Chapter 103
Approach to Tropical Infections in the ICU

103.1 Introduction

Tropical infections represent a significant challenge in the ICU due to their diverse etiologies and potential for severe outcomes. These infections are prevalent in specific geographic regions such as Southeast Asia, sub-Saharan Africa, and parts of South America, often exacerbated by environmental, occupational, or travel-related factors. Data from the GeoSentinel database highlight regions where infections like malaria, dengue, and rickettsial diseases are endemic. The monsoon season, characterized by heavy rainfall and flooding, is a peak time for certain infections such as leptospirosis and melioidosis, particularly in countries like India, Thailand, and northern Australia. Effective management in the ICU demands a structured approach to rapidly identify and treat the underlying pathogen while mitigating complications [1–4] [Ref: Algorithm 103.1].

103.2 Clinical Presentation

The initial assessment focuses on categorizing acute febrile illness based on associated clinical features:

- Fever, Rash, or Eschar:
- Suggestive of rickettsial infections (e.g., Scrub Typhus) or Dengue.
- Rash or eschar is an essential clinical clue; an eschar is particularly pathognomonic of rickettsial diseases.
- Fever with Respiratory Symptoms:
- Raises suspicion for Malaria, Leptospirosis, Melioidosis, or Tuberculosis.

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- Key differentials include malaria-associated pulmonary edema, leptospirosis-induced acute respiratory distress syndrome (ARDS), or severe pneumonia in melioidosis.
- Leptospirosis may progress to Weil's disease, characterized by jaundice, renal failure, hemorrhagic manifestations, severe acidosis, and atypical features like necrotizing pancreatitis.
- Fever with Shock or Bleeding Diathesis:
- Prioritize evaluating for Viral Hemorrhagic Fevers such as Dengue or severe Malaria.
- Shock may indicate capillary leak syndrome or sepsis, while bleeding points to thrombocytopenia or disseminated intravascular coagulation.
- Fever with Altered Mentation:
- Indicates possible Scrub Typhus, Dengue encephalitis, Tuberculosis meningitis, or Cerebral Malaria.
- Central nervous system involvement necessitates prompt imaging and lumbar puncture to rule out meningitis or encephalitis.
- Fever with Adrenal Insufficiency:
- Tuberculosis can cause adrenal insufficiency, leading to hypotension unresponsive to vasopressors.
- Consider adrenal insufficiency in patients with TB-related shock.
- Recent Travel to Endemic Areas:
- Helps narrow the diagnosis to regional infections like Japanese encephalitis or Malaria.
- Occupational or Environmental Exposure:
- Environmental cues, such as contact with soil or rodents, suggest Leptospirosis or Melioidosis.
- Melioidosis can present with severe pneumonia, septic shock, or abscess formation in various organs.

103.3 Laboratory Investigations

Laboratory workup is essential for identifying the pathogen and assessing organ dysfunction:

- General Tests:
- Include complete blood count (CBC), liver and renal function tests, and coagulation profile to assess systemic involvement.
- Findings such as thrombocytopenia (Dengue), elevated liver enzymes (Leptospirosis), or pancytopenia (severe Malaria) guide management.
- Specific Tests:
- Peripheral Smear/Rapid Diagnostic Test (RDT):
- Confirms Malaria; a peripheral smear also provides insight into parasite density.
- IgM ELISA or MAT (Microscopic Agglutination Test):

- Used to confirm Leptospirosis.
- For difficult-to-diagnose cases, advanced techniques like nested PCR can increase diagnostic yield.
- RT-PCR/NS1 Antigen, IgM ELISA:
- RT-PCR/NS1: Highly sensitive for early detection of Dengue.
- Early rapid diagnostic tests in endemic regions help reduce delays in management and improve outcomes.
- GeneXpert or (*Mycobacteria* Growth Indicator Tube) MGIT Culture:
- For diagnosing tuberculosis, especially in extrapulmonary cases.
- In suspected tuberculosis-related adrenal insufficiency, cortisol levels and Adrenocorticotrophic hormone (ACTH) stimulation tests may be necessary.
- Blood Culture:
- Identifies organisms in Melioidosis (*Burkholderia pseudomallei*) or Enteric fever.
- Whole-genome sequencing can be utilized for precise identification and antibiotic susceptibility profiling, especially in rickettsial infections.
- Scrub Typhus IgM ELISA:
- A specific test to confirm Scrub Typhus.

103.4 Imaging

Imaging complements laboratory investigations by identifying organ-specific involvement:

- Chest X-ray:
- Evaluate for ARDS or consolidation, which is common in Leptospirosis, Tuberculosis, Melioidosis, or secondary bacterial infections.
- Abdominal Ultrasound:
- Used to detect organomegaly, abscesses, or hepatosplenomegaly, which are hallmark features of Melioidosis, Enteric fever, or Malaria.
- Computed Tomography (CT scan)
- CT scan of thorax for Tuberculosis and CT scan of abdomen (with contrast) for Tuberculosis, Melioidosis.

103.5 Prognostic Indicators

Prognostic tools aid in risk stratification and guide management decisions:

- Leptospirosis:
- Tools like the SPiRO (Sequential Organ Failure Assessment for Leptospirosis) or THAI LEPTO score help predict severe disease and mortality risk.
- These scores consider factors such as age, organ dysfunction, and laboratory parameters.

- Dengue:
- The World Health Organization (WHO) classification stratifies patients into dengue without warning signs, with warning signs, and severe dengue, guiding monitoring and treatment intensity.
- Malaria:
- High parasite density, severe anemia, or cerebral involvement indicates a poor prognosis.

103.6 Initial Empiric Therapy

Early empiric therapy is vital while awaiting confirmatory diagnostics. Treatment selection is based on clinical suspicion:

- **Severe Malaria**: [5]
- Definition: Severe Malaria is defined as *Plasmodium parasitemia* plus one or more of the following:
  - Altered level of consciousness: Glasgow Coma Scale (GCS) score below 11 in adults
  - Prostration: Severe weakness rendering the patient unable to sit, stand, or walk without help
  - Recurrent seizures: More than two convulsive episodes within a 24-hour timeframe
  - Metabolic acidosis: Evidenced by a base deficit exceeding 8 mEq/L, plasma bicarbonate below 15 mmol/L, or venous lactate concentration of 5 mmol/L or higher
  - Hypoglycemia: Blood or plasma glucose <40 mg/dL
  - Severe malarial anemia: Hemoglobin concentration < 7 g/dL or a hematocrit of ≤20% with a parasite count >10,000/μL (count only for *P. falciparum*)
  - Renal impairment: Plasma or serum creatinine >265 μmol/L (3 mg/dL) or blood urea >20 mmol/L
  - Jaundice: Plasma or serum bilirubin >3 mg/dL with a parasite count >100,000/μL (count only for *P. falciparum*).
  - Pulmonary edema: Radiologically confirmed or oxygen saturation < 92% on room air with a respiratory rate > 30/min
  - Significant bleeding refers to persistent or repeated bleeding episodes, such as from the nose, gums, or venipuncture sites, as well as gastrointestinal bleeding presenting as hematemesis or melena.
  - Shock is categorized as follows:
  - Compensated shock is indicated by a capillary refill time of 3 seconds or more, or a noticeable temperature gradient between the mid and proximal parts of the limb, without the presence of hypotension.
  - Decompensated shock is defined by a systolic blood pressure lower than 80 mmHg in adults.

  - Hyperparasitemia*: P. falciparum* parasitemia >10% (not to be considered in case of *vivax*). *P. knowlesi* > 100,000/μL or jaundice and parasite density > 20,000/μL.
  - Splenic rupture (a complication)

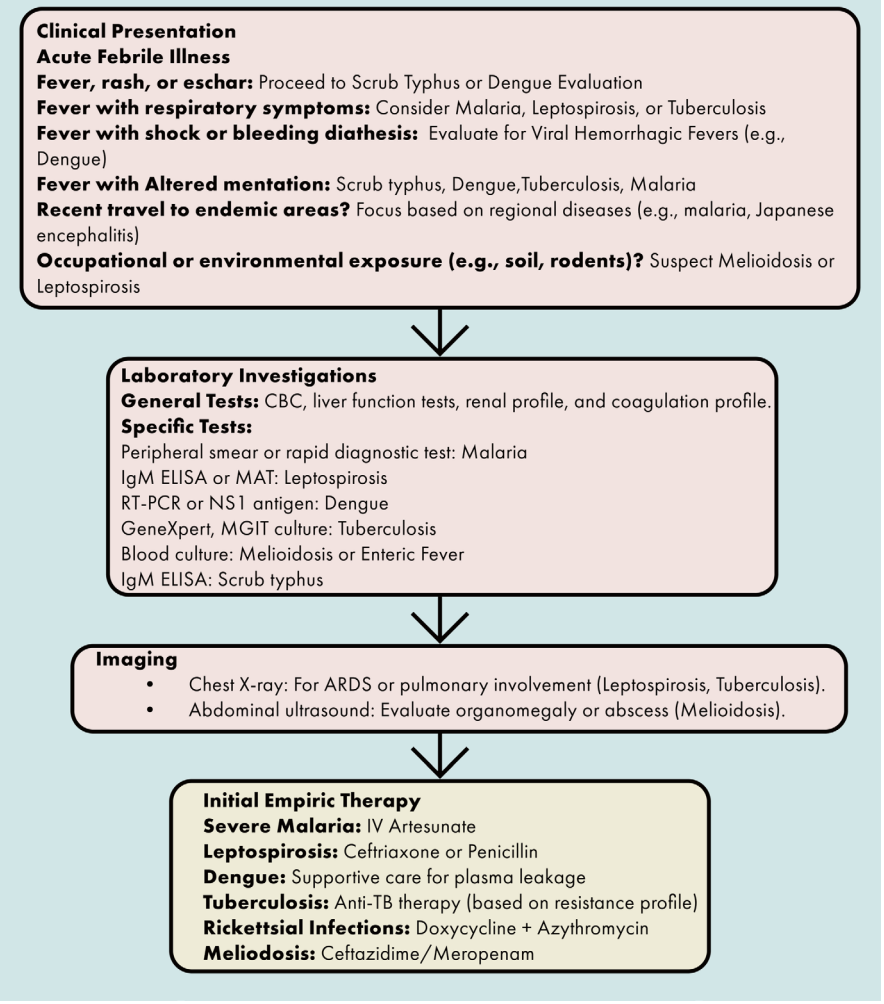
- IV Artesunate is the first-line therapy for *Plasmodium falciparum* malaria.
- Dose: 2.4 mg/kg body weight each dose, three doses in first 24 hours (0, 12, and 24 hours) and then once daily for three more days. At least 1 day of IV therapy is recommended. It may be switched to ACT [Artemisinin-based combination therapy, e.g., Artemether-lumefantrine (80 mg BD + 480 mg BD x 3 days), Artesunate-mefloquine (Artesunate 100 mg BD x 3 days + Mefloquine 750 mg on second day and 500 mg on third day), Artesunate-amodiaquine, Artesunate-sulfadoxine-pyrimethamine (Artesunate 100 mg BD x 3 days + Sulfadoxine 1500 mg and Pyrimethamine 75 mg single dose)] on day 2 if patient is able to take orally. This ACT should be given for 3 days.
- Adjunct therapies include managing complications like hypoglycemia, cerebral malaria, hyperpyrexia, convulsions, severe anemia, pulmonary edema, acute kidney injury, coagulopathy, metabolic acidosis or shock.
- **Leptospirosis**:
- IV Ceftriaxone (1 g IV every 24 hours) or Penicillin (1.5 MU IV every 6 hours) to address leptospiral sepsis. Doxycycline 100 mg BD or Azithromycin 500 mg once daily can also be given as second line of therapy.
- Consider doxycycline prophylaxis for high-risk exposures.
- **Dengue**:
- Supportive care with fluid resuscitation for plasma leakage syndrome.
- Platelet transfusion is indicated only for severe thrombocytopenia with active bleeding.
- Monitor for rare complications like encephalitis, which may require specific supportive measures.
- **Tuberculosis**:
- Initiate anti-TB therapy per resistance patterns or empiric regimens if drug sensitivity testing is pending.
- In cases of adrenal insufficiency, stress-dose steroids (hydrocortisone) may be necessary to manage hypotension and other symptoms.
- **Rickettsial Infections:**
- Doxycycline (100 mg IV twice daily) is effective against Scrub Typhus and other rickettsioses. Azithromycin is an alternative (500 mg IV once daily).
- In severe cases, a combination with Azithromycin may be beneficial.
- **Melioidosis:**
- IV Ceftazidime (2 g every 8 hour by a continuous infusion after a 2 g bolus) or Meropenem (1 g every 8 hour by a continuous infusion after a 1 g bolus) is critical for this potentially fatal infection. Most of the time, IV therapy extends to beyond 10 days. This is defined as the acute phase/intensive phase.

- Following initial intensive therapy, an eradication phase with oral antibiotics such as doxycycline and trimethoprim-sulfamethoxazole (160 mg/800 mg tablets; two tablets every 12 h) is essential to prevent relapses.
- Combination therapy (Co-trimoxazole+ Ceftazidime, Ceftazidime + Meropenem, Meropenem + Co-trimoxazole) may be given in case of poor clinical response to individual regimen. Combination therapy is important due to the organism's resistance patterns. The dose for IV Co-trimoxazole being 160 mg/800 mg–320 mg/1600 mg.
- Adjunctive therapies like granulocyte colony-stimulating factor (G-CSF) may be considered in septic shock to enhance neutrophil function. Adjunctive management also involves comprehensive supportive care for sepsis, which includes maintaining hemodynamic stability, ensuring proper blood glucose control, addressing respiratory and renal failure, and performing drainage of abscesses when feasible.

103.7 Conclusion

Managing tropical infections in the ICU requires a structured approach tailored to the clinical presentation, regional epidemiology, and individual patient factors. Recognizing symptom patterns and understanding the epidemiological context are crucial for early diagnosis. Comprehensive laboratory and imaging studies, including advanced diagnostic techniques, facilitate accurate identification of pathogens. Prognostic indicators and statistical tools aid in risk stratification and inform clinical decision-making. Initiating prompt empiric therapy and appropriate adjunctive treatments, while awaiting confirmatory diagnostics, improves patient outcomes. Early intervention and supportive care are pivotal in managing severe cases like Dengue, Malaria, or Melioidosis. Understanding the nuances of each condition and maintaining vigilance for complications—such as adrenal insufficiency or severe acidosis—are crucial for optimizing patient care.

Algorithm 103.1: Approach to tropical infections in the ICU



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