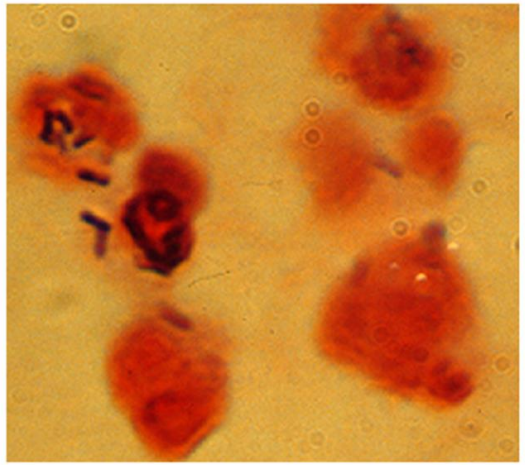
ACUTE INFECTIONS OF NERVOUS SYSTEM

PROF. LEILA RINATOVNA AKHMADEEVA

UFA, SEP 8, 2022

***Listeria monocytogenes* in cerebrospinal fluid**



Gram stain of cerebrospinal fluid (x1000) shows inflammatory cells and small, gram-positive rods and coccobacilli. Culture of this specimen revealed moderate-sized beta-hemolytic colonies composed of small, motile gram-positive rods, confirmed to be *Listeria monocytogenes*.

Courtesy of Harriet Provine.

UpToDate®

PLAN

- GENERAL INFORMATION
- CLASSIFICATION
- MAIN EXAMPLES
- LITERATURE TO STUDY

INFECTIONS OF NERVOUS SYSTEM

A GROUP OF THE DISORDERS CAUSED BY INFECTIOUS AGENTS WITH SYMPTOMS AND SIGNS OF IMPAIRMENT IN NERVOUYS SYSTEM

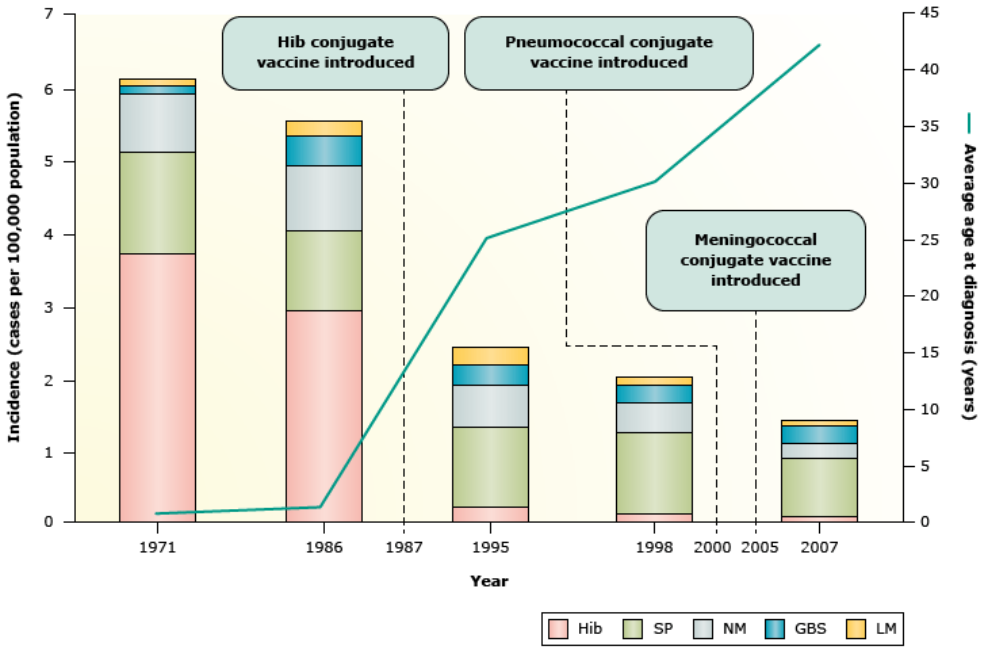
IMPORTANT

- COMMON
- OFTEN SEVERE
- MORTALITY - 15–70%
- BACTERIAL MENINGITIS: 1, 2 MILLION CASES EVERY YEAR IN THE WORLD
  - 135 000 DIE
- >50% PATIENTS HAVE RESIDUAL SIGNS EITHER FOR LIFETIME OR FOR LIMITED TIME

The introduction of vaccines has reduced the burden of the two most common etiological agents for **bacterial** meningitis in adults and older children, Streptococcus pneumoniae and Neisseria meningitidis. Haemophilus influenzae type B (Hib) is also becoming a rare cause of meningitis in Europe

1. van Ettekoven CN, van de Beek D, Brouwer MC. Update on communityacquired bacterial meningitis: guidance and challenges. Clin Microbiol Infect. 2017;23(9):601–6.
2. McIntyre PB, O'Brien KL, Greenwood B, van de Beek D. Effect of vaccines on bacterial meningitis worldwide. Lancet. 2012;380(9854):1703–11.
3. van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT, et al. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect. 2016;(22):S37-S62.

Effect of conjugate vaccines on bacterial meningitis infections



Incidence (left axis, bars) and average age at diagnosis (right axis, line) are shown for patients with bacterial meningitis in the United States from 1971 to 2007[1-4]. The decreasing proportion of disease caused by *Haemophilus influenzae* type b (Hib) and, later, *Streptococcus pneumoniae* (SP) and the increase in overall age of remaining cases show the effect of routine infant vaccination programs.

GBS: group B streptococcus; LM: *Listeria monocytogenes*; NM: *Neisseria meningitidis*.

References:

1. *Thigpen MC, Whitney CG, Messonnier NE, et al. Bacterial meningitis in the United States, 1998–2007. N Engl J Med 2011; 364:2016.*
2. *Schuchat A, Hilger T, Farley MM, et al. Active bacterial core surveillance of the emerging infections program network. Emerg Infect Dis 2001; 7:92.*
3. *Wenger JD, Hightower AW, Facklam RR, et al. Bacterial meningitis in the United States, 1986: report of a multistate surveillance study. J Infect Dis 1990; 162:1316.*
4. *Fraser DW, Geil CC, Feldman RA. Bacterial meningitis in Bernalillo County, New Mexico: a comparison with three other American populations. Am J Epidemiol 1974; 100:29.*

The most commonly diagnosed causes of **viral** CNS infections in Europe are Herpes simplex virus (HSVs), enteroviruses, Varicella-zoster virus (VZV) and arthropod-borne viruses (arboviruses)

Boucher A, Herrmann JL, Morand P, Buzele R, Crabol Y, Stahl JP, et al. Epidemiology of infectious encephalitis causes in 2016. Med Mal Infect. 2017;47(3):221–35..

MODERN PATTERNS

- MORE CONDITIONS WITH NO OBVIOUS SIGNS
- DIFFERENT AGES (INCLUDING ELDERLY)
- MORE CNS INVOLVEMENT
- MORE VIRAL INFECTIONS
- DIFFICULT TO TREAT (RESISTANT TO ANTIBIOTICS) BACTERIAL INFECTIONS
- MORE MIXED INFECTIONS
- NEW INFECTIONS!

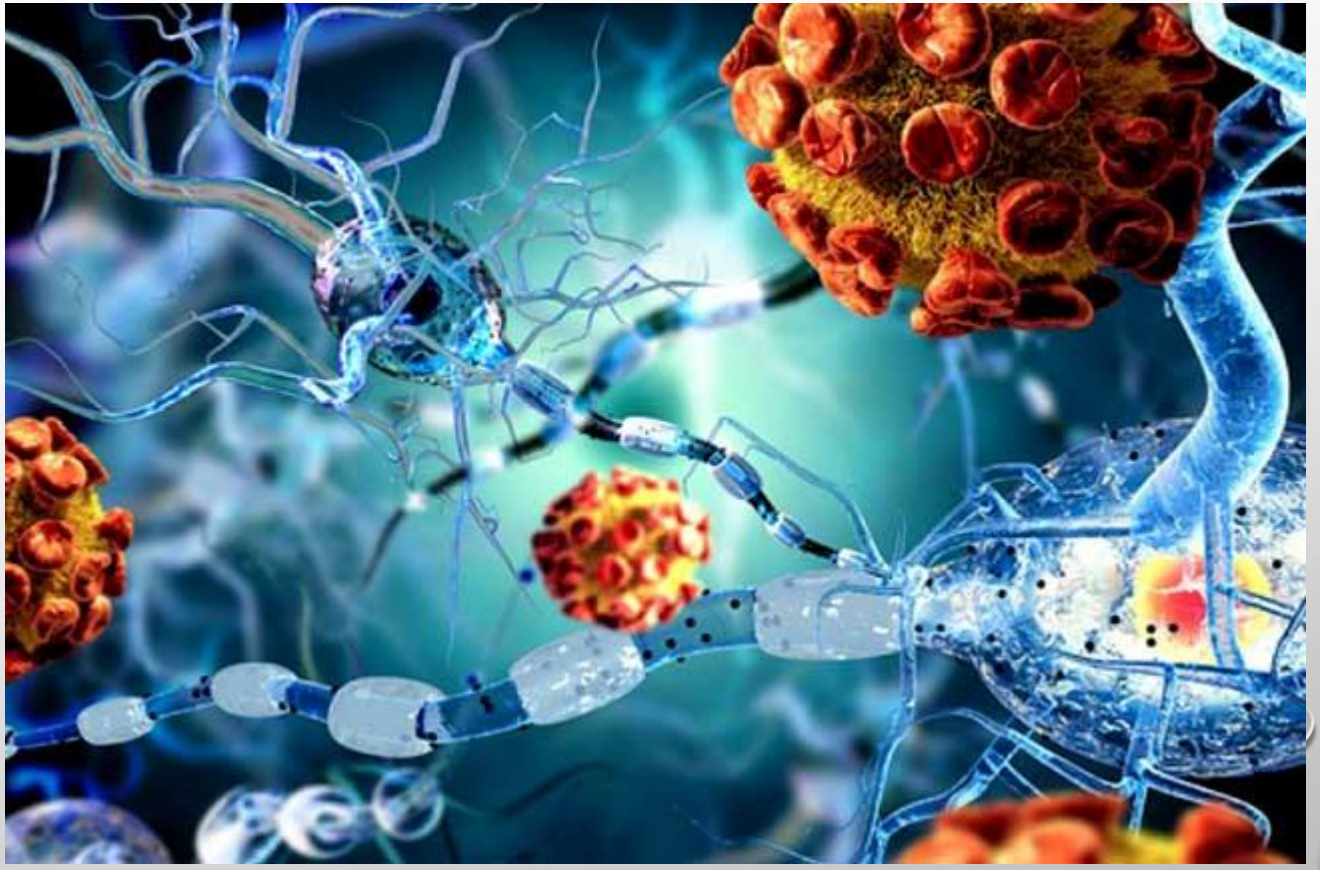
CLASSIFICATION

PRIMARY

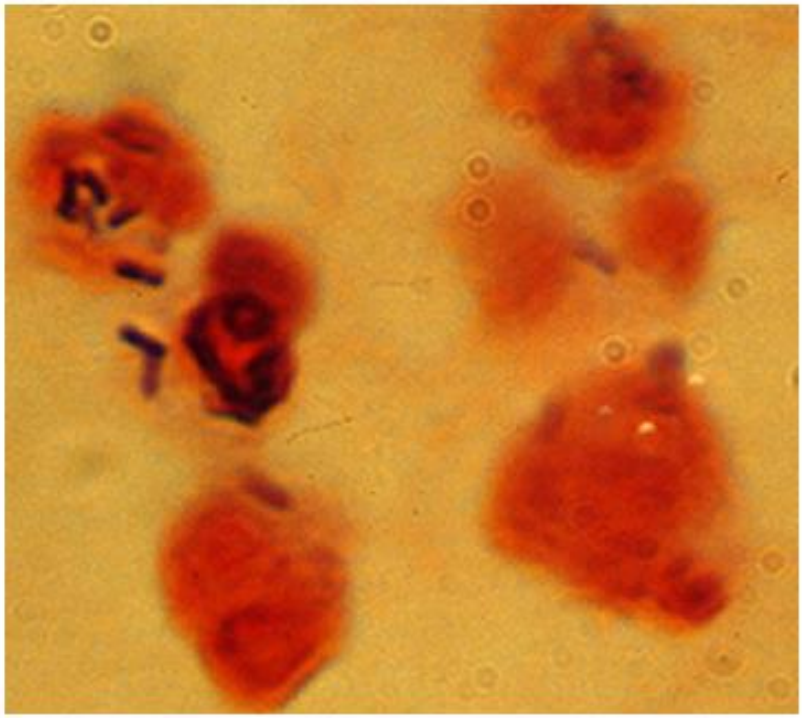
SECONDARY

CLASSIFICATION

- BACTERIAL
- VIRAL
- FUNGAL
- PROTOZOAL



Listeria monocytogenes in cerebrospinal fluid

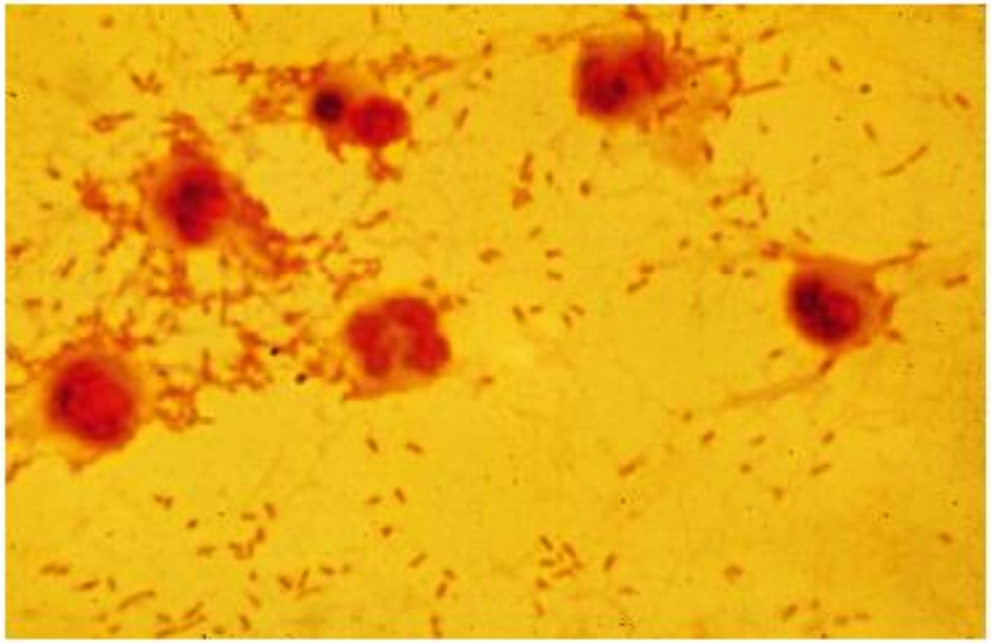


Gram stain of cerebrospinal fluid (x1000) shows inflammatory cells and small, gram-positive rods and coccobacilli. Culture of this specimen revealed moderate-sized beta-hemolytic colonies composed of small, motile gram-positive rods, confirmed to be *Listeria monocytogenes*.

Courtesy of Harriet Provine.

UpToDate®

Haemophilus influenzae in cerebrospinal fluid

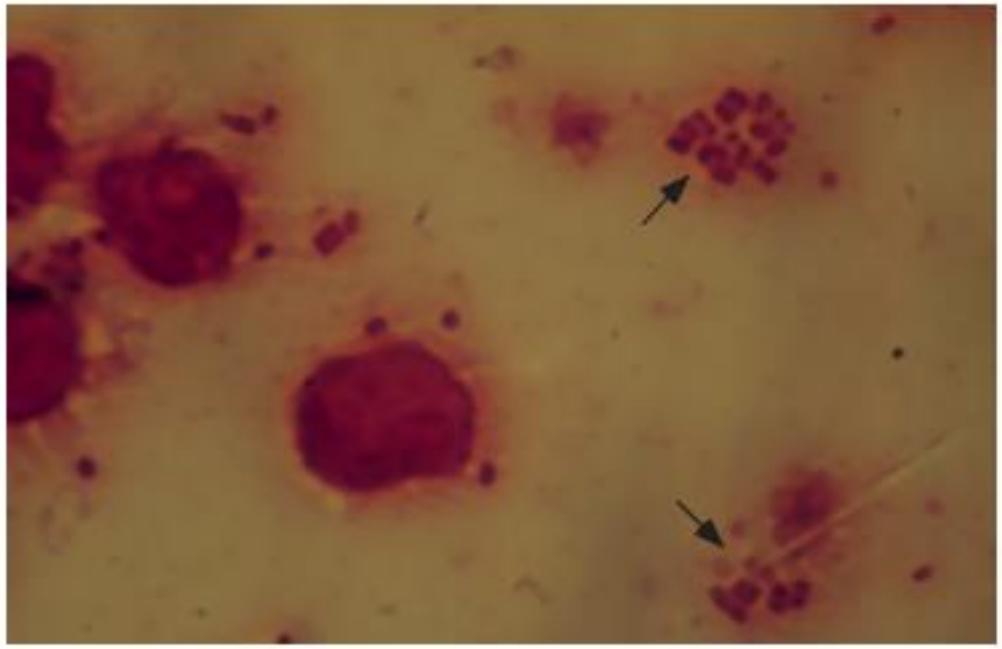


Gram stain of cerebrospinal fluid (x1000) shows inflammatory cells and small, pleomorphic, gram-negative coccobacilli. *Haemophilus influenzae* grew from this specimen.

Courtesy of Harriet Provine.

UpToDate®

Neisseria meningitidis in cerebrospinal fluid

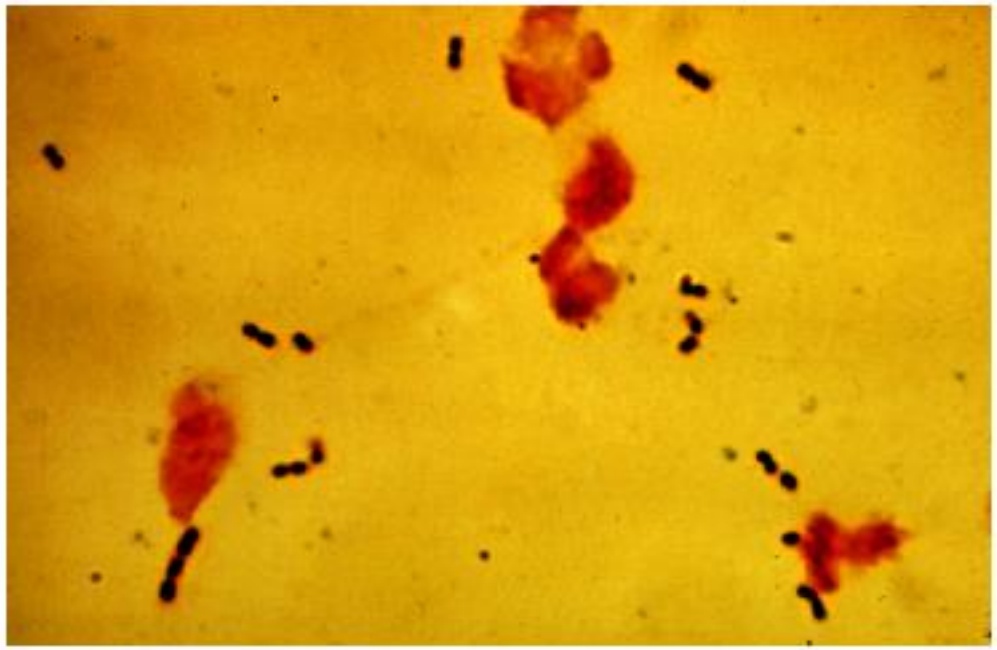


Gram stain of cerebrospinal fluid (x1000) shows inflammatory cells and kidney-shaped, gram-negative diplococci (arrows). *Neisseria meningitidis* grew from this specimen.

Courtesy of Harriet Provine.

UpToDate®

Streptococcus pneumoniae in cerebrospinal fluid



Gram stain of cerebrospinal fluid (x1000) shows inflammatory cells and gram-positive diplococci. *Streptococcus pneumoniae* grew from this specimen.

Courtesy of Harriet Provine.

UpToDate®

MICROORGANISMS CAPABLE OF CAUSING DISEASE—OR PATHOGENS—USUALLY ENTER OUR BODIES THROUGH THE EYES, MOUTH, NOSE, OR UROGENITAL OPENINGS, OR THROUGH WOUNDS OR BITES THAT BREACH THE SKIN BARRIER. ORGANISMS CAN SPREAD, OR BE TRANSMITTED, BY SEVERAL ROUTES.

КЛАССИФИКАЦИЯ

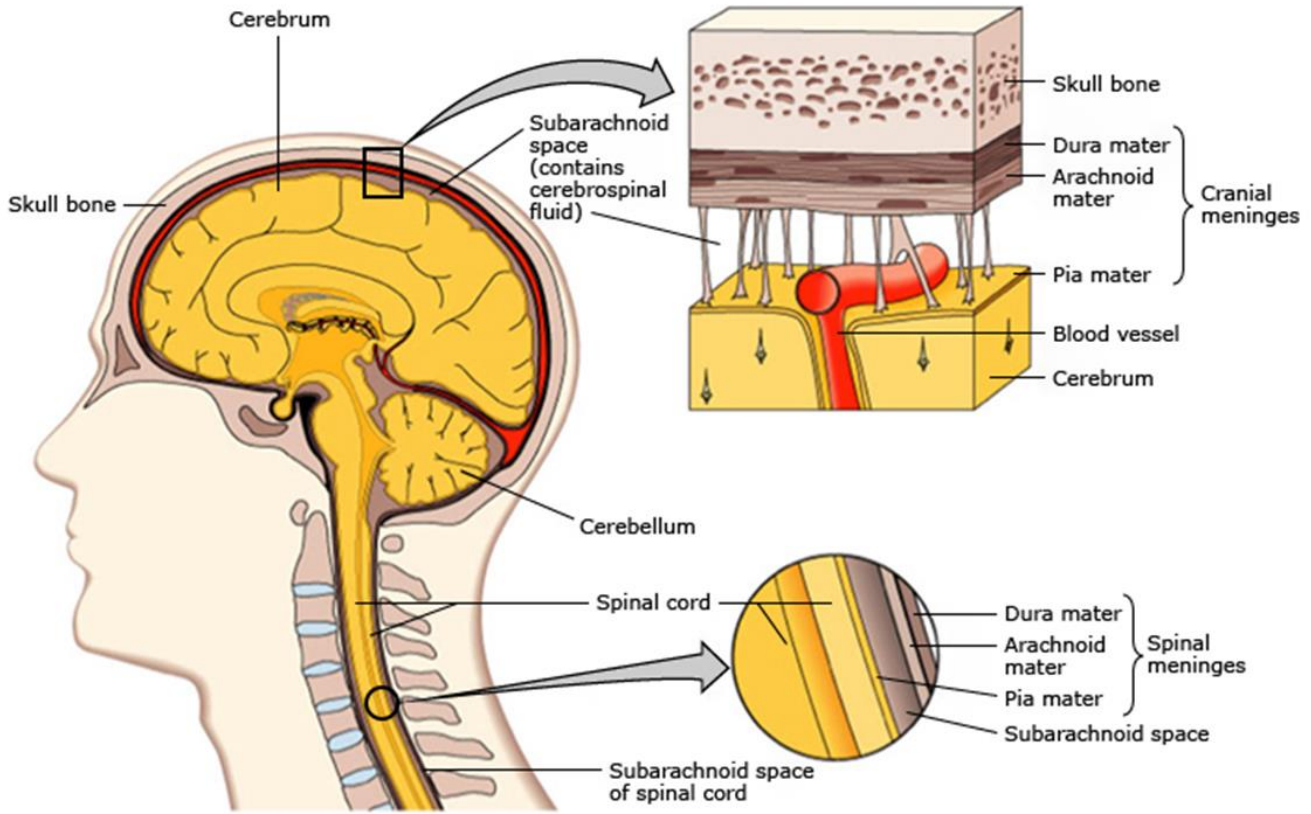
- **ПО СПОСОБУ ПРОНИКНОВЕНИЯ ИНФЕКЦИОННОГО АГЕНТА (ВХОДНЫМ ВОРОТАМ) :**
- ВОЗДУШНО-КАПЕЛЬНЫЕ
- КОНТАКТНЫЕ (ПРИ ТРАВМАХ, ЗАБОЛЕВАНИЯХ ЛОР-ОРГАНОВ), ГЕМАТОГЕННЫЕ
- ЛИМФОГЕННЫЕ
- ПЕРИНЕВРАЛЬНЫЕ (ПО ПУТИ СЛЕДОВАНИЯ ПЕРИФЕРИЧЕСКИХ НЕРВОВ)

CLASSIFICATION

LOCATION

- MENINGITIS
- ENCEPHALITIS
- MYELITIS
- GANGLIONITIS
- NEURITIS
- ETC

Meningeal layers of the brain and spinal cord



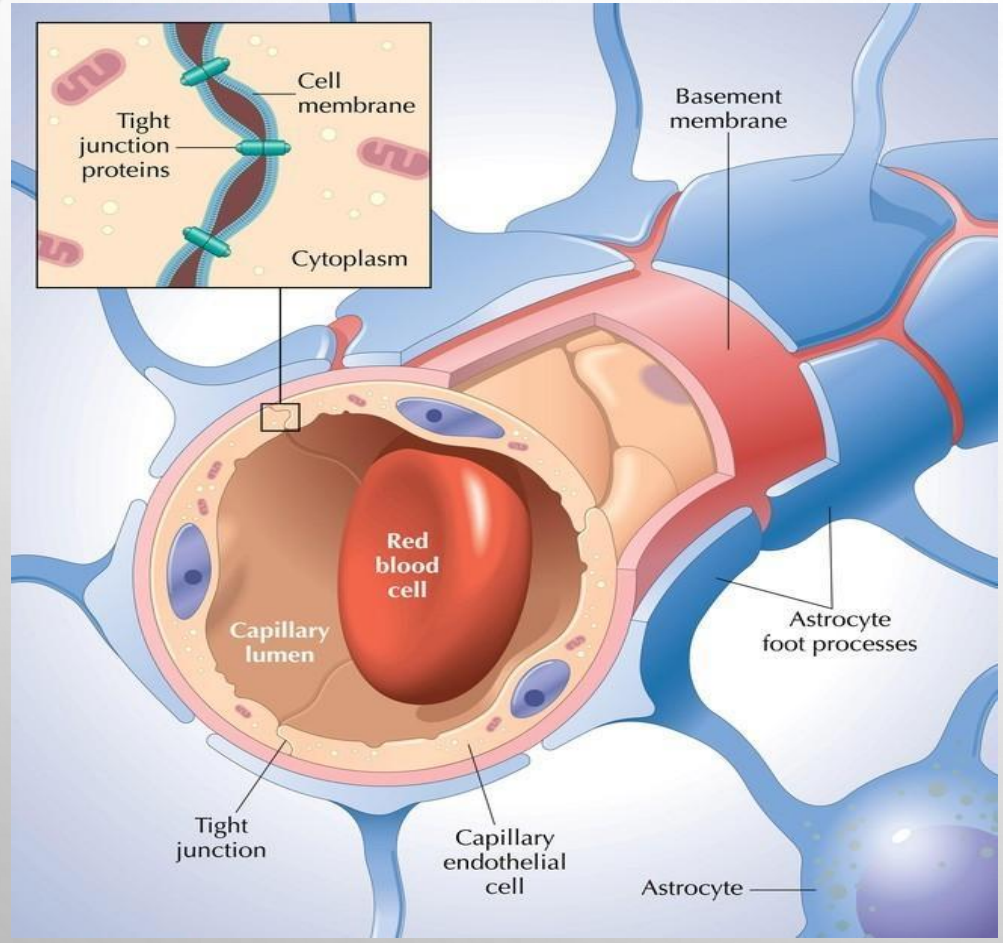
Reproduced with permission from: Microbial diseases of the nervous system. In: Microbiology: An Introduction, 8th ed, Tortora GJ, Funke BR, Case CL (Eds), Pearson Education, Inc., San Francisco 2004. p.617. Copyright © 2004 The Authors.

UpToDate®

IN THE P**RE-ANTIBIOTIC** ERA BACTERIAL MENINGITIS WAS VIRTUALLY 100 PERCENT FATAL.

DESPITE THE EFFECTIVENESS OF CURRENT ANTIBIOTICS IN CLEARING BACTERIA FROM THE CEREBROSPINAL FLUID (CSF), BACTERIAL **MENINGITIS** CONTINUES TO CAUSE **SIGNIFICANT MORBIDITY AND MORTALITY** WORLDWIDE.

ГЕМАТОЭНЦЕФАЛИЧЕСКИЙ БАРЬЕР (ГЭБ)

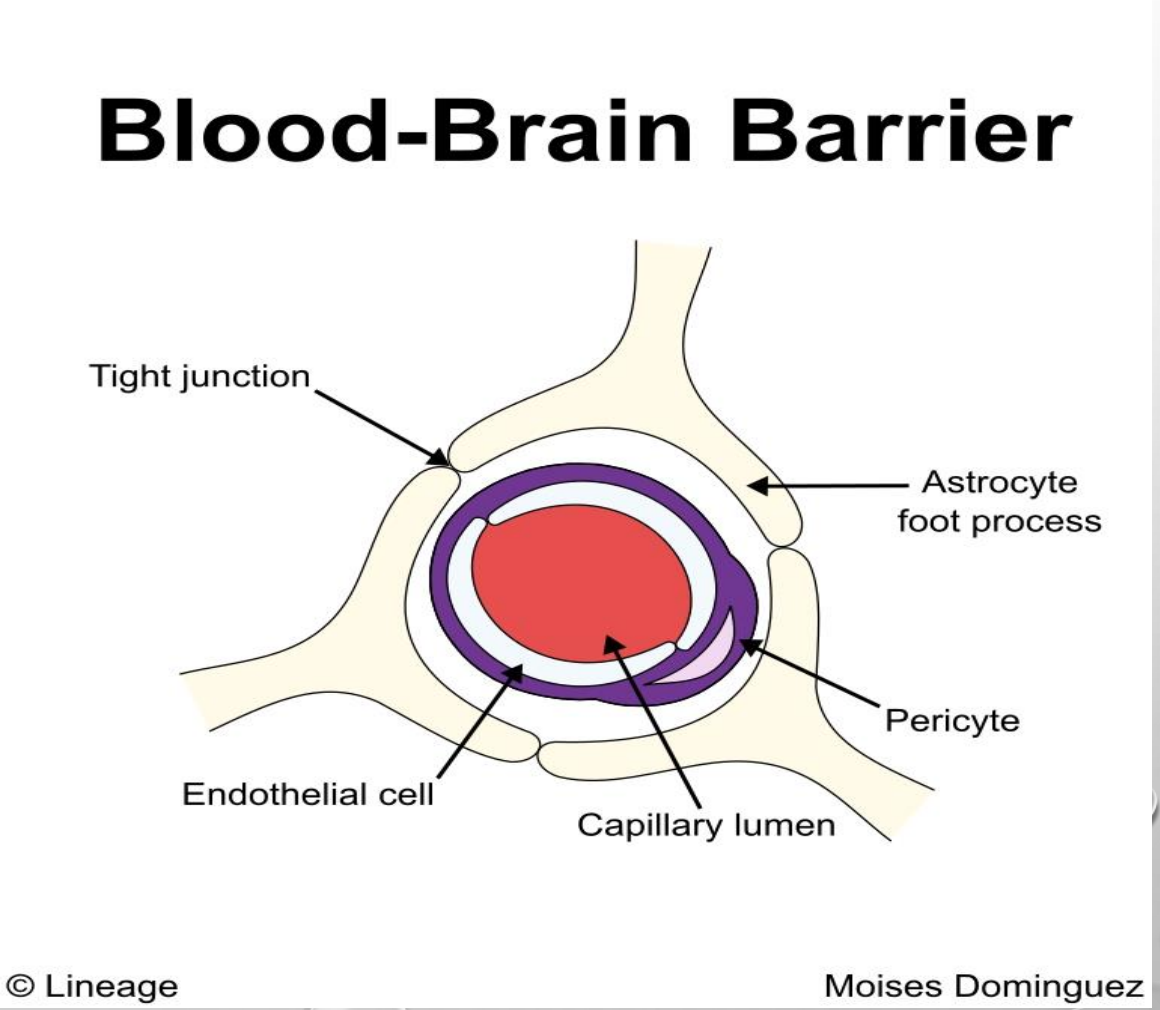


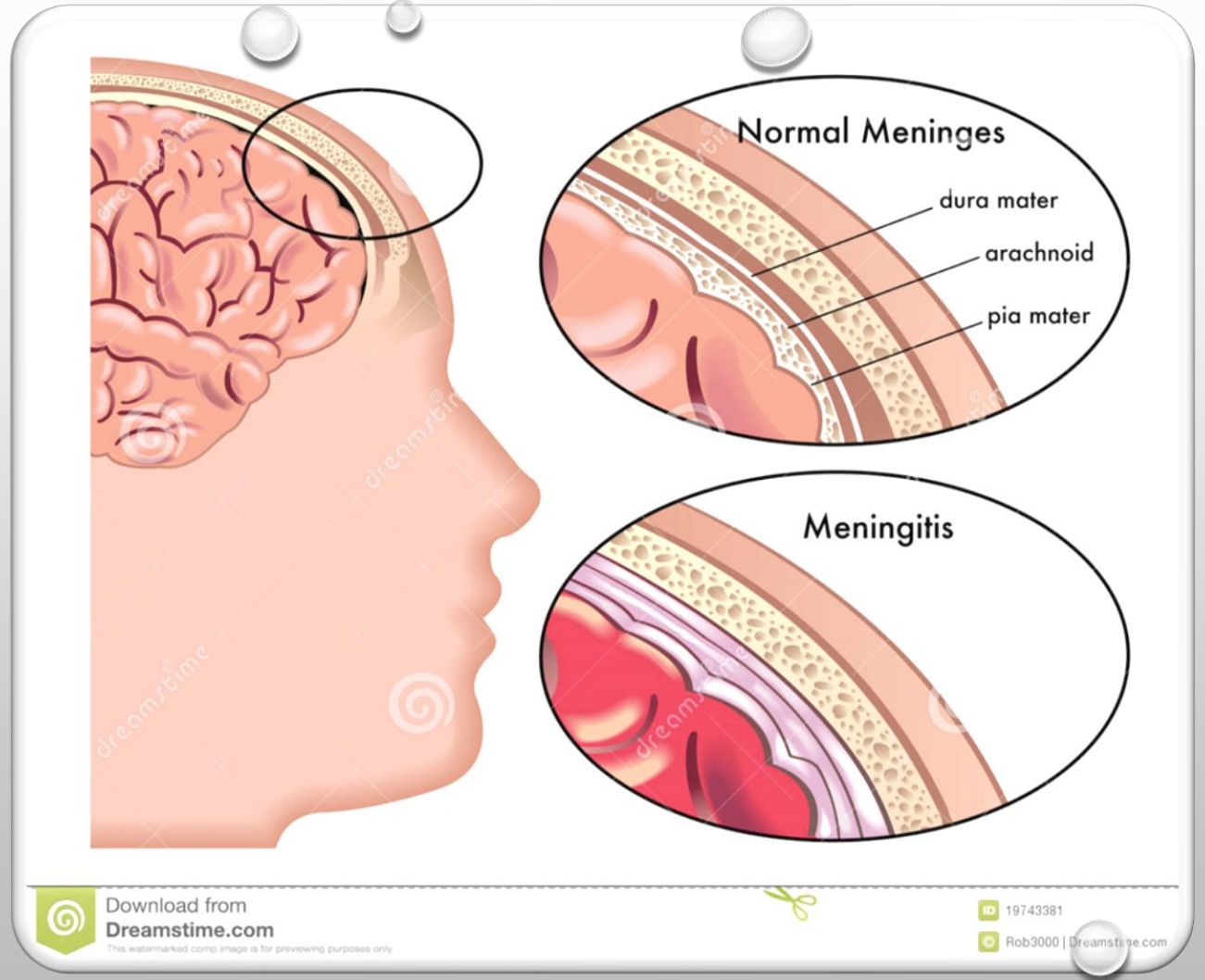
СОВОКУПНОСТЬ МОРФОЛОГИЧЕСКИХ ОБРАЗОВАНИЙ, УЧАСТВУЮЩИХ В РЕГУЛЯЦИИ СОСТАВА ЛИКВОРА И ЛИМИТИРУЮЩИХ ПРОНИКНОВЕНИЕ ИЗ КРОВИ В ВЕЩЕСТВО МОЗГА МЕТАБОЛИТОВ, МИКРОБНЫХ АГЕНТОВ, ТОКСИНОВ, ХИМИЧЕСКИХ ВЕЩЕСТВ.

ГЕМАТОЭНЦЕФАЛИЧЕСКИЙ БАРЬЕР (ГЭБ)

ОБРАЗОВАН СТЕНКАМИ КАПИЛЛЯРОВ, СОСТОЯЩИМИ ИЗ ТРЕХ СЛОЕВ:

- ЭНДОТЕЛИЙ КАПИЛЛЯРОВ
- БАЗАЛЬНАЯ МЕМБРАНА
- СЛОЙ ОТРОСТКОВ НЕЙРОГЛИИ (АСТРОЦИТОВ)

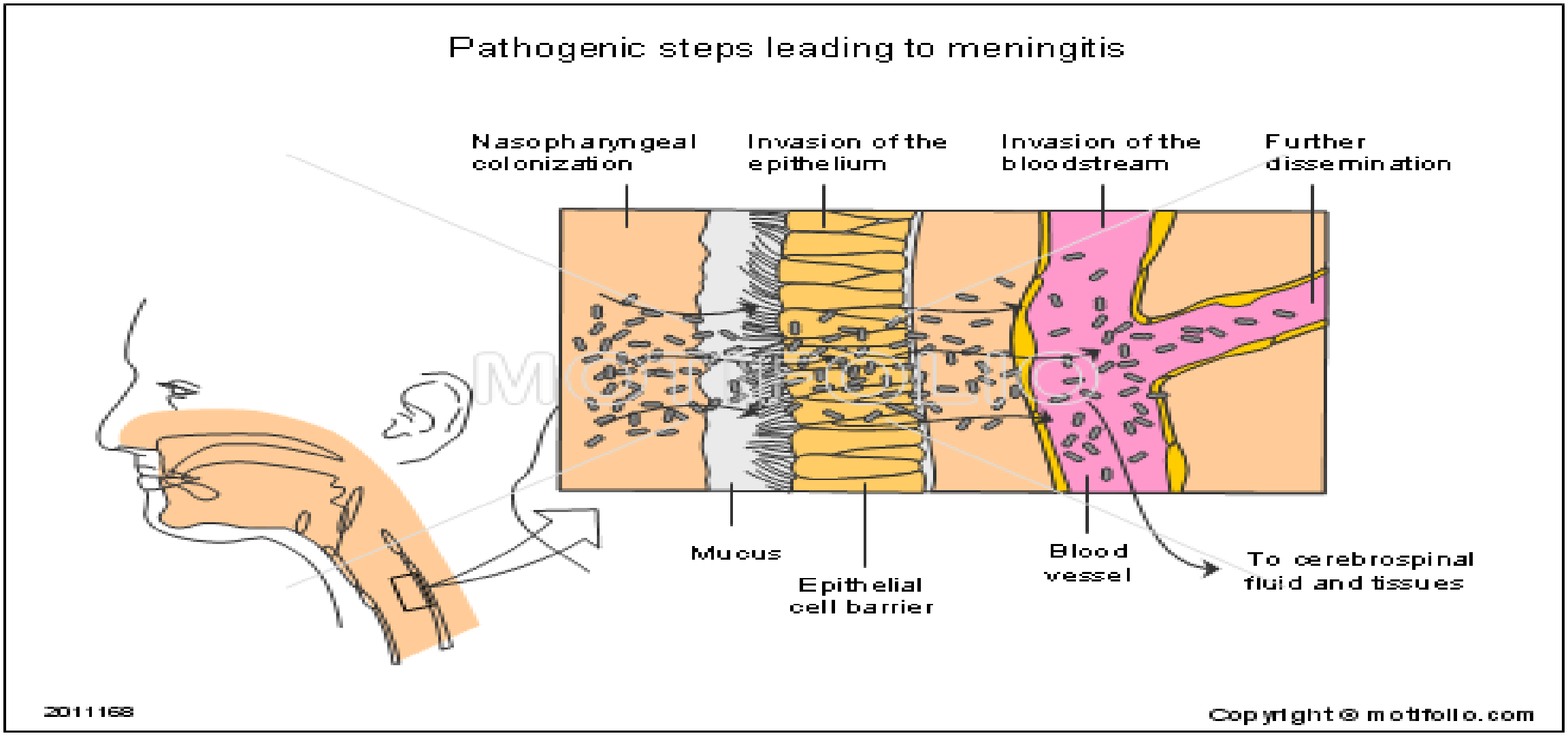


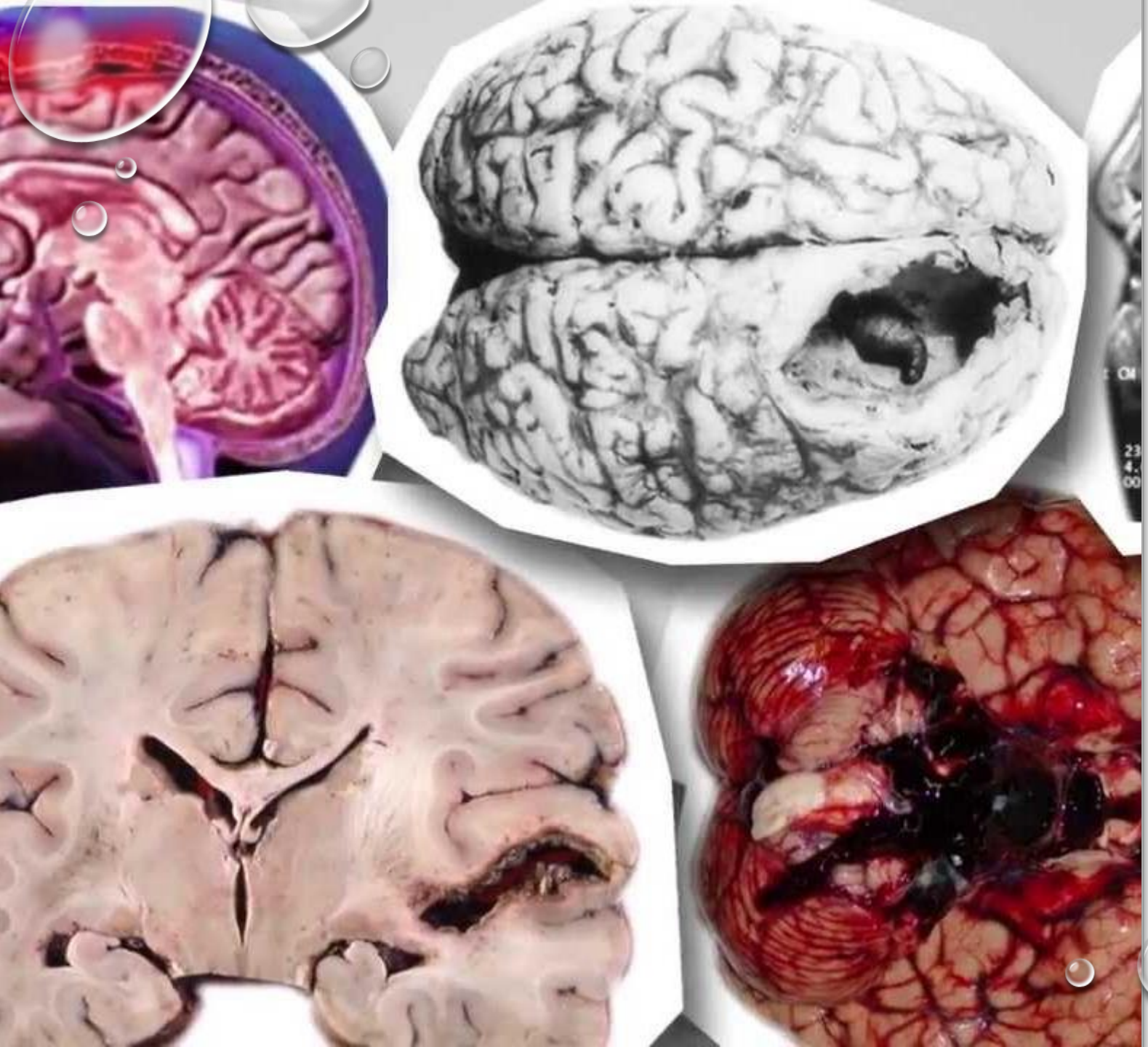

Normal Meninges
dura mater
arachnoid
pia mater
Meningitis
Download from
Dreamstime.com
This watermarked comp image is for previewing purposes only.
ID 19743381
Rob3000 | Dreamstime.com

MENINGITIS

ВОЗБУДТЕЛИ БАКТЕРИАЛЬНОГО МЕНИНГИТА

- **НОВОРОЖДЕННЫЕ:** ЭНТЕРОБАКТЕРИИ, СТРЕПТОКОККИ, LISTERIA MONOCYTOGENES
- **ДЕТИ:** STREPTOCOCCUS PNEUMONIAE, NEISSERIA MENINGITIDIS
- **ВЗРОСЛЫЕ:** STREPTOCOCCUS PNEUMONIAE, NEISSERIA MENINGITIDIS, LISTERIA MONOCYTOGENES (> 50-ЛЕТНИХ)


Pathogenic steps leading to meningitis
Nasopharyngeal colonization
Invasion of the epithelium
Invasion of the bloodstream
Further dissemination
Mucus
Epithelial cell barrier
Blood vessel
To cerebrospinal fluid and tissues
2011168
Copyright © mottfollo.com



КЛАССИФИКАЦИЯ МЕНИНГИТОВ

- ПО ТЕМПУ РАЗВИТИЯ
- ПО ТЯЖЕСТИ ТЕЧЕНИЯ
- ПО ЛОКАЛИЗАЦИИ ПРОЦЕССА
- ПО ПУТЯМ ИНФИЦИРОВАНИЯ

Clinical features and diagnosis of acute bacterial meningitis in adults

Author: Rodrigo Hasbun, MD, MPH, FIDSA
Section Editor: Allan R Tunkel, MD, PhD, MACP
Deputy Editor: Jennifer Mitty, MD, MPH

Contributor Disclosures

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Aug 2022.** | This topic last updated: **Mar 07, 2022.**

- IN THE UNITED STATES, FOLLOWING THE INSTITUTION OF ROUTINE INFANT IMMUNIZATION WITH THE CONJUGATE *HAEMOPHILUS INFLUENZAE* TYPE B VACCINE IN 1990 AND THE 7-VALENT *STREPTOCOCCUS PNEUMONIAE* (PNEUMOCOCCUS) CONJUGATE VACCINE IN 2000 (PCV7) FOLLOWED BY THE 13-VALENT PNEUMOCOCCAL VACCINE (PCV13) IN 2010, BACTERIAL MENINGITIS HAS DECREASED IN FREQUENCY, AND THE *PEAK INCIDENCE OF BACTERIAL MENINGITIS HAS SHIFTED FROM CHILDREN UNDER FIVE YEARS OF AGE TO* ***ADULTS***.

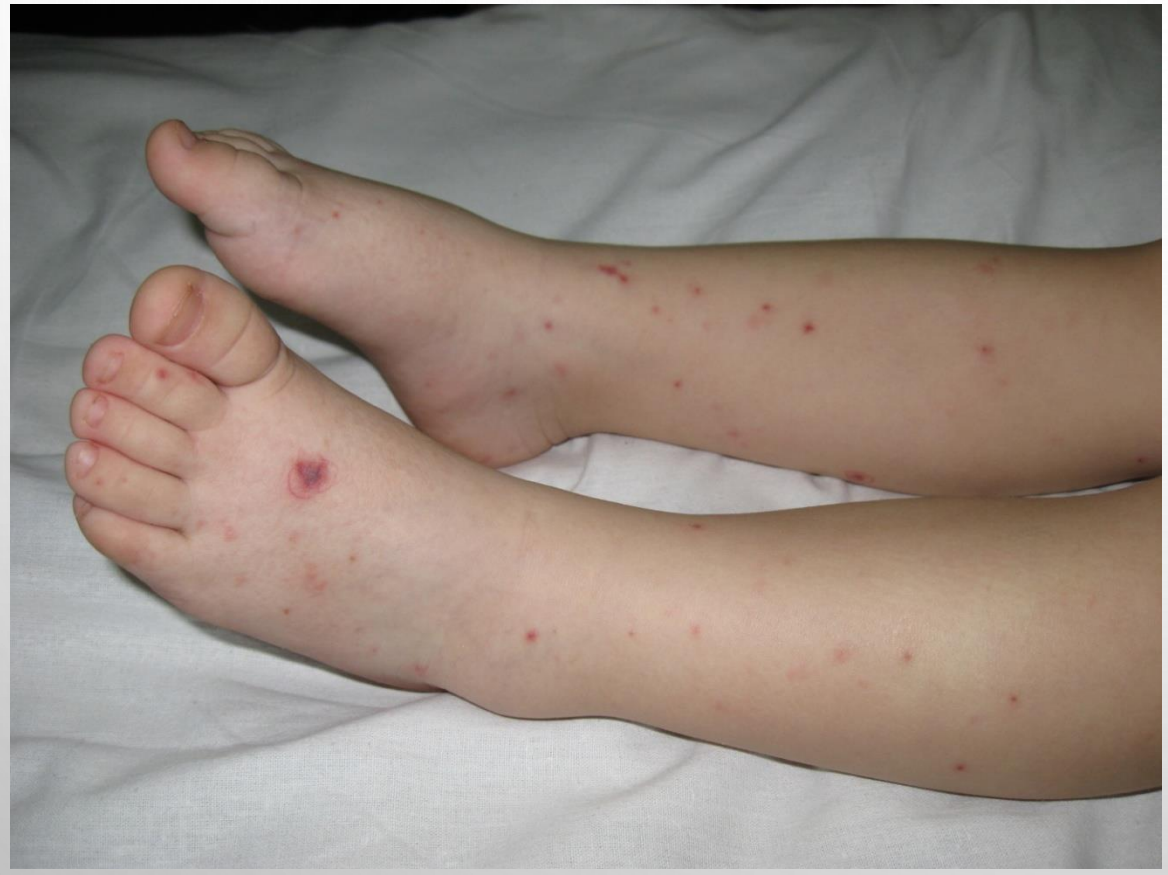
- *S. PNEUMONIAE REM*AINS THE LEADING PATHOGEN OF COMMUNITY-ACQUIRED BACTERIAL MENINGITIS GLOBALLY AND CONTINUES TO BE ASSOCIATED WITH A HIGH MORTALITY RATE

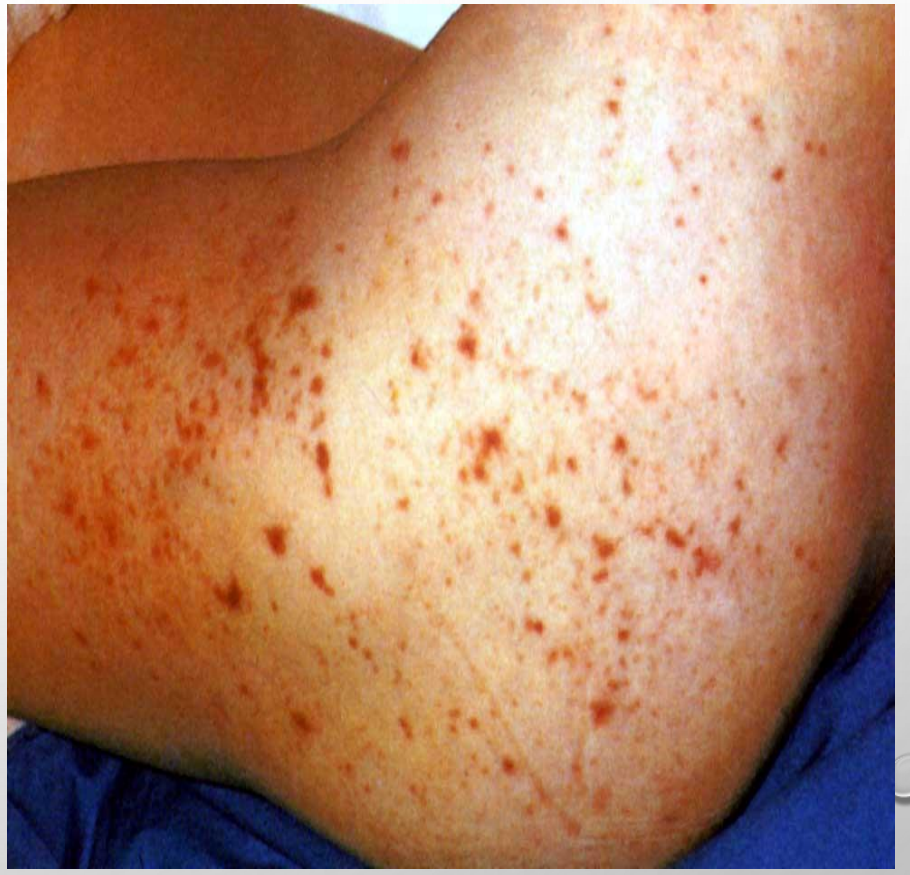
Characteristic features of common causes of bacterial meningitis

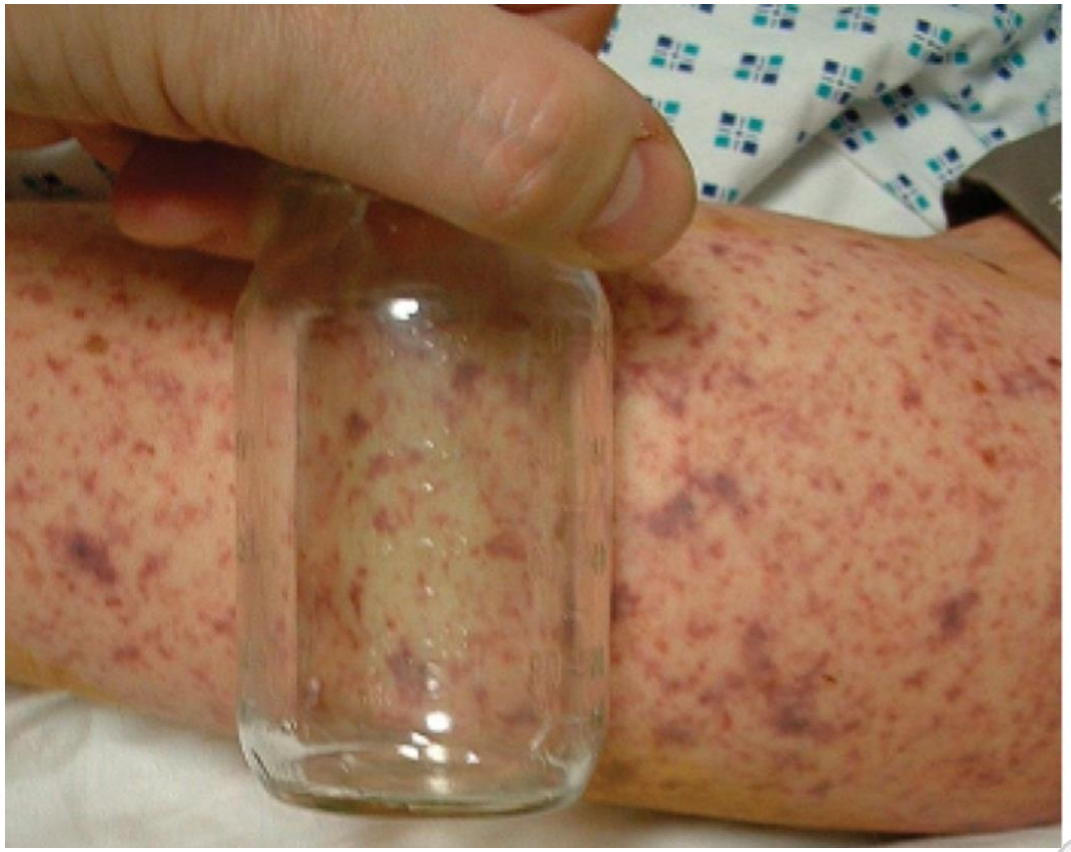
Organism	Site of entry	Age range	Predisposing conditions
Neisseria meningitidis	Nasopharynx	All ages	Usually none, rarely complement deficiency
Streptococcus pneumoniae	Nasopharynx, direct extension across skull fracture, or from contiguous or distant foci of infection	All ages	All conditions that predispose to pneumococcal bacteremia, fracture of cribriform plate, cochlear implants, cerebrospinal fluid otorrhea from basilar skull fracture, defects of the ear ossicle (Mondini defect)
Listeria monocytogenes	Gastrointestinal tract, placenta	Older adults and neonates	Defects in cell-mediated immunity (eg, glucocorticoids, transplantation [especially renal transplantation]), pregnancy, liver disease, alcoholism, malignancy
Coagulase-negative staphylococci	Foreign body	All ages	Surgery and foreign body, especially ventricular drains
Staphylococcus aureus	Bacteremia, foreign body, skin	All ages	Endocarditis, surgery and foreign body, especially ventricular drains; cellulitis, decubitus ulcer
Gram-negative bacilli	Various	Older adults and neonates	Advanced medical illness, neurosurgery, ventricular drains, disseminated strongyloidiasis
Haemophilus influenzae	Nasopharynx, contiguous spread from local infection	Adults; infants and children if not vaccinated	Diminished humoral immunity

- *STREPTOCOCCUS SUIS* IS AN EMERGING ZOONOSIS THAT CAUSES MENINGITIS IN ASIA AND HAS BEEN LINKED TO EXPOSURE TO PIGS OR PORK.
- DESPITE THE DECREASED MORTALITY OF MENINGITIS WITH THE ADVENT OF EFFECTIVE ANTIBIOTICS, MORTALITY FROM MENINGITIS STILL REMAINS SIGNIFICANT. THE USE OF ADJUNCTIVE DEXAMETHASONE IN PNEUMOCOCCAL MENINGITIS HAS BEEN SHOWN IN CLINICAL TRIALS AND OBSERVATIONAL STUDIES TO DECREASE MORTALITY IN HIGH-INCOME COUNTRIES.
- HEALTH CARE-ASSOCIATED VENTRICULITIS AND MENINGITIS ARE PRIMARILY DISEASES OF NEUROSURGICAL PATIENTS. THE MOST COMMON PATHOGENS ARE GRAM-POSITIVE BACTERIA (EG, *STAPHYLOCOCCUS*, *STREPTOCOCCUS*, ETC) AND GRAM-NEGATIVE ORGANISMS (EG, *PSEUDOMONAS*, ENTEROBACTERIACEAE, ETC). SPECIFIC RISK FACTORS FOR THE DEVELOPMENT OF HEALTH CARE-ASSOCIATED MENINGITIS INCLUDE CRANIOTOMY, PLACEMENT OF VENTRICULAR OR LUMBAR CATHETERS, CSF LEAK, AND HEAD TRAUMA.
- THE ORGANISM RESPONSIBLE FOR ACUTE BACTERIAL MENINGITIS DEPENDS IN PART UPON THE ROUTE OF ACQUISITION AND UNDERLYING HOST FACTORS. THERE ARE THREE MAJOR MECHANISMS FOR DEVELOPING MENINGITIS:
  - COLONIZATION OF THE NASOPHARYNX, WITH SUBSEQUENT BLOODSTREAM INVASION FOLLOWED BY CENTRAL NERVOUS SYSTEM (CNS) INVASION
  - INVASION OF THE CNS FOLLOWING BACTEREMIA DUE TO A LOCALIZED SOURCE, SUCH AS INFECTIVE ENDOCARDITIS
  - DIRECT ENTRY OF ORGANISMS INTO THE CNS FROM A CONTIGUOUS INFECTION (EG, SINUSES, MASTOID), TRAUMA, NEUROSURGERY, A CSF LEAK, OR MEDICAL DEVICES (EG, CSF SHUNTS, INTRACEREBRAL PRESSURE MONITORS, OR, IN CHILDREN, COCHLEAR IMPLANTS WITH POSITIONERS)

ЭКЗАНТЕМА ПРИ МЕНИНГИТЕ







ЭКЗАНТЕМА ПРИ МЕНИНГИТЕ

ЭЛЕМЕНТЫ СЫПИ НЕ ИСЧЕЗАЮТ, НЕ БЛЕДНЕЮТ ПРИ НАДАВЛИВАНИИ

MAJOR CAUSES OF COMMUNITY-ACQUIRED BACTERIAL MENINGITIS

OF COMMUNITY-ACQUIRED BACTERIAL MENINGITIS

- *STREPTOCOCCUS PNEUMONIAE*,
- *NEISSERIA MENINGITIDIS*, AND,
- PRIMARILY IN PATIENTS OVER AGE 50 YEARS OR THOSE WHO HAVE DEFICIENCIES IN CELL-MEDIATED IMMUNITY, *LISTERIA MONOCYTOGENES*.

OF HEALTH CARE-ASSOCIATED BACTERIAL MENINGITIS

- STAPHYLOCOCCI AND
- AEROBIC GRAM-NEGATIVE BACILLI.

BACTERIAL MENINGITIS

- PATIENTS WITH BACTERIAL MENINGITIS ARE USUALLY **QUITE ILL** AND OFTEN **PRESENT SOON** AFTER SYMPTOM ONSET.
- THE CLASSIC TRIAD OF ACUTE BACTERIAL MENINGITIS CONSISTS OF
  1. FEVER,
  2. NUCHAL RIGIDITY, AND
  3. A CHANGE IN MENTAL STATUS, USUALLY OF SUDDEN ONSET.

  HOWEVER, AN APPRECIABLE NUMBER OF PATIENTS DO NOT HAVE ALL THREE FEATURES.

Signs of meningeal irritation

Signs of meningeal irritation	Maneuver	Positive test
Kernig sign	Place patient supine with hip flexed at 90 degrees. Attempt to extend the leg at the knee.	The test is positive when there is resistance to extension at the knee to >135 degrees or pain in the lower back or posterior thigh.
Brudzinski sign	Place patient in the supine position and passively flex the head toward the chest.	The test is positive when there is flexion of the knees and hips of the patient.
Jolt accentuation of headache	Patient rotates his/her head horizontally two to three times per second.	The test is positive if the patient reports exacerbation of his/her headache with this maneuver.

Video - patients

BACTERIAL MENINGITIS

INITIAL BLOOD TESTS SHOULD INCLUDE

- A COMPLETE BLOOD COUNT WITH DIFFERENTIAL AND PLATELET COUNT AND
- TWO AEROBIC BLOOD CULTURES OF APPROPRIATE VOLUME (IDEALLY, PRIOR TO THE INITIATION OF ANTIMICROBIAL THERAPY).

SERUM ELECTROLYTES AND GLUCOSE, BLOOD UREA NITROGEN, AND CREATININE CONCENTRATIONS ARE HELPFUL IN DETERMINING THE CEREBROSPINAL FLUID- (CSF) TO-BLOOD GLUCOSE RATIO.

COAGULATION STUDIES MAY BE INDICATED, ESPECIALLY IF PETECHIAE OR PURPURIC LESIONS ARE NOTED.

BLOOD CULTURES ARE OFTEN POSITIVE AND CAN BE USEFUL IN THE EVENT THAT CSF CANNOT BE OBTAINED BEFORE THE ADMINISTRATION OF ANTIMICROBIALS.

APPROXIMATELY 50 TO 90 PERCENT OF PATIENTS WITH BACTERIAL MENINGITIS HAVE POSITIVE BLOOD CULTURES.

Host immune defects predisposing to meningitis

Host problem	Organism favored	Frequency of defect actually leading to infection
Absence of opsonizing antibody	*Streptococcus pneumoniae*	Common in all age groups
	Haemophilus influenzae	Common in very young children
Asplenia: surgical or functional	*S. pneumoniae*	Rare
	Neisseria meningitidis	Very rare
Complement deficiency	*N. meningitidis*	Very rare
Glucocorticoid excess	*Listeria monocytogenes*	Rare
	Cryptococcus neoformans	Rare
HIV infection	*C. neoformans*	About 5 percent eventually get cryptococcal meningitis
	S. pneumoniae	Common presenting illness
	L. monocytogenes	Rare
Bacteremia/endocarditis	*Staphylococcus aureus*; various gram-negative rods	Rare
Basilar skull fracture	*S. pneumoniae*; other upper respiratory tract flora	Very rare

HIV: human immunodeficiency virus.

IMPORTANT!

- EVERY PATIENT WITH SUSPECTED MENINGITIS SHOULD HAVE **CSF** OBTAINED UNLESS A LUMBAR PUNCTURE (LP) IS CONTRAINDICATED. A CT SCAN IS SOMETIMES PERFORMED BEFORE LP TO EXCLUDE A MASS LESION OR INCREASED INTRACRANIAL PRESSURE, WHICH RARELY LEADS TO CEREBRAL HERNIATION DURING SUBSEQUENT CSF REMOVAL. HOWEVER, A SCREENING CT SCAN IS NOT NECESSARY IN THE MAJORITY OF PATIENTS.
- *A CT SCAN OF THE HEAD BEFORE LP SHOULD BE PERFORMED IN ADULT PATIENTS WITH SUSPECTED BACTERIAL MENINGITIS WHO HAVE ONE OR MORE OF THE FOLLOWING RISK FACTORS:*
  - *IMMUNOCOMPROMISED STATE (EG, HIV INFECTION, IMMUNOSUPPRESSIVE THERAPY, SOLID ORGAN OR HEMATOPOIETIC STEM CELL TRANSPLANTATION)*
  - *HISTORY OF CENTRAL NERVOUS SYSTEM (CNS) DISEASE (MASS LESION, STROKE, OR FOCAL INFECTION)*
  - *NEW ONSET SEIZURE (WITHIN ONE WEEK OF PRESENTATION)*
  - *PAPILLEDEMA*
  - *ABNORMAL LEVEL OF CONSCIOUSNESS*
  - *FOCAL NEUROLOGIC DEFICIT*

MORE TO KNOW

- IF LP IS DELAYED OR DEFERRED, BLOOD CULTURES SHOULD BE OBTAINED AND ANTIMICROBIAL THERAPY SHOULD BE ADMINISTERED **EMPIRICALLY** BEFORE THE IMAGING STUDY, *FOLLOWED AS SOON AS POSSIBLE BY THE LP*.
- IN ADDITION, DEXAMETHASONE (0.15 MG/KG INTRAVENOUSLY EVERY SIX HOURS) SHOULD BE GIVEN *SHORTLY BEFORE OR AT THE SAME TIME AS THE ANTIMICROBIAL* AGENTS IF THE PREPONDERANCE OF CLINICAL AND LABORATORY EVIDENCE SUGGESTS BACTERIAL MENINGITIS WITH A PLAN TO STOP THERAPY, IF INDICATED, WHEN THE EVALUATION IS COMPLETE.
- ADJUNCTIVE DEXAMETHASONE **SHOULD NOT** BE GIVEN TO PATIENTS WHO HAVE ALREADY RECEIVED ANTIMICROBIAL THERAPY BECAUSE IT IS *UNLIKELY TO IMPROVE PATIENT OUTCOME*.

CSF

THE USUAL CSF FINDINGS IN PATIENTS WITH BACTERIAL MENINGITIS ARE

A WHITE BLOOD CELL (WBC) COUNT OF 1000 TO 5000/MICROL (RANGE OF <100 TO >10,000) WITH A PERCENTAGE OF NEUTROPHILS USUALLY GREATER THAN 80 PERCENT,

PROTEIN OF 100 TO 500 MG/DL (1000 TO 5000 MG/L), AND

GLUCOSE <40 MG/DL (2.22 MM/L; WITH A CSF:SERUM GLUCOSE RATIO OF ≤0.4).

DESPITE THESE TYPICAL CSF FINDINGS, THE SPECTRUM OF CSF VALUES IN BACTERIAL MENINGITIS IS SO WIDE THAT THE ABSENCE OF ONE OF MORE OF THE TYPICAL FINDINGS IS OF LITTLE VALUE.

Typical cerebrospinal fluid findings in central nervous system infections*

	Glucose (mg/dL)		Protein (mg/dL)		Total white blood cell count (cells/microL)		
	<10¶	10 to 40Δ	100 to 500◇	50 to 300§	>1000	100 to 1000	5 to 100
More common	Bacterial meningitis	Bacterial meningitis	Bacterial meningitis	Viral meningitis Nervous system Lyme disease (neuroborreliosis) Encephalitis Neurosyphilis TB meningitis¥	Bacterial meningitis	Bacterial or viral meningitis TB meningitis	Early bacterial meningitis Viral meningitis Neurosyphilis TB meningitis
Less common	TB meningitis Fungal meningitis	Neurosyphilis Some viral infections (such as mumps and LCMV)		Early bacterial meningitis	Some cases of mumps and LCMV	Encephalitis	Encephalitis

TB: tuberculosis; LCMV: lymphocytic choriomeningitis virus.

* It is important to note that the spectrum of cerebrospinal fluid values in bacterial meningitis is so wide that the absence of one or more of these findings is of little value. Refer to the UpToDate topic reviews on bacterial meningitis for additional details.

¶ <0.6 mmol/L.

Δ 0.6 to 2.2 mmol/L.

◇ 1 to 5 g/L.

§ 0.5 to 3 g/L.

¥ Cerebrospinal fluid protein concentrations may be higher in some patients with tuberculous meningitis; concentrations >500 mg/dL are an indication of blood-brain barrier disruption or increased intracerebral production of immunoglobulins, and extremely high concentrations, in the range of 2 to 6 g/dL, may be found in association with subarachnoid block.

ACUTE BACTERIAL MENINGITIS SHOULD BE SUSPECTED

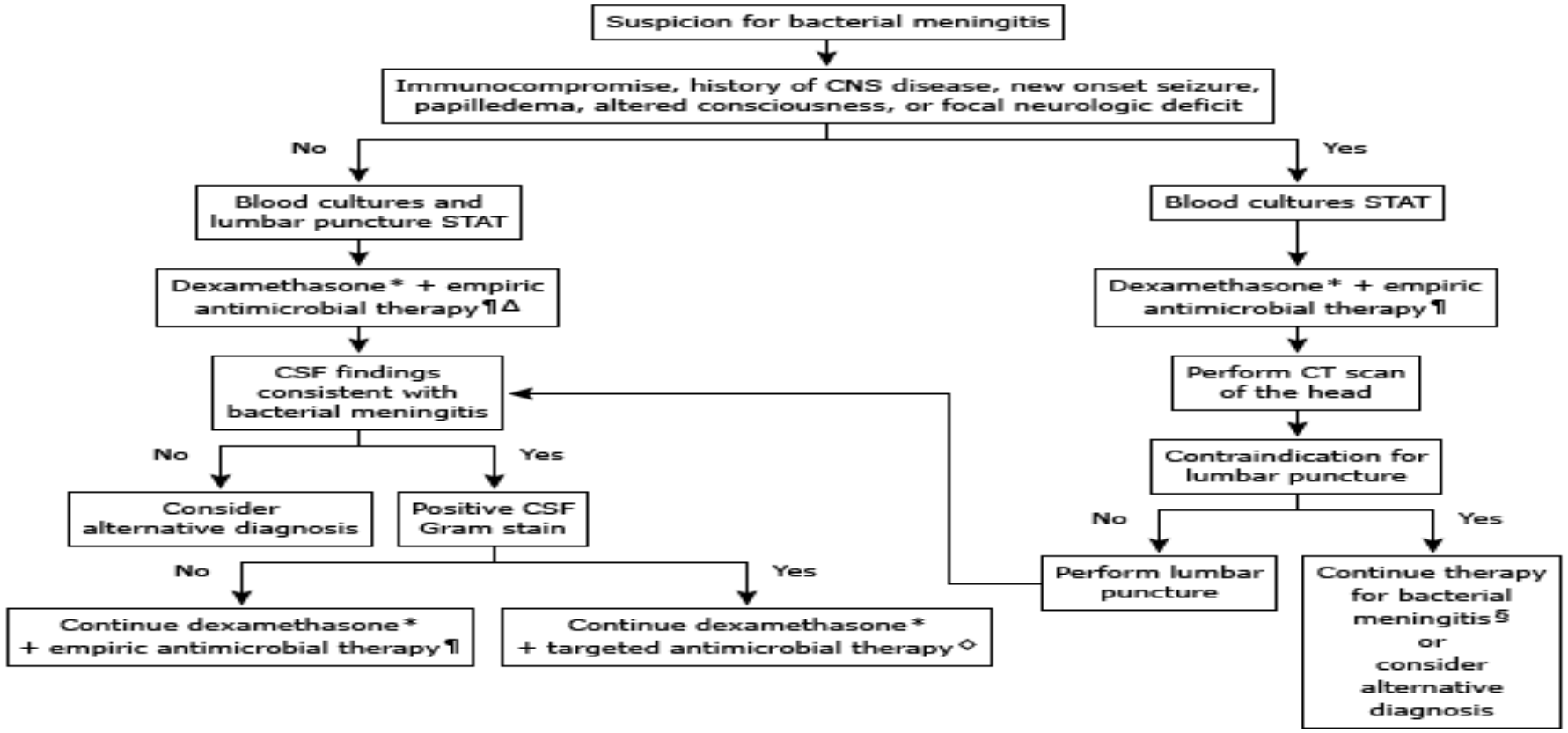
IN ADULTS WHO PRESENT WITH **FEVER** AND **SIGNS OF MENINGEAL INFLAMMATION**.

- ISOLATION OF A BACTERIAL PATHOGEN FROM THE CSF (BY CULTURE OR OTHER DIAGNOSTIC TECHNIQUES) CONFIRMS THE DIAGNOSIS OF BACTERIAL MENINGITIS. ISOLATION OF BACTERIA FROM BLOOD CULTURES IN A PATIENT WITH CSF PLEOCYTOSIS ALSO CONFIRMS THE DIAGNOSIS, EVEN IF THE CSF CULTURE REMAINS NEGATIVE.
- THE CLINICAL AND LABORATORY FINDINGS OF BACTERIAL MENINGITIS OVERLAP WITH THOSE OF MENINGITIS CAUSED BY VIRUSES, MYCOBACTERIA, FUNGI, OR PROTOZOA. DIFFERENTIATION OF THESE DISORDERS FROM BACTERIAL MENINGITIS REQUIRES CAREFUL EXAMINATION OF CSF PARAMETERS, NEUROIMAGING (WHEN INDICATED), AS WELL AS CONSIDERATION OF ANY EPIDEMIOLOGIC FACTORS THAT WOULD RAISE THE POSSIBILITY OF SPECIFIC BACTERIAL OR NONBACTERIAL CNS INFECTIONS.

Characteristic features of common causes of bacterial meningitis

Organism	Site of entry	Age range	Predisposing conditions
Neisseria meningitidis	Nasopharynx	All ages	Usually none, rarely complement deficiency
Streptococcus pneumoniae	Nasopharynx, direct extension across skull fracture, or from contiguous or distant foci of infection	All ages	All conditions that predispose to pneumococcal bacteremia, fracture of cribriform plate, cochlear implants, cerebrospinal fluid otorrhea from basilar skull fracture, defects of the ear ossicle (Mondini defect)
Listeria monocytogenes	Gastrointestinal tract, placenta	Older adults and neonates	Defects in cell-mediated immunity (eg, glucocorticoids, transplantation [especially renal transplantation]), pregnancy, liver disease, alcoholism, malignancy
Coagulase-negative staphylococci	Foreign body	All ages	Surgery and foreign body, especially ventricular drains
Staphylococcus aureus	Bacteremia, foreign body, skin	All ages	Endocarditis, surgery and foreign body, especially ventricular drains; cellulitis, decubitus ulcer
Gram-negative bacilli	Various	Older adults and neonates	Advanced medical illness, neurosurgery, ventricular drains, disseminated strongyloidiasis
Haemophilus influenzae	Nasopharynx, contiguous spread from local infection	Adults; infants and children if not vaccinated	Diminished humoral immunity

Management algorithm for adults with suspected bacterial meningitis



"STAT" indicates that the intervention should be done emergently.
CNS: central nervous system; CSF: cerebrospinal fluid; CT: computed tomography.
* Refer to UpToDate topic review on dexamethasone to prevent neurologic complications of bacterial meningitis in adults for specific recommendations.
¶ Refer to UpToDate table on recommendations for empiric antimicrobial therapy for purulent meningitis based on patient age and specific predisposing condition.
Δ Administer dexamethasone and antibiotic therapy immediately after CSF is obtained.
◇ Refer to UpToDate table on recommendations for antimicrobial therapy in adults with presumptive pathogen identification by positive Gram stain.
§ If the diagnosis of bacterial meningitis is likely.
Modified with permission from: Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis 2004; 39:1267. Copyright © 2004 University of Chicago Press.

Initial therapy and prognosis of bacterial meningitis in adults

- Bacterial meningitis is a medical emergency, and immediate steps must be taken to establish the specific cause and initiate effective therapy. The mortality rate of untreated disease approaches 100 percent and, even with optimal therapy, there is a high failure rate.

- If possible, crucial historical information (eg, serious drug allergies, recent exposure to an individual with meningitis) should be obtained before antibiotic treatment of presumed bacterial meningitis is instituted.

- As part of empiric therapy for adults in the developed world with suspected bacterial meningitis in whom the organism is not yet known, we recommend administration of dexamethasone (Grade 1B). Adjunctive dexamethasone should be given shortly before or at the same time as the first dose of antibiotics, when indicated. Dexamethasone should be only continued if the CSF Gram stain and/or the CSF or blood cultures reveal Streptococcus pneumoniae. The indications for dexamethasone for patients with suspected or confirmed bacterial meningitis in the developing world depend on the patient population and are discussed in detail elsewhere.

- Once the CSF Gram stain results are available, the antimicrobial regimen should be tailored to cover the most likely pathogen. If the CSF findings are consistent with the diagnosis of acute bacterial meningitis but the Gram stain is negative, empiric antibiotic therapy should be continued.

- The antibiotic regimen should be modified further, when indicated, based on the CSF culture and susceptibility results.

- Cessation of antimicrobial therapy is not recommended in patients who have received prior or are receiving concurrent antimicrobial therapy with a negative CSF culture and who are suspected of having bacterial meningitis based on clinical and laboratory findings (eg, CSF pleocytosis). The choice of antimicrobial regimen and duration of administration should be individualized based on risk factors and likely infecting pathogens.

Recommendations for empiric antimicrobial therapy for purulent meningitis based on patient age and specific predisposing condition*

Predisposing factor	Common bacterial pathogens	Antimicrobial therapy
Age		
<1 month	*Streptococcus agalactiae, Escherichia coli, Listeria monocytogenes*	Ampicillin plus cefotaxime; OR ampicillin plus an aminoglycoside
1 to 23 months	*Streptococcus pneumoniae, Neisseria meningitidis, S. agalactiae, Haemophilus influenzae, E. coli*	Vancomycin plus a third-generation cephalosporin¶Δⵔⵔ
2 to 50 years	*N. meningitidis, S. pneumoniae*	Vancomycin plus a third-generation cephalosporin¶Δⵔⵔ
>50 years	*S. pneumoniae, N. meningitidis, L. monocytogenes*, aerobic gram-negative bacilli	Vancomycin plus ampicillin plus a third-generation cephalosporin¶Δ
Head trauma		
Basilar skull fracture	*S. pneumoniae, H. influenzae*, group A beta-hemolytic streptococci	Vancomycin plus a third-generation cephalosporin¶Δ
Penetrating trauma	*Staphylococcus aureus*, coagulase-negative staphylococci (especially *Staphylococcus epidermidis*), aerobic gram-negative bacilli (including *Pseudomonas aeruginosa*)	Vancomycin plus cefepime; OR vancomycin plus ceftazidime; OR vancomycin plus meropenem
Postneurosurgery	Aerobic gram-negative bacilli (including *P. aeruginosa*), *S. aureus*, coagulase-negative staphylococci (especially *S. epidermidis*)	Vancomycin plus cefepime; OR vancomycin plus ceftazidime; OR vancomycin plus meropenem
Immunocompromised state	*S. pneumoniae, N. meningitidis, L. monocytogenes*, aerobic gram-negative bacilli (including *P. aeruginosa*)	Vancomycin plus ampicillin plus cefepime; OR vancomycin plus meropenem§

* For recommended doses, refer to the UpToDate content on treatment of bacterial meningitis in children and adults.

¶ Ceftriaxone or cefotaxime.

Δ Some experts would add rifampin if dexamethasone is also given.

ⵔⵔ Add ampicillin if meningitis caused by *Listeria monocytogenes* is suspected.

§ Meropenem provides sufficient coverage for *Listeria* when used as part of an initial regimen. However, if *Listeria* is identified, the patient should generally be switched to a regimen that includes ampicillin. Refer to the UpToDate topic that discusses treatment of *Listeria* for a discussion of regimen selection.

Recommendations for antimicrobial therapy of bacterial meningitis in adults with presumptive pathogen identification by positive Gram stain*

Microorganism	Recommended therapy	Alternative therapies
Streptococcus pneumoniae	Vancomycin plus a third-generation cephalosporin¶Δ	Fluoroquinolone◇
Neisseria meningitidis	Third-generation cephalosporin¶	Chloramphenicol, fluoroquinolone, aztreonam
Listeria monocytogenes	Ampicillin§ or penicillin G§	Trimethoprim-sulfamethoxazole
Haemophilus influenzae	Third-generation cephalosporin¶	Chloramphenicol, cefepime, meropenem, fluoroquinolone

* For recommended dosages, refer to the UpToDate table on recommended intravenous dosages of antimicrobial therapy for adults with bacterial meningitis.

¶ Ceftriaxone or cefotaxime.

Δ Some experts would add rifampin if dexamethasone is also given.

◇ Moxifloxacin is recommended given its excellent cerebrospinal fluid penetration and in vitro activity against *Streptococcus pneumoniae*, although there are no clinical data available. If used, many authorities would combine moxifloxacin with vancomycin or a third-generation cephalosporin (cefotaxime or ceftriaxone).

§ Addition of an aminoglycoside should be considered.

Recommended intravenous dosages of antimicrobial therapy for adults with bacterial meningitis who have normal renal and hepatic function

Antimicrobial agent	Dose (adult)
Amikacin	5 mg/kg every 8 hours*
Ampicillin	2 g every 4 hours
Aztreonam	2 g every 6 to 8 hours
Cefepime	2 g every 8 hours
Cefotaxime	2 g every 4 to 6 hours
Ceftazidime	2 g every 8 hours
Ceftriaxone	2 g every 12 hours
Chloramphenicol	1 to 1.5 g every 6 hours¶
Ciprofloxacin	400 mg every 8 to 12 hours
Gentamicin	1.7 mg/kg every 8 hours*
Meropenem	2 g every 8 hours
Moxifloxacin	400 mg every 24 hours△
Nafcillin	2 g IV every 4 hours
Oxacillin	2 g IV every 4 hours
Penicillin G potassium	4 million units every 4 hours
Rifampin	600 mg every 24 hours◇
Tobramycin	1.7 mg/kg every 8 hours*
Trimethoprim-sulfamethoxazole (cotrimoxazole)	5 mg/kg every 8 hours§ ¥
Vancomycin	15 to 20 mg/kg every 8 to 12 hours‡ †

IV: intravenously; MRSA: methicillin-resistant *Staphylococcus aureus*; IDSA: Infectious Diseases Society of America.

* Dose based on ideal body weight or dosing weight except in underweight patients. A calculator for ideal body weight and dosing weight is available in UpToDate. Dosage and interval must be individualized to produce a peak serum concentration of 7 to 9 mg/L and trough <1 to 2 mg/L for gentamicin or tobramycin and a peak of 25 to 40 mg/L and trough <4 to 8 mg/L for amikacin. For additional information, refer to the UpToDate topic on aminoglycosides.

¶ The higher dose is recommended for patients with pneumococcal meningitis.

△ No data on optimal dosage needed in patients with bacterial meningitis.

◇ For the treatment of MRSA meningitis, the IDSA suggests a rifampin dose of 600 mg orally once daily or 300 to 450 mg twice daily.[1]

§ Dosage is based on the trimethoprim component.

¥ We administer trimethoprim-sulfamethoxazole at a dose of 5 mg/kg (based on the trimethoprim component) IV every 8 hours in patients with normal renal function. However, there are limited data on the preferred dosing interval, and in case reports, the dose of trimethoprim-sulfamethoxazole has been administered anywhere from every 6 to every 12 hours. For the treatment of MRSA meningitis, the IDSA suggests a trimethoprim-sulfamethoxazole dose of 5 mg/kg (based on the trimethoprim component) intravenously twice or three times daily.[1]

‡ For treatment of meningitis due to pathogens other than *S. aureus*, the vancomycin dose should not exceed 2 g per dose or a total daily dose of 60 mg/kg. Adjust dose to achieve vancomycin serum trough concentrations of 15 to 20 mcg/mL.[1]

† For treatment of meningitis due *S. aureus*, a vancomycin loading dose (20 to 35 mg/kg) is appropriate;[2] within this range, we use a higher dose for critically ill patients. The loading dose is based on actual body weight, rounded to the nearest 250 mg increment and not exceeding 3000 mg. The initial maintenance dose and interval are determined by nomogram (typically 15 to 20 mg/kg every 8 to 12 hours for most patients with normal renal function). Subsequent dose and interval adjustments are based on AUC-guided or trough-guided serum concentration monitoring. Refer to the UpToDate topic on vancomycin dosing for a sample nomogram and discussion of vancomycin monitoring.

Reference:

1. *Liu C, Bayer A, Cosgrove SE, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant Staphylococcus Aureus Infections in Adults and Children: Executive Summary. Clin Infect Dis 2011; 52:285.*
2. *Rybak MJ, Le J, Lodise TP, et al. Therapeutic Monitoring of Vancomycin for Serious Methicillin-Resistant Staphylococcus Aureus Infections: A Revised Consensus Guideline and Review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm 2020; 77:835.*

Recommendations for specific antimicrobial therapy of bacterial meningitis in adults based on isolated pathogen and susceptibility testing*

Microorganism, susceptibility	Standard therapy	Alternative therapies¶
Streptococcus pneumoniae		
Penicillin MIC		
≤0.06 mcg/mL	Penicillin G or ampicillin	Third-generation cephalosporinΔ, chloramphenicol
≥0.12 mcg/mL		
Third-generation cephalosporinΔ MIC <1 mcg/mL	Third-generation cephalosporinΔ	Cefepime, meropenem
Third-generation cephalosporinΔ MIC ≥1 mcg/mL	Vancomycin plus a third-generation cephalosporinΔ◇	Fluoroquinolone§
Neisseria meningitidis		
Penicillin MIC		
<0.1 mcg/mL	Penicillin G or ampicillin	Third-generation cephalosporinΔ, chloramphenicol
0.1 to 1.0 mcg/mL	Third-generation cephalosporinΔ	Fluoroquinolone, meropenem, chloramphenicol
Listeria monocytogenes	Ampicillin¥ or penicillin G¥	Trimethoprim-sulfamethoxazole
Streptococcus agalactiae (group B *Streptococcus*)	Ampicillin or penicillin G	Third-generation cephalosporinΔ
Escherichia coli and other Enterobacteriaceae‡	Third-generation cephalosporinΔ	Aztreonam, fluoroquinolone, meropenem, trimethoprim-sulfamethoxazole, ampicillin
Pseudomonas aeruginosa‡	Cefepime or ceftazidime	Aztreonam, ciprofloxacin, meropenem
Acinetobacter baumannii	Meropenem	Colistin (usually formulated as colistimethate sodium)† or polymyxin B†
Haemophilus influenzae		
Beta-lactamase negative	Ampicillin	Third-generation cephalosporinΔ, cefepime, fluoroquinolone, aztreonam, chloramphenicol
Beta-lactamase positive	Third-generation cephalosporinΔ	Cefepime, fluoroquinolone, aztreonam, chloramphenicol
Staphylococcus aureus		
Methicillin susceptible	Nafcillin or oxacillin	Vancomycin, meropenem, linezolid, daptomycin
Methicillin resistant	Vancomycin**	Trimethoprim-sulfamethoxazole, linezolid, daptomycin
Staphylococcus epidermidis	Vancomycin**	Linezolid
Enterococcus species		
Ampicillin susceptible	Ampicillin plus gentamicin	...
Ampicillin resistant	Vancomycin plus gentamicin	...
Ampicillin and vancomycin resistant	Linezolid	...

MIC: minimum inhibitory concentration.

* For recommended dosages, refer to the UpToDate table on the recommended intravenous doses of antimicrobial therapy for adults with bacterial meningitis.

¶ There may not be clinical data to support all recommendations for alternative antibiotics in patients with bacterial meningitis, but specific agents are recommended based on cerebrospinal fluid (CSF) penetration in experimental animal models and in vitro activity against the offending organism.

Δ Ceftriaxone or cefotaxime.

◇ Consider addition of rifampin if the MIC of ceftriaxone is >2 mcg/mL.

§ Moxifloxacin is recommended given its excellent CSF penetration and in vitro activity against *Streptococcus pneumoniae*, although there are no clinical data available. If used, many authorities would combine moxifloxacin with vancomycin or a third-generation cephalosporin (cefotaxime or ceftriaxone).

¥ Addition of an aminoglycoside should be considered.

‡ Choice of a specific antimicrobial regimen must be guided by in vitro susceptibility test results.

† Should be administered not only by the intravenous route but also by the intraventricular or intrathecal route.

** Consider addition of rifampin.

Reference:
1. van de Beek D, Brouwer MC, Thwaites GE, Tunkel AR. Advances in the treatment of bacterial meningitis. Lancet 2012; 380:1693.

Treatment of bacterial meningitis caused by specific pathogens in adults

Among adults with bacterial meningitis in the United States, *Streptococcus pneumoniae* and *Neisseria meningitidis* are the most common infecting organisms.

●There are a number of general principles of antimicrobial therapy in patients with bacterial meningitis. The most important initial issues are avoidance of delay in administering therapy and the choice of drug regimen.

●For the initial therapy of *S. pneumoniae*, we recommend vancomycin **plus either** ceftriaxone **or** cefotaxime rather than a third-generation cephalosporin alone (**Grade 1B**). In countries where the incidence of ceftriaxone-resistant pneumococcus is <1 percent, it is appropriate to use ceftriaxone monotherapy for empiric coverage although some authorities would recommend continuation of dual therapy until the results of in vitro susceptibility testing are available.

•If the isolate is proven to be **susceptible to penicillin** (minimum inhibitory concentration [MIC] ≤0.06 mcg/mL), monotherapy with penicillin G or ampicillin can be used. It is also reasonable to continue therapy with a third-generation cephalosporin alone instead of changing to penicillin or ampicillin, given the excellent efficacy, convenient dosing, and affordability of these agents.

•If the isolate is **resistant to penicillin** (MIC ≥0.12 mcg/mL), but susceptible to third-generation cephalosporins (MIC <1.0 mcg/mL), either cefotaxime or ceftriaxone should be used.

If the isolate is **resistant to both penicillin and third-generation cephalosporins**, vancomycin plus a third-generation cephalosporin should be continued for the total duration of therapy

The dosing for patients with normal renal function is:

-Vancomycin – 15 to 20 mg/kg intravenously (IV) every 8 to 12 hours (not to exceed 2 g per dose or a total daily dose of 60 mg/kg; adjust dose to achieve vancomycin serum trough concentrations of 15 to 20 mcg/mL)

-Ceftriaxone – 2 g IV every 12 hours

-Cefotaxime – 2 g IV every four to 6 hours

-Penicillin G – 4 million units IV every 4 hours

-Ampicillin – 2 g IV every 4 hours

For the initial therapy of *N. meningitidis*, we recommend a third-generation cephalosporin, such as cefotaxime or ceftriaxone, rather than penicillin, while awaiting susceptibility data (**Grade 1C**). If the isolate is susceptible to penicillin, either a third-generation cephalosporin or penicillin may be used to complete the course of therapy

- The preferred regimens for other causes of bacterial meningitis are discussed above.
- The optimal regimens for patients with severe drug allergies depends upon the organism.

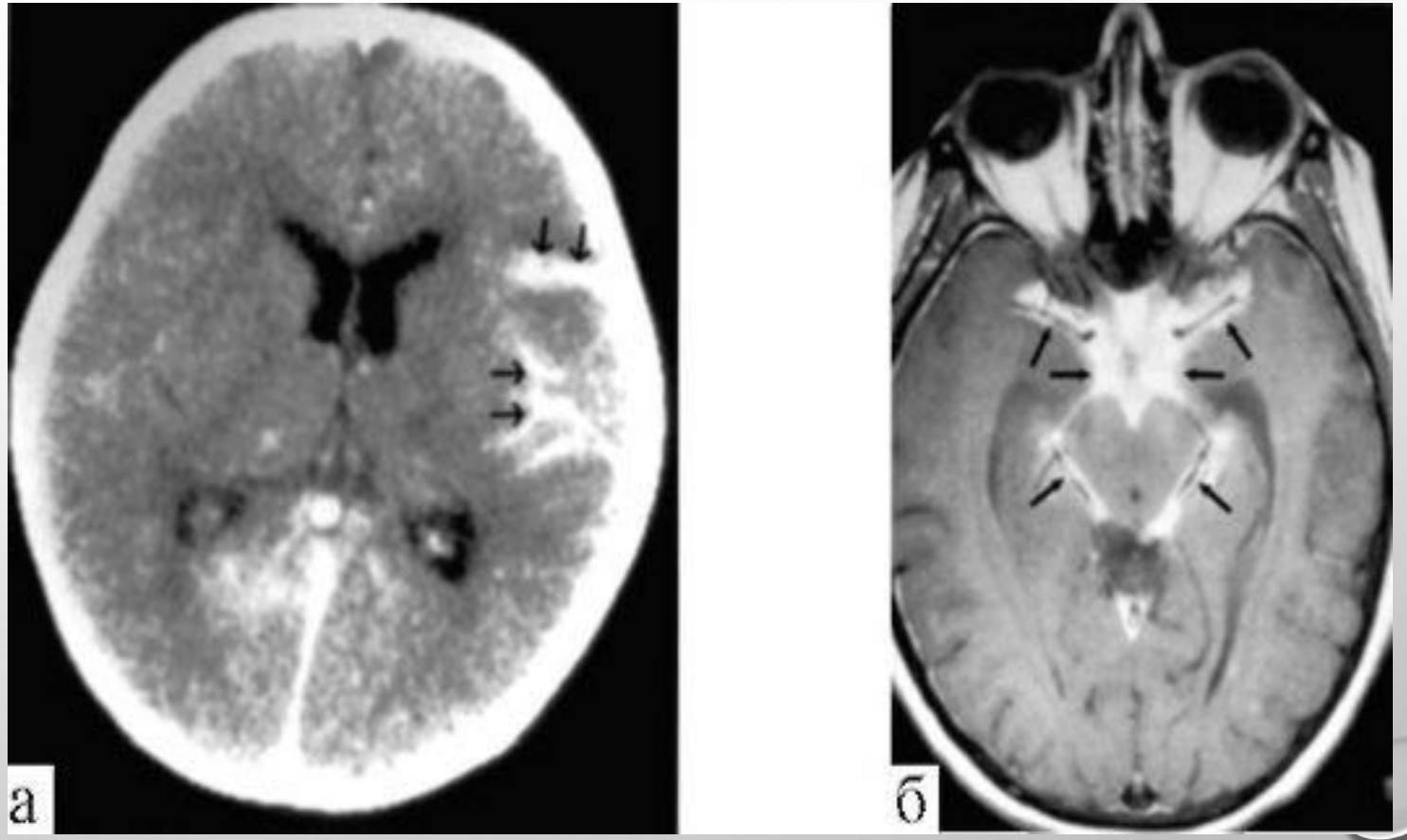
- Vaccines against *N. meningitidis* and *S. pneumoniae* are recommended for adults at increased risk of these infections.
- There is a role for postexposure chemoprophylaxis to prevent spread of meningococcal and *Haemophilus* meningitis under certain circumstances.
- For patients with a basilar skull fracture and a CSF leak, we recommend **against** using prophylactic antimicrobials (**Grade 1B**). If the CSF leak persists for >7 days, an attempt should be made to repair it. Patients with a CSF leak (due to either basilar skull fracture or another cause) should receive pneumococcal vaccination.

PCR TESTING FOR THE DIAGNOSIS OF HERPES SIMPLEX VIRUS IN PATIENTS WITH ENCEPHALITIS OR MENINGITIS

- ALTHOUGH ENCEPHALITIS IS A RARE COMPLICATION OF HERPES SIMPLEX VIRUS (HSV) INFECTION, HSV IS THE MOST COMMON CAUSE OF NONEPIDEMIC, SPORADIC, ACUTE FOCAL ENCEPHALITIS IN THE UNITED STATES.
- PRIOR TO THE WIDE AVAILABILITY OF MOLECULAR TESTING METHODOLOGY, BRAIN BIOPSY WAS CONSIDERED THE "GOLD STANDARD" FOR THE DIAGNOSIS OF HERPES SIMPLEX VIRUS ENCEPHALITIS; HSV WAS IDENTIFIED IN TISSUE BY CELL CULTURE OR IMMUNOHISTOCHEMICAL STAINING. ALTHOUGH BRAIN BIOPSY HAS A SENSITIVITY OF 99 PERCENT AND A SPECIFICITY OF 100 PERCENT, IT REMAINS AN INVASIVE PROCEDURE AND THE RESULTS MAY NOT BE AVAILABLE FOR SEVERAL DAYS. CULTURE AND SEROLOGIC TECHNIQUES ARE NOT GOOD ALTERNATIVES BECAUSE THEY HAVE LOWER SENSITIVITY AND SPECIFICITY THAN BRAIN BIOPSY.
- POLYMERASE CHAIN REACTION (PCR) TESTING ON CEREBROSPINAL FLUID (CSF) OFFERS RAPID RESULTS WITH HIGH SENSITIVITY AND SPECIFICITY OF 98 AND 94 PERCENT, RESPECTIVELY, WHEN COMPARED WITH BRAIN BIOPSY SPECIMENS. DETECTION OF HSV DNA IN CSF BY PCR HAS BECOME THE STANDARD FOR THE DIAGNOSIS OF HERPES SIMPLEX VIRUS ENCEPHALITIS IN ADULTS AND NEONATES.
- PCR TESTING IS POSITIVE EARLY IN THE COURSE OF THE ILLNESS (WITHIN THE FIRST 24 HOURS OF ONSET OF SYMPTOMS) AND REMAINS POSITIVE DURING THE FIRST WEEK OF ANTIVIRAL THERAPY
- MOST HSV PCR ASSAYS REQUIRE BETWEEN 0.5 AND 1 ML OF CSF FOR HSV TESTING. SPECIMENS ARE STORED REFRIGERATED OR FROZEN UNTIL TESTING IS PERFORMED.
- HSV PCR RESULTS SHOULD ALWAYS BE INTERPRETED WITHIN THE CONTEXT OF THE CLINICAL PRESENTATION OF THE PATIENT. IF TESTING RESULTS DO NOT CORRELATE WITH THE CLINICAL IMPRESSION, REPEAT TESTING SHOULD BE PERFORMED.
- HSV CAN ALSO CAUSE ASEPTIC MENINGITIS, A SELF-LIMITED DISEASE USUALLY ASSOCIATED WITH HSV TYPE 2 INFECTION. THE PREFERRED DIAGNOSTIC TEST FOR PATIENTS WITH SUSPECTED HSV MENINGITIS IS PCR TESTING ON CEREBRAL SPINAL FLUID.

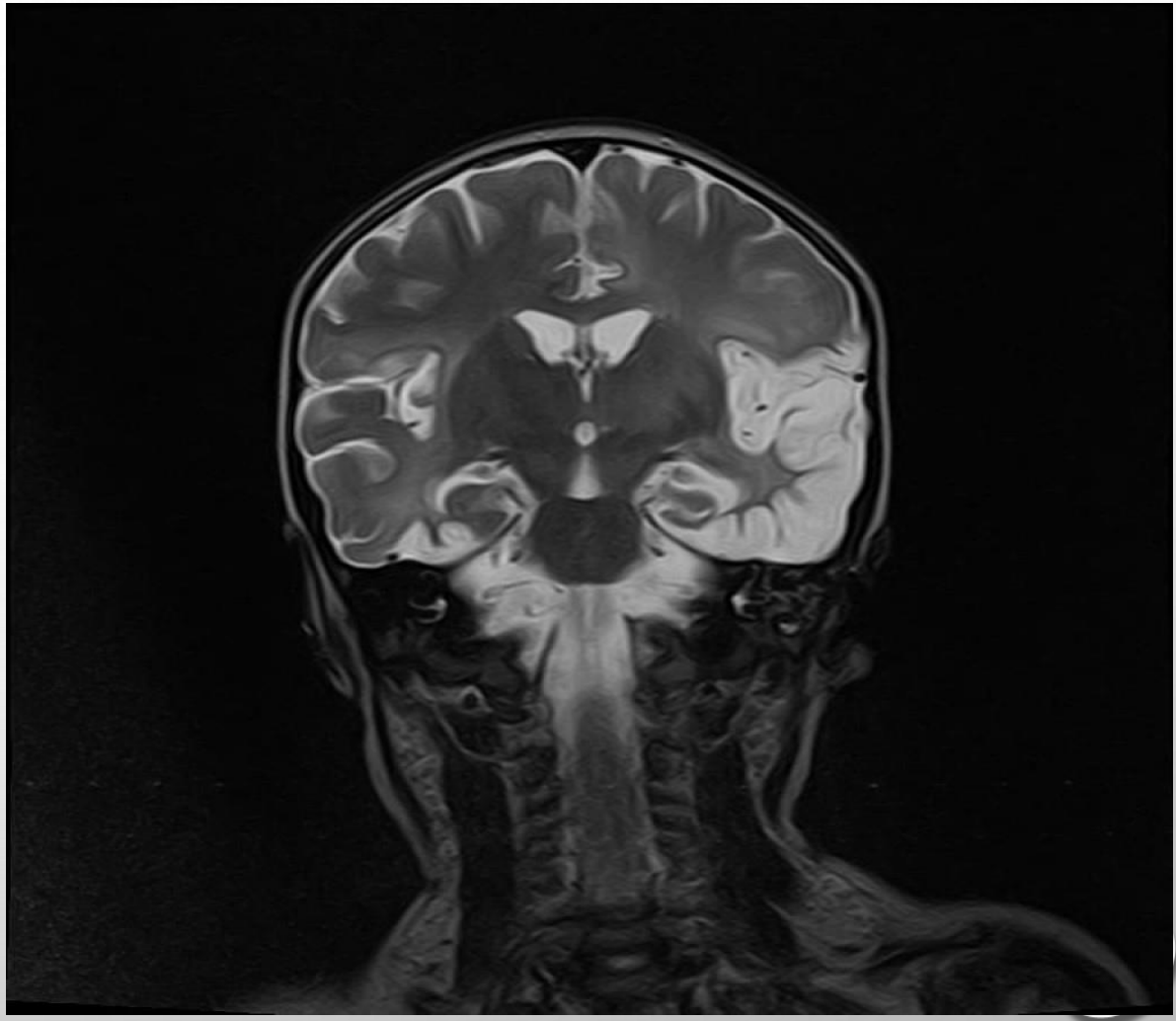
ТУБЕРКУЛЕЗНЫЙ МЕНИНГИТ

- ПРОДРОМАЛЬНЫЙ ПЕРИОД
- ПЕРИОД РАЗДРАЖЕНИЯ ЦНС
- ПЕРИОД ПАРЕЗОВ И ПАРАЛИЧЕЙ



ЭНЦЕФАЛИТЫ

- **ЭНЦЕФАЛИТ -** ВОСПАЛЕНИЕ ГОЛОВНОГО МОЗГА, КОГДА ИМЕЮТСЯ КЛИНИЧЕСКИЕ И ПАТОЛОГОАНАТОМИЧЕСКИЕ ПРИЗНАКИ ВОВЛЕЧЕНИЯ В ИНФЕКЦИОННЫЙ ПРОЦЕСС ГЕМИСФЕР ГОЛОВНОГО МОЗГА, СТВОЛА МОЗГА И МОЗЖЕЧКА.



ЭНЦЕФАЛИТЫ

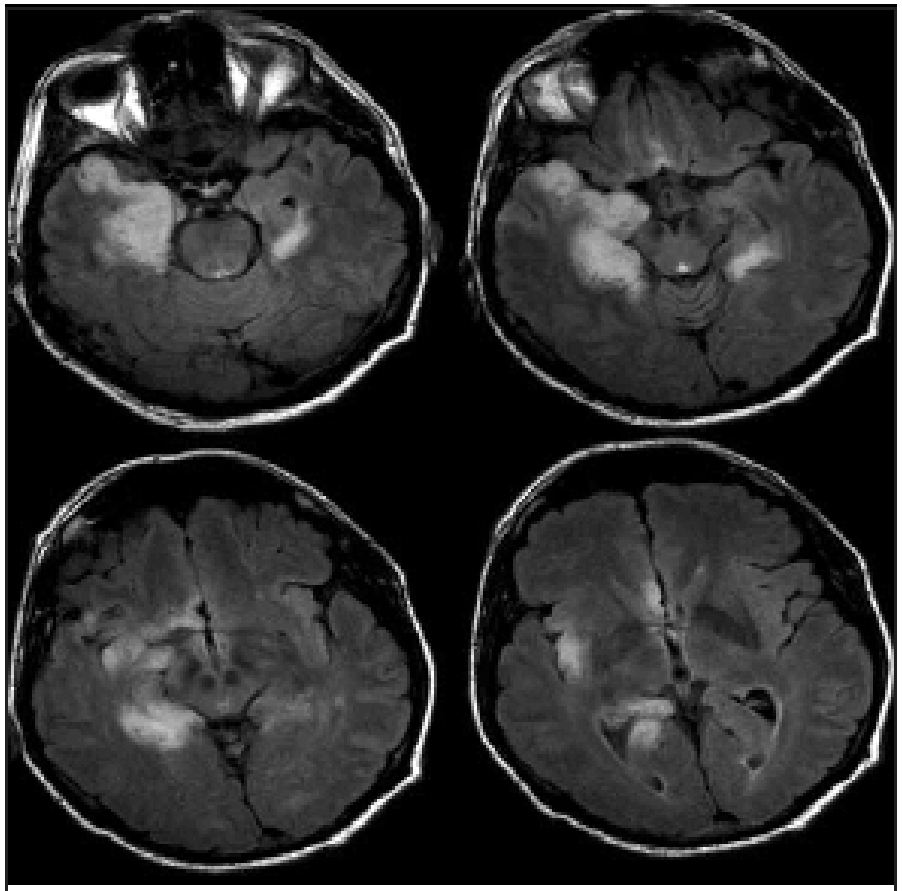


Рис. 1. МРТ головного мозга больного энцефалитом, вызванным вирусом герпеса 1-го типа. Выявляется асимметричное поражение обеих височных долей, больше справа

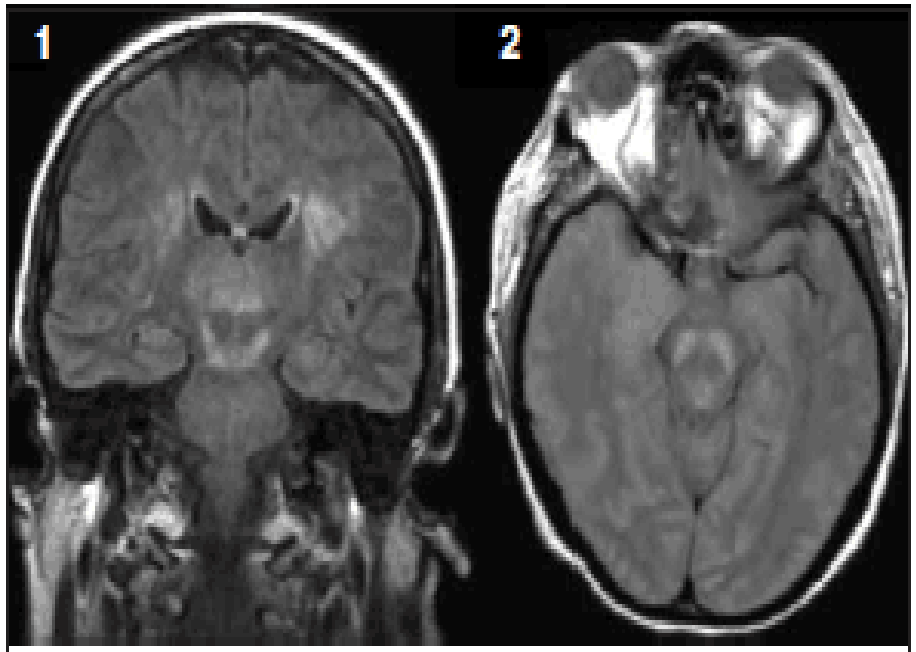


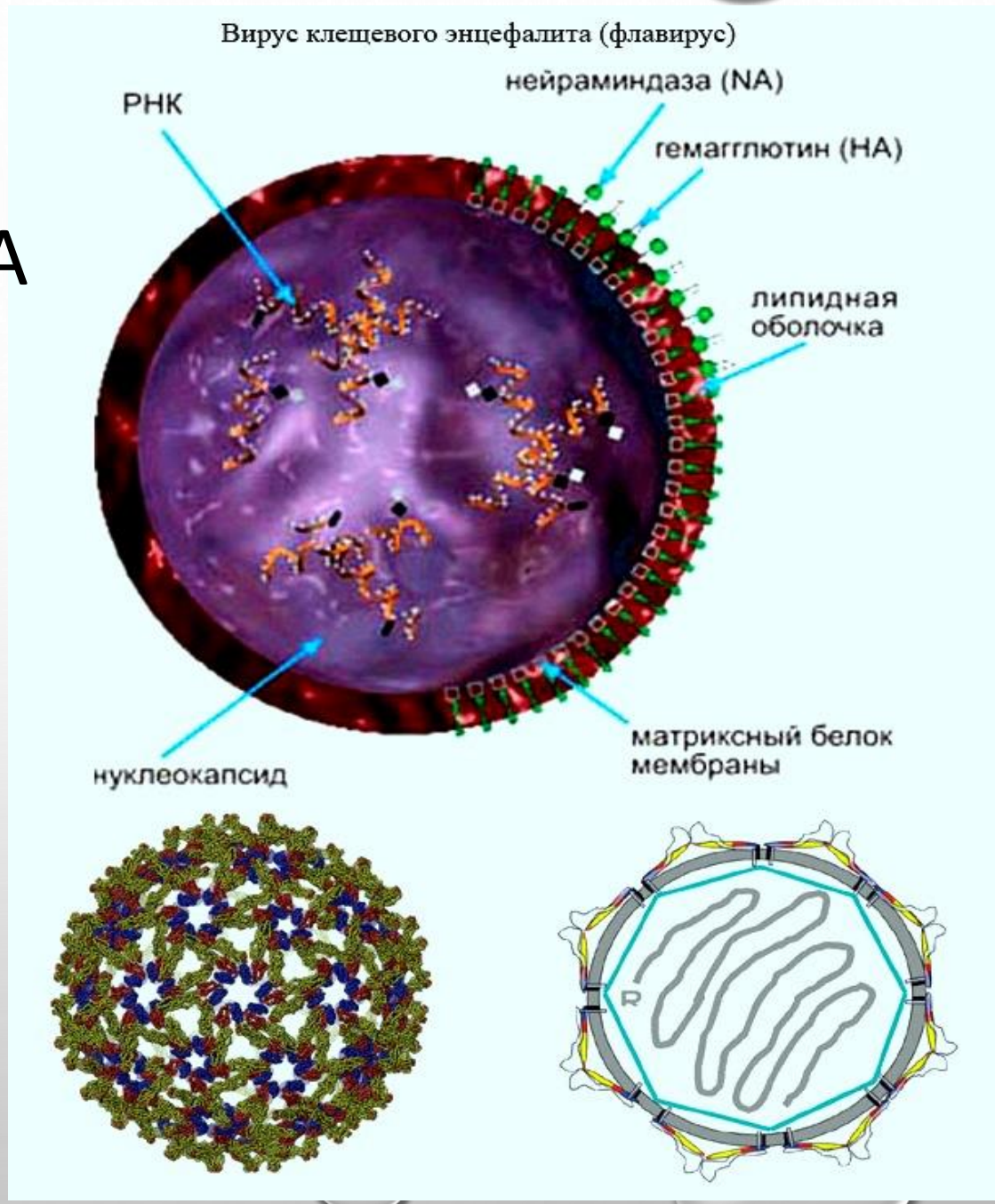
Рис. 2. МРТ больного с энцефалитом, вызванным вирусом лихорадки Западного Нила.
1 – коронарный срез, выявляются двусторонние очаги в верхних отделах ствола головного мозга, таламусе, базальных ганглиях.
2 – аксиальный срез, двусторонние очаги в черной субстанции

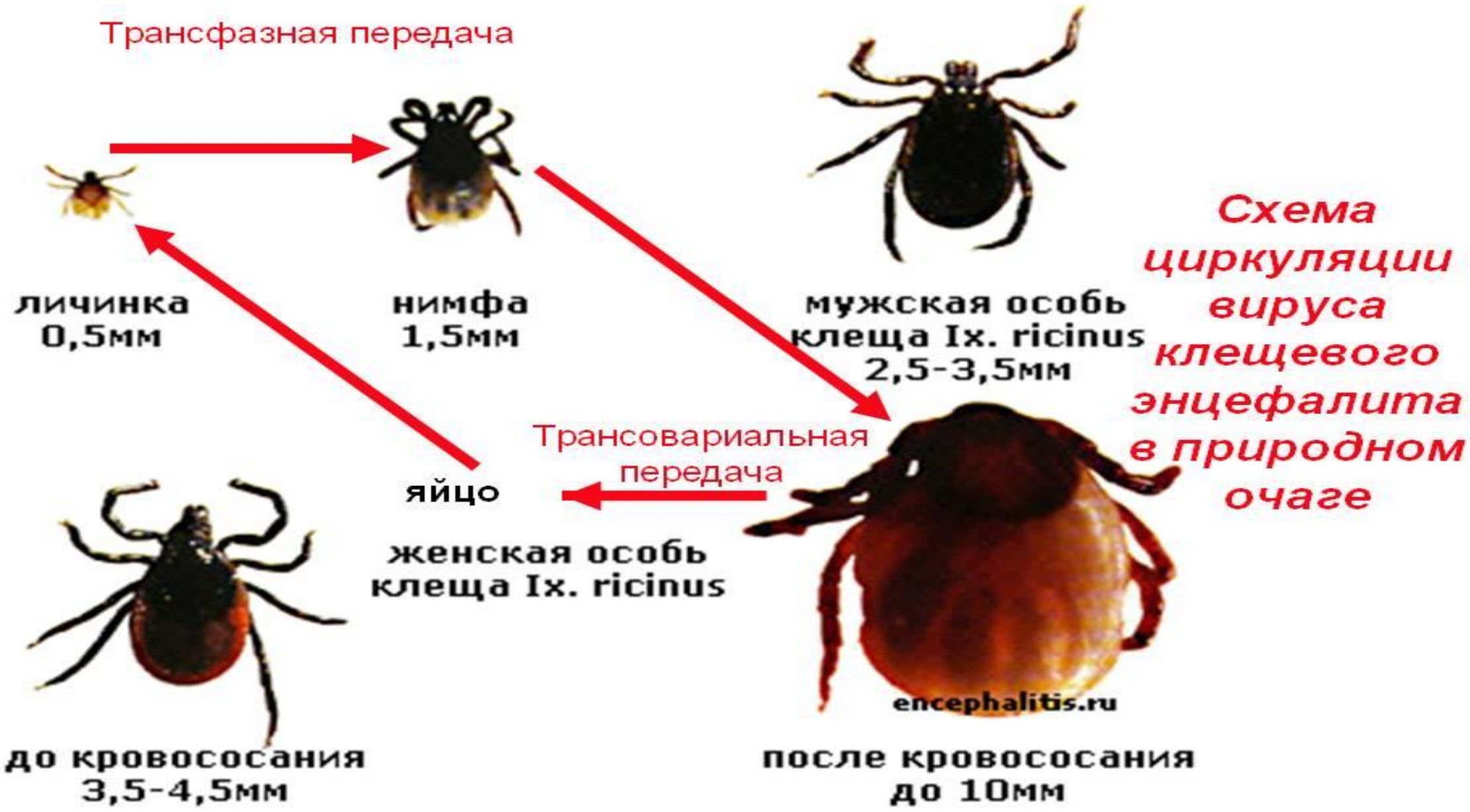
Котов С.В., Елисеев С.В.,Котов А.С. Возвращение нейроинфекций в клинику. РМЖ 2015;12:656

TICK BORNE ENCEPHALITIS AND LYME DISEASE

ВИРУС КЛЕЩЕВОГО ЭНЦЕФАЛИТА

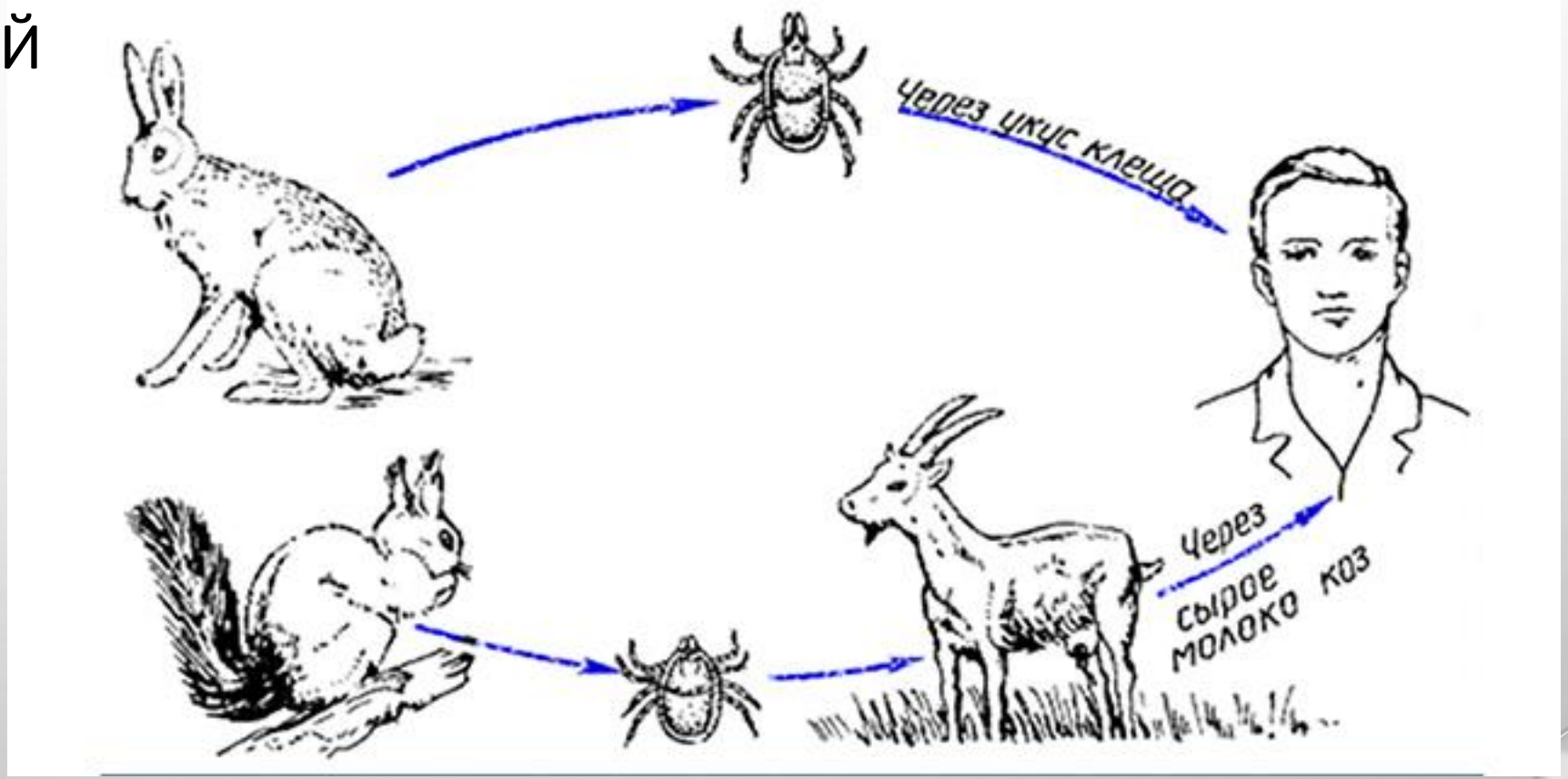
- РОД : FLAVIVIRUS (ГРУППА B)
- СЕМЕЙСТВО: TOGAVIRIDAE
- ЭКОЛОГИЧЕСКАЯ ГРУППА:ARBOVIRIDAE
- 3 ВИДА:
- ДАЛЬНЕВОСТОЧНЫЙ
- **УРАЛО-СИБИРСКИЙ**
- ЗАПАДНЫЙ



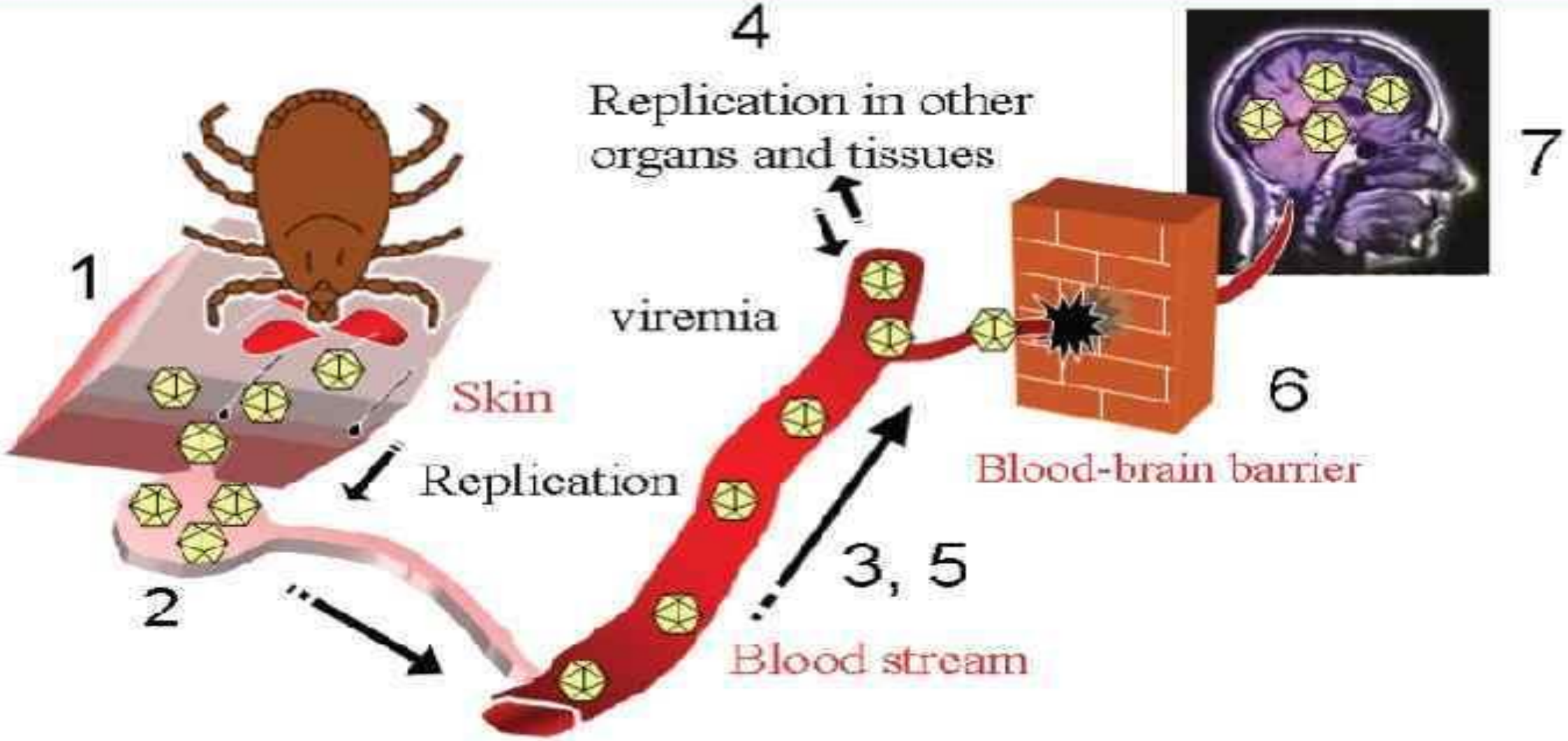

Трансфазная передача
личинка
0,5мм
нимфа
1,5мм
мужская особь
клеща Ix. ricinus
2,5-3,5мм
Схема циркуляции вируса клещевого энцефалита в природном очаге
Трансовариальная передача
яйцо
женская особь
клеща Ix. ricinus
encephalitis.ru
до кровососания
3,5-4,5мм
после кровососания
до 10мм

ПУТИ ПЕРЕДАЧИ КЭ

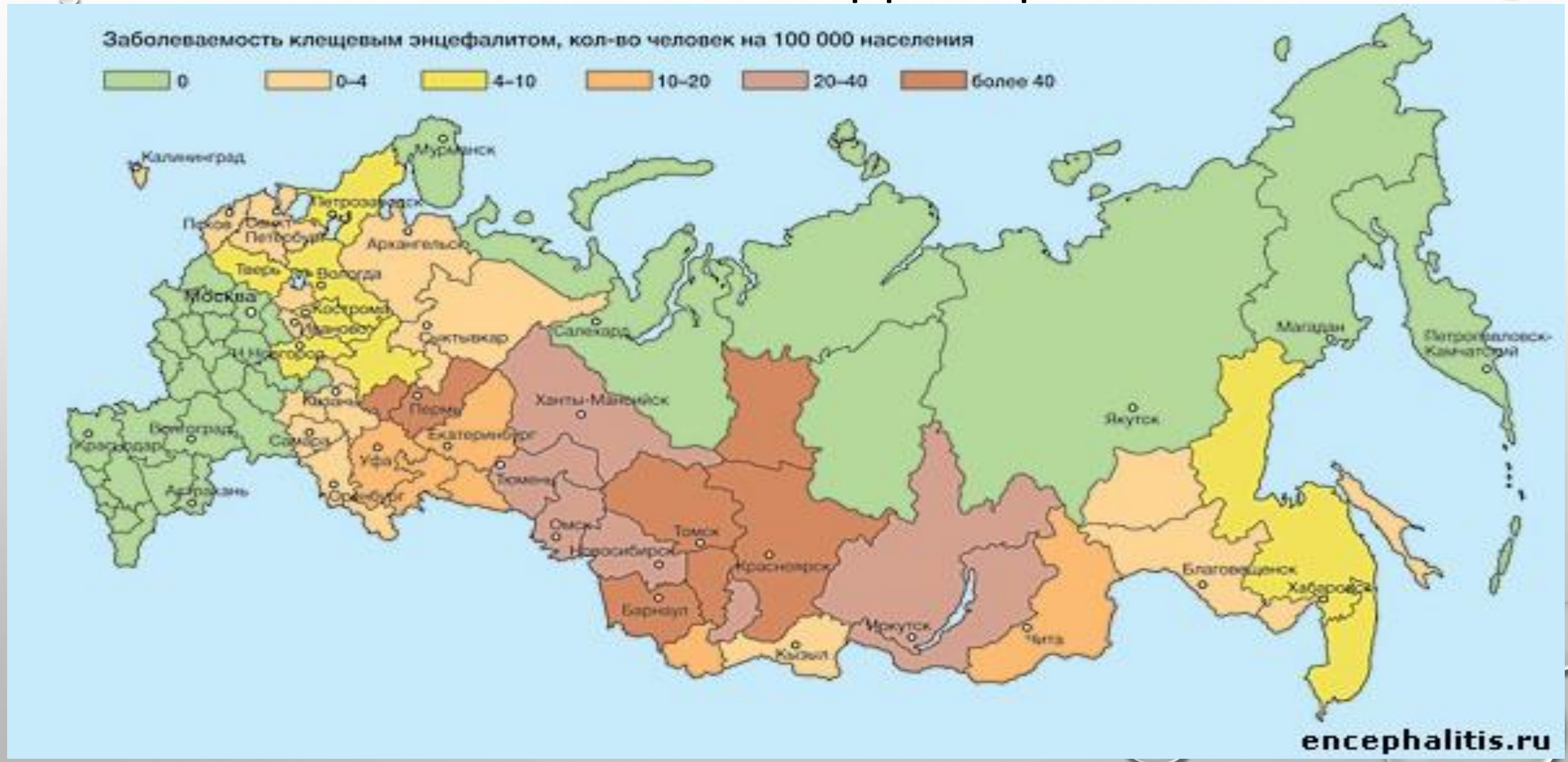
- ТРАНСМИССИВНЫЙ
- АЛИМЕНТАРНЫЙ



Патогенез заболевания



ЗАБОЛЕВАЕМОСТЬ КЛЕЩЕВЫМ ЭНЦЕФАЛИТОМ В РОССИЙСКОЙ ФЕДЕРАЦИИ



РЕСПУБЛИКА БАШКОРТОСТАН – ЭНДЕМИЧНЫЙ РЕГИОН ДЛЯ КЛЕЩЕВОГО ЭНЦЕФАЛИТА

- 42 РАЙОНА РБ ЭНДЕМИЧНЫ

ДЛЯ КЛЕЩЕВОГО ЭНЦЕФАЛИТА

- ЗОНА НАИБОЛЬШЕГО РИСКА ЗАРАЖЕНИЯ

КЭ НА ТЕРРИТОРИИ РБ - ПРЕДУРАЛЬЕ И ЮЖНЫЙ УРАЛ

LYME DISEASE

Clinical manifestations of Lyme disease

Early localized disease, occurring a few days to one month after the tick bite*
Erythema migrans - occurs in approximately 80 percent of patients
Associated symptoms and signs may include: fatigue, malaise, lethargy, mild headache, mild neck stiffness, myalgias, arthralgias, regional lymphadenopathy
Early disseminated disease¶, occurring weeks to months after the tick bite*Δ
Carditis - about 1 percent of patients reported to the CDC◇
Manifestations include AV nodal block, mild cardiomyopathy or myopericarditis
Neurologic disease - occurs in approximately 15 percent of untreated patients◇
Manifestations include lymphocytic meningitis, cranial neuropathy (most often facial, can be bilateral), peripheral neuropathy; rarely myelitis or encephalitis
Musculoskeletal involvement - occurs in approximately 60 percent of untreated patients◇
Manifestations include migratory arthralgias
Skin involvement - multiple erythema migrans lesionsΔ, borrelial lymphocytoma (in Europe)
Lymphadenopathy - regional or generalized
Eye involvement§ - conjunctivitis, iritis, choroiditis, vitritis, retinitis
Liver disease - liver function test abnormalities, hepatitis
Kidney disease - microhematuria, asymptomatic proteinuria
Late disease¶, occurring months to years after the tick bite*
Musculoskeletal symptoms - approximately 60 percent of untreated patients develop intermittent monoarticular or oligoarticular arthritis; approximately 10 percent of untreated patients develop persistent monoarthritis, usually affecting the knee
Neurologic disease - incidence has not been established
Peripheral neuropathy or encephalomyelitis (both rare)
Cutaneous involvement - acrodermatitis chronica atrophicans, morphea/localized scleroderma-like lesions (both described only in Europe)

CDC: United States Centers for Disease Control and Prevention.

* Only about 25 percent of patients with erythema migrans recall the tick bite that transmitted Lyme disease.

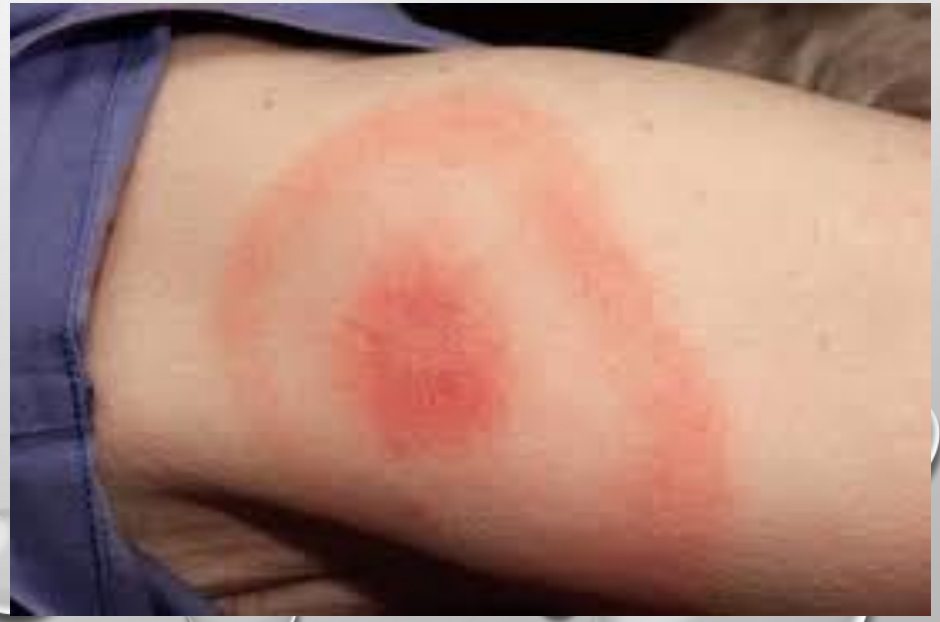
¶ Can occur in the absence of any prior features of Lyme disease.

Δ The multiple erythema migrans lesions of early disseminated disease typically occur days to weeks following infection.

◇ Incidence following treated erythema migrans is not known but is very low.

§ Observation based on individual case reports.

UpToDate®



Clinical manifestations of Lyme disease

Early localized disease, occurring a few days to one month after the tick bite*
Erythema migrans - occurs in approximately 80 percent of patients
Associated symptoms and signs may include: fatigue, malaise, lethargy, mild headache, mild neck stiffness, myalgias, arthralgias, regional lymphadenopathy
Early disseminated disease¶, occurring weeks to months after the tick bite*Δ
Carditis - about 1 percent of patients reported to the CDC◇
Manifestations include AV nodal block, mild cardiomyopathy or myopericarditis
Neurologic disease - occurs in approximately 15 percent of untreated patients◇
Manifestations include lymphocytic meningitis, cranial neuropathy (most often facial, can be bilateral), peripheral neuropathy; rarely myelitis or encephalitis
Musculoskeletal involvement - occurs in approximately 60 percent of untreated patients◇
Manifestations include migratory arthralgias
Skin involvement - multiple erythema migrans lesionsΔ, borrelial lymphocytoma (in Europe)
Lymphadenopathy - regional or generalized
Eye involvement§ - conjunctivitis, iritis, choroiditis, vitritis, retinitis
Liver disease - liver function test abnormalities, hepatitis
Kidney disease - microhematuria, asymptomatic proteinuria
Late disease¶, occurring months to years after the tick bite*
Musculoskeletal symptoms - approximately 60 percent of untreated patients develop intermittent monoarticular or oligoarticular arthritis; approximately 10 percent of untreated patients develop persistent monoarthritis, usually affecting the knee
Neurologic disease - incidence has not been established
Peripheral neuropathy or encephalomyelitis (both rare)
Cutaneous involvement - acrodermatitis chronica atrophicans, morphea/localized scleroderma-like lesions (both described only in Europe)

CDC: United States Centers for Disease Control and Prevention.

* Only about 25 percent of patients with erythema migrans recall the tick bite that transmitted Lyme disease.

¶ Can occur in the absence of any prior features of Lyme disease.

Δ The multiple erythema migrans lesions of early disseminated disease typically occur days to weeks following infection.

◇ Incidence following treated erythema migrans is not known but is very low.

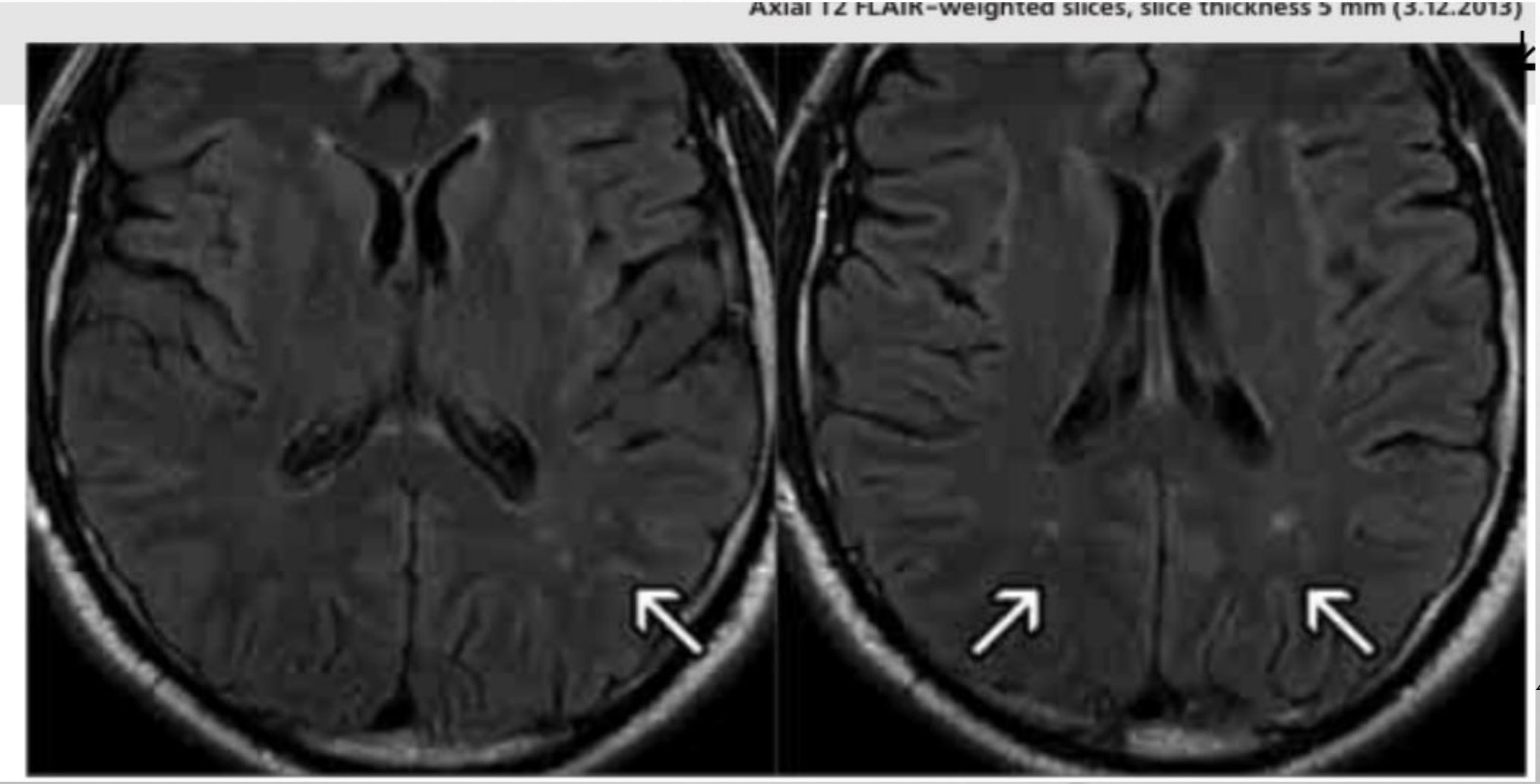
§ Observation based on individual case reports.

UpToDate®

TREATMENT OF LYME DISEASE

Neurologic disease[§]				
•Acute neurologic disease, such as:Cranial nerve palsy (eg, facial nerve palsy) •Meningitis •Radiculoneuropathy (early disseminated disease)	Doxycycline[¶Δ◊]	100 mg orally twice daily for 14 to 21 days	4.4 mg/kg/day orally divided twice daily (maximum 100 mg per dose) for 14 to 21 days	•For patients with isolated facial nerve palsy (eg, no evidence of meningitis or radiculoneuropathy), amoxicillin or cefuroxime is an alternative in patients with contraindications to doxycycline. For patients with other forms of acute neurologic disease, most experts would initiate IV therapy (eg, ceftriaxone) if doxycycline cannot be used. •In the United States, most practitioners favor using longer courses of antibiotics (eg, 28 days) for those with evidence of severe neurologic disease.
Severe neurologic disease, including encephalitis	Ceftriaxone[¥‡]	2 g IV once daily for 14 to 28 days	50 to 75 mg/kg IV once daily (maximum 2 g per dose) for 14 to 28 days	
Carditis				

ПОДОСТРЫЙ КЛЕЩЕВОЙ ЭНЦЕФАЛИТ



4 (3) : 66-72.

4.8.2. Критерии лабораторного подтверждения диагноза

Признак	Критерии	Сила*
IgM КЭ, IgG КЭ	Нарастание титра IgG-антител в парных сыворотках (в остром периоде инфекции и периоде выздоровления), а также повышение уровней IgG и IgM указывает на наличие клещевого энцефалита.	B
РНК вируса КЭ в крови и ликворе	Выявление РНК вируса клещевого энцефалита методом ПЦР в крови и ликворе	B
Антигены вируса КЭ в крови и ликворе	Выявление антигенов вируса клещевого энцефалита в крови и ликворе	B

Примечание: * - Оценка силы рекомендаций в соответствии с рейтинговой схемой

«Клещевой вирусный энцефалит у взрослых» Клинические рекомендации. Научное общество Клинические инфекционистов,2014

ЛЕЧЕНИЕ КЭ: ЭТИОТРОПНОЕ

- **ПРОТИВОКЛЕЩЕВОЙ ИММУНОГЛОБУЛИН** ПО СХЕМЕ: ПО 6,0-12,0 В/М 1-2 РАЗ/ДЕНЬ, ПРИ НАЛИЧИИ СИМПТОМОВ ВИРЕМИИ (ЛИХОРАДОЧНЫЙ СИНДРОМ), ДОЗА И КРАТНОСТЬ ВВЕДЕНИЯ ОПРЕДЕЛЯЕТСЯ ФОРМОЙ КЭ. (А)
- НАЗНАЧЕНИЕ **СЗП ПРОТИВОКЛЕЩЕВОЙ** ДО 300 МЛ/СУТ РЕКОМЕНДУЕТСЯ ПРИ ТЯЖЕЛОЙ ФОРМЕ ЗАБОЛЕВАНИЯ (С ОБОСНОВАНИЕМ) (А)
- **ИНТЕРФЕРОН АЛЬФА-2В ЧЕЛОВЕЧЕСКИЙ РЕКОМБИНАНТНЫЙ** ПО СХЕМЕ: ПО 1 МЛН МЕ - 1 РАЗ В ДЕНЬ В/М В СОЧЕТАНИИ **С РИБАВИРИНОМ** В ДОЗЕ 400 МГ 2 РАЗА В СУТКИ ДО КУПИРОВАНИЯ СИМПТОМОВ ВИРЕМИИ (ЛИХОРАДОЧНОГО СИНДРОМА)(В)
- РЕКОМЕНДОВАНА ТЕРАПИЯ ИММУНОМОДУЛЯТОРАМИ(МЕГЛЮМИНА АКРИДОНАЦЕТАТ И ДР.) НЕ РАНЕЕ 7 СУТОК ТЕРАПИИ (В)

- КЛЕЩЕВОЙ ВИРУСНЫЙ ЭНЦЕФАЛИТ У ВЗРОСЛЫХ. КЛИНИЧЕСКИЕ РЕКОМЕНДАЦИИ, 2016.

ЛЕЧЕНИЕ КЭ

- ВСЯ ЭТИОТРОПНАЯ ТЕРАПИЯ НЕЭФФЕКТИВНА НА ПОЗДНИХ СТАДИЯХ ЗАБОЛЕВАНИЯ, КОГДА ВИРУС УЖЕ ПОРАЗИЛ ЦЕНТРАЛЬНУЮ НЕРВНУЮ СИСТЕМУ.
- В ЭТОМ СЛУЧАЕ ЛЕЧЕНИЕ НАПРАВЛЕНО НЕ НА БОРЬБУ С ВОЗБУДИТЕЛЕМ БОЛЕЗНИ, А НА ПАТОЛОГИЧЕСКИЕ МЕХАНИЗМЫ, УГРОЖАЮЩИЕ ЖИЗНИ ПАЦИЕНТА

- КЛЕЩЕВОЙ ВИРУСНЫЙ ЭНЦЕФАЛИТ У ВЗРОСЛЫХ. КЛИНИЧЕСКИЕ РЕКОМЕНДАЦИИ, 2016.

ПРОФИЛАКТИКА КЭ

- СПЕЦИФИЧЕСКАЯ :

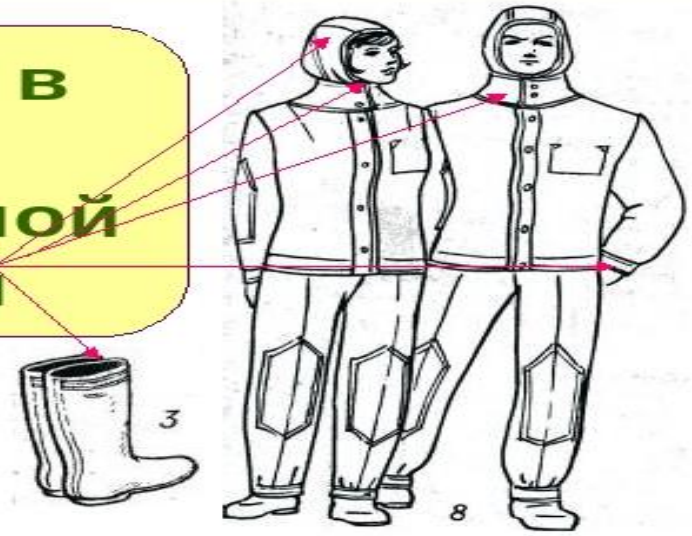
ВАКЦИНАЦИЯ ЭКСТРЕННАЯ И ОСНОВНАЯ

- НЕСПЕЦИФИЧЕСКАЯ

НЕСПЕЦИФИЧЕСКАЯ ПРОФИЛАКТИКА КЛЕЩЕВОГО ЭНЦЕФАЛИТА

Профилактика клещевого энцефалита

Ношение в лесу специальной одежды



Кипячение сырого козьего и коровьего молока

Само- и взаимоосмотры на выходе из леса и на привалах

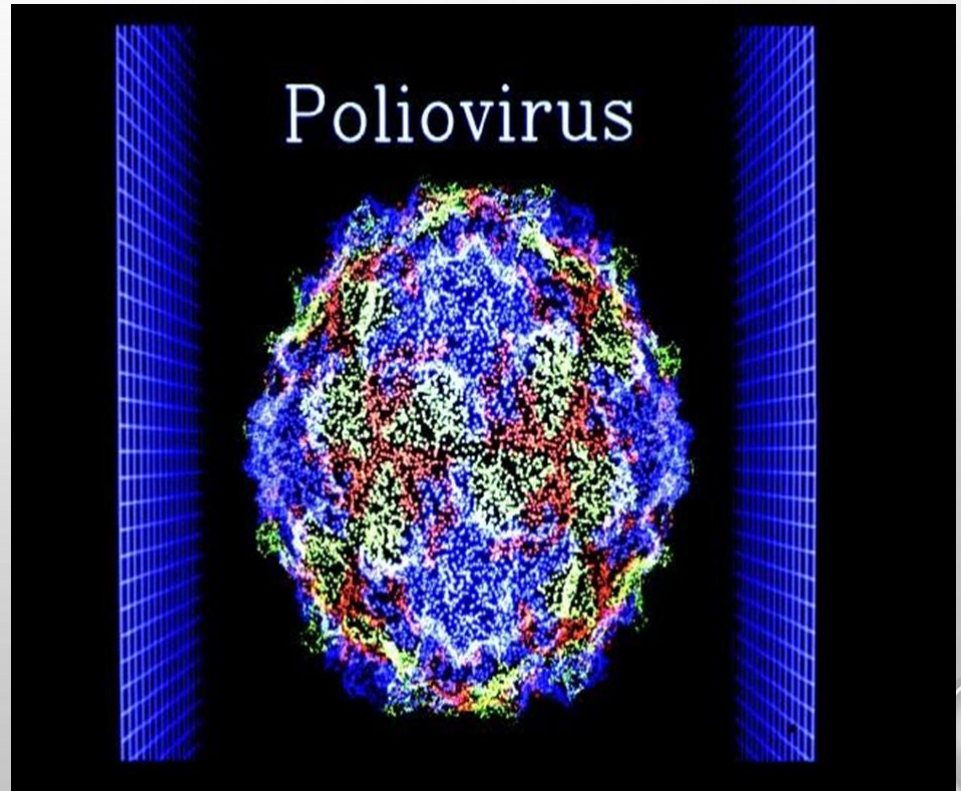
Применение жидких и аэрозольных препаратов для борьбы с насекомыми

ЭКСТРЕННАЯ ПРОФИЛАКТИКА

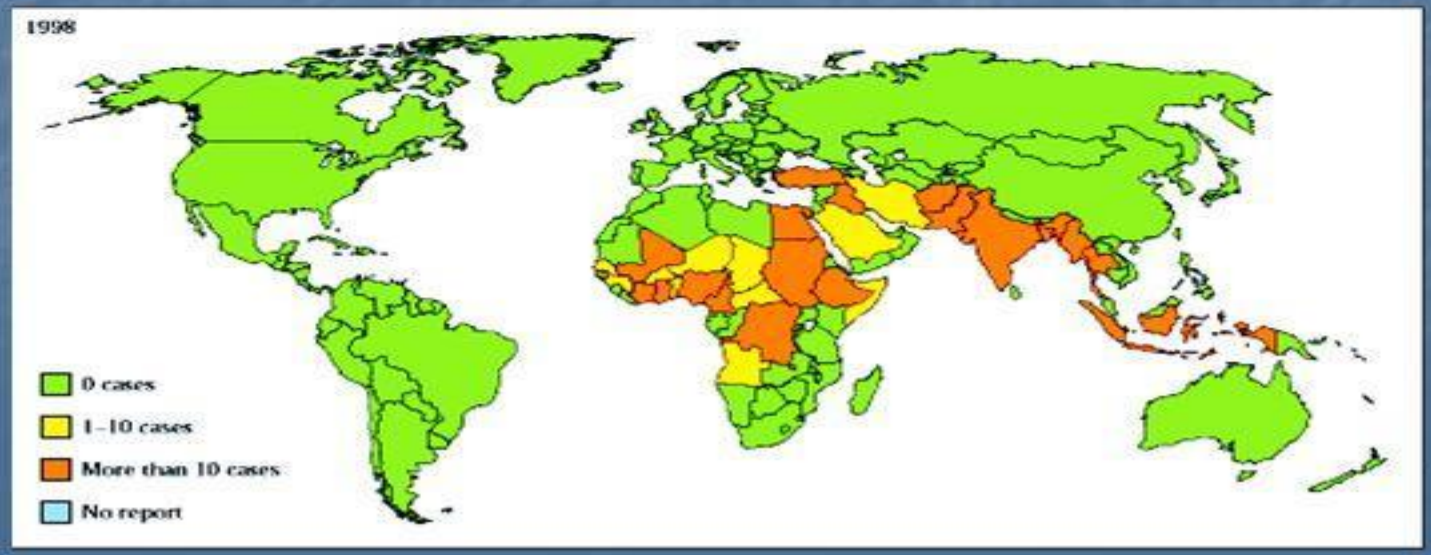
- В ПЕРВЫЕ 96 ЧАСОВ ПОСЛЕ ПРИСАСЫВАНИЯ РЕКОМЕНДОВАНО ВВОДИТЬ ИММУНОГЛОБУЛИН ПРОТИВ КЛЕЩЕВОГО ЭНЦЕФАЛИТА ВНУТРИМЫШЕЧНО ОДНОКРАТНО, В ДОЗИРОВКЕ 0,1 МЛ/КГ (В)

- ОСНОВНАЯ СХЕМА ВАКЦИНАЦИИ : 0, 1-3, 9-12 МЕСЯЦЕВ С ПОСЛЕДУЮЩЕЙ РЕВАКЦИНАЦИЕЙ КАЖДЫЕ 3-5 ЛЕТ
- ЭКСТРЕННАЯ СХЕМА ВАКЦИНАЦИИ: (ДВЕ ИНЪЕКЦИИ С ИНТЕРВАЛОМ В 14 ДНЕЙ) РЕКОМЕНДОВАНО ПРИМЕНЯТЬ ДЛЯ НЕ ВАКЦИНИРОВАННЫХ РАНЕЕ ЛИЦ, ПРИЕЗЖАЮЩИХ В ЭНДЕМИЧНЫЕ ОЧАГИ ВЕСНОЙ-ЛЕТОМ. (А)

POLYOMYELITIS



Карта распространения заболеванием полиомиелитом до (вверху) и после (внизу) проведения массовых вакцинаций ВОЗ



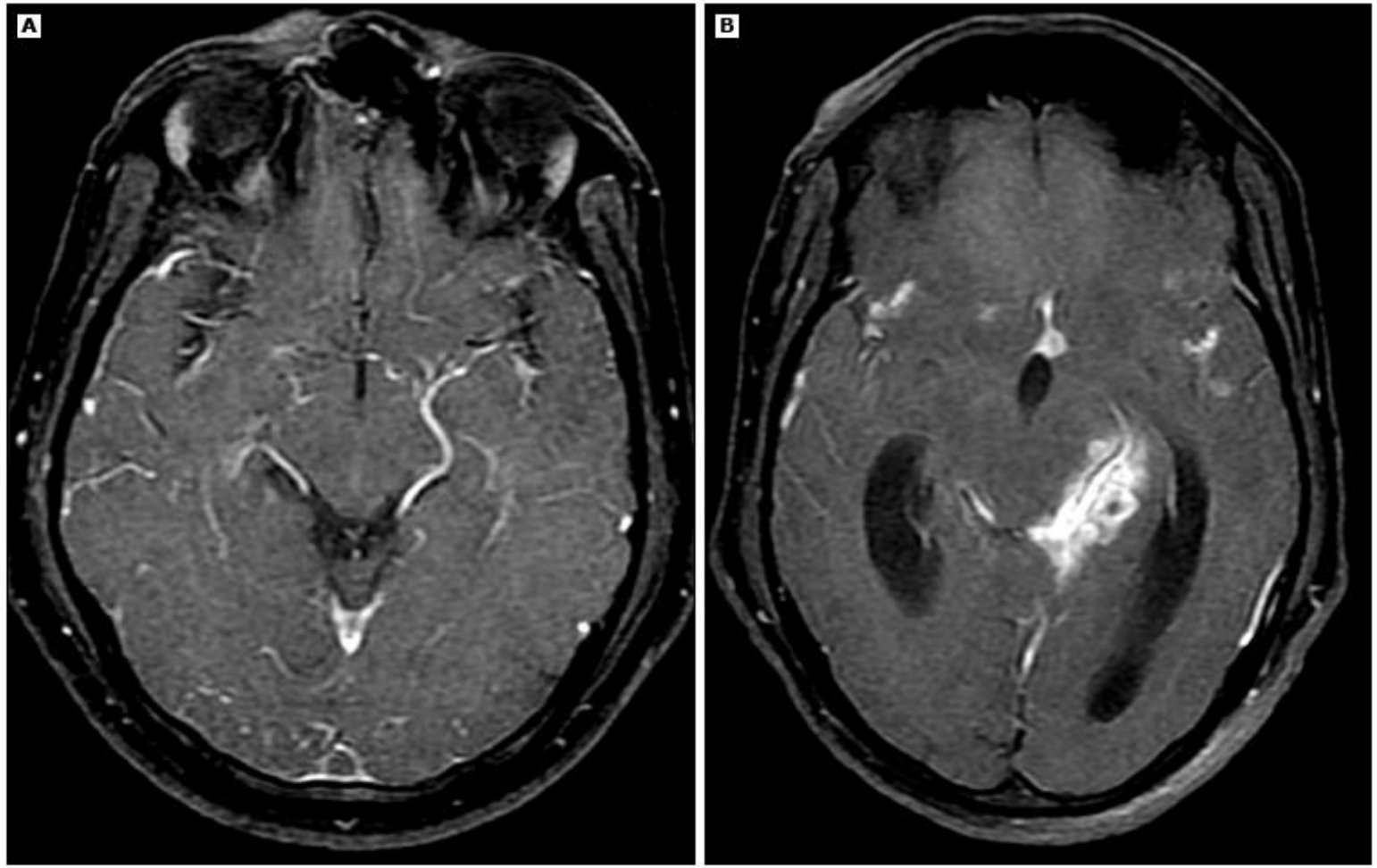
РЕЗИДУАЛЬНЫЙ ПЕРИОД

CENTRAL NERVOUS SYSTEM TUBERCULOSIS

FORMS OF CENTRAL NERVOUS SYSTEM (CNS) INFECTION DUE TO MYCOBACTERIUM TUBERCULOSIS INCLUDE

- MENINGITIS,
- TUBERCULOMA, AND
- SPINAL ARACHNOIDITIS.

Tuberculous meningitis paradoxical reaction



(Panel A) Initial brain magnetic resonance imaging in patient with tuberculous meningitis.

(Panel B) Follow-up imaging 8 weeks after initiation of antituberculous treatment demonstrates paradoxical worsening including hydrocephalus, tuberculoma and exudates in peri-mesencephalic cistern.

UpToDate®

First-line antituberculosis drugs for treatment of CNS tuberculosis: Adult dosing*

Drug	Preparations	Daily dose
Isoniazid¶	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 mL); aqueous solution (100 mg/mL) for intravenous or intramuscular injection	5 mg/kg (usual maximum dose 300 mg)
Rifampin (rifampicin)Δ	Capsules (150 mg, 300 mg); capsule contents may be suspended for oral administration; aqueous solution for intravenous injection	10 mg/kg (usual maximum dose 600 mg)
RifabutinΔ	Capsule (150 mg)	5 mg/kg (usual maximum dose 300 mg)
Pyrazinamide◇	Tablet (500 mg, scored)	Patient weight 40 to 55 kg§: 1000 mg (18.2 to 25 mg/kg)
		Patient weight 56 to 75 kg§: 1500 mg (20 to 26.8 mg/kg)
		Patient weight 76 to 90 kg§¥: 2000 mg‡ (22.2 to 26.3 mg/kg)
Ethambutol†	Tablets (100 mg, 400 mg)	Patient weight 40 to 55 kg§: 800 mg (14.5 to 20 mg/kg)
		Patient weight 56 to 75 kg§: 1200 mg (16 to 21.4 mg/kg)
		Patient weight 76 to 90 kg§: 1600 mg‡ (17.8 to 21.1 mg/kg)

- Adult dosing listed in this table is used in patients ≥15 years old or weighing >40 kg.
- Antituberculous agents are used in multidrug combination regimens of varying duration, which are described in detail in a separate table (refer to the UpToDate table on regimens for treatment of drug-susceptible tuberculosis) and in the accompanying text.

CNS: central nervous system.

* Dosing based on actual weight is acceptable in patients who are not obese. For obese patients (>20% above ideal body weight [IBW]), dosing based on IBW may be preferred for initial doses. Some clinicians prefer a modified IBW (IBW + [0.40 × (actual weight − IBW)]) as is done for initial aminoglycoside doses. Because tuberculosis drug dosing for obese patients has not been established, therapeutic drug monitoring may be considered for such patients.

¶ Pyridoxine (vitamin B6; 25 to 50 mg/day) is given with isoniazid to individuals at risk for neuropathy (eg, pregnant women, breastfeeding infants, and individuals with HIV infection, diabetes, alcoholism, malnutrition, chronic renal failure, or advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.

Δ Rifabutin dose may need to be adjusted when there is concomitant use of protease inhibitors or nonnucleoside reverse transcriptase inhibitors. Refer to the UpToDate topic on treatment of pulmonary tuberculosis in HIV-infected adults for specific dose adjustments.

◇ For patients with creatinine clearance <30 mL/min (by Cockroft-Gault equation) or for patients receiving intermittent hemodialysis, pyrazinamide dosing consists of 25 to 35 mg/kg (ideal body weight) per dose orally 3 times per week (NOT daily); max 2.5 g per dose. On the day of hemodialysis, medications should be administered after hemodialysis. Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption without excessive accumulation and to assist in avoiding toxicity.

§ Based on estimated lean body weight.

¥ Patients >90 kg should have serum concentration monitoring. In obese patients, weight-based dosing is likely best based on measurements of ideal (versus total) body weight.

‡ Maximum dose regardless of weight.

† For patients with creatinine clearance <30 mL/min (by Cockroft-Gault equation) or for patients receiving intermittent hemodialysis, ethambutol dosing consists of 20 to 25 mg/kg (ideal body weight) per dose orally 3 times per week (NOT daily); max 1.6 g per dose. On the day of hemodialysis, medications should be administered after hemodialysis. Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption without excessive accumulation and to assist in avoiding toxicity.

Data adapted from:
1. *Nahid P, Dorman SE, Alipanah N, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of American clinical practice guidelines: Treatment of drug-susceptible tuberculosis. Clin Infect Dis 2016; 63:e147.*
2. *Curry International Tuberculosis Center and California Department of Public Health, 2016: Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, Third Edition.*

CENTRAL NERVOUS SYSTEM TUBERCULOSIS

- PROMPT ANTITUBERCULOUS THERAPY IS ESSENTIAL IN THE TREATMENT OF CENTRAL NERVOUS SYSTEM (CNS) TUBERCULOSIS (TB). BECAUSE OF THE HIGH ASSOCIATED MORTALITY, TREATMENT SHOULD BE INITIATED WHEN THE DIAGNOSIS IS SUSPECTED AND NOT DEFERRED UNTIL A DIAGNOSIS IS ESTABLISHED
- IN GENERAL, TREATMENT OF CNS TB CONSISTS OF AN INTENSIVE PHASE (4 DRUGS ADMINISTERED FOR 2 MONTHS) FOLLOWED BY A CONTINUATION PHASE (2 DRUGS ADMINISTERED FOR AN ADDITIONAL 7 TO 10 MONTHS), FOR A TOTAL TREATMENT DURATION OF 9 TO 12 MONTHS.
- FOR ADULTS, THE INTENSIVE PHASE CONSISTS OF FOUR DRUGS (ISONIAZID, RIFAMPIN, PYRAZINAMIDE, AND ETHAMBUTOL) ADMINISTERED FOR TWO MONTHS. THIS APPROACH IS DERIVED FROM MANAGEMENT OF PULMONARY TB, THE EVIDENCE FOR WHICH IS DISCUSSED SEPARATELY.
- FOR CHILDREN, THE INTENSIVE PHASE CONSISTS OF FOUR DRUGS (ISONIAZID, RIFAMPIN, PYRAZINAMIDE, AND EITHER ETHIONAMIDE OR AN AMINOGLYCOSIDE [IN PLACE OF ETHAMBUTOL, GIVEN DIFFICULTY ASSOCIATED WITH MONITORING FOR ETHAMBUTOL-ASSOCIATED OPTIC NEURITIS]) ADMINISTERED FOR TWO MONTHS.
- •FOR ADULTS AND CHILDREN, THE CONTINUATION PHASE CONSISTS OF 2 DRUGS (ISONIAZID AND RIFAMPIN); WE SUGGEST A DURATION OF 7 TO 10 MONTHS OVER A SHORTER DURATION (**GRADE 2C**).

CENTRAL NERVOUS SYSTEM TUBERCULOSIS

FOR PATIENTS WITH ISONIAZID-RESISTANT CNS TB, WE FAVOR TREATMENT WITH DAILY RIFAMPIN, ETHAMBUTOL, PYRAZINAMIDE, AND A FLUOROQUINOLONE. THIS APPROACH IS DERIVED FROM MANAGEMENT OF DRUG-RESISTANT PULMONARY TB, THE EVIDENCE FOR WHICH IS DISCUSSED SEPARATELY. IN ADDITION, THE DURATION OF THERAPY SHOULD BE EXTENDED TO 18 TO 24 MONTHS, TAKING INTO ACCOUNT THE SEVERITY OF ILLNESS, CLINICAL RESPONSE TO THERAPY, AND THE PATIENT'S IMMUNE STATUS.

CENTRAL NERVOUS SYSTEM TUBERCULOSIS

THE APPROACH TO USE OF GLUCOCORTICOIDS DEPENDS ON THE CLINICAL PRESENTATION:

- FOR PATIENTS WITH ESTABLISHED OR SUSPECTED TUBERCULOUS MENINGITIS IN THE ABSENCE OF HIV INFECTION, WE RECOMMEND ADJUNCTIVE GLUCOCORTICOID THERAPY (GRADE 1A). CLINICAL TRIAL DATA HAVE FOUND THAT SUCH TREATMENT IMPROVES SHORT-TERM SURVIVAL.
- FOR PATIENTS WITH HIV INFECTION, WE ALSO SUGGEST ADJUNCTIVE GLUCOCORTICOID THERAPY (GRADE 2C). DATA SHOWING A SURVIVAL BENEFIT IN PATIENTS WITH HIV INFECTION ARE LIMITED.
- FOR PATIENTS WITH TUBERCULOMA, WE SUGGEST ADJUNCTIVE GLUCOCORTICOID THERAPY FOR PATIENTS WITH CEREBRAL **EDEMA** (PARTICULARLY WHEN EDEMA IS OUT OF PROPORTION TO MASS EFFECT IN THE SETTING OF ASSOCIATED ALTERED MENTAL STATUS OR FOCAL NEUROLOGIC DEFICITS), AND/OR **ELEVATED INTRACRANIAL PRESSURE** (GRADE 2C).
- FOR PATIENTS WITH SPINAL ARACHNOIDITIS, WE SUGGEST ADJUNCTIVE GLUCOCORTICOID THERAPY FOR PATIENTS WITH SPINAL BLOCK (CEREBROSPINAL FLUID PROTEIN ≥500 MG/DL) AND/OR PATIENTS WITH ACUTE CORD COMPRESSION (GRADE 2C).

Sigfrid *et al. BMC Medicine* (2019) 17:170
https://doi.org/10.1186/s12916-019-1387-5

BMC Medicine

RESEARCH ARTICLE Open Access

A systematic review of clinical guidelines on the management of acute, community-acquired CNS infections

Louise Sigfrid[1*†], Chelsea Perfect[2†], Amanda Rojek[1], Kajsa-Stina Longuere[3], Sam Lipworth[4], Eli Harriss[5], James Lee[1], Alex Salam[6], Gail Carson[1], Herman Goossens[7] and Peter Horby[1]

Abstract

Background: The epidemiology of CNS infections in Europe is dynamic, requiring that clinicians have access to up-to-date clinical management guidelines (CMGs) to aid identification of emerging infections and for improving quality and a degree of standardisation in diagnostic and clinical management practices. This paper presents a systematic review of CMGs for community-acquired CNS infections in Europe.

Methods: A systematic review. Databases were searched from October 2004 to January 2019, supplemented by an electronic survey distributed to 115 clinicians in 33 European countries through the CLIN-Net clinical network of the COMBACTE-Net Innovative Medicines Initiative. Two reviewers screened records for inclusion, extracted data and assessed the quality using the AGREE II tool.