

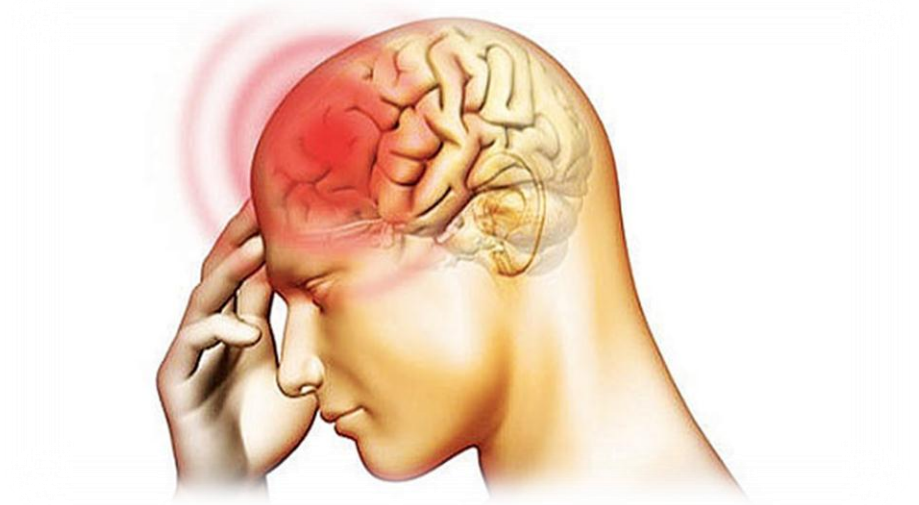
CNS 1NFECTION1ONS

WHAT 1S NEW?

By GÜ1řah IKRIKI IřIK, M.D.

5th International Critical Care and Emergency Medicine Congress

ANTALYA-2018

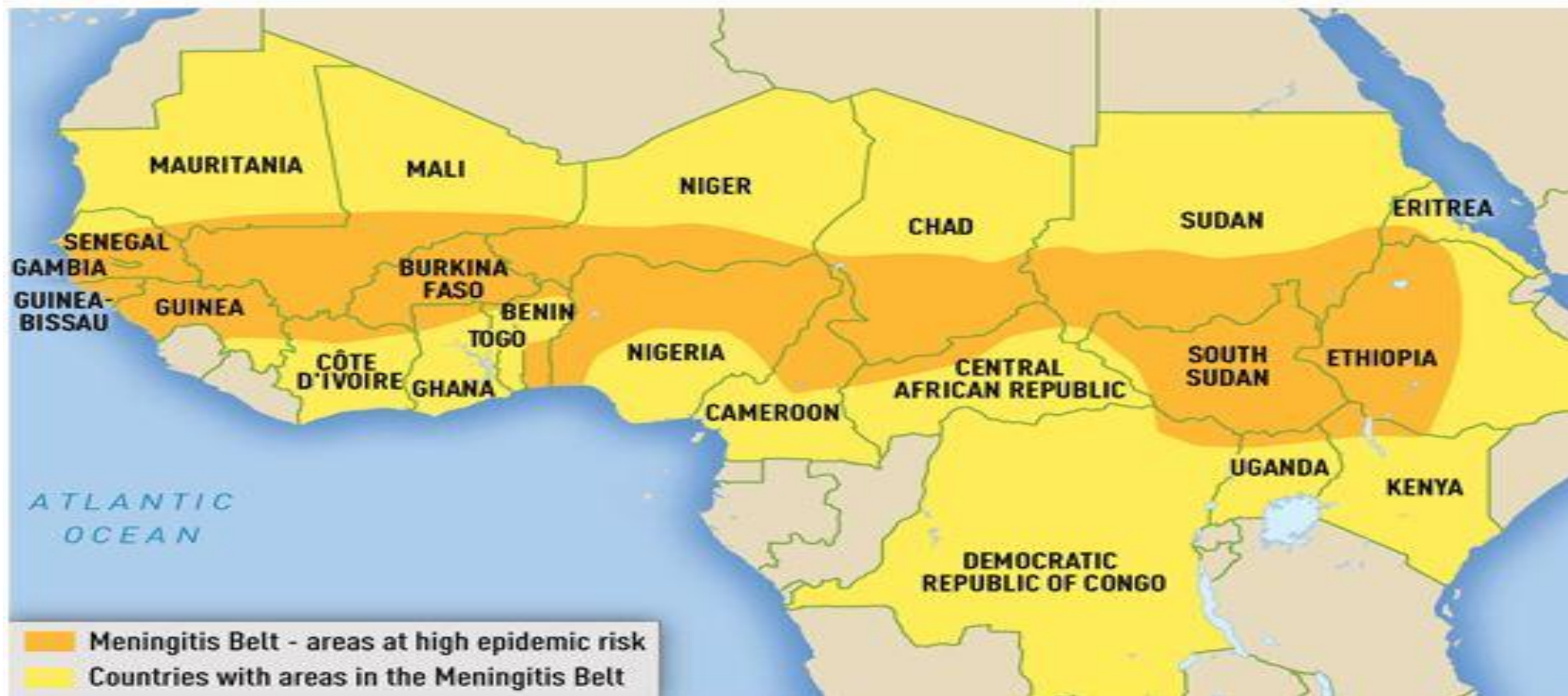


MENINGITIS ?

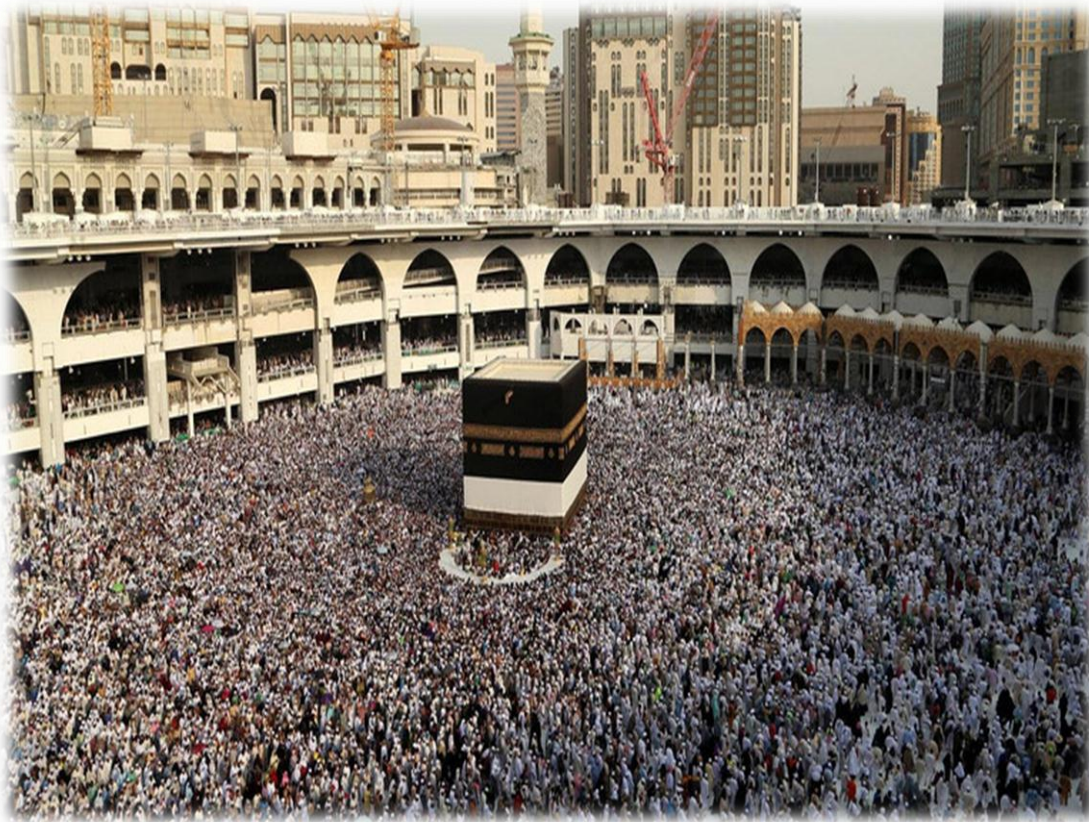


- Meningitis is an inflammation of the meninges, the membranes covering the brain and spinal cord.
- It can be caused by variety of organisms that include bacteria, fungi and viruses.

Map 3-11. Areas with frequent epidemics of meningococcal meningitis



IS MENINGITIS JUST A PROBLEM FOR AFRICA?



- **Meningococcal disease during the Hajj and Umrah mass gatherings.²**

- The pilgrimages have been associated with a number of local and international outbreaks of meningococcal disease.
 - Serogroup A disease outbreaks in 1987 and throughout the 1990s
 - Serogroup W135 outbreaks in 2000 and 2001

1. <http://english.alarabiya.net/en/News/middle-east/2016/09/16/Saudi-Arabia-recorded-least-number-of-Hajj-pilgrims-this-year.html>

2. Meningococcal disease during the Hajj and Umrah mass gatherings. Int J Infect Dis. 2016 Jun;47:60-4.

IS MENENGITIS JUST A PROBLEM FOR AFRICA?



- **Immigration₂**

- Paediatric tuberculosis cases increased in Stockholm from 1971 to 2015 following the rising number of children with immigrant backgrounds.
 - 2001 to 2015, 79% of cases, or at least one parent, were born in high-incidence countries.
 - The incidence in this group was **35** per 100 000, but remained at 0.9 per 100 000 in other children

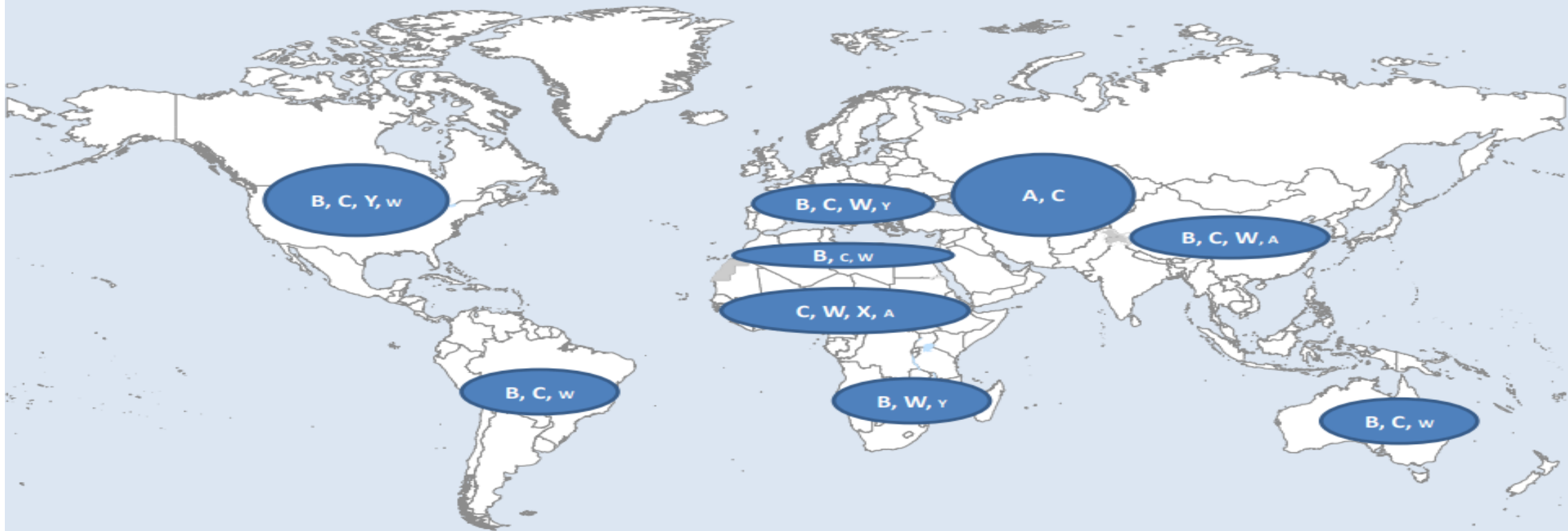
1. <http://www.yesmagazine.org/peace-justice/call-for-submissions-sanctuary-communities>

2. Paediatric tuberculosis cases increased in Stockholm from 1971 to 2015 following the rising number of children with immigrant backgrounds. Acta Paediatr. 2016 Dec;105(12):1480-1486.

Invasive Meningococcal Disease – Serogroup distribution, 2018



Map date: 16/02/2018



SEROGROUP Most frequent
SEROGROUP Less frequent

Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

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CLINICAL PRESENTATION

SIGNS AND SYMPTOMS OF **MENINGITIS**



- Are they specific?

Patients without meningitis

- Headache (81%)
- Fever (67%)
- n&v (53%)
- Photophobia (51%)
- Stiff neck (45%)
- Focal symptoms/seizure (21%)

Patients with meningitis

- Headache (92%)
- Fever (71%)
- n&v (70%)
- Photophobia (57%)
- Stiff neck (48%)
- Focal symptoms/seizure (18%)

1. <http://www.millenniumfamilypractice.com/meningitis-what-is-it/>

2. The Diagnostic Accuracy of Kernig's Sign, Brudzinski's Sign, and Nuchal Rigidity in Adults with Suspected Meningitis, Clinical Infectious Diseases 2002; 35:46–52

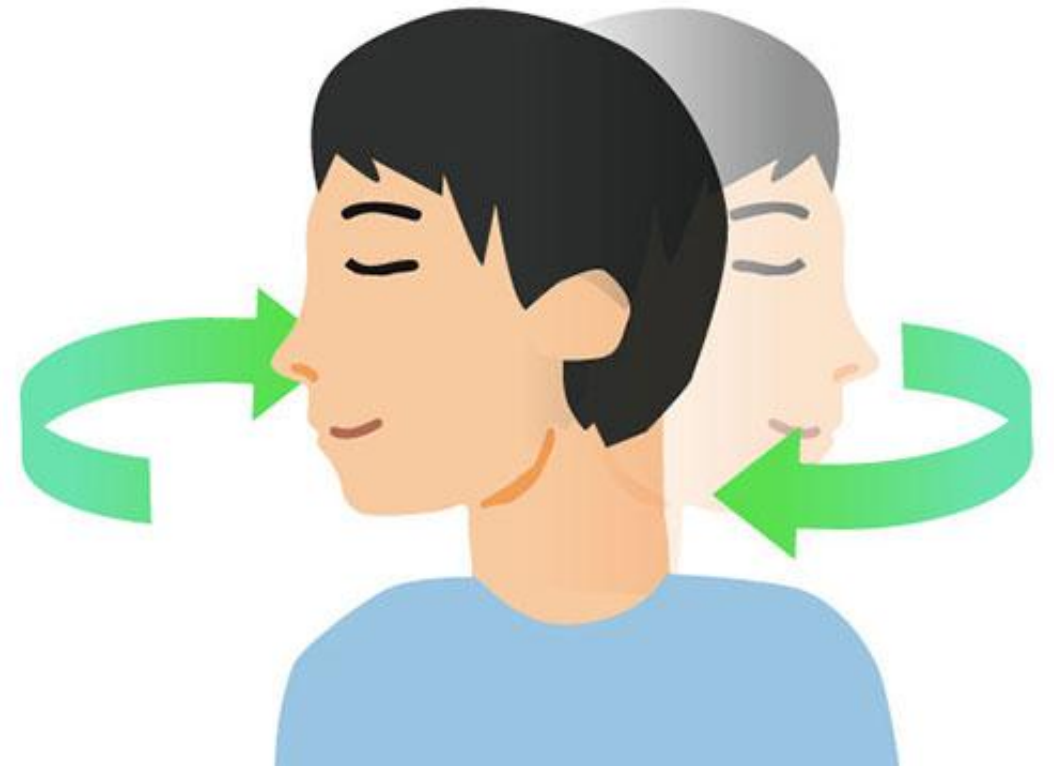
SIGNS OF MENINGITIS

Patients without meningitis

- Temperature $>38^{\circ}\text{C}$ (52%)
- Neck stiffness (32%)
- Kernig's sign (5%)
- Brudzinski's sign (5%)
- GCS <13 (7%)
- Mean wbc in CSF 1

Patients with meningitis

- Temperature $>38^{\circ}\text{C}$ (43%)
- Neck stiffness (30%)
- Kernig's sign (5%)
- Brudzinski's sign (5%)
- GCS <13 (10%)
- Mean wbc in CSF 359



SKIN RASHES



MENINGITIS



NOT MENINGITIS



Take a glass and apply it to the rash. Press it firmly against your skin until it goes totally pale.

- If those spots on your skin become white the person doesn't have meningitis
- If that rash stays the same, then you should immediately go see your doctor

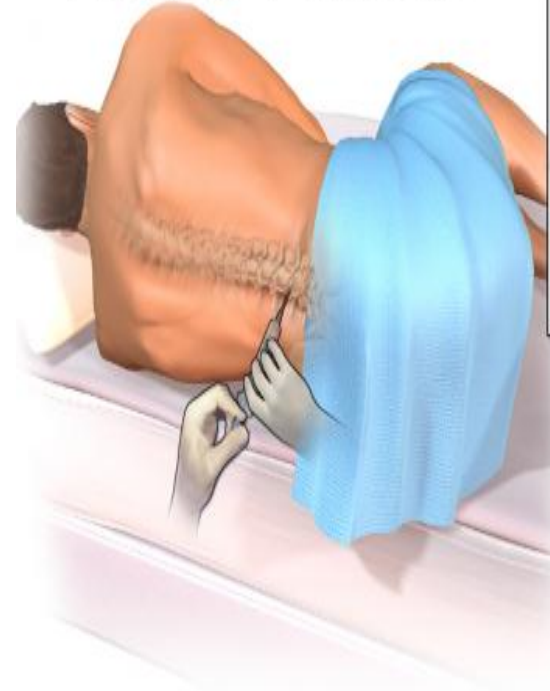
DIAGNOSIS= LP

- **2004 Infectious Diseases Society of America (IDSA) guidelines**

- 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

CT scan of the head before LP should be performed

Lumbar Puncture



Lying Position



Sitting Position

Lumbar Puncture Performed Promptly or After Neuroimaging in Acute Bacterial Meningitis in Adults: A Prospective National Cohort Study Evaluating Different Guidelines.

Glimåker M^{1,2}, Sjölin J³, Åkesson S^{1,2}, Naucle P^{1,2}.

⊕ Author information

Abstract

BACKGROUND: Early treatment is pivotal for favorable outcome in acute bacterial meningitis (ABM). Lumbar puncture (LP) is the diagnostic key. The aim was to evaluate the effect on outcome of adherence to European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Infectious Diseases Society of America (IDSA), and Swedish guidelines regarding neuroimaging before LP.

METHODS: The cohort comprised 815 adult ABM patients in Sweden registered prospectively between 2008 and 2015. Primary endpoint was in-hospital mortality and secondary endpoint was favorable outcome at 2-6 months of follow-up.

RESULTS: Indications for neuroimaging before LP existed in 7%, 32%, and 65% according to Swedish, ESCMID, and IDSA guidelines, respectively. The adjusted odds ratio (aOR) was 0.48 (95% confidence interval [CI], .26-.89) for mortality and 1.52 (95% CI, 1.08-2.12) for favorable outcome if Swedish guidelines were followed. ESCMID guideline adherence resulted in aOR of 0.68 (95% CI, .38-1.23) for mortality and 1.05 (95% CI, .75-1.47) for favorable outcome. Following IDSA recommendations resulted in aOR of 1.09 (95% CI, .61-1.95) for mortality and 0.59 (95% CI, .42-.82) for favorable outcome. Performing prompt vs neuroimaging-preceded LP was associated with aOR of 0.38 (95% CI, .18-.77) for mortality and 2.11 (95% CI, 1.47-3.00) for favorable outcome. The beneficial effect of prompt LP was observed regardless of mental status and immunosuppression.

CONCLUSIONS: Adherence to Swedish guidelines in ABM is associated with decreased mortality and increased favorable outcome in contrast to adherence to ESCMID or IDSA recommendations. Our findings support that impaired mental status and immunocompromised state should not be considered indications for neuroimaging before LP in patients with suspected ABM.

- **CSF should be sent for**
 - Cell count and differential
 - Glucose concentration
 - Protein concentraion
 - Gram stain and bacterial culture
 - Other appropriate tests

	Normal	Bacterial	Viral	Fungal/TB
Pressure (cmH20)	5-20	> 30	Normal or mildly increased	
Appearance	Normal	Turbid	Clear	Fibrin web
Protein (g/L)	0.18-0.45	> 1	< 1	0.1-0.5
Glucose (mmol/L)	2.5-3.5	<2.2	Normal	1.6-2.5
Gram stain	Normal	60-90% Positive	Normal	
Glucose - CSF:Serum Ratio	0.6	< 0.4	> 0.6	< 0.4
WCC	< 3	> 500	< 1000	100-500
Other		90% PMN	Monocytes 10% have >90% PMN 30% have >50% PMN	Monocytes

CSF LACTATE LEVELS

[Infect Dis \(Lond\)](#). 2018 Feb 28;1-8. doi: 10.1080/23744235.2018.1441539. [Epub ahead of print]

Cerebrospinal fluid lactate as a marker to differentiate between community-acquired acute bacterial meningitis and aseptic meningitis/encephalitis in adults: a Danish prospective observational cohort study.

[Buch K](#)¹, [Bodilsen J](#)², [Knudsen A](#)¹, [Larsen L](#)³, [Helweg-Larsen J](#)⁴, [Storgaard M](#)⁵, [Brandt C](#)⁶, [Wiese L](#)⁷, [Østergaard C](#)⁸, [Nielsen H](#)², [Lebech AM](#)¹; [Danish Study Group for Infections in the Brain](#).

⊕ Author information

Abstract

BACKGROUND: The ability of cerebrospinal fluid (CSF) lactate to distinguish between acute bacterial meningitis (ABM) and aseptic meningitis/encephalitis (AME) is debated. We assessed the diagnostic value of CSF lactate to discriminate between ABM and AME.

METHODS: We included 176 patients from a prospective adult cohort with neuroinfections. In total, 51 ABM and 125 AME patients with clinically and/or microbiologically diagnosed acute meningitis were examined with CSF-lactate and traditional markers for infection. Receiver operating characteristic (ROC) curves were used to assess diagnostic performance.

RESULTS: In CSF, lactate, leukocytes, fraction of neutrophils, protein and glucose ratio, were significantly different between the ABM and AME groups. CSF lactate had the best diagnostic value, with an area under the curve (AUC) of 0.976 (95%CI 0.966-0.997) and using a cut-off of 3.5 mmol/L a sensitivity of 96% and specificity of 85%. Antibiotic treatment before lumbar puncture had no significant effect on the AUC of CSF lactate.

CONCLUSIONS: Compared to traditional CSF-markers, CSF lactate is more accurate to distinguish between ABM and AME.

TREATMENT

- Don't DELAY!



- Time to antibiotic therapy and outcome in bacterial meningitis: a Danish population-based cohort study.
 - The median door-to-antibiotic time was 2.0 h (interquartile range (IQR) 1.0-5.5). We observed **increased adjusted risk ratios** for in-hospital mortality of 1.6 (95 % CI 0.8-3.2) and an unfavourable outcome at discharge of 1.5 (95 % CI 1.0-2.2, $p=0.03$) **when treatment delays exceeded 6 h versus treatment within 2 h of admission**
 - Delay in antibiotic therapy was associated with unfavourable outcome at discharge

1. <https://teamarin.net/2015/05/18/3-reasons-not-to-delay-your-ipv6-deployment/>

2. Time to antibiotic therapy and outcome in bacterial meningitis: a Danish population-based cohort study. BMC Infect Dis. 2016 Aug 9;16:392

CHOICE OF REGIMEN

- **Antimicrobial selection must be empiric**

- immediately after CSF is obtained
- or when lumbar puncture is delayed
- directed toward the most likely pathogens and should be adjusted by patient age and risk factors

Age or Predisposing Feature	Antibiotics
Age 0-4 wk	Ampicillin plus either cefotaxime or an aminoglycoside
Age 1 mo-50 y	Vancomycin plus cefotaxime or ceftriaxone
Age >50 y	Vancomycin plus ampicillin plus ceftriaxone or cefotaxime plus vancomycin
Impaired cellular immunity	Vancomycin plus ampicillin plus either cefepime or meropenem
Recurrent meningitis	Vancomycin plus cefotaxime or ceftriaxone
Basilar skull fracture	Vancomycin plus cefotaxime or ceftriaxone
Head trauma, neurosurgery, or CSF shunt	Vancomycin plus ceftazidime, cefepime, or meropenem

ADJUNCTIVE DEXAMETHASONE

Childs Nerv Syst. 2018 Feb;34(2):217-223. doi: 10.1007/s00381-017-3667-8. Epub 2017 Nov 29.

Meta-analysis of adjunctive dexamethasone to improve clinical outcome of bacterial meningitis in children.

Wang Y^{1,2}, Liu X³, Wang Y³, Liu Q⁴, Kong C⁵, Xu G⁶.

⊕ Author information

Erratum in

Correction to: Meta-analysis of adjunctive dexamethasone to improve clinical outcome of bacterial meningitis in children.

Abstract

BACKGROUND: The current recommended therapies for bacterial meningitis are based on childhood vaccination programs. However, the role of adjunctive dexamethasone remains unclear.

METHODS: Using meta-analysis, this study aims to investigate the effect of adjunctive dexamethasone compared with antibiotic therapy. Documents of randomized controlled trials (RCT) related to the treatment of bacterial meningitis in children with dexamethasone published since the establishment of the databases to December in 2016 were retrieved from the databases of Cochrane Library, Pubmed, MEDLINE, EMBASE, Chinese BioMedical Literature Database, and China National Knowledge Infrastructure. The references in RCT were retrieved by hands at the same time. Full texts of screened documents were searched and given qualitative review, and then, all RCT included were analyzed statistically by using Review Manager 5.3 software.

RESULTS: The search yielded 15 studies (2409 children cases), among which 4 fall in grade A and 11 were grade B. The results of meta-analysis have shown that patients who received dexamethasone have significantly lower risks in incidence of hearing loss (OR = 0.68, 95%CI 0.53-0.89, P = 0.004) and severe neurological sequelae (OR = 0.59, 95%CI 0.37-0.95, P = 0.03), but the follow-up mortality is hardly effected (OR = 0.86, 95%CI 0.67-1.10, P = 0.23).

CONCLUSIONS: Evidence has proven that the adjunctive administration of dexamethasone is conducive to treating children with bacterial meningitis to a certain extent, to decreasing the possibility of hearing loss and severe neurological sequelae, but has no significant effect on the follow-up mortality.

Dexamethasone **0.15mg/kg every 6 hours for 4 days** started with first dose of antibiotics especially if pneumococcal meningitis is suspected; stop if non-bacterial cause is identified

PROTEIN C CONCENTRATE

Thromb Res. 2014 Jul;134(1):63-7. doi: 10.1016/j.thromres.2014.04.019. Epub 2014 Apr 29.

Non-activated plasma-derived PC improves amputation rate of children undergoing sepsis.

Piccin A¹, O' Marcaigh A², Mc Mahon C², Murphy C³, Okafor I², Marcheselli L⁴, Casey W⁵, Claffey L⁶, Smith OP⁷

⊕ Author information

Abstract

Low circulating protein C (PC) levels have been observed in sepsis, especially in paediatric patients. Low PC levels are associated with poor clinical outcome and high limb amputation rates have been associated in infected patients. Using activated PC replacement therapy patients with sepsis have shown reduced mortality and fewer severe bleeding events. Paediatric sepsis studies using non-activated plasma-derived PC have been limited. We conducted a retrospective study in children with sepsis who were treated with Ceprotrin® focusing on the amputation rate. Median age at diagnosis was 2 years. Twenty-one (70%) were treated for meningococcal sepsis, another 8 (26%) patients with malignancies were treated for neutrophilic sepsis. There was a significant increase in leukocyte count ($p=0.004$), neutrophil count ($p=0.001$) and PC levels ($p=0.001$) were seen. Prothrombin time (pretreatment =30.3 seconds, posttreatment =16.5; $p=0.001$) and activated partial thromboplastin time (pretreatment =61.8 sec, posttreatment =42.6 sec; $p=0.000$) were significantly reduced. Fibrinogen levels (pretreatment =1.9 g/dL, posttreatment =4.4 g/dL; $p=0.000$). The median time between admission to intensive care and Ceprotrin® administration was 10 hrs. Limb amputation rate was reduced (16-23% versus 30-50% from previous studies) and there were no haemorrhagic events observed. This study demonstrates the safe administration of non-activated plasma-derived PC concentrate in patients with sepsis who are coagulopathic and it associated with a reduction in amputation rates.

Protein C concentrate has been approved by the **US Food and Drug Administration for use intravenously in severe sepsis**. Suggested dose is:

100 to 120 international units/kg initially

followed every six hours for three subsequent doses of **60 to 80** international units/kg.

PREVENTION

[Hum Vaccin Immunother.](#) 2018 Jan 2;14(1):209-212. doi: 10.1080/21645515.2017.1377380. Epub 2017 Dec 11.

Neisseria meningitidis Serogroup X ST-5799 (ST-22 complex) in Turkey: A unique pediatric case.

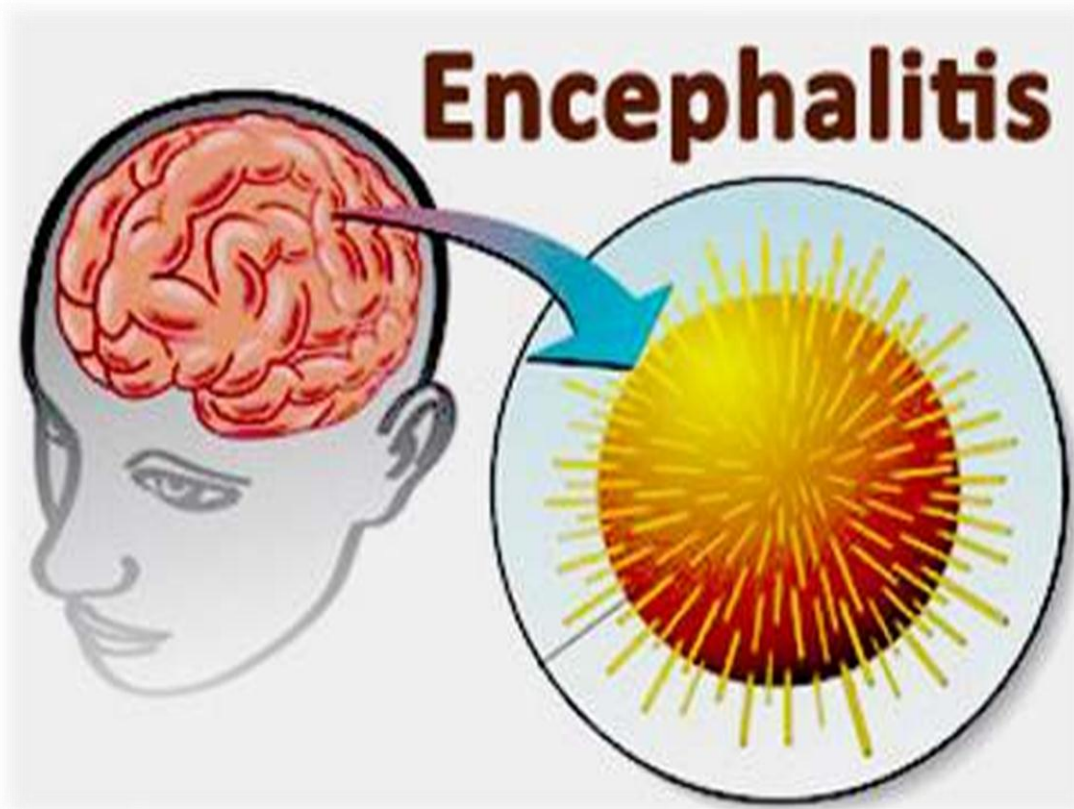
[Tanır G¹](#), [Ozsarekci Y²](#), [Lucidarme J³](#), [Yaşar Durmuş S¹](#), [Lekshmi A³](#), [Akisoglu Ö⁴](#), [Aycan AE²](#), [Borrow R³](#), [Ceyhan M²](#).

⊕ Author information

Abstract

Although outbreaks of *Neisseria meningitidis* serogroup X occurred in a couple of African countries, a limited number of serogroup X meningococcal cases were reported in America and Europe as well as Turkey. Additionally, serogroup X is still not represented in current conjugated meningococcal vaccines. Here, we describe the first pediatric case with meningitis caused by *Neisseria meningitidis* serogroup X ST-5799 (ST-22 complex) that formed a distinct lineage.

ENCEPHALITIS



- Encephalitis is inflammation of the brain.
- There are several causes, but the most common is **viral infection**.
 - One review demonstrated that viruses were recovered from only 6 percent of 22,394 viral cultures of CSF samples.
 - When nucleic acid amplification testing is performed, viral culture may have no additional benefit ⁽²⁾

1. <http://www.assignmentpoint.com/science/medical/encephalitis.html>

2. Assessment of the utility of viral culture of cerebrospinal fluid. Clin Infect Dis. 2006 Dec 15;43(12):1578-9

Review of Viral Encephalitis Cases Seen at a Tertiary Care Center in Turkey: Focus on Herpes Simplex Type 1.

Çiftçi Kavaklıoğlu B¹, Çoban E¹, Şen A¹, Söylemezoğlu E¹, Aldan MA¹, Atakli R¹, Çiğdem S¹

➕ Author information

Abstract

INTRODUCTION: The objective of this study was to determine the incidence of viral encephalitis, a common, potentially mortal, and treatable cause of sporadic encephalitis.

METHODS: The demographic, clinical, laboratory, imaging, electrophysiology, and polymerase chain reaction (PCR) DNA results of patients examined with a pre-diagnosis of encephalitis were retrospectively examined.

RESULTS: A total of 68 patients were included in the study. The most common presenting symptom was altered behavior (67.6%), while temporal T2 hyperintensity was determined in the magnetic resonance imaging (MRI) of 27.9% of the patients and electroencephalography (EEG) abnormalities were determined in 66.2% of the patients. Lymphocytic pleocytosis was determined in the cerebrospinal fluid (CSF) in 35 patients. Fifty-seven patients had been diagnosed with viral encephalitis, 3 with bacterial meningitis, 3 with tuberculous meningitis, 2 with sporadic Creutzfeld-Jakob disease, 2 with acute disseminating encephalomyelitis, and 1 with Brucella encephalitis. Seven (10.2%) cases of viral encephalitis were found to be positive for herpes simplex virus (HSV) DNA by PCR.

CONCLUSION: Viral encephalitis is the most common cause of infectious encephalitis; however, other atypical causes should also be noted. Negative PCR results for HSV DNA should not exclude the need for antiviral therapy in patients with a strong pre-diagnosis of HSE because diagnostic modalities, including PCR, may fail in acute settings and HSE remains the sole treatable cause of infectious encephalitis.

Grade 1A RECOMANDATION:
Rapid initiation of **acyclovir** 10 mg/kg three times daily intravenously for empiric treatment of HSV ⁽¹⁾

[illegible]