



**Stepwise Guide for Diagnosis
and Management of Acute Fever
in Primary Care**



Acute fever

Acute undifferentiated febrile illness (AUFI)

Algorithm 1

Acute onset of fever $>38.3^{\circ}\text{C}$ (101.0°F) for >2 days and lasting up to 14 days without organ- or system-specific signs at the onset¹

Note: With history of no localizing symptoms except accompaniments of fever, such as chills, headaches, retro-orbital pain, myalgia, malaise, nausea, or vomiting.¹

Acute febrile illness (AFI) due to localized infections^{1,2}

Algorithm 2

- RTIs: Cough, dyspnea
- UTIs: Dysuria, hematuria
- IAIs: Abdominal pain, diarrhea, vomiting
- SSTIs: Abscess, cellulitis
- Bone and joint infections
- Viral fever/COVID-19

Fever of unknown origin (FUO)

Defined as fever 38.3°C (101°F) for >21 days that remains undiagnosed after a hospital workup^{3,4}

- Malignancy: Colorectal cancer, leukemia
- Noninfectious inflammatory disease: Rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, sarcoidosis, vasculitis syndromes

Note: Symptoms that can help direct the evaluation toward noninfectious causes include heart palpitations, sweating, heat intolerance (hyperthyroidism), recurrent or cyclic symptoms (rheumatoid, inflammatory, or hereditary disorder)⁵

- Drug-induced fever due to medications, such as carbamazepine, cimetidine, captopril, heparin, methyl dopa, and allopurinol

For management approach for FUO, refer to specialist



Acute undifferentiated febrile illness (Algorithm 1)

Step 1: Evaluation of medical history of the patient^{1,2}

- Consider factors: age, comorbidities, immunosuppression, and pregnancy.

Step 2: Thorough clinical examination of the patient^{1,2}

- A complete and thorough physical examination is mandatory.
- A search is required for hidden foci, such as throat examination, sinus tenderness, renal or hepatic tenderness, heart murmurs, chest examination, lymph nodes, and splenomegaly.
- Fundus examination (if headache or bleeding tendency) and examination of the skin for eschar and petechiae or purpura must be made.

Footnotes: Pneumonia, SSTI, UTI, and gastroenteritis are well-recognized issues among elderly patients with fever.⁶ Pregnancy-related immunosuppression is associated with increased severity of falciparum malaria. Other causes of fever in pregnancy include urinary tract infections, influenza, pneumonia, tonsillitis, viral gastroenteritis, and pyelonephritis (kidney infection).^{2,7,8}

Review of systems should include (i) febrile seizures; (ii) runny nose and congestion (viral UTI); (iii) headache (sinusitis, meningitis);

(iv) ear pain or waking in the night with signs of discomfort (otitis media); (v) cough or wheezing (pneumonia, bronchiolitis), abdominal pain (pneumonia, strep pharyngitis, gastroenteritis, abdominal abscess); and (vi) back pain (pyelonephritis), and any history of joint swelling or redness (osteomyelitis).^{2,5,7,8}

Special attention should be provided for specific underlying conditions that predispose them to select infections, such as diabetes mellitus, COPD, poor swallowing or gag reflex, long-term indwelling urinary catheters, prosthetic devices (artificial joints leading to septic arthritis), altered mental status (for aspiration pneumonia), or chronic immobility.⁶



Acute undifferentiated febrile illness (Algorithm 1)

Step 3: Assessment of Clinical Signs and Complications of Different AUFIs

Malaria^{9,10}

Clinical features:

Plasmodium falciparum
(IP: 9–14 days)

Plasmodium vivax
(IP: 10–14 days)

- Acute onset of high-grade intermittent fever
- Paroxysm of fever, shaking chills, and sweats occur every 48 hours or 72 hours, depending on species

Manifestations of severe malaria

- Cerebral malaria, severe anemia, metabolic acidosis, and acute renal failure
- ARDS and shock

Dengue^{9,10}

Clinical features:

IP: 3–14 days with acute onset of high-grade continuous fever

Dengue fever:

Headache, retro-orbital pain, myalgia, arthralgia, and rash

Dengue hemorrhagic fever:

Thrombocytopenia, mucosal and gastrointestinal bleeds, rise in hematocrit

Dengue shock syndrome:

Weak pulse, hypotension

Expanded dengue syndrome:

Encephalitis, myocarditis, hepatitis, renal failure, ARDS, and hemophagocytosis

Enteric fever^{9,10}

Clinical features:

IP: 1–14 days

First week:

Fever, headache, and relative bradycardia

Second week:

Abdominal pain, diarrhea, constipation, hepatosplenomegaly, and encephalopathy

Third week:

Intestinal bleeding, perforation, and MODS

Chikungunya¹¹

Clinical features:

Acute onset of moderate-to-high-grade continuous fever, rash, malaise, arthralgia, myalgia, and red eyes

Complications

- Respiratory failure
- Cardiovascular decompensation
- Myocarditis
- Acute hepatitis
- Renal failure
- Hemorrhage
- Meningoencephalitis
- Acute flaccid paralysis

Leptospirosis^{9,10}

Clinical features:

IP: 2–26 days with acute onset of moderate-to-high-grade continuous fever

Anicteric leptospirosis:

- Abrupt onset of fever, chills, headache, and myalgia
- Abdominal pain, conjunctival suffusion, and transient skin rash

Icteric leptospirosis:

- Jaundice, proteinuria, hematuria, oliguria, and/or anuria
- Pulmonary hemorrhages, ARDS, and myocarditis

Japanese encephalitis^{9,10}

Clinical features:

IP: Averages 6–8 days, with a range of 4–15 days.

- Prodromal period-fever, headache, vomiting, and myalgia
- Neurological features range from mild confusion to agitation to overt coma.
- Parkinson-like extrapyramidal signs are common, including tremor, rigidity, and choreoathetoid movements

Scrub typhus^{9,10}

Clinical features:

IP: 1–3 weeks

- Fever, headache, and myalgia
- Breathing difficulty, delirium, vomiting, cough, and jaundice

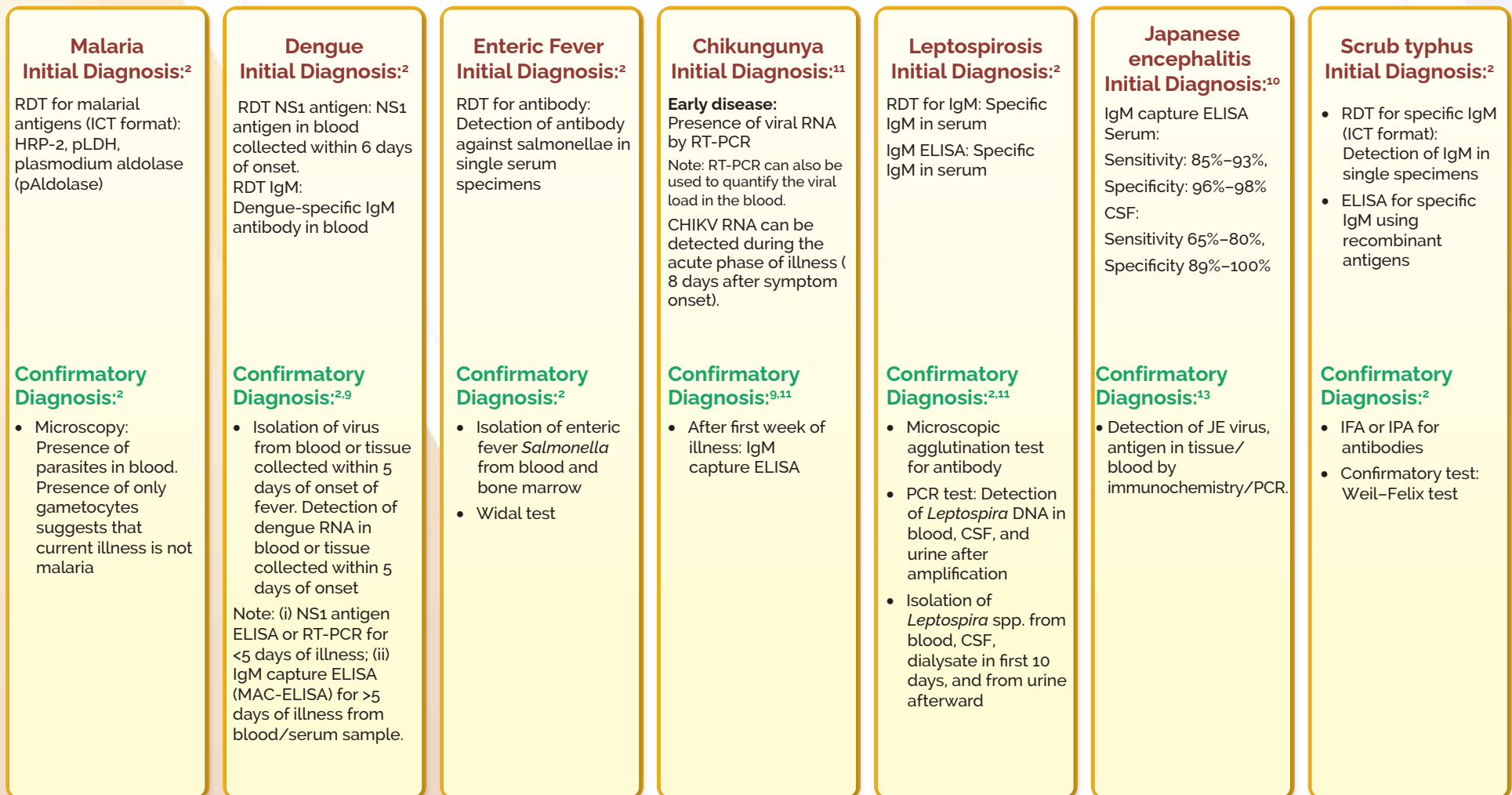
Complications

- Overwhelming pneumonia with ARDS-like presentation
- Hepatitis
- Aseptic meningitis
- Myocarditis and disseminated intravascular coagulation



Acute undifferentiated febrile illness (Algorithm 1)

Step 4: Confirmatory Diagnosis of Different AUFIs





Acute undifferentiated febrile illness (Algorithm 1)

Step 5: Treatment Options for Different AUFIs

Malaria

Vivax malaria::

Chloroquine (25 mg/kg b.w divided over three days, i.e. 10 mg/kg on day 1, 10 mg/kg on day 2, and 5 mg/kg on day 3) and primaquine (0.25 mg/kg b.w daily for 14 days).⁹

Note: Primaquine is used to prevent relapse but is contraindicated in pregnant women and infants.

Falciparum malaria:

Artesunate 4 mg/kg b.w. daily for 3 days plus sulfadoxine (25 mg/kg b.w) and pyrimethamine (1.25 mg/kg b.w) on day 1. This is to be accompanied by single dose of primaquine (0.75 mg/kg b.w) preferably on day 2.⁹

Chemoprophylaxis (< 6 weeks):

Doxycycline: 100 mg daily in adults and 1.5 mg/kg b.w for children more than 8 years old. The drug should be started 2 days before travel and continued for 4 weeks after leaving the malarious area.

Note: Doxycycline is contraindicated in pregnant and lactating women and children less than 8 years.¹⁴

Dengue

Antipyretics (avoid salicylates/ibuprofen) and tepid water sponging if temperature is above 39°C. Tablet paracetamol 10 mg/kg TDS.¹⁵

Increase fluid intake:¹⁵

- Children: 50 mL/kg b.w fluids during first 4–6 hours. Maintenance: 80–100 mL/kg b.w in the next 24 hours
- Adults: 2.5–4 L/day

Enteric fever¹⁶

- Oral amoxicillin 25 mg/kg TDS for 10–14 days.
- Oral trimethoprim/sulfamethoxazole 4/20 mg/kg BD for 10–14 days.

Chikungunya¹¹

- Patient may be treated symptomatically with paracetamol.
- If the pain is intractable, then NSAIDs, such as ibuprofen (400 mg TDS), naproxen (250 mg BD), diclofenac (50 mg BD), can be used.
- To minimize gastric intolerance, H₂ blockers ranitidine 150 mg BD or proton pump inhibitors, such as omeprazole 20 mg OD, may be used.

Leptospirosis¹²

- Adults: Doxycycline 100 mg twice a day for 7 days.
- Pregnant and lactating mothers should be given capsule ampicillin 500 mg every 6 hourly.
- Children (<8 years): Amoxicillin/ampicillin 30–50 mg/kg/day in divided doses for 7 days.
- Chemoprophylaxis: During the peak transmission season doxycycline 200 mg, once a week.

Note: Chemoprophylaxis should be for 6 weeks and should never be extended for more than 8 weeks.

Japanese Encephalitis

- Paracetamol 15 mg/kg diluted in 50 mL saline as retention enema. Oral syrup may be diluted 1:1 with ordinary water and used.¹³
- Supportive-airway management, seizure control, and management of raised intracranial pressure.^{10,13}

Scrub typhus¹⁰

- First line: Doxycycline 100 mg BD for 7 days.
- Azithromycin or rifampicin or chloramphenicol as alternative in children and pregnant women.

Note: For severely ill patients with nonmalarial, nonarboviral AUFIs, use a combination (third-generation cephalosporin+ doxycycline) as empirical therapy to cover rickettsioses, leptospirosis, and enteric fever. Doxycycline can serve as a companion antimalarial drug to artesunate and ceftriaxone and address concomitant bacterial sepsis frequently seen in such patients.²



Acute undifferentiated febrile illness (Algorithm 1)

Criteria for immediate attention and referral in fever in pediatric patients.⁵

Age <1 month	Petechiae or purpura
Lethargy, listlessness, or toxic appearance	Inconsolable crying
Respiratory distress	Seizures, difficulty to stay awake, and stiff neck

Red flag signs in patients with AUFIs, indicating the need for hospitalization, referral, and urgent treatment.²

- **Prostration**—Unable to stand, sit, or walk without
- **Temperature**—Hyperpyrexia (>41.5°C) or hypothermia (temperature <36°C) or rigors
- **Respiration**—Shortness of breath, respiratory rate >22 breaths/minute, cyanosis, arterial oxygen saturation <92% on room air
- **Circulation**—Blood pressure <100 mmHg systolic, cold clammy extremities, capillary refill >3 seconds
- **Neurological**—Altered mental status (Glasgow Coma Scale <13), convulsions, positive meningeal signs (such as neck stiffness and Kernig's sign)
- **Abdominal pain**—Severe or persistent vomiting
- **Severe conjunctival or palmar pallor**
- **Jaundice on examination of sclera**
- **Petechial or purpuric rash**
- **Bleeding**—From nose, gums, or venipuncture sites; hematemesis melena

FUO: Fever of unknown origin; AUFIs: Acute undifferentiated febrile illnesses; ARDS: Acute respiratory distress syndrome; IP: Incubation period; MODS: Multiple organ dysfunction syndrome; RDT: Rapid diagnostic test; HRP-2: Histidine-rich protein 2; ICT: Immunochromatographic test; IgG: Immunoglobulin G; NS-1: Nonstructural antigen 1; ELISA: Enzyme-linked immunosorbent assay; IFA: Immunofluorescent assay; IPA: Immunoperoxidase assay; BD: Twice a day; UTI: Urinary tract infection; SSTI: Skin and soft tissue infection; IAI: Intra-abdominal infection; BJI: Bone and joint infections; RTIs: Respiratory tract infections; COVID-19: Coronavirus disease of 2019; HCPS: Healthcare professionals; b.w: body weight; TDS: Thrice a day; OD: Once a day; WBC: White blood cell count; AFI: Acute febrile illness; COPD: Chronic obstructive pulmonary disease; PLDH: plasmodium lactate dehydrogenase; RT-PCR: Reverse transcription-polymerase chain reaction; CHIKV-RNA: Chikungunya viral ribonucleic acid; CSF: Cerebrospinal fluid; JE virus: Japanese encephalitis virus; MAC-ELISA: IgM antibody capture ELISA.



AFI due to localized infections (Algorithm 2)

Step 1: Evaluation of medical history of the patient^{1,2}

- Consider factors: age, comorbidities, immunosuppression, and pregnancy.

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AFI due to localized infections (Algorithm 2)

Step 3: Assessment of Clinical Signs and Complications of Different AFIs Due to Localized Infections

Fever due to URTI¹

Presenting features of URTI include sore throat, runny/blocked nose, cough with or without systemic symptoms, including fever and malaise.

- Streptococcal pharyngitis: sudden onset of fever and sore throat with pain during swallowing.
- Bacterial sinusitis: Worsening of symptoms or signs include new-onset fever, headache, or increase in nasal discharge following a typical viral URTI that lasts for 5–6 days and was initially improving (double sickening).

Fever due to LRTI¹

CAP is characterized by (i) symptoms of acute lower respiratory tract illness (cough with or without expectoration, shortness of breath, pleuritic chest pain) for less than 1 week and (ii) at least one systemic feature (temperature >37.7°C, chills, and rigors, and/or severe malaise).

Viral fever^{1,9,17}

Viral pneumonia due to adenovirus, influenza A & B, human metapneumovirus, parainfluenza, RSV, rhinovirus, cytomegalovirus. Characterized by high-grade fever, cough, sore throat, or myalgia

Note: Influenza-like illness is characterized by systemic signs, such as fever and malaise, along with the upper respiratory symptoms. The patients should be warned about symptoms, which indicate complications, such as breathing difficulty, persistent fever beyond 4–5 days, or ear pain.

COVID-19 caused by SARS-CoV-2 is characterized by low-to-moderate-grade continuous fever. IP: 2–4 days (onset of symptom average: 5–7 days).

- Symptoms include cough, dyspnea, myalgia, headache, sore throat, diarrhea, rhinorrhea, tachypnea, decreased oxygen saturation, and multiorgan involvement.

Complications include ARDS, arrhythmias, acute cardiac injury shock, pulmonary embolism, and acute stroke.

Fever due to UTI¹

- Acute cystitis characterized by dysuria, frequency, and urgency with or without fever with chills.

- Acute pyelonephritis characterized by flank pain, tenderness, or both and fever associated with dysuria, urgency, and frequency.

Fever due to IAI¹

Invasive bacterial (inflammatory) diarrhea characterized by fever, tenesmus, and grossly bloody stool.

Fever due to SSTI¹

SSTIs involve features of inflammatory response, with other manifestations, such as fever, rapid progression of lesions, and bullae.

Cellulitis is characterized by clinically rapidly intensifying pain and redness. Fever and lymphadenopathy may be present.

Fever due to BJI¹

Septic arthritis includes acute onset of high-grade fever with tender swollen joint.



AFI due to localized infections (Algorithm 2)

Step 4: Confirmatory Diagnosis of Different AFIs Due to Localized Infections

Fever due to URTI

- Examination findings include tonsillopharyngeal erythema and exudates, palatal petechiae, tender anterior cervical adenopathy, and sometimes scarlatiniform rash.¹
- Confirmation of diagnosis by rapid antigen test or throat swab culture is desirable.^{1,18}

Fever due to LRTI¹⁸

- X-ray PNS is done usually only if there is a chronic sinusitis to look for a fluid level.
- If duration of illness is >10 days with purulent nasal discharge, nasal obstruction, and facial pain, then a bacterial cause should be considered.

Viral fever

Laboratory findings for viral pneumonia:¹⁷
RT-PCR positive for the underlying virus, elevated lymphocyte counts

Laboratory findings for COVID-19 fever:¹⁷
RT-PCR positive for SARS-CoV-2, lymphopenia, elevated aminotransferases, CRP, and D-dimer

Chest CT findings for viral pneumonia:¹⁷ Interstitial inflammation, high-attenuation reticular patterns, localized atelectasis, or pulmonary edema

Chest CT findings for COVID-19:¹⁷

- Early stage: GGOs
- Progressive stage: Multiple GGOs, consolidation patches, crazy-pavement pattern
- Advanced stage: Diffuse exudative lesions, whiteout lung

Fever due to UTI

Routine urine analysis: Significant pyuria and/or dipstick leukocyte esterase test positive.¹

Fever due to IAI

A stool culture is indicated if the patient has symptoms lasting for more than 3–7 days, or is immunosuppressed. Microscopic evidence containing red blood cells can provide sufficient evidence.¹

Fever due to SSTI

Initial diagnosis involves morphologic features of lesion and the clinical setting. If drainage or an open wound is present, Gram's stain and culture can provide a definitive diagnosis. In the absence of culture findings, the bacterial etiology is difficult to establish.¹⁹

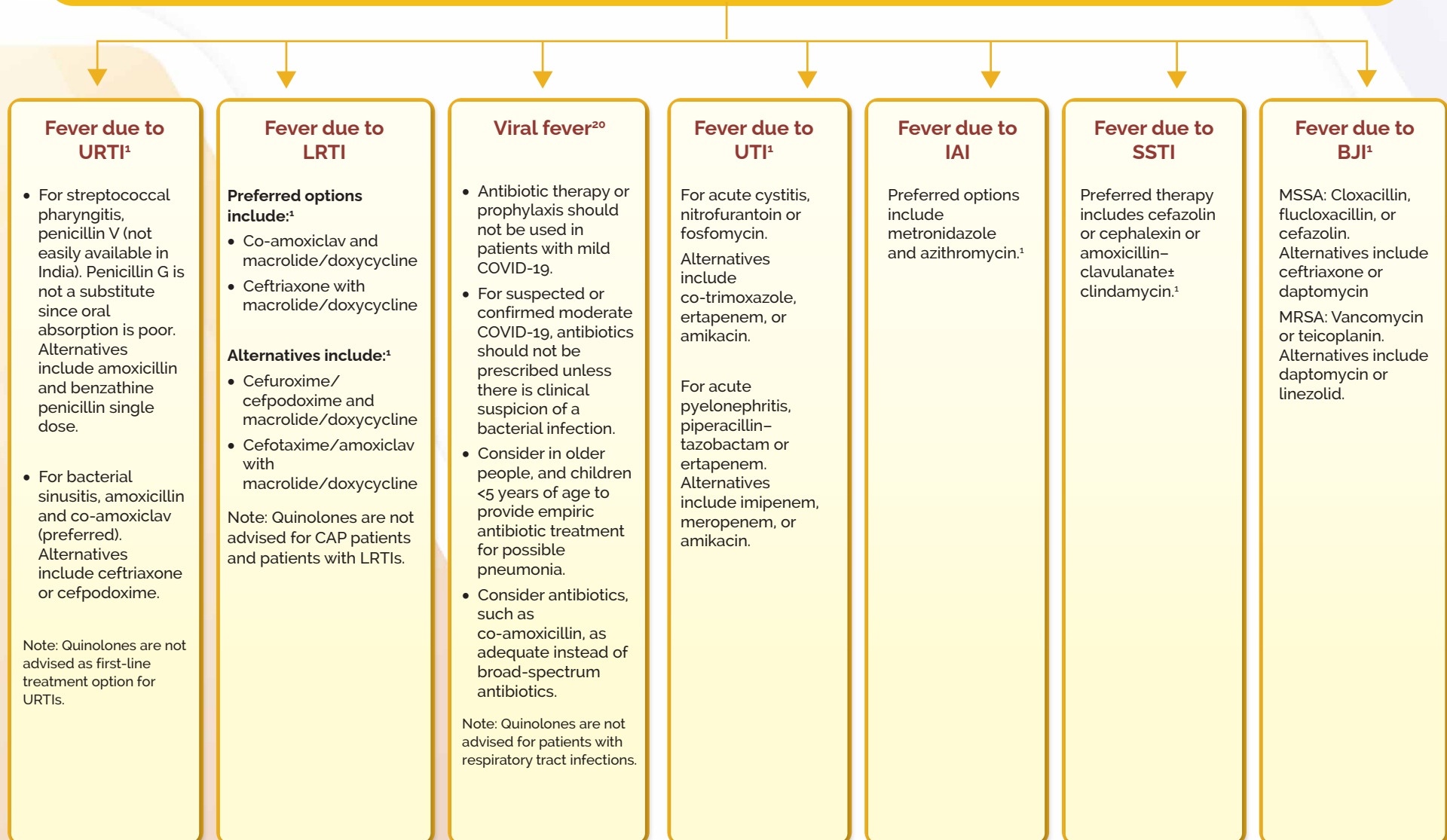
Fever due to BJI¹

- Leucocytosis, high ESR, and CRP are features of septic arthritis.
- Synovial fluid from the infected joint should send for WBC counts, Gram stain, and culture before starting antibiotics.
- Blood cultures should be obtained for all suspected cases of septic arthritis before starting antibiotics.



AFI due to localized infections (Algorithm 2)

Step 5: Treatment Options for Different AFIs Due to Localized Infections





In case of limited resources in management of fever and in certain compelling indications; empirical use of broad-spectrum antibiotics like doxycycline can be considered in the management of acute febrile illness.²¹

Do's of fever management^{1,22}

- Start antibiotics for a presumed bacterial infection promptly, but adjust the drug's dosage and duration, switch to a new drug, or end antibiotic therapy when results do not support or justify the need to continue.
- Reassess the situation within 48 hours based on test results and patient status.
- Supportive therapy: Acetaminophen 650 mg every 6 hours is advisable, accompanied by tepid sponging for fever >103°F.
- Supportive therapy should include adequate oral hydration to maintain the fluid balance and prevent dehydration. A minimum fluid intake of 50 mL/kg of b.w. in 24 hours should be maintained.

Don'ts of fever management^{1,22}

- Antibiotics should not be prescribed without an obvious clinical diagnosis or during strong suspicion of viral fever.
- Corticosteroids are not recommended in the treatment of AUFIs.
- Avoid indiscriminate use of antibiotic agents, NSAIDs, and steroids in patients with AUFIs.

Use mercury-free digital thermometers over traditional mercury thermometers. Note to HCPs: (i) Digital thermometers should not be used beyond 1 year; (ii) Sterilization: after every use wipe with 70%–90% of alcohol; and (iii) in clinics and hospitals, auxiliary thermometry is preferred over oral thermometry to avoid cross-contamination.



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