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# Acute Meningitis: Diagnosis, Interpretation, & Controversy

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## 2009 MEMC V Meeting



Valencia, Spain  
16 September 2009

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## Disclosures

- FERNE Executive Board
- FERNE grant support by industry

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## Objectives

- Present a relevant patient case
- Discuss contraindications for lumbar puncture (LP)
- Review the procedure of LP
- Discuss the role of antibiotics , anti-virals, and steroids.

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## A Clinical Case

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## ED Presentation


- 77 yo previously healthy female
- 3 day history of fever, confusion, and lethargy
- Glasgow Coma Scale 13 (E4,V4,M5)
- Key Aspects of Physical Exam:
  - Unable to cooperate with neurological exam, +neck stiffness upon neck flexion

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## Indications for pre-LP head CT scan


Table 2. Recommended criteria for adult patients with suspected bacterial meningitis who should undergo CT prior to lumbar puncture (B-II).

Criterion	Comment
Immunocompromised state	HIV infection or AIDS, receiving immunosuppressive therapy, or after transplantation
History of CNS disease	Mass lesion, stroke, or focal infection
New onset seizure	Within 1 week of presentation; some authorities would not perform a lumbar puncture on patients with prolonged seizures or would delay lumbar puncture for 30 min in patients with short, convulsive seizures
Papilledema	Presence of venous pulsations suggests absence of increased intracranial pressure
Abnormal level of consciousness	---
Focal neurologic deficit	Including dilated nonreactive pupil, abnormalities of ocular motility, abnormal visual fields, gaze palsy, arm or leg drift


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## Contraindications


- Skin infection near site of LP
- Suspicion of increased intracranial pressure due to cerebral mass
- Uncorrected coagulopathy
- Acute spinal cord trauma

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## Positioning



INCORRECT




CORRECT

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### Predicting difficult and traumatic lumbar punctures.


**The American Journal of Emergency Medicine**  
 2007, Volume 25, Issue 6, Pages 608-611  
 K. Shah, D. McGillicuddy, J. Spear, J. Edlow

- Difficult LP
  - Requires 3 or more needle sticks or attempt by another clinician
- Spine visibility
  - Ability to see the contour of the spinous processes
- Spine palpability
  - Ability to palpate distinct spinous processes

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### Comparison of Clinical Groups

	Difficult	Traumatic
• Spine visible	20.0	8.6
• Spine not visible	42.0	21.8
• Spine palpable	26.7	12.4
• Spine not palpable	44.2	23.3
• BMI > 30	42.1	18.4
• BMI < 30	28.2	14.6
• Age >65	42.9	14.3
• Age <65	29.9	15.8

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## Ultrasound Assisted Lumbar Puncture

- 46 patients
  - 22 Palpation Landmarks (PL)
  - 24 Ultrasound Landmarks (UL)
- Failure Rates
  - 6/22 PLs
  - 1/24 ULs
- Obese Patients
  - 4/7 failed PLs
  - 0/5 failed ULs

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Nomura JT, et al. A randomized controlled trial of ultrasound-assisted lumbar puncture. J Ultrasound Med. 2007 ; 26(10):1341-8

## Understanding Opening Pressures

- Normal: 60-200 mm H<sub>2</sub>O (obese patients up to 250mm H<sub>2</sub>O)
- Elevated: Suggest increased intracranial pressures (>250 mm H<sub>2</sub>O)
  - Mass lesion (neoplasm, hemorrhage, infection)
  - Overproduction of CSF
  - Defective Outflow Mechanics

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## CSF Composition

- Color
  - Clear and colorless
  - Turbid
    - 200 WBCs or 400 RBCs
  - Grossly Bloody
    - 6000 RBCs

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## CSF Composition

- Cells
  - Acellular ( up to 5 WBCs and 5 RBCs)
  - More than 3 polymorphonuclear leukocytes (PMNs) abnormal

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## CSF Pleocytosis

- CSF pleocytosis
  - 10 white blood cells/ $\mu$ L, corrected for CSF red blood cells using a ratio of 1 WBC per 500 RBCs

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## Calculating Predicted CSF WBC count

Predicted CSF WBC count/ $\mu$ L =

CSF RBC count X (peripheral blood WBC count  $\div$  peripheral RBC count)

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## Validation of Prediction Calculation in Adults

- 720 patients
  - CSF WBC count >10X predicted value
    - Positive Predictive Value 48% for Bacterial Meningitis
  - CSF WBC count < 10X predicted value
    - Negative Predictive Value 99% for meningitis

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## Validation of Prediction Calculation in Children

- 92 children
  - CSF WBC count >10X predicted value
    - 28/30 children (93%) bacterial meningitis
- 57 children
  - CSF WBC count < 10X predicted
    - 100% for predicting the absence of meningitis

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## CSF Composition

- Protein
  - Largely excluded from CSF by blood-CSF barrier
  - Normal range (adults) 23-38 mg/dL
  - False elevation
    - Diabetes, Presence of RBCS
  - True elevation
    - Infectious and Noninfectious Conditions

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## CSF Composition

- Glucose
  - CSF-to-serum glucose ratio
    - Normal 0.6
  - Low CSF glucose concentrations
    - Bacterial meningitis
    - Mycobacterial and Fungal CNS infections
    - M. pneumoniae and Noninfectious processes
    - Less than 18 mg/dL strongly predictive of bacterial meningitis

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## CSF Composition

- Glucose
  - CSF-to-serum glucose ratio
    - Limited utility in Neonates, and severe hyperglycemia
  - Normal CSF glucose concentrations
    - Viral CNS infections
    - Exceptions:
      - mumps, enteroviruses, lymphocytic choriomeningitis(LCM), herpes simplex

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## CSF Composition


- Lactate
  - Elevated in bacterial meningitis
  - One study higher sensitivity and specificity than blood glucose ratio

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## CSF in CNS Infection

- **Bacterial Meningitis**
  - CSF WBC > 1000/microL ( with PMNs )
  - CSF Protein >250 mg/dL
  - CSF Glucose < 45 mg/dL (2.5 mmol/L)
  - CSF-blood glucose ratio 0.4 or less (LR 18)
  - CSF Lactate >31.53 mg/dL(3.5 mmol/L)

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## CSF in CNS Infection

- **Viral Meningitis**
  - CSF WBC < 250 /microL ( with lymphocytes )
  - CSF Protein <150 mg/dL
  - CSF Glucose more than 50% of serum concentration

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## Summary of Typical CSF Findings

	Normal	Bacterial	Viral	Fungal
Opening Pressure	<170 mm	>300	200	300
Cells	0-5	>1000	<1000	< 500
Polymorphs	0	Predominate	Early	+/- increased
Lymphocytes	5	Late	Predominate	Increased
Glucose	60-80	<40	>40	<40
CSF plasma: Glucose ratio	66%	<40%	Normal	< 30%
Protein	5-40	Increased >200	+/- Increased <200	Increased >200
Culture	Negative	Positive	Negative	Positive

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## Organisms

- < 3 months
  - *E.Coli* , *Listeria*, *Streptococci*
- 3 months- 18 yrs
  - *N. meningitidis*, *H. influenzae*, *S. pneumoniae*
- 18yrs – 50 yrs.
  - *N. meningitidis*, *S. pneumoniae*
- > 50 yrs.
  - *S. pneumoniae*, *Listeria*, *gram-negative bacilli*

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## Antibiotic Choices (Recommendations)

- **Good CNS penetration**
  - Ceftriaxone
  - Cefotaxime
  - Vancomycin (controversial in children)
- **Listeria (young, old, immunosuppressed)**
  - Add high-dose ampicillin
- **PCN or Cephalosporin Allergy**
  - Meropenem or Chloramphenicol + Vancomycin

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# PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## Early Vancomycin Therapy and Adverse Outcomes in Children With Pneumococcal Meningitis


*PEDIATRICS* Vol. 117 No. 5 May 2006, pp. 1688-1694

- Associated with a substantially increased risk of hearing loss.
- Recommend delaying the first dose of vancomycin therapy until 2 hours after the first dose of parenteral cephalosporin


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## Antivirals & Meningitis

- Viruses
  - Arbovirus
  - Herpes Simplex \*
  - Cytomegalovirus
  - Adenovirus
  - HIV
  - \* Protracted course (Acyclovir 10mg/kg IV Q8 hours)

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## Controversy Steroid Use In Bacterial Meningitis

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## Steroids & Meningitis

European Journal of Neurology 2009, 16: 662-673 doi:10.1111/j.1468-1331.2009.02615.x

REVIEW ARTICLE

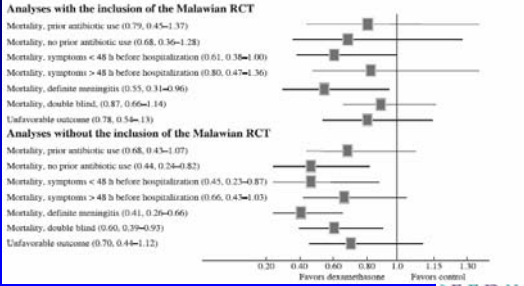
Adjunctive dexamethasone therapy for bacterial meningitis in adults: a meta-analysis of randomized controlled trials

K. Z. Vardakas<sup>a</sup>, D. K. Matthaiou<sup>a</sup> and M. E. Falagas<sup>a,b</sup>

<sup>a</sup>Alfa Institute of Biomedical Sciences (AIBS), Athens, Greece; and <sup>b</sup>Department of Medicine, Tufts University School of Medicine, Boston, MA, USA

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## Meta-Analysis & Malawian RCT




**Analyses with the inclusion of the Malawian RCT**

- Mortality, prior antibiotic use (0.79, 0.45-1.37)
- Mortality, no prior antibiotic use (0.68, 0.36-1.28)
- Mortality, symptoms < 48 h before hospitalization (0.61, 0.36-1.00)
- Mortality, symptoms > 48 h before hospitalization (0.80, 0.47-1.36)
- Mortality, definite meningitis (0.55, 0.31-0.96)
- Mortality, double blind, (0.87, 0.66-1.14)
- Unfavorable outcome (0.78, 0.54-1.13)


**Analyses without the inclusion of the Malawian RCT**

- Mortality, prior antibiotic use (0.68, 0.43-1.07)
- Mortality, no prior antibiotic use (0.44, 0.24-0.82)
- Mortality, symptoms < 48 h before hospitalization (0.45, 0.23-0.87)
- Mortality, symptoms > 48 h before hospitalization (0.66, 0.43-1.03)
- Mortality, definite meningitis (0.41, 0.26-0.66)
- Mortality, double blind (0.60, 0.39-0.93)
- Unfavorable outcome (0.70, 0.44-1.12)

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## Meta-Analysis Results

- Treatment with Dexamethasone Benefits:
  - Lower mortality than Placebo (non-significant OR= 0.58)
  - Lower mortality with definite meningitis (OR=0.55)
  - Shorter duration of symptoms (OR=0.61)
  - *Streptococcus Pneumoniae* meningitis (OR=0.26)

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## Meta-Analysis Conclusions

- Treatment with Dexamethasone
  - Did not decrease mortality in all patients
  - Beneficial in the following groups
    - Early presentation (< 48 hours)
    - Definite meningitis
    - *Streptococcus Pneumoniae* meningitis
    - Countries with medium or high HDI


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ScienceDirect  
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www.em-consulte.com  
MÉDECINE ET MALADIES INFECTIEUSES  
ELSEVIER MASSON  
Medicine et maladies infectieuses 39 (2009) 531–538

Texts of experts  
Corticosteroids for acute adult bacterial meningitis<sup>☆</sup>  
Corticothérapie pour les méningites bactériennes de l'adulte  
D. van de Beek  
Department of Neurology, Care of Infection and Immunity of Amsterdam (CIIMA), Academic Medical Centre, University of Amsterdam, P.O. Box 22700, 1100 Amsterdam, The Netherlands  
Received 15 January 2009; accepted 20 February 2009  
Available online 21 April 2009

- Dexamethasone given before or with 1<sup>st</sup> dose of antibiotics
- No serious adverse effects
- Consistent beneficial effect on mortality and borderline statistical beneficial effect on neurologic sequels

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## Corticosteroids for Acute Bacterial Meningitis

Ann Emerg Med. 2009 Jul;54(1):136-7

To the Editor:

We are writing in response to the systematic review abstract entitled “Corticosteroids for Acute Bacterial Meningitis”

However, we disagree with some of the conclusions:

*Both sets of authors, as a result of the review, advocate corticosteroids for all adults and children with suspected bacterial meningitis. While undoubtedly correct in the era before the H. influenzae vaccine, we feel this recommendation may not be the current best course of action for pediatric patients.*

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## Case Resolution

- CT scan: No mass lesion
  - CSF Results
    - WBC 5000 / $\mu$ L
    - RBC 5 /microL
    - CSF blood glucose ratio 0.2
  - Gram stain: gram positive rods
- Diagnosis: Meningitis due to Listeria

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## Recommendations

- Calculate CSF-blood glucose ratio.
  - 0.4 or less (LR 18) bacterial meningitis
- Determine the predicted CSF WBC count
  - Negative Predictive Value 99% for bacterial meningitis

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## Recommendations

- Do not delay administering antibiotics as delays have been associated with worsening clinical outcomes
- Empiric antibiotic choice is based upon broad spectrum coverage of common pathogens
- Use of dexamethasone has shown benefit in selected cases of adult bacterial meningitis less so in children

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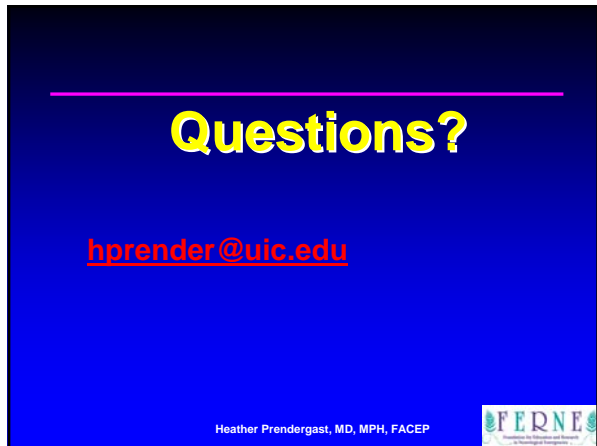


## Conclusions

- Primary indications for LP is to assess for meningitis or subarachnoid hemorrhage
- Most patients do not require CT scan to rule out mass lesions prior to LP
- Clinical examination can guide decision for neuroimaging
- Elevated opening pressures indicate increase intracranial pressures

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**Questions?**

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