وزارة الصحة
Ministry of Health

MOH Clinical Protocol for Emergency Management of Community Acute Bacterial Meningitis and Meningoencephalitis in Adults

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1. Introduction

a. Meningitis is an inflammatory process that affects the protective membranes surrounding the brain and spinal cord. Acute bacterial meningitis is a potentially fatal illness that has an overall mortality in excess of 50% if not promptly diagnosed and treated and even when treated early, may still be associated with permeant morbidities like seizures, hearing loss, and learning disabilities. High index of suspicion and good clinical judgment are the keys to a good outcome.

2. Purpose of this document is

a. To standardize the timely recognition, evaluation, and management of acute bacterial meningitis and meningoencephalitis in order to optimize patient outcomes, minimize complications, and ensure effective utilization of diagnostic and therapeutic resources.

3. Scope

a. This protocol applies to all adults' patients presenting to the emergency department with signs or symptoms suggestive of a community acquired acute bacterial meningitis. It covers:
   i. Patient stabilization and initial assessment.
   ii. Indicated laboratory and radiological investigations.
   iii. Empiric and targeted antimicrobial/antiviral therapy.
   iv. Supportive care and monitoring.
   v. Reassessment, follow-up, and quality assurance.

4. Clinical presentation

a. Typically present with a sudden onset of high-grade fever, headache, altered level of consciousness, irritability, and vomiting as well as signs of meningeal irritation like nuchal rigidity, Kernig's, Brudzinski's signs and Jolt accentuation of headache may be present.
b. A patient with recurrent meningitis should be examined and investigated for:
   i. Immune-deficient states, notably defects of the complement system and agammaglobulinemia
   ii. Ear or sinus infections or CSF leakage.

5. Definitions

- **Acute CNS Infection:** Inflammation of the meninges, brain parenchyma, or both, typically caused by bacteria, viruses, fungi, or parasites.
- **Empiric Therapy:** Initial treatment based on clinical suspicion, administered prior to definitive diagnostic confirmation.
- **Lumbar Puncture (LP):** A diagnostic procedure to obtain cerebrospinal fluid (CSF) for analysis.

6. Protocol Details

A. Initial Patient Assessment & Stabilization

1. **Triage and Stabilization**
    - Assess Airway, Breathing, and Circulation (ABCs)
    - Ensure immediate stabilization.
    - Initiate resuscitation measures if needed.
    - Evaluate for impaired level of consciousness (LOC).
    - Recognize and treat clinical and subclinical seizures.

2. **Implement Infection Control Measures:**
    - Apply droplet / airborne precautions & contact precautions if a highly transmissible pathogen (e.g., meningococcal meningitis) is suspected.
    - Apply isolation for suspected cases.

3. **History and Physical Examination**
    - Elicit a detailed history emphasizing:
        - Fever, headache, neck stiffness.
        - Altered mental status, photophobia, seizures, or focal neurologic deficits.
        - Recent infections, travel, exposures, and immuno-compromising conditions.
        - Associated skin rash (extensive purpura)
    - Perform a thorough physical and neurological examination:
        - Check for meningeal signs (Kernig's / Brudzinski's / Jolt accentuation of headache).
        - Assess mental status and cranial nerve functions.

B. Diagnostic Workup

1. **Laboratory Studies**
    - **Blood Tests:**
        - Complete blood count (CBC), coagulation profile (PT / PTT / INR), serum lactate and inflammatory biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and procalcitonin (PCT).
        - **Blood Cultures:**
            - Collect at least two sets *before* initiating antibiotics.
    - **Additional Tests:**
        - Basic metabolic panel and any tests based on clinical suspicion (e.g., HIV status if immunocompromise is suspected).

2. **Neuroimaging**
    - Performing a neuro imaging prior to LP carries a risk of delaying empiric antibiotics therapy waiting for LP to be performed. Empiric prompt antibiotic therapy and lumbar puncture are the two corner stone steps that resulted in decreased mortality and neurological sequelae. Intracranial hypertension, commonly observed in severe meningitis is not a contraindication to LP by itself, however expert opinion in such cases is recommended.

- **Indications for CT Prior to LP:**
    - Focal neurologic deficits
    - Cranial nerve deficits
    - Signs and symptoms of increased ICP like (papilledema and 6th nerve palsy)
    - Persisting or new-onset seizures
    - Altered mental status
    - Immunocompromised state

- **Procedure:**
    - Obtain a non-contrast CT scan of the head if neurological contraindications to lumbar puncture are suspected.
    - If imaging is normal and no other contraindications exist, proceed with LP and CSF analysis after taking the informed consent.

3. **Lumbar Puncture (LP) and CSF Analysis**

- Informed consent to be taken from the patient or his representative prior to LP.
- Early cerebrospinal fluid examination should be performed before starting antibiotics in all patients with suspected meningitis unless there is an absolute contraindication for lumbar puncture.
- LP should be performed within 1 hour from arrival at the emergency room and before the initiation of antibiotic therapy (however antibiotics should not be held if LP will take more than one hour)
- If empirical antibiotics are administrated before lumbar puncture and it is safe to do LP, it should still be done and preferably within 4 hours of commencing antibiotics.
- LP should not be delayed for the results of blood tests unless there is a high clinical suspicion of a bleeding diathesis.
- LP should not be delayed on patients on aspirin and other non-steroidal anti-inflammatory drugs.
- In patients on clopidogrel or newer anticoagulants consider hematology consultation particularly in high-risk for bleeding patients.
- Patients on prophylactic LMWH should not have LP within 12 h after the last dose.
- Patients on is on therapeutic LMWH should not have LP within 24 h after the last dose.
- In patients on warfarin, LP should be delayed until the INR is ≤ 1.4
- LP should not be performed if platelets count is <50 ×109/L or rapidly falling platelets count (benefit vs. risk ratio must be taken into consideration)
- LP sample should be sent for
    - CSF white blood cell count (WBC)
    - CSF total protein
    - CSF glucose concentrations (with concurrent plasma glucose)
    - CSF gram stain and culture sensitivities
    - CSF lactate (if available & antibiotic therapy was not initiated yet)
    - CSF PCR for pneumococci and meningococcal (particularly for patients who received antibiotics prior to LP), and Immunochromatographic test for N. meningitides and S. pneumoniae (if available).
- The Laboratory should have the results of CSF analysis made available within 4 h of LP

- **Pre-LP Considerations:**
  - Absolute contraindications for LP
    - Cutaneous infection spreading to the lumbar puncture site
    - Uncontrolled hemodynamic or respiratory instability (the lumbar puncture should be delayed until stabilization)
    - Hemostasis disorders (hemophilia, another coagulopathy, platelet count < 50,000/mm3, INR is ≥ 1.4)
    - Spontaneous bleedings indicative of disseminated intravascular coagulation (DIC)

- **Post LP consideration**
  - Therapeutic intravenous unfractionated heparin could be restarted 1 h after LP and LMWH could be started 4 hours post LP
  - In high-risk for bleeding patients therapeutic intravenous unfractionated heparin could be restarted 6 - 8 hours after LP and LMWH could be started 12 hours post LP (consider hematology consultation)

- **Repeated LP possible indications**
  - Patients with no clinical response after 48 h of appropriate antimicrobial therapy
  - Neurological deterioration while on that is not explainable
  - Patients with CSF shunt infections after removal of the shunt.

4. **Documentation**
   - Record all findings, including timing of blood cultures, neuroimaging, and LP details.
   - Ensure clear communication of any contraindications or abnormalities.
   - Conduct reporting through "Weqayah" for positive cases.
   - Trace and give prophylactic antibiotic treatment for household contacts and other close contacts with positive meningococcal meningitis cases.

C. Empiric Pharmacologic Management

- The selection of an empiric antibiotic depends on the patient's age, location, potential organisms and the presence of antibiotic resistance.
- The antibiotic therapy should be initiated within the first hour following presentation to the hospital, irrespective of the presumed time since meningitis onset.
- The investigation and laboratory work up should not delay the administration of the first doses of antimicrobial drugs.

1. **Antibacterial Therapy**
   - **Immediate empiric therapy**
     - **Recommended Regimen (Healthy Adults less than 50 with no added risk Factors and with No penicillin allergy):**
       - **Ceftriaxone or Cefotaxime** plus **Vancomycin** as first-line agents.
         - Ceftriaxone dose 2 g q12h IV
         - Cefotaxime dose: 2 g q4–6 h IV

- Vancomycin loading dose of 25 to 30 mg/kg – (actual body weight) followed by maintenance dose of 15–20 mg/kg q8–12h IV to achieve serum trough concentrations of 15–20 µg/mL

- **Recommended regimen in case of risk factors for Listeria monocytogenes infection: (Age over 50 years, pregnancy, immunosuppressive therapy • organ transplantation • malignancy • advanced HIV disease • diabetes mellitus • end-stage kidney disease • liver cirrhosis • alcohol abuse.)**
  - **Above regimen plus**

    1. Ampicillin loading dose 2 g IV
    2. Ampicillin maintenance dose 2 g q4h IV

- **Recommended Regimen (Healthy Adults less than 50 with no added risk Factors and with mild penicillin allergy):**
- **Meropenem** plus **Vancomycin** as first-line agents

  - Meropenem 2 gm IV q 8 h
  - Vancomycin loading dose of 25 to 30 mg/kg (actual body weight) followed by maintenance dose of 15–20 mg/kg q8–12h IV to achieve serum trough concentrations of 15–20 µg/mL

- **Recommended Regimen (Healthy Adults less than 50 with no added risk Factors and with sever penicillin allergy):**
- **Trimethoprim/ sulfamethoxazole** plus **Vancomycin** plus **Aztreonam** or **Ciprofloxacin**

  - Vancomycin + Aztreonam 2 gm IV q6 h + Trimethoprim/ sulfamethoxazole 5 mg/kg q6-8 h IV

    OR:

  - Vancomycin + Ciprofloxacin 400 mg IV q8 h or (other Fluoroquinolones i.e. Levofloxacin 750 mg IV q 24 h or Moxifloxacin 400 mg IV q 24 h) + Trimethoprim/ sulfamethoxazole 5 mg/kg q6-8 h IV

  - Vancomycin loading dose of 25 to 30 mg/kg – (actual body weight) followed by maintenance dose of 15–20 mg/kg q8–12h IV to achieve serum trough concentrations of 15–20 µg/mL

- **Recommended regimen (Adults with sever immune compromising state) / (Adults with HIV)**
- **Same as above but consider fungal meningitis coverage with appropriate antifungal drugs.**

- **Adjunctive Therapy**
    - Intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) should be initiated with the first dose of antibiotics in adults with suspected acute bacterial meningitis.
        - Dexamethasone dose: 10 mg q6h IV for 4 days.
    - If CSF characteristics are consistent with bacterial meningitis and a bacterial pathogen other than S. pneumoniae or H. influenzae type b is detected through culture or molecular testing, intravenous corticosteroids can be discontinued.
    - This treatment is **not** recommended in immunocompromised patients or in patients presenting with neuro invasive listeriosis.
    - During meningococcal disease epidemics, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) should not be routinely used in adults with suspected or probable meningococcal meningitis.

2. **Antiviral Therapy**
    - **Herpes Encephalitis Suspicion:**
        - Start intravenous **Acyclovir** promptly when there is clinical or imaging suspicion of herpes simplex virus (HSV) encephalitis.
            - Acyclovir dose: 10mg/kg q8h IV

3. **Targeted Therapy Adjustments**
    - Once culture and PCR results are available, tailor the antimicrobial/antiviral regimen to the specific pathogen and its susceptibilities.
    - Consult infectious diseases service and clinical pharmacist accordingly.
    - The doses for normal kidney function - refer to MOH formulary for dose adjustment

4. **Recommended duration of therapy according to isolated pathogen:**

Pathogen	Specific therapy	Overall duration
Unspecified bacterial meningitis	Empirical antimicrobial therapy	10–14 days
Streptococcus pneumoniae Penicillin-susceptible	Penicillin G or ampicillin or amoxicillin	10–14 days
Streptococcus pneumoniae Penicillin-resistant	Ceftriaxone or cefotaxime	
Streptococcus pneumoniae Cephalosporin-resistant	Vancomycin + rifampicin, or Vancomycin + ceftriaxone/cefotaxime, or Rifampicin + ceftriaxone/cefotaxime	
Neisseria meningitidis Penicillin-susceptible	Penicillin G or ampicillin or amoxicillin	5–7 days
Neisseria meningitidis Penicillin-resistant	Ceftriaxone or cefotaxime	
Haemophilus influenzae Beta-lactamase-negative	Ampicillin or amoxicillin	7–10 days
Haemophilus influenzae Beta-lactamase-positive	Ceftriaxone or cefotaxime	
Streptococcus agalactiae	Penicillin G or ampicillin or amoxicillin	14–21 days
Listeria monocytogenes	Penicillin G or ampicillin or amoxicillin	21 days
Gram-negative bacillary and Pseudomonal meningitis	According to antibiotic sensitivity	21–28 days
Herpes simplex virus	Acyclovir	14–21 days

D. Supportive Care and Monitoring

1. **Monitoring**
    - **Continuous Neurologic Assessment:**
        - Frequent checks of mental status, focal neurological deficits, and signs of increased ICP.
    - **Vital Signs and Laboratory Monitoring:**
        - Regular monitoring of temperature, heart rate, blood pressure, and repeat laboratory tests as indicated.

2. **Symptom Management**
    - **Analgesics:**
        - For headache and pain
    - **Antiemetics:**
        - For nausea and vomiting
    - **Antipyretics:**
        - For fever control
    - **Anticonvulsants:**
        - Administer if seizures are present or there's a high suspicion of subclinical seizure activity.
        - Consult neurology service accordingly.
    - **Fluid and Electrolyte Management:**
        - Maintain balance and optimize cerebral perfusion.
        - Correct electrolytes disorders.
        - Avoid hypoglycemia or hyperglycemia.

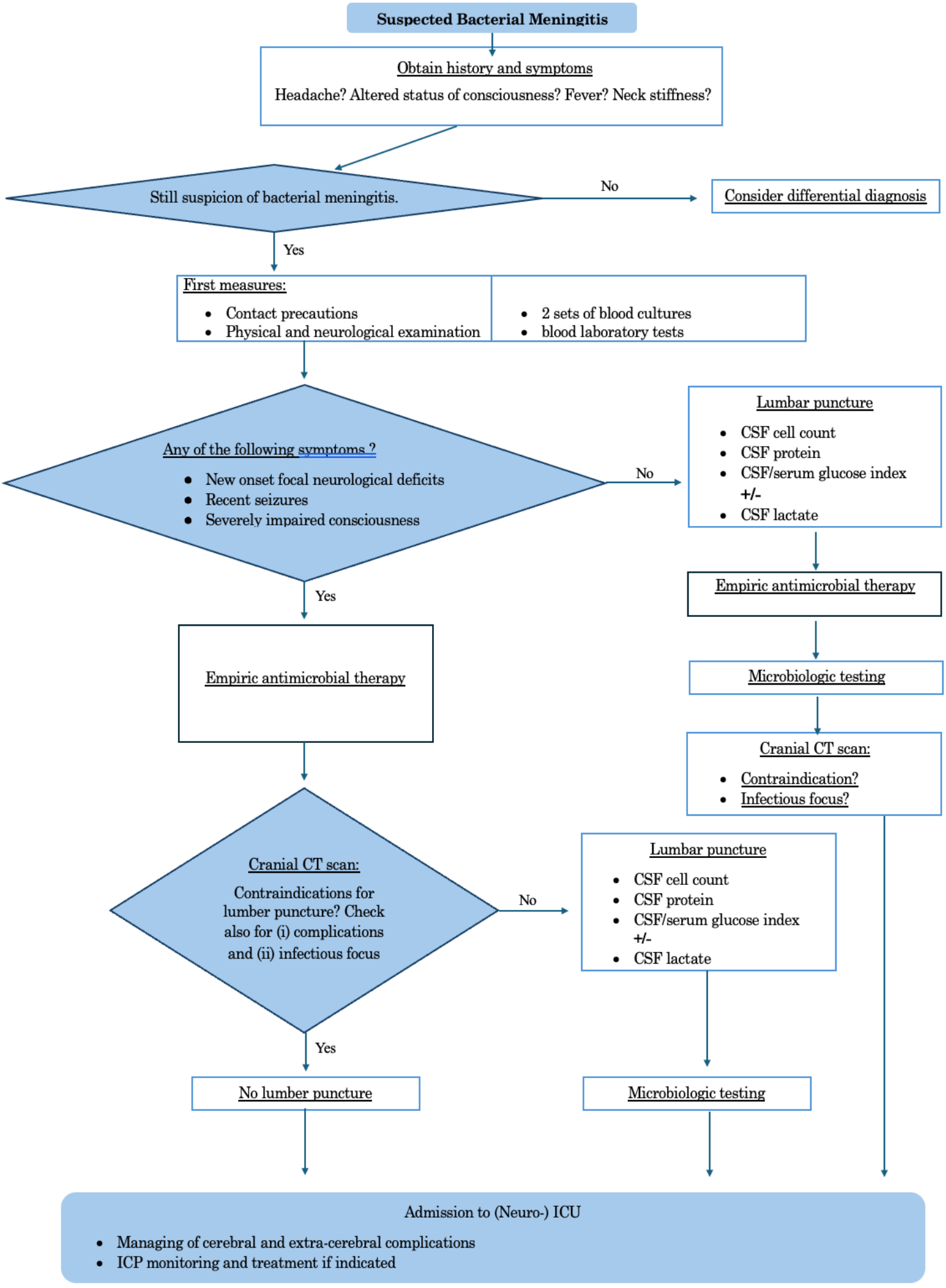
3. **Supportive ICU Care**
    - Admit patients with severe presentations or complications to an intensive care unit for advanced monitoring and intervention, especially if any of the following is present:
        - Extensive purpura
        - Glasgow score ≤ 10 or Focal neurological signs
        - Signs of brainstem involvement, usually indicative of intracranial hypertension: (bradycardia, tachycardia, respiratory rate or pattern abnormalities)
        - Status epilepticus or uncontrolled frequent seizures
        - Hemodynamic instability / septic shock.
        - Any other ICU admission as per MOH ICU admission criteria (https://www.moh.gov.sa/en/Ministry/MediaCenter/Publications/Documents/Adult-ICU-Triage-Admission-and-Discharge-Criteria.pdf)

E. Reassessment, Follow-Up, and Discharge Planning

1. **Reassessment**
    - **Timeframe:**
        - Reevaluate the patient's response to treatment within 48–72 hours.
        - Consider EEG incases presenting with seizures or have persistence low LOC.
    - **Monitoring:**
        - Monitor for clinical improvement, potential complications (e.g., hydrocephalus, abscess formation), and therapy-related adverse effects.
        - Consult neurosurgery service accordingly.
2. **Follow-Up Testing**
    - Consider repeat imaging brain (CT or MRI) if the patient shows no clinical improvement.
    - Liaise with infectious disease and neurology for continued management and consultation.
    - Consider repeating CSF analysis if indicated.
3. **Discharge Planning**
    - **Criteria for Discharge:**
        - Resolution or stable improvement of clinical symptoms.
        - Completion of the appropriate course of intravenous therapy.
    - **Rehabilitation:**
        - Arrange follow-up neurological evaluations and rehabilitation services for any persistent deficits.
4. **Documentation & Communication**
    - Clearly document all reassessments, changes in therapy, and patient progress.
    - Ensure detailed handover notes for ongoing care providers.
    - Give post discharge follow up appointments in clinic for reevaluation.

F. Quality Assurance and Process Improvement

- **Performance Metrics:**
    - Time from presentation to antibiotic/antiviral administration.
    - Rates of culture-proven infections.
    - Patient outcomes (mortality, morbidity, length of stay).
- **Auditing:**
    - Regular audits of protocol compliance and outcomes reports.
    - Multidisciplinary meetings to review cases and integrate recent evidence or guideline changes.



** Adapted from: Dyckhoff-Shen, S., Koedel, U., Pfister, H. W., & Klein, M. (2021). SOP: emergency workup in patients with suspected acute bacterial meningitis. *Neurological research and practice*, *3*(1), 2.

Remarks

This clinical protocol is intended as a dynamic tool reflecting current best practices. It should be reviewed periodically and adjusted as new evidence emerges. Use of diagnostic algorithms may be helpful to guide management in individual patients with suspected acute bacterial meningitis, but clinical judgement is key when considering whether to start empiric antibiotic and adjunctive therapy.

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