Doncaster and Bassetlaw Teaching Hospitals
NHS Foundation Trust

POLICY FOR TREATMENT OF CENTRAL NERVOUS SYSTEM INFECTIONS IN ADULTS

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This document is part of antibiotic formulary guidance

Formulary guidance holds the same status as Trust policy

Amendment table

Version	Date Issued	Brief Summary of Changes	Author
3	March 2022	• Change in recommendation from Cefotaxime to Ceftriaxone due to reduced cost and ease of administration • Duration of treatment for meningococcal sepsis/meningitis changed from 7d to 5d • Re-wording of the cotrimoxazole dosing regimen to improve clarity • Advice to review antibiotics/antivirals with results of CSF PCRs performed using in-house FilmArray • Advice to contact microbiologist if additional CSF PCR testing is required (in samples that do not meet testing criteria for FilmArray) • Highlighting the need for notification to Health Protection team for any confirmed or suspected case of meningitis – to ensure prompt prophylaxis of contacts where indicated	Dr Bala Subramanian

CONTENTS

1) Meningitis

Definition

Inflammation of the meninges – may be bacterial, viral or aseptic meningitis. The classic triad of fever, neck stiffness and altered mental status (GCS ≤ 14) is not always present. May have signs specific to the infecting organism e.g. purpuric rash in meningococcal meningitis. In culture-proven bacterial meningitis*:*

95% of patients have 2 of the following symptoms and signs
99% of patients have at least 1

- Headache
- Fever
- Neck stiffness
- Altered mental state

Viral meningitis is thought to account for about 50 – 80% of all cases of 'meningitis'.

Common causative organisms

Bacterial meningitis	**Viral meningitis**
• *Neisseria meningitidis* • *Haemophilus influenzae, type B* • *Streptococcus pneumoniae* • *Listeria monocytogenes* (especially in patients who are immunocompromised, diabetic or alcohol dependent) • *M.tuberculosis*	• *Herpes simplex virus(HSV)-usually HSV-2* • *Varicella Zoster virus(VZV)* • *Enterovirus*

Please note: CSF PCR testing (using FilmArray) is available at DRI labs to facilitate rapid diagnosis and rationalisation of antimicrobials. Please review antibiotics and antivirals based on PCR testing and discontinue treatments as appropriate.

Notification to Health Protection team

- All cases of meningitis (regardless of aetiology) should be notified to the local HPT
- Please refer to 'PAT/IC 12 Meningococcal Infections – Management of Cases and Contacts'

Management of Suspected Meningitis

Contraindications to immediate LP?
Focal neurological signs, presence of papilloedema, continuous/uncontrolled seizures, GCS <13

No → **If delay in LP >1 hour, start empirical antibiotics**

Yes → **Urgent CT**

Urgent CT → **Alternative diagnosis?**

Alternative diagnosis? Yes → **Treat as appropriate**

Alternative diagnosis? No → **Radiological contraindication to LP?**

Radiological contraindication to LP? No → **Perform LP sending CSF for following:**

- Opening pressure
- Cell count, microscopy & culture (Bottles 1 & 3). If CSF WCC >5, PCRs will be performed using FilmArray with same day results
- Biochemistry – Protein, glucose (Bottle 2)

If TB meningitis is suspected, take large volume sample >10mls for AAFB & culture

Radiological contraindication to LP? Yes → **Start empirical antibiotics**

	1st line	**2nd line or if history of Penicillin anaphylaxis**	**Duration**
Adults < 60 years	Ceftriaxone (IV) 2g 12-hourly	Chloramphenicol* (IV) 25mg/kg 6-hourly for 48h, then reduce to 12.5mg/kg 6-hourly	*Meningococcal* – 5 days if good clinical recovery *Pneumococcal* – 10 - 14 days *Haemophilus influenzae* – 10 days *Listeria* – 21 days *Enterobacteriacae* (eg E.coli)- 21 days Viral – Stop antibiotics, treatment is supportive
Adults ≥ 60 years Immunocompromised, diabetes or alcohol excess	Ceftriaxone (IV) 2g 12-hourly AND Amoxicillin* (IV) 2g 4-hourly (**OR** if rash allergy to Penicillin, Co-trimoxazole IV 120mg/kg in 4 divided doses	Chloramphenicol* (IV) 25mg/kg 6-hourly for 48h, then reduce to 12.5mg/kg 6-hourly **AND** Co-trimoxazole* (IV) 120mg/kg in 4 divided doses	
If travel in last 6 months to country with high penicillin resistance	**Discuss further with Microbiologist.** High risk countries include: *Canada, China, Croatia, Greece, Italy, Mexico, Pakistan, Poland, Spain, Turkey*		

All cases of **suspected bacterial meningitis** should receive **IV dexamethasone 8.3mg QDS within 12 hours** of **first dose of antibiotic.** If pneumococcal meningitis is confirmed, then continue dexamethasone for total 4 days.
***May need dose adjustment in renal impairment. Discuss with Pharmacist if required.**

Additional testing

- 2 sets blood cultures (preferably before antibiotics)
- Pneumococcal & meningococcal PCR on blood
- Blood Borne Virus testing
- Bacterial throat swab for MC&S
- If viral meningitis is likely: Viral T/S for respiratory viruses & enterovirus and stool for enterovirus PCR
- If HIV positive, please discuss with Infectious Diseases in Sheffield regarding additional testing
- CSF PCR testing will be performed based on clinical information and CSF results. If additional CSF PCR testing is required, please discuss with Microbiologist

2) Meningococcal septicaemia

Definition

Evidence of sepsis +/- characteristic petechial/purpuric skin rash and hypoperfusion. *Neisseria meningitidis* may be identified from blood, CSF or skin lesions.

Patients with meningococcal septicaemia can deteriorate rapidly. The classic petechial or purpuric rash occurs in ≈ 60%, but this can be a late sign. Certain symptoms that should raise alarm are severe muscle pain (a possible feature of systemic bacterial sepsis) or thirst (a prominent feature of impending shock even when the blood pressure is normal). Temperature may be high, low or normal.

Common causative organism	**Microbiological Investigations**
Neisseria meningitidis	• Blood cultures • Meningococcal and pneumococcal PCR (1 x EDTA tube to microbiology) • Throat swab for MC&S **Note: LP should NOT be performed in these patients.**

Treatment

1st line	**Penicillin anaphylaxis**	**Duration**
Ceftriaxone (IV) 2g every 12h	Chloramphenicol (IV) 25mg/kg 6-hourly	5 days (provided good clinical recovery)

3) Encephalitis

Definition

Inflammation of the brain substance. Involvement of particular areas of the brain can occur with specific pathogens.

Usually presents with headache, fever, change in cognitive state (e.g. confusion, personality change). Focal features, such as reduced GCS or seizures, may occur.

The most frequent cause of encephalitis in the UK is HSV-1. It tends to affect the temporal and/or frontal lobes.

Bacterial, parasitic and fungal causes are rare in the UK. However, if there is a relevant travel history and additional CSF PCR testing is needed, discuss with Virologist (at Northern General Hospital) or the Microbiologist for further advice.

Common causative organisms	**Microbiological Investigations**	**Additional tests**
Herpes simplex virus (HSV) – usually HSV-1 *Varicella zoster virus (VZV)* *Enterovirus*	• Blood cultures • Lumbar puncture • CSF microscopy, culture • CSF PCR testing will be done (using FilmArray with same day results) if CSF WCC >5 or where there is high suspicion for encephalitis (please indicate this on the request form) • Throat swab & stool for enterovirus PCR • If vesicles present, send viral skin swabs • Meningococcal and pneumococcal PCR (EDTA sample) to help rule out bacterial meningo-encephalitis **Note:** **Additional CSF investigations may be indicated if immunocompromised, recent travel or if at risk exposure. Please discuss with Virologist (based at Northern General Hospital) if appropriate.**	• MRI brain • Consider EEG

Treatment

Treatment of patients early in the course of the illness, before the development of necrosis, is essential for better outcome.

1st line	**Duration**
Aciclovir 10mg/kg 8-hourly (IV) **In obese patients, ideal body weight should be used to calculate dose, to avoid excessive doses.** <u>Ideal body weight (IBW) calculation:</u> Female IBW (kg) = height (cm) -105 Male IBW (kg) = height – 100	• If proven HSV encephalitis, continue aciclovir for 14 days (or 21 days if immunocompromised) • Repeat LP at the end of treatment to confirm that HSV PCR negative before stopping treatment • If CSF still positive, then continue treatment with weekly LPs until HSV PCR negative • Maintain good hydration and monitor U&E whilst on aciclovir

Note:

HSV PCR may be negative in the first few days of illness. If the initial LP is done < 72 hours of symptom onset and HSV PCR is negative, then consider repeat LP if high clinical suspicion of viral encephalitis.

References

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