ANTIBIOTIC GUIDELINES FOR THE MANAGEMENT OF COMMUNITY-ACQUIRED MENINGITIS AND ENCEPHALITIS IN ADULTS

Version	• 4.0
Date ratified	• February 2009
Review date	• February 2011
Ratified by	• Nottingham Antimicrobial Guidelines Committee • Nottingham University Hospitals Drugs and Therapeutics Committee
Authors	• Dr Richard Lessells updated by Dr I Elliott • Drs Sumeet Singhal and Adrian Wills
Consultation	• Nottingham Antibiotic Guidelines Committee members • Neurologists • Neuroradiologists
Evidence base	• Local microbiological sensitivity surveillance • Recommended best practice based on clinical experience of guideline developers • British Infection Society Guidelines on the early management of patients with suspected bacterial meningitis or meningococcal septicaemia in adults
Changes from previous Guideline	• Addition of chloramphenicol as an alternative treatment for those patients with a history of anaphylaxis to penicillins or rash with cephalosporins
Inclusion criteria	• Immuno-competent adult patients admitted with community acquired meningitis or meningo-encephalitis
Exclusion criteria	Post-operative meningitis, suspected TB meningitis, known or high clinical suspicion of immunospuppression e.g. HIV
Distribution	• This guideline will be available on the Clinical Effectiveness Department Intranet page: http://nuhnet/diagnostics_clinical_support/antibiotics and the City and QMC intranet antibiotics guidelines website: http:www.nuh.nhs.uk/antibiotics • This guideline will be included in the NUH Formulary update
Local contacts	• Dr V Weston Consultant Microbiologist

This guideline has been registered with the Trust.
Clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague. Caution is advised when using guidelines after a review date.

ANTIBIOTIC GUIDELINES FOR THE MANAGEMENT OF COMMUNITY-ACQUIRED MENINGITIS AND ENCEPHALITIS IN ADULTS

The following guidelines have been produced in conjunction with the Infectious Diseases and Microbiology Services and are intended to provide general advice on antimicrobial and adjunctive treatment of community-acquired meningitis and encephalitis in adults.

NB These guidelines are not to be used for the following patients:

- Post-operative meningitis
- Suspected TB meningitis
- Known or high clinical suspicion of immunosupression e.g. HIV
- Recent history of travel

In these cases please refer urgently to Microbiology/Infectious Diseases for advice.

All patients with suspected meningococcal sepsis/or community-acquired bacterial meningitis should be notified to the Consultant for Communicable Disease Control (CCDC) and discussed with Microbiology/Infectious Diseases.

Introduction

Bacterial meningitis remains a relatively common and potentially fatal condition, which can affect any age group. Acute viral encephalitis is relatively uncommon but again is potentially fatal and can affect any age group. **Optimum management depends on early recognition of the syndrome, rapid diagnostic evaluation, and rapid initiation of appropriate antimicrobial and adjunctive therapy**. It is key to involve Infectious Diseases/Microbiology and Neurology at the earliest opportunity.

Clinical presentation

Neurological infections usually present with a history of fever, headache, and altered mental state. There may or may not be focal neurological deficits and seizures. The presence of altered mental state is more common in acute encephalitis than meningitis but there is often a degree of overlap.

Initial management may require treatment for causes of meningitis and encephalitis until further information is obtained from investigation e.g. brain imaging and lumbar puncture

Common causes of CNS infections in adults:

Bacteria: *Neisseria meningitidis* (Meningococcus)
Streptococcus pneumoniae (Pneumococcus)
Listeria monocytogenes
Haemophilus influenzae

Viruses: Herpes simplex virus (HSV)
Varicella-zoster virus (VZV)
Enteroviruses

Investigations

- Blood cultures (2 sets prior to antibiotics)
- EDTA blood for meningococcal PCR
- Acute serum (for storage)
- Throat swab x 2
    - Bacterial transport medium for meningococcal culture
    - Viral transport medium for viral investigation
- Consider Brain imaging, see: http://intratemp/radref/neuro/neuro_ct_lp_guidelines.htm
    - CT usually first choice, though may be normal early in encephalitis; especially useful in emergency if there are LP contraindications
    - MRI is more sensitive in encephalitis, but is not an emergency investigation and should be discussed with a neurologist/radiologist
- Lumbar puncture (LP) unless contraindicated
- LP contraindications
    - Platelet count <50
    - INR >1.2 (always check if suspected liver disease or on warfarin)
    - Known bleeding disorder (eg haemophilia)
    - Evidence of significant raised intracranial pressure
        - Obtunded (GCS <13)
        - Papilloedema
        - Mass effect, cerebral oedema and other features on CT
        - Convulsions (in context of suspected intra-cranial infection
    - Meningococcal septicaemia (purpuric rash)
    - If in doubt, avoid LP until discussed with a senior
- LP measurements
    - Opening pressure *must* be documented
    - Microscopy, stain and culture (2 sterile universals to microbiology)
    - Protein (sterile universal to biochemistry)
    - Glucose (fluoride-oxalate to biochemistry with blood glucose)
    - Meningococcal, pneumococcal and viral PCRs (sterile universal to microbiology)

Always try and take *at least* 1ml of CSF per universal container. Lumbar puncture and brain imaging are key to making a diagnosis of CNS infections. The initial CSF

results (even if negative gram stain) may help to direct therapy. Interpretation of CSF findings can always be discussed with Microbiology/Infectious Diseases.

Empirical Antimicrobial Treatment

Bacterial meningitis is suspected without any specific features:

IV Ceftriaxone 2g bd

In severely ill patients this should be given immediately i.e. before performing a lumbar puncture (if not contraindicated) but after blood cultures

If the patient has signs suggestive of meningococcal septicaemia with or without meningitis (i.e. typical petechial/purpuric rash), **Ceftriaxone** as above should be given immediately after blood cultures have been taken. A lumbar puncture is contraindicated in individuals with meningococcal septicaemia.
If the patient has received Benzylpenicillin from the GP they should still receive Ceftriaxone as above.

If the patient has a history of anaphylaxis with penicillins or rash with cephalosporins.use IV chloramphenicol, but discuss urgently with Microbiology/Infectious Diseases.

IV Chloramphenicol 12.5 mg/kg qds (maximum dose 1g qds)

If patient pregnant, please discuss with microbiology/infectious diseases.

In individuals >55yrs old or who are immunosuppressed, cover for *Listeria* is required **in addition to Ceftriaxone**:

IV Amoxicillin 2g 4-hrly

Please discuss with Microbiology/ Infectious Diseases alternatives to amoxicillin if penicillin allergic

If an individual has altered mental state and a there is a suspicion of acute viral encephalitis:

IV Aciclovir 10mg/kg tds

All these treatments are empirical and should be discussed at the earliest opportunity with Infectious Diseases/Microbiology - treatment may be rationalised as further information is gained from investigations.

The doses above are for those patients with normal renal function. For those patients with renal impairment please see separate guidance
"Antibiotic doses for adults with renal impairment" available at:
http://nuhnet/diagnostics_clinical_support/antibiotics or
http://www.nuh.nhs.uk/antibiotics.

Ongoing treatment

Culture positive meningitis should be treated with **IV Ceftriaxone 2g bd** as follows:

Neisseria meningitidis (meningococcus)	7 days
Streptococcus pneumoniae (pneumococcus)	14 days
Haemophilus influenzae	7 days

Listeria monocytogenes: **IV Amoxicillin 2g 4-hrly** for at least 21 days. Gentamicin may be added but this should be discussed with Infectious Diseases/Microbiology**.**

If an organism is not isolated but clinical findings and CSF are consistent with bacterial meningitis then patients should have 7-14 days intravenous treatment with **IV Ceftriaxone 2g bd** (The duration of therapy should be determined according to clinical response and repeat CSF examination where appropriate).

If viral encephalitis is proven due to HSV or VZV then therapy with **IV Aciclovir 10mg/kg tds** should be continued for 14-21 days. Oral therapy is not appropriate. If the diagnosis is not proven then length of treatment should be discussed with Infectious Diseases/Microbiology.

Adjunctive Therapy

Dexamethasone has been shown to improve the outcome of bacterial meningitis caused by pneumococcus but not by meningococcus. There is also evidence that dexamethasone reduces the neurological and audiological sequelae that can complicate *Haemophilus influenzae* meningitis. There is no role for steroids routinely in viral encephalitis.

It is recommended to give **IV Dexamethasone (base) 8mg qds** for 4 days
N.B. (8mg dexamethasone base is approximately equivalent to 10mg dexamethasone sodium phosphate).

This should be administered before or with the first dose of antibiotic in suspected bacterial meningitis. Further results may then guide whether to continue or stop steroids.

The following are contraindications to the use of steroids:

- Viral meningitis
- Patients where the diagnosis is in doubt
- Patients already treated with antibiotics (including benzylpenicillin from GP)
- Patients with sepsis
- Immunosuppressed patients
- Meningitis following surgery

Prophylaxis against Disease

Meningococcus (*N. meningitidis)*

Treatment to eliminate pharyngeal carriage **(index case)**

Ceftriaxone eliminates carriage of meningococcus. Patients with meningococcal disease who have **not received ceftriaxone** should be given oral **Ciprofloxacin 500mg stat** or **Rifampicin 600mg bd for 2 days** (if ciprofloxacin intolerant). Both are contra-indicated in pregnancy and advice should be sought from Microbiology.

Treatment to eliminate pharyngeal carriage **(close contacts)**

Close contacts of patients with meningococcal disease should be given **Rifampicin** (<12 years) or **Ciprofloxacin** prophylaxis (>12 years), both are contra-indicated in pregnancy see alternative page 6 . These include those living in the same household and those with kissing/secretion contact with the patient within the previous 10 days, or performed mouth to mouth resuscitation, or have had definite droplet contamination from respiratory secretions. If the patient attends school, college or university, contact the Consultant for Communicable Disease Control (CCDC) for further advice (out of hours the on call doctor for Public Health Medicine via switchboard).
The doses for rifampicin are:

<12 months:	5mg/kg bd for 2 days
1-12 years:	10mg/kg bd for 2 days (maximum 600mg bd)
>12 years/adult:	600mg bd for 2 days

Pneumococcus (*S. pneumoniae)*

No prophylaxis required.

***Haemophilus influenzae* type b:**

If an unvaccinated child <4 years of age lives in the same household as the patient, **Rifampicin** prophylaxis should be given to the entire household for 4 days (including the patient).

(NB most children in the UK are vaccinated at 2, 3 and 4 months of age).

Oral Doses:	1-3 months	10mg/kg once daily for 4 days
	3 months – 12 yrs	20mg/kg once daily for 4 days (max 600 mg)
	>12 yrs/adult	600 mg once daily for 4 days

Side effects/drug interactions of Rifampicin

Rifampicin causes orange-red discoloration of tears, urine and soft contact lenses. It may also cause skin rashes and itching. It reduces the effectiveness of most oral contraceptives (and some contraceptive patches) so additional contraceptive precautions should be taken whilst taking Rifampicin and for at least 4 weeks after stopping it: the next new packet being started immediately without a break.

Contra-indications to the use of Rifampicin

Pregnancy
Severe liver disease

Alternatives for prophylaxis in such cases

Ciprofloxacin 500 mg po stat (Adults only) (not in pregnancy)
Ceftriaxone 250 mg I.M. stat (125 mg 1 month-12 years) (unlicensed indication)

If in doubt about any aspect of patient management, please contact Microbiology/Infectious Diseases Services.