q4h | 1.5-2 g q4h |
| ticarcillin | 75-100 mg/kg q12h | 75 mg/kg q6h | 3 g q4h |
| gentamicin | 2.5 mg/kg q12h → q8h | 2.5 mg/kg q8h | 1.66 mg/kg q8h |
| amikacin | 7,5-10 mg/kg q12h → q8h | 10 mg/kg q8-12h | 7.5 mg/kg q12h |
| cefotaxime | 50 mg/kg q12h →  50 mg/kg q6-8h | 50 mg/kg q6h | 1.5-2 g q4h |
| ceftriaxone | - (displaces bilirubin from albumin-binding sites) | 40-50 mg/kg q12h | **2**-3 g q12h |
| ceftazidime | 30 mg/kg q12h → q8h | 40-50 mg/kg q8h | 2 g q8h |
| vancomycin R | 15 mg/kg q12h → q8h | 10 mg/kg q6h | Load 25-30 mg/kg  (max. 3000 mg)  ↓  500-750 mg q6h  (check trough level after 3rd dose) |
| chloramphenicol | 25 mg/kg q24h → q12h | 20-25 mg/kg q6h | 1 g q6h |
| metronidazole |  | 7.5 mg/kg q8h | 500 mg q6h |
| SMX/TMP |  |  | 15-20 mg/kg/d divided equally as q6h or q8h doses |
| oral rifampin |  | > 1 yr.: 10 mg/kg q12h  < 1 yr.: 5 mg/kg ql2h | 600 mg q12h |

\*may produce convulsions if large concentrations are introduced into CSF

R dose adjustment necessary for Creatinine Clearance < 60 mL/min

N.B. only **3rd generation** cephalosporins are used; cefuroxime enters CSF, but frequent treatment failures!

|  |  |
| --- | --- |
| **Antibiotic** | **Ratio CSF to serum** |
| penicillin G | 2-5% |
| ampicillin | 15-20% |
| cefotaxime | 27-63% |
| nafcillin | 10-15% |
| vancomycin | 10-15% |

Antivirals

1. ganciclovir 5 mg/kg q12h IVI over 1 h for minimum 14-21 days → 6 mg/kg/d for indefinite period.
2. foscarnet 40-60 mg/kg q8h (or 100 mg/kg q12h) IVI over 1 h for 14-21 days → maintenance 60-120 mg/kg/d IV for indefinite period.
3. acyclovir
   1. 10 mg/kg (or 500 mg/m2) IVI q8h over 60 min (to minimize risk of renal dysfunction).

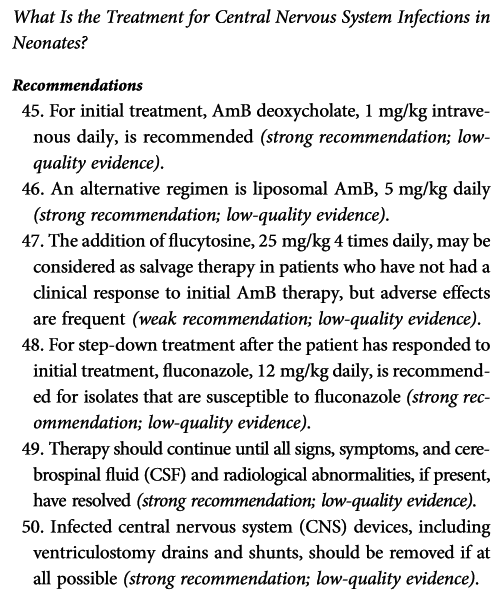
* dilute to concentration ≤ 7 mg/mL (e.g. 70-kg person - 700 mg is diluted in 100 mL).
* extravasation → local inflammation and phlebitis.
* excellent CSF penetration.
* acyclovir-resistant strains are problem only in AIDS patients.
  1. 800 mg orally ×5/d.

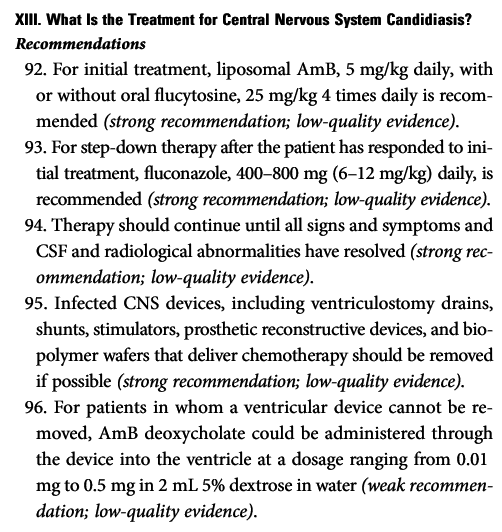
1. valacyclovir 1.0 g orally ×3/d.
2. famciclovir 500-750 mg orally ×3/d.

Antifungals

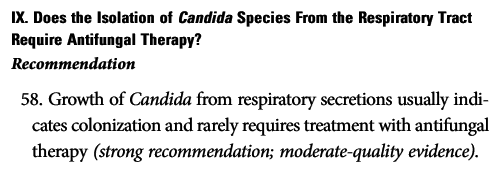
Candida

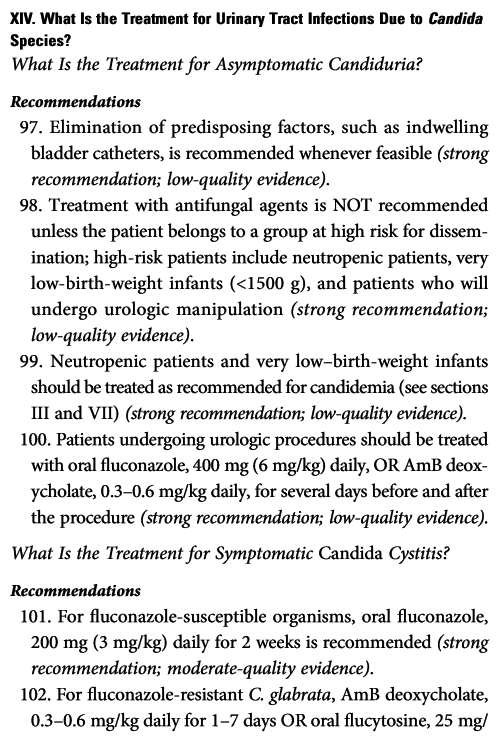
From 2016 guidelines:

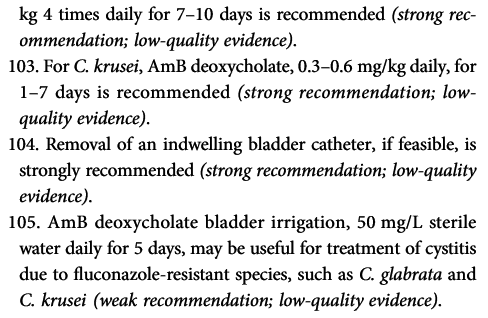




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