Infections that are unique to or predominantly seen in the tropical region are referred to as tropical infections. It is a broad term that encompasses a multitude of viral, bacterial, fungal and parasitic infections (Bhargava et al. 2018). These diseases are of significant public health concern as they affect a large section of the world population many of whom do not have access to adequate medical care. With increase in international travel these infections are no longer concern of the developing or underdeveloped nations alone (Marks et al. 2016).

If not identified and treated early, many of these infections can develop life threatening complications that require intensive care. This includes acute respiratory distress syndrome, myocarditis, hepatic failure, acute kidney injury, alteration in sensorium, shock and life threatening metabolic abnormalities (Table 3.1). Patients with these complications are better managed in intensive care units with adequate monitoring and life support systems.

The epidemiology of tropical infections requiring intensive care varies with seasons and regions. Many of these diseases are transmitted by mosquitoes and there is an increase in the incidence of these disease post rainfall due to the increase in vector density (Singhi et al. 2017). Common infections that necessitate hospital care and intensive care are dengue, scrub typhus, acute encephalitis syndromes, malaria and leptospirosis (Chrispal et al. 2010; Mittal et al. 2015). This profile however can vary from region to region and a good knowledge of the local epidemiology of tropical infections is a must for any physician working in these areas. Tropical infections are important cause of morbidity in returning western travellers after visiting these regions. Malaria, enteric fever, dengue fever and leishmaniasis are important tropical infections seen in returning travellers, many of which can have life threatening complications (Marks et al. 2016; Jensenius et al. 2013).
| Tropical infection | Life threatening complications requiring intensive care |
|--------------------|----------------------------------------------------------|
| **Viral infections** |                                                          |
| Dengue fever        | Shock, Fluid accumulation with respiratory distress, Severe bleeding, Impaired consciousness, Liver failure, Myocarditis |
| Yellow fever disease| Hepatic failure, Renal dysfunction, Severe bleeding |
| Japanese encephalitis| Impaired consciousness, Seizures |
| Kyasanur forest disease| Severe bleeding, Impaired sensorium |
| Chandipura virus    | Impaired sensorium |
| Nipah virus disease | Impaired consciousness, Seizures, ARDS |
| Crimean-Congo haemorrhagic fever| Severe bleeding |
| Ebola virus disease | Hypovolemic shock, Severe bleeding, Impaired sensorium, Respiratory distress |
| **Rickettsial infections** |                                                          |
| Scrub typhus        | Impaired consciousness, ARDS, Myocarditis, Renal dysfunction, DIC |
| Murine typhus       | Impaired sensorium, Renal dysfunction, ARDS |
| **Bacterial infections** |                                                          |
| Leptospirosis       | Renal impairment, Hepatic failure, Pulmonary haemorrhage, ARDS, Myocarditis |
| Enteric fever       | Intestinal perforation, Impaired sensorium |
| Traveller’s diarrhoea| Hypovolemia |
| Cholera             | Severe diarrhoea and hypovolemia |
| Melioidosis         | Pneumonia, Septic shock |
A Syndromic Approach to Diagnosis of Tropical Fevers

Many tropical infections have overlapping clinical features. Reaching a specific diagnosis may be difficult especially in resource limited settings without adequate diagnostic facilities. Moreover many of the serological tests used to diagnose tropical infections may be negative in the early part of the illnesses. A syndromic approach is therefore suggested for the diagnosis and management of undifferentiated tropical infections (Singhi et al. 2014; Karnad et al. 2018a; Kothari et al. 2006).
3.1.1  Fever with Hepatic and/or Renal Impairment

Many tropical infections can be complicated by acute kidney injury, hepatic involvement or both. Mild to moderate elevations in the levels of alanine transaminase (ALT) and aspartate transaminase (AST) levels are common in dengue fever, whereas bilirubin and alkaline phosphatase levels are usually normal (Trung et al. 2010). Elevated serum transaminase levels (ALT and AST >500 IU/ml) are independent predictors of mortality in dengue fever (Jain et al. 2017). Dengue patients with ALT or AST levels ≥1000 IU/L should be classified and managed as severe dengue (World Health Organization 2009).

Hepatic involvement in leptospirosis is characterised by marked increase serum bilirubin leading to jaundice (Fig. 3.1). AST, ALT and alkaline phosphatase are moderately elevated (Katz et al. 2001; Talwani et al. 2011). The kidneys are also

Fig. 3.1  Jaundice and conjunctival suffusion in a patient with leptospirosis (Image courtesy: Latha Rajeevan, Physician, District Hospital, Kannur, Kerala, India)
commonly involved in leptospirosis. Urine analysis may show microscopic haematuria, leucocytes and proteinuria. In severe cases renal involvement can be marked with elevated blood urea nitrogen and serum creatinine (Katz et al. 2001; Levett 2001).

Liver dysfunction in scrub typhus commonly manifests as mild to moderate elevation in serum transaminase levels. Elevated levels of bilirubin and alkaline phosphatase levels are relatively uncommon. Acute kidney injury also complicates a significant number of scrub typhus cases especially in the setting of multi-organ dysfunction (Rajapakse et al. 2017). Though elevated levels of hepatic transaminases are seen commonly in enteric fever, clinically significant hepatitis is uncommon (Sur et al. 2018).

Both hepatic and renal involvement are common in complicated malaria. Hepatic dysfunction in malaria is multifactorial including haemolysis, hepatitis and cholestasis. Acute kidney injury in malaria is due to acute tubular necrosis and is usually oliguric (White et al. 2014).

Liver involvement is characteristic of yellow fever and should be suspected in inhabitants of the endemic areas (South America and sub-Saharan Africa) as well as travellers visiting or returning from these areas (Barnett 2007). In its initial phase it resembles any other viral fever with fever, headache, malaise, myalgia, nausea and vomiting. Most patients enter a period of remission after the initial febrile period. Fifteen to twenty percent of patients may enter a period of intoxication after a brief afebrile period. Fever reappears and patient can develop multiple organ dysfunctions. Liver enzymes are elevated and unlike in other viral fevers AST is elevated more than ALT (Monath 2001). Serum transaminase levels correlate with the severity of the disease (Tuboi et al. 2007). There can be moderate increase in bilirubin levels (5–10 mg/dl), while alkaline phosphatase levels are usually normal. Patients can also develop acute kidney injury, proteinuria and bleeding manifestations.

3.1.2 Fever with Thrombocytopenia and/or Coagulopathy

Thrombocytopenia is seen in almost all patients with symptomatic dengue fever, while coagulopathy occurs in severe cases. Disseminated intravascular coagulation (DIC) can complicate dengue and is a predictor of mortality (Jain et al. 2017). Other viral illnesses that can present with haemorrhagic manifestations include yellow fever, Crimean-Congo haemorrhagic fever, Ebola virus disease and Marburg virus disease. A knowledge of the local epidemiology and patient’s detailed travel history may give valuable clues to the diagnosis (Hidalgo et al. 2017).

Ebola and Marburg viruses are two members of the Filoviridae family which can cause life threatening complications. Ebola viral disease has been reported from Central Africa, West Africa and Sudan. An outbreak is currently ongoing in the North Kivu region of the Democratic Republic of Congo. Many patients can develop bleeding manifestations (petechiae, ecchymoses, mucosal bleeding and blood in stools). Severe bleeding may occur towards the terminal phase of the illness. Volume
depletion due to severe vomiting and profuse watery diarrhoea is a major cause of severity and mortality (Schieffelin et al. 2014; Bah et al. 2015). Delirium and seizures can also occur (Chertow et al. 2014).

After its first outbreak in Germany (from imported vervet monkeys from Uganda) all cases of Marburg virus diseases were reported from Africa. It presents as a febrile illness progressing to severe hypotension, shock and coma. Bleeding manifestations occur in many patients, but clinically significant bleeding occurs mostly in terminal stages (Centers for Disease Control and Prevention (CDC) 2005; Kortepeter et al. 2011).

Thrombocytopenia in leptospirosis is transient and usually does not result in DIC (Levett 2001). Thrombocytopenia can occur in scrub typhus as well, and severe cases may be complicated by DIC (Lee et al. 2017). Thrombocytopenia and coagulopathy often complicate malaria, though spontaneous bleeding is uncommon (Karnad et al. 2018b). Thrombocytopenia occurs more commonly in adult patients of enteric fever than in paediatric patients (Azmatullah et al. 2015).

### 3.1.3 Fever with Rash

A maculopapular/morbilliform rash is common in dengue fever. Petechiae, ecchymosis and mucosal bleeding may indicate a severe disease (Thomas et al. 2007). Similar lesions can occur in other haemorrhagic fevers as well. A transient macular rash may be seen in some patients with leptospirosis (Levett 2001).

A macular or maculopapular rash is common in most of the rickettsial infections. A characteristic eschar can occur at the site of chigger bite in scrub typhus. Its frequency in scrub typhus varies, ranging from 7 to 80% in various studies (Rajapakse et al. 2017). It begins as a papule which enlarges and later necrosis to be covered with a black crust.

Meningococcal infection is to be considered as a differential diagnosis in any patient presenting with fever and rash, though the disease is not limited to the tropics. Skin lesions can be seen in meningococcal meningitis and meningococcemia and can be petechial, purpuric or ecchymotic lesions (Fig. 3.2).

### 3.1.4 Fever with Encephalopathy

Fever with altered sensorium in a patient living in a tropical country should raise suspicion of various diagnostic possibilities apart from common bacterial and viral pathogens causing central nervous system infections. Japanese encephalitis (JE) has been considered as the common cause of viral encephalitis in Asian countries. However various other viruses can also give rise to clinically indistinguishable encephalitic syndromes. Dengue virus, Chikungunya virus, Kyasanur forest disease, Chandipura virus and scrub typhus are other important causes of acute encephalitis syndrome (Joshi et al. 2012; Ravi et al. 2019). Cerebral malaria should be another important differential diagnosis in any patient with fever and altered sensorium or seizures.
Japanese encephalitis is a mosquito borne flavivirus which is endemic to Asia and western Pacific (Le Flohic et al. 2013; Mackenzie et al. 2006). In endemic areas it predominantly affects the paediatric population (Kabilan et al. 2004). However in non-immune travellers, persons of any age group can be affected. Most of the infections are asymptomatic or mild. However, those who develop neuroinvasive disease can develop life threatening complications. In such patients JE presents as a febrile illness followed after few days with alteration of mental status, focal neurological deficits, seizures and movement disorders. CSF opening pressure may be elevated and CSF studies may show mild to moderate lymphocytic pleocytosis. CSF protein may be mildly elevated and CSF glucose is usually normal. Lesions in the thalamus are characteristic finding on magnetic resonance imaging (MRI) but may not be seen in all patients (Dung et al. 2009). Basal ganglia as well as the brainstem can also be involved. In those who present as an encephalitis syndrome mortality is high (upto 25%) and many of the survivors will have long-term neurological sequelae (Kumar et al. 2017; McNaughton et al. 2018).

Kyasanur forest disease is endemic to the Western Ghats region of southern India (Munivenkatappa et al. 2018). It is a tick borne flavivirus disease which causes a self-limiting febrile disease in most patients. But around 20% of the patients can develop bleeding manifestations or neurological manifestations. Neurological manifestations occur later in the phase of disease in the form of alteration in sensorium,
convulsion and loss of consciousness (Wadia 1975). The Chandipura virus is an arbovirus belonging to the Rhabdoviridae family. Outbreaks were reported from Indian states of Gujarat, Maharashtra and Andhra Pradesh (Sudeep et al. 2016). The disease manifests as an acute encephalitis syndrome with high case fatality rate (50–75%) (Rao et al. 2004; Chadha et al. 2005).

In outbreak settings Nipah virus also should be considered as an important cause of encephalitis especially if the patients have coexisting acute respiratory distress syndrome (Banerjee et al. 2019). Nipah has caused outbreaks in Malaysia, Singapore, Bangladesh, Philippines, West Bengal (India) and recently in the southern Indian state of Kerala (Arunkumar et al. 2018).

### 3.1.5 Fever with Respiratory Distress

Respiratory distress in tropical infection can occur due to various reasons like pneumonia, acute respiratory distress syndrome, myocarditis and pleural effusion. ARDS and myocarditis are well-known complications of tropical infections like dengue, malaria, scrub typhus and leptospirosis (Kumar et al. 2018). Pleural effusion caused by plasma leakage and third space fluid accumulation can cause respiratory distress in dengue patients (Suwarto et al. 2016). Pulmonary haemorrhage is dreaded complication of leptospirosis that can be fatal (Trevejo et al. 1998).

### 3.2 Laboratory Investigations

#### 3.2.1 Routine Laboratory Investigations

Routine haemogram and blood chemistry can give valuable clues to the diagnosis of tropical fevers (Bhargava et al. 2018). While leucocytosis is common in leptospirosis, leucopenia is seen in most cases of viral illnesses including dengue fever. As mentioned above thrombocytopenia occurs in many tropical infections. A rising haematocrit may indicate haemocencentration in dengue fever. Alterations in hepatic and renal parameters occur in many tropical infections and the pattern of involvement may indicate specific diagnosis (Table 3.2). Creatine phosphokinase may be elevated in leptospirosis (Johnson et al. 1975). A peripheral smear is of utmost importance for the diagnosis of malaria.

#### 3.2.2 Culture and Sensitivity Testing

Appropriate microbiological investigations should be sent for all critically ill patients with suspected tropical infections. If any focus of infection is suspected, appropriate samples should be sent for gram staining, bacterial culture and sensitivity testing. Similarly if a fungal infection is suspected, samples should be send for microscopy (KOH staining, Calcofluor-white stain, etc.) and fungal culture and sensitivity testing.
| Tropical infection | Epidemiology | Clinical features | Abnormalities in routine laboratory testing | Diagnosis | Specific management |
|-------------------|--------------|------------------|------------------------------------------|-----------|--------------------|
| Dengue fever      | Caused by: Dengue virus (serotypes 1–4)  
Principle vector: Aedes aegypti mosquitoes  
Incubation period: 4–6 days  
Seasonal increase in rainfall leads to increase in the vector density and an increase in number of dengue cases. However many tropical countries are hyperendemic for dengue and cases can present in any season | Fever (usually lasting for 2–7 days)  
Headache  
Myalgia  
Retroorbital pain  
Rash and haemorrhagic manifestations | Leucopenia  
Thrombocytopenia  
Elevated haematocrit  
Elevation in transaminase levels | Dengue NS1 antigen detection (first 6 days of illness)  
Nucleic acid detection by RT-PCR (first 5 days of illness)  
IgM ELISA (after 5 days of illness) | Fluid resuscitation for shock  
Blood transfusion in patients with significant internal bleeding  
Platelet transfusion in those with platelet count less than 10,000/mm³ and/active bleeding |
| Leptospirosis     | Caused by Leptospira spp.  
Incubation period: 1–2 weeks  
Transmitted commonly by exposure to water contaminated by rat urine. Increase in number of cases can be seen following rainfall and flooding in endemic areas | Fever (1–2 weeks duration)  
Muscle pain  
Calf muscle tenderness  
Conjunctival suffusion  
Jaundice  
Oliguria | Leucocytosis  
Thrombocytopenia  
Hyperbilirubinemia (marked increase may be seen)  
Moderate increase in hepatic transaminase levels  
Elevated blood urea, serum creatinine, creatinine phosphokinase  
Urine analysis may show proteinuria, WBCs and RBCs | IgM ELISA is the most commonly available test. May be negative in early phase of illness  
Microscopic agglutination test (MAT) and PCR are more sensitive and specific, but are not widely available and are expensive | For critically ill patients intravenous therapy is preferred. Effective drugs include crystalline penicillin (1.5 MU IV q6h) for 7 days  
Alternate agents  
Ceftriaxone (2 g IV q24h) or Doxycycline (100 mg IV q12h) |
Table 3.2 (continued)

| Tropical infection | Epidemiology | Clinical features | Abnormalities in routine laboratory testing | Diagnosis | Specific management |
|--------------------|--------------|------------------|-------------------------------------------|-----------|--------------------|
| Scrub typhus       | Scrub typhus is caused by *Orientia tsutsugamushi* and is transmitted by the bite of the infected larval stages (chiggers) of the trombiculid mites during feeding. Incubation period: 7–10 days. It is endemic in many countries in the Asia-Pacific region including China, India, Japan, Korea, Thailand, Indonesia and Sri Lanka. | Fever (usually prolonged; median duration of 2 weeks). Headache. Myalgia. A characteristic eschar at the site of chigger bite may be seen. | Leucopenia or leucocytosis. Thrombocytopenia. Mild to moderate increase in transaminase levels. Creatinine may be elevated. | IgM ELISA is the test is widely available. Indirect fluorescent antibody test is considered as gold standard in serology. Weil–Felix test has poor sensitivity and specificity. Serological tests may be negative in early part of the illness. | Doxycycline 100 mg IV/PO q12h × 7 days OR Azithromycin 500 mg PO/IV q24h × 3 days |
| Enteric fever      | *Caused by Salmonella enterica* serotype Typhi. Incubation period: 10–14 days. Transmitted usually through contaminated food and water. It is more prevalent in areas with poor sanitation. | Fever (usually prolonged). Diarrhoea or constipation. Headache. | Leucopenia or leucocytosis. Mild to moderate increase in serum transaminase levels. | Blood culture (sensitivity: 50–70%). Bone marrow culture is more sensitive. Serological tests including the Widal test are unreliable. | Ceftriaxone 2 g IV q12h for 10 to 14 days OR Azithromycin 1 g PO/IV for 5–7 days |
| Tropical Infections in ICU |
|---------------------------|
| **Malaria**               |
| Transmitted by the bite of female anopheles mosquito |
| Incubation period: 1–4 weeks |
| Malaria is endemic to most of the tropical countries. Severe disease is usually caused by *P. falciparum* but can occur in infections due to other species also |
| High grade fever with chills and sweating |
| Malaise |
| Headache |
| Abdominal pain |
| Splenomegaly |
| Anaemia |
| Thrombocytopenia |
| Coagulation abnormalities |
| Increased bilirubin, hepatic transaminases |
| Elevated serum creatinine |
| Metabolic acidosis |
| Direct microscopy of giemsa stained peripheral blood smears (cannot detect low level parasitaemia) |
| Rapid diagnostic tests: based on detection of malarial antigens |
| Commonly used antigens include HRP2, LDH and aldolase. These tests are fairly accurate and easy to use |
| Parenteral artesunate is the drug of choice for severe malaria. It should be given at least for 24 h and till oral administration is possible (Dose: 2.4 mg/kg/dose stat followed by at 12 h, 24 h and then daily once) |
| Treatment should be completed with a three course of artemisinin combination therapy |
| **Yellow fever** |
| Caused by yellow fever virus, a flavivirus and transmitted by the bite of Aedes aegypti mosquitoes |
| Endemic to sub-Saharan Africa and South America |
| Disease begins as a non-specific viral illness with fever, headache, malaise and myalgia. This may be followed by an afebrile period. Around 15% patients enters a period of intoxication characterised by hepatic and renal dysfunction |
| Leukopenia |
| Elevated liver enzymes, (AST >> ALT) |
| Moderately elevated levels of Bilirubin |
| Azotemia, elevated creatinine, and significant proteinuria |
| Anti YF IgM antibody detection ELISA |
| Cross reactivity with other Flavivirus can occur) |
| IgM antibodies can persist after vaccination |
| RT-PCR |
| High sensitivity and specificity |
| Can differentiate between wild virus and 17D vaccine strain |
| LAMP (loop-mediated isothermal amplification) |
| RT-PCR: rapid, sensitive test |
| Do not require thermocycler, can be used in field settings |
| No anti-viral treatment available |
| Supportive care, including fluid management, correction of metabolic abnormalities, correction of coagulopathy, dialysis, treatment of secondary bacterial infections |
Many tropical infections can be complicated by secondary bacterial infections leading to bacteraemia and sepsis (Syue et al. 2018; West et al. 2014). Blood culture is therefore a mandatory investigation in these patients. Blood culture is the diagnostic investigation for enteric fever and is positive in about 50–70% of patients. Bone marrow culture offers sensitivity more than 90% in enteric fever and may be attempted if diagnosis remains elusive despite routine tests (Mogasale et al. 2016). Blood and urine culture for the diagnosis of leptospirosis are of low sensitivity and are seldom clinically useful.

### 3.2.3 Serological Tests

Specific serological tests for tropical infections should be done based on pre-test probabilities (Table 3.2). Considering the potential life threatening complications rapid diagnostic tests are often helpful in guiding therapy.

Serological tests for the diagnosis of dengue fever should be chosen based on the day of illness. In the initial 5 days of illness NS1 antigen detection by ELISA is preferred, while after 5 days IgM antibody by ELISA is used for diagnosis. Rapid tests for the diagnosis of dengue though less time consuming are not completely reliable (Hunsperger et al. 2009, 2014).

Peripheral blood smear examination has been traditionally used as the standard test for the diagnosis of malaria. However the procedure is operator dependent and cases with low level of parasitaemia can be missed (Kilian et al. 2000). Rapid diagnostic tests based on malarial antigens have revolutionised the diagnosis of malaria. The RDT kits are easy to use and give results in a short span of time. Commonly used kits are immunochromatography based flow through assays which detects one or more malarial antigens (histidine-rich protein 2 (HRP2), Plasmodium lactate dehydrogenase (pLDH) and aldolase). Current kits can also differentiate between Plasmodium falciparum malaria from malaria due to other species. The sensitivity and specificity of these RDTs are over 90% (Wilson 2012).

The microscopic agglutination test (MAT) considered as the reference standard serological test for the diagnosis of leptospirosis is cumbersome to perform and is not readily available. It also requires paired sera demonstrating a fourfold rise in titre for a definitive diagnosis. Various RDTs are commercially available which may help in presumptive diagnosis especially in acute settings. For confirmation it is recommended to perform testing by two different RDTs (National Centre for Disease Control 2015). IgM Immunofluorescence assay (IFA) is considered as the gold standard serological test for the diagnosis of scrub typhus. IgM ELISA is an alternative test with comparable sensitivity and specificity. IgM rapid flow assay is a point of care test that may be useful in resource limited setting (Gupta et al. 2016). Currently available serological tests for the diagnosis of enteric fever are not completely reliable (Wijedoru et al. 2017).

It should be emphasised that many serological tests may be negative in the initial phase of illness, and a negative serological test should not deter the clinician from initiating specific antimicrobial therapy in critically ill patients, especially if clinical possibility is high.
3.3 **Management of Critically Ill Patients with Tropical Infections**

The initial focus of management should be on correction of haemodynamic instability, hypoxemia, protection of airway and early initiation of antimicrobial agents. Hypovolemia and hypoperfusion can complicate many tropical infections. Moreover many tropical infections may be complicated by super added sepsis. Fluid and vasopressor therapy should be administered in accordance with the current sepsis guidelines (Singer et al. 2016; Rhodes et al. 2017). Fluid resuscitation is of at most importance in the management of dengue fever (Dutta et al. 2011). Hypoxemia and ARDS may require invasive or non-invasive ventilation. Endotracheal intubation may be required for the protection of airway in those patients with depressed sensorium.

### 3.3.1 Empirical Antimicrobial Therapy

If a tropical infection is suspected in a critically ill patient, appropriate antibiotics should be initiated without waiting for confirmatory laboratory residents. An attempt to make a clinical diagnosis based on the local epidemiology, travel and exposure history, physical examination and basic laboratory investigations should be made. A syndromic approach as mentioned above can be helpful in the initiation of antibiotics. Often a specific diagnosis may take time and meanwhile a combination of antibiotics may have to be used. For example, a combination of intravenous artesunate, ceftriaxone and doxycycline can cover most of the tropical infections and may have to be used in critically ill patients with suspected tropical infections awaiting a specific diagnosis (Karnad et al. 2018a).

3.4 **Management Issues in Specific Tropical Infections**

#### 3.4.1 Dengue Fever

Most complications in dengue fever occur during the critical phase of illness (day 3–7 of illness). During this period there is an increase in capillary permeability leading to plasma leakage. When patients lose a critical amount of plasma, shock develops. Thrombocytopenia and coagulation abnormalities during this time lead to bleeding manifestations which sometimes can be severe.

Patients with severe dengue should be managed ideally in an intensive care setup. Criteria for severe dengue is given in Table 3.3.

Fluid management with intravascular volume repletion forms the cornerstone of management of patients with plasma leakage. Crystalloids can be used as the fluid for initial resuscitation as randomised studies has shown no significant advantage of colloids over crystalloids (Wills et al. 2005). Details of fluid management in dengue patients with shock is summarised in Figs. 3.3 and 3.4 (World Health Organization 2009). In patients with significant bleeding leading to hypovolemia blood transfusion should be
Improvement

IV crystalloid 5–7 ml/kg/hr for 1–2 hours, then:
reduce to 3–5 ml/kg/hr for 2–4 hours;
reduce to 2–3 ml/kg/hr for 2–4 hours.

If patient continues to improve, fluid can be further reduced.
Monitor HCT 6–8 hourly.

If the patient is not stable, act according to HCT levels:
if HCT increases, consider bolus fluid administration or increase fluid administration; if HCT decreases, consider transfusion with fresh whole transfusion.

Stop at 48 hours.

If patient improves, reduce to 7–10 ml/kg/hr for 1–2 hours
Then reduce further.

Compensated shock (systolic pressure maintained but has signs of reduced perfusion) Fluid resuscitation with isotonic crystalloid 5–10 ml/kg/hr over 1 hour

Check HCT

HCT ↑ or high

Administer 2nd bolus of fluid 10–20 ml/kg/hr for 1 hour

Consider significant occult/overt bleed
Initiate transfusion with fresh whole blood

HCT ↓

Yes

No

Fig. 3.3 Fluid management in Dengue fever with compensated shock (World Health Organisation 2009)

Table 3.3 Criteria for severe dengue (World Health Organisation 2009)

| Severe plasma leakage                  |
|----------------------------------------|
| – Dengue shock syndrome                |
| – Fluid accumulation with respiratory distress |

| Severe bleeding as evaluated by the clinician |
|-----------------------------------------------|

| Severe organ involvement                      |
|-----------------------------------------------|
| – Liver: AST or ALT ≥ 1000 IU/L                |
| – CNS: impaired consciousness                 |
| – Heart and other organs                      |
Hypotensive shock
Fluid resuscitation with 20 ml/kg isotonic crystalloid or colloid over 15 minutes
Try to obtain a HCT level before fluid resuscitation

Improvement

Crystalloid/colloid 10 ml/kg/hr for 1 hour, then continue with: IV crystalloid 5–7 ml/kg/hr for 1–2 hours;
reduce to 3–5 ml/kg/hr for 2–4 hours;
reduce to 2–3 ml/kg/hr for 2–4 hours.
If patient continues to improve, fluid can be further reduced.
Monitor HCT 6-hourly.
If the patient is not stable, act according to HCT levels:
If HCT increases, consider bolus fluid administration or increase fluid administration; if HCT decreases,
consider transfusion with fresh whole transfusion. Stop at 48 hours.

Review first HCT

HCT ↑ or high

Administer 2nd bolus fluid (colloid) 10–20 ml/kg over ½ to 1 hour

Improvement

Yes

No

Repeat 2nd Hct

HCT ↓

Consider significant occult/overt bleed
Initiate transfusion with fresh whole blood

Administer 3rd bolus fluid (colloid) 10–20 ml/kg over 1 hour

Improvement

Yes

No

Repeat 3rd HCT

Fig. 3.4 Fluid management in Dengue fever with hypotensive shock (World Health Organization 2009)
There is no role for prophylactic platelet therapy in the absence of severe thrombocytopenia (<10,000/mm³) or active bleeding manifestations (World Health Organization 2009; Dutta et al. 2011). There is no sufficient evidence to support the use of corticosteroids in the management of dengue fever (Zhang and Kramer 2014).

### 3.4.2 Malaria

Severe malaria is a life threatening emergency and needs intensive monitoring and critical care. The definition of severe *P. falciparum* and *P. vivax* malaria is given in Table 3.4. All patients with severe malaria, irrespective of the infecting species, should be treated with parenteral artesunate for at least 24 h and until oral therapy is tolerated, after which treatment should be completed with artemisinin based combination therapy (artemether plus lumefantrine, artesunate plus amodiaquine or dihydroartemisinin plus piperaquine) for three days (WHO 2015; Sinclair et al. 2012). The same treatment is recommended in pregnant and lactating women as well. If artesunate is not available intramuscular, artemether is preferred over quinine in treating severe malaria (Esu et al. 2014).

| Table 3.4 | Criteria for severe malaria (from WHO 2015) |
|-----------|------------------------------------------|
| Severe *falciparum* malaria is defined as one or more of the following in the absence of an identified alternative cause and in the presence of *P. falciparum* parasitaemia |
| Impaired consciousness—Glasgow coma score <11 in adults or Blantyre coma score <3 in children |
| Prostration—generalised weakness so that a person is unable to sit, stand or walk without assistance |
| Multiple convulsions—more than two episodes within 24 h |
| Acidosis—a base deficit of >8 mEq/L, a plasma bicarbonate level of <15 mmol/L, or venous plasma lactate ≥5 mmol/L. Clinical indicators of acidosis include rapid, deep, laboured breathing |
| Hypoglycemia—blood or plasma glucose <40 mg/dL (<2.2 mmol/L) |
| Severe malarial anaemia—haemoglobin concentration ≤5 g/dL or haematocrit ≤15% in children <12 years of age (<7 g/dL and <20%, respectively, in adults) with parasite count >10,000/mcL |
| Renal impairment—plasma or serum creatinine >3 mg/dL (265 mc mol/L) or blood urea >20 mmol/L |
| Jaundice—plasma or serum bilirubin >50 mc mol/L (3 mg/dL) with a parasite count >100,000/mcL (approximately 2%) |
| Pulmonary edema—radiographically confirmed or oxygen saturation <92% on room air with respiratory rate >30/min, often with chest indrawing and crepitation on auscultation |
| Significant bleeding—including recurrent or prolonged bleeding from the nose, gums, or venipuncture sites, hematemesis, or melena |
| Shock—compensated shock is defined as capillary refill ≥3 s or temperature gradient on leg (mid to proximal limb) but no hypotension. Decompensated shock is defined as systolic blood pressure <70 mmHg in children or <80 mmHg in adults, with evidence of impaired perfusion (cool peripheries or prolonged capillary refill) |
| *P. falciparum* parasitaemia >10% (>500,000/mcL) |
| Severe *P. vivax* malaria is defined as falciparum malaria, except that there are no parasite density thresholds |

given. There is no role for prophylactic platelet therapy in the absence of severe thrombocytopenia (<10,000/mm³) or active bleeding manifestations (World Health Organization 2009; Dutta et al. 2011). There is no sufficient evidence to support the use of corticosteroids in the management of dengue fever (Zhang and Kramer 2014).
Apart from anti-malarial therapy supportive care and management of complications is of utmost significance in the management of severe malaria. Fluid status should be carefully assessed and managed accordingly. Impaired consciousness is a common complication of severe malaria. Airway has to be protected in such patients and in severe cases intubation may be needed to secure the airway. Convulsions should be managed with short acting benzodiazepines (diazepam, lorazepam or midazolam). Patients should be monitored for hypoglycaemia, and those with blood glucose level less than 40 mg/dl should be treated with continuous dextrose infusion. Severe anaemia (Haemoglobin <7 g/dL in adults) requires treatment with blood transfusion. Severe acute kidney injury and metabolic acidosis may warrant use of renal replacement therapy. Patients with poor sensorium may require endotracheal intubation for airway protection. ARDS in these patients should be managed as per standard ARDS protocols with lung protective ventilation (Taylor et al. 2012).

### 3.4.3 Leptospirosis

Antibiotics should be started at the earliest in critically ill patients of leptospirosis (Tubiana et al. 2013). Parenteral therapy is indicated in these patients. Effective agents include crystalline penicillin, doxycycline, ceftriaxone and cefotaxime. Antibiotics are usually continued for 7 days.

Acute kidney injury is common in severe leptospirosis. Pre-renal AKI may respond to fluid replacement; however, many patients will require renal replacement therapy. Hypokalemia is common, serum potassium levels should be monitored regularly and levels should be corrected if indicated.

The role of steroids in the management of severe leptospirosis is controversial. It has been tried in cases of severe leptospirosis with pulmonary involvement. While the only randomised control trial in this regard found that corticosteroids were ineffective and increased the risk of nosocomial infections, four prospective studies found benefit in those treated with steroids (Rodrigo et al. 2014; Azevedo et al. 2011).

### 3.4.4 Scrub Typhus

The preferred antibiotic is doxycycline given for a duration of seven days. Other effective agents include azithromycin, rifampicin and chloramphenicol (Jang et al. 2014).

Scrub typhus can be complicated by ARDS, meningo-encephalitis, myocarditis and disseminated intravascular coagulation and should be managed as accordingly as they arise.

### 3.4.5 Acute Encephalitis Syndromes

All patients presenting with acute encephalitis syndrome should be first stabilised and airways should be protected. Convulsions should be initially managed using short acting benzodiazepines. In case of recurrent seizures or status epilepticus, other anti-convulsants may have to be used. All metabolic abnormalities should be
corrected. A lumbar puncture and CSF analysis should be done for all patients presenting with acute onset fever and altered sensorium. If the CSF is showing possibility of pyogenic meningitis, patients should be started on ceftriaxone and vancomycin pending culture reports. In case an encephalitis syndrome is suspected an MRI of the brain can be done. If MRI is suggestive of Herpes encephalitis (temporal lobe involvement), IV acyclovir should be initiated. If thalamic involvement is prominent, Japanese encephalitis can be suspected. If the patient has other systemic involvement in addition to fever and altered sensorium, patients should be worked up for malaria, dengue, scrub typhus and leptospirosis. Empirical doxycycline should be added to treatment if scrub typhus or leptospirosis is suspected. For definitive diagnosis serological investigations and nucleic acid amplification tests (NAAT) in serum and CSF will have to be sent (Misra et al. 2017).

3.5 Conclusion

Tropical infections can cause life threatening complications requiring intensive monitoring and treatment. They account for a significant proportion of ICU admissions in the tropical countries. Early identification of the clinical syndrome and prompt initiation of empirical therapy is of paramount importance. Supportive therapy in the ICU including fluid management, correction of electrolyte imbalances and ventilatory support is also essential for successful management of critically ill patients with tropical infections.

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