

COMMON ILLNESSES IN CHILDREN WITH HIV/AIDS

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OBJECTIVES

1. Discuss the assessment of a child with human immunodeficiency virus (HIV) who presents with fever.
2. Discuss the differential diagnosis of serious causes of fever, which includes sepsis, pneumonia, meningitis, and urinary tract infections.
3. Describe common signs and symptoms associated with the serious causes of fever.
4. Discuss the appropriate management of fever on the basis of the child's age.
5. Discuss the management of fever in children living in regions at high risk for malaria.

KEY POINTS

1. Infection is the most common cause of fever in children with HIV. Other causes of fever rarely include HIV infection itself or medications used to treat HIV.
2. Serious causes of fever include sepsis, pneumonia, meningitis, and urinary tract infections. These infections may be more severe or more rapidly progressive in children with HIV.
3. Respiratory infection is the most common complaint in HIV-infected children and may be manifested by one or more of the following signs and symptoms: fever, cough, difficulty breathing, sore throat, runny nose/nasal congestion, and ear pain or ear drainage.
4. Treatment of febrile illnesses in children depends on the age of the child.
5. Measles remains a cause of fever for children in most developing countries.
6. Malaria should be considered for any child with fever who lives in areas at high risk for malaria transmission.
7. All children younger than 2 months with fever and/or pneumonia and older children with severe disease should be assessed, stabilized, and referred to a hospital as quickly as possible.

OVERVIEW

Regardless of human immunodeficiency virus (HIV) status, any sick child who is brought to a clinic or hospital requires a complete and thorough assessment. If the child is assessed only for the major complaint or symptom, other important signs of diseases such as pneumonia, tuberculosis, diarrhea, malaria, measles, or malnutrition may be overlooked. If left untreated, these diseases can be serious or even fatal in young children.

This module reviews the assessment and treatment of a child who presents with fever and/or respiratory symptoms in areas at both high and low risk of malaria transmission. This module first discusses common infections in children aged 2 months to 5 years such as meningitis, sepsis, malaria, measles, urinary tract infection, and respiratory infections including pneumonia, otitis media, mastoiditis and sore throat. Fever in infants aged 1 week to 2 months is discussed later. Fever in newborns (aged <7 days) is beyond the scope of this discussion. Other diseases, including diarrhea, pneumocystis jirovecii (previously pneumocystis carinii) pneumonia, tuberculosis, and neurological manifestations of HIV/AIDS, are reviewed in other modules.

FEVER IN CHILDREN AGED 2 MONTHS TO 5 YEARS

Fever is one of the most common parental concerns for a child with HIV. Caregivers often view fever as an illness rather than a sign or symptom. Fever is defined by the World Health Organization (WHO) as a temperature greater than 37.5°C (measured under the arm) continuously for more than 24 h or intermittently for more than 24 h in a 72-h period.

Assessment

The first step in assessing a sick child is to ask the mother or caregiver to describe the problem(s) that the child is having and to check for general danger signs.

Subjective data include the following:

1. What is the child's temperature? What is the highest that it has been?
2. How long has the child had fever?
3. Has the child been alert and playful or lethargic and quiet?
4. How has the child's appetite been? Has the child been able to drink liquids?
5. Is the child experiencing any other signs/symptoms, such as ear pain, runny nose, cough, sore throat, abdominal pain, vomiting, or diarrhea?
6. Has the child been in contact with anyone who is ill?
7. Which treatments or medications have been given?

Assessment for general danger signs should include asking the child's caregiver the following:

1. Is the child unable to drink or breast-feed?
2. Does the child vomit every meal?
3. Has the child had convulsions?
4. Is the child unusually irritable or restless?
5. Has the child been less playful or sleeping more than usual?
6. Has the child been less interactive with the caregiver?
7. Has the child's urine output decreased?
8. Has the child lost weight?
9. Is the child having difficulty in breathing?

Danger Signs

- Lethargy
- Poor oral intake
- Fever (>37.5°C) or hypothermia (<35°C)
- Tachypnea
- Wheezing
- Retractions
- Nasal flaring
- Cyanosis
- Stridor when calm
- Altered mental status
- Severe malnutrition

Objective data include the following:

1. Accurate vital signs are essential in the assessment of a sick child. (See **Table A5** [in the appendix] for normal vital signs.)
2. Assessment of the child's general appearance. (Is the child toxic appearing or not?)
3. Does the child have a rash or appear pale or cyanotic (blue around the lips or face)?

4. Is the child's respiration labored? Does the child have retractions or nasal flaring?
5. A complete physical examination is needed to locate a source for the fever. Fever in persons with HIV infection should be evaluated based on clinical signs and symptoms, as well as the stage of HIV disease. The physical examination should pay particular attention to auscultation of the lungs, abdominal exam, skin, lymph nodes, and neurologic examination.
6. When possible, laboratory investigations may be helpful in identifying the source of infection and guiding treatment.

A child who has any of these general danger signs needs immediate, urgent attention. The assessment and initial treatment, such as administering a dose of the appropriate antibiotic, should be completed as quickly as possible, and a referral should be made for further treatment at a hospital. If the child is not responsive, causes such as hypoglycemia should be considered and empirically treated. If the child appears dehydrated, intravenous fluids or aggressive oral rehydration should be considered.

DIFFERENTIAL DIAGNOSIS OF FEVER IN CHILDREN AGED 2 MONTHS TO 5 YEARS

Fever may be caused by infection (bacterial, viral, fungal, or protozoal) or malignancy but is rarely caused by HIV infection itself or by medications used to treat HIV infection. In children in the early stages of HIV infection, before substantial immune suppression develops, a child with fever should be evaluated as an immunocompetent host. It is not until the child develops severe immunosuppression (CD4⁺ count of <15%) that he or she becomes more susceptible to opportunistic infections. When severely immunocompromised children present with fever, the assessment and initial treatment, such as administering a dose of the appropriate antibiotic, should be completed as quickly as possible, and the patient should be referred urgently to the hospital.

In children aged 2 months to 5 years, the differential diagnosis for fever may include the following:

- Severe bacterial infections
 - Meningitis
 - Severe pneumonia
 - Septicemia (overwhelming sepsis)
 - Severe malaria (in malaria-endemic areas)

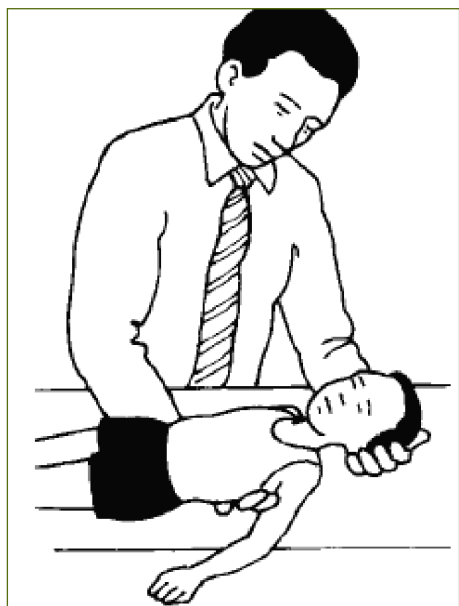


Figure 1. Examining a child for neck stiffness. (World Health Organization. Management of the child with a serious infection or severe malnutrition. Guidelines for care at the first-referral level in developing countries, 2000.)



Figure 2. A child with opisthotonos and rigid posture: a sign of raised intracranial pressure. (World Health Organization. Management of the child with a serious infection or severe malnutrition. Guidelines for care at the first-referral level in developing countries, 2000.)

- Pneumonia (nonsevere)
- Measles
- Urinary tract infections
- Upper respiratory infections
- Others
 - Septic arthritis
 - Dengue hemorrhagic fever
 - Typhoid

- Convulsions
- Lethargy
- Headache or pain in the back of the neck

Examination for bacterial meningitis includes the following:

- Neck stiffness (**Figure 1**)
- Repeated convulsions
- Petechial rash or purpura
- Lethargy
- Irritability
- Bulging fontanel
- Evidence of head trauma suggesting possibility of recent skull fracture
- Signs of raised intracranial pressure (**Figure 2**)
 - Unequal pupils
 - Opisthotonos or rigid posture
 - Irregular respirations
 - Focal paralysis in any of the limbs or trunk

This module will focus mainly on the prehospital care of the most common conditions; detailed inpatient management is beyond the scope of this module.

Bacterial Meningitis

Acute bacterial meningitis is a bacterial infection of the meninges and cerebrospinal fluid (CSF) resulting in meningeal inflammation, obstruction of the circulation of the CSF caused by purulent exudate, cerebral edema, and local necrosis of nerve fibers and cerebral vessels. Bacterial meningitis has high mortality and morbidity rates, especially if not treated early; therefore, early diagnosis and prompt effective treatment are essential. Diagnosis of bacterial meningitis includes the following:

History

- Vomiting
- Inability to drink or breast-feed
- Irritability

Nuchal rigidity, or neck stiffness, is reflected in the inability of a patient to place the chin on the chest, limitation of passive neck flexion, and Kernig and Brudzinski signs. Kernig sign is present if the patient, in the supine position with the hip and knee flexed at 90°, cannot extend the knee more than 135° and/or there is flexion of the opposite knee.

The Brudzinski sign is present if the patient, while in the supine position, flexes the lower extremities during attempted passive flexion of the neck.

Any child showing any of the preceding symptoms and signs should be quickly assessed for clinical stability, treated empirically with intravenous (IV) or intramuscular (IM) antibiotics, and transferred urgently to a hospital for further assessment and inpatient management. In children known or suspected to have HIV/AIDS, the differential diagnosis includes bacterial, tuberculous, viral and fungal (particularly cryptococcal) meningitis.

Laboratory investigations. Whenever possible, the diagnosis of meningitis should be confirmed with a lumbar puncture and CSF collection prior to the administration of antibiotics. CSF should be examined for full blood count, gram stain, culture, glucose, and protein. A lumbar puncture should not be carried out if there are signs of raised intracranial pressure (as outlined earlier) or there is local infection at the lumbar puncture site. Also, because of the invasive nature of the lumbar puncture, lumbar puncture is not recommended in settings in which reliable examination and culture of the CSF obtained is not possible.

Management. In the prehospital setting, if there is high suspicion of meningitis, and a lumbar puncture is not possible, then antibiotic therapy should be commenced promptly before the child is transferred to the hospital. Choose one of the following regimens:

- Chloramphenicol, 25 mg/kg of body weight IV (or IM) every 6 h plus ampicillin, 50 mg/kg IV (or IM) every 6 h
- Chloramphenicol, 25 mg/kg IV (or IM) every 6 h plus benzylpenicillin, 60 mg/kg (100,000 U/kg) every 6 h IV (or IM)

Where there is known significant drug resistance of common organisms (e.g., *Haemophilus influenzae* or *Streptococcus pneumoniae*) to the preceding antibiotics, national guidelines (based on susceptibility tests) should be followed. Often the most appropriate antibiotic will be a third-generation cephalosporin such as the following:

- Cefotaxime, 50 mg/kg IV (or IM) every 6 h
- Ceftriaxone, 50 mg/kg IV (or IM) over 30-60 min every 12 h

Measles

Measles is a highly contagious viral disease with serious complications (such as blindness in children with preexisting vitamin A deficiency) and a high mortality rate. It is rare in infants younger than 3 months. After a 1- to 2-week incubation period, the infection presents with a prodrome of high fever followed by cough, coryza (runny nose), conjunctivitis, and a fine maculopapular rash behind the ears and along the hairline, spreading to become generalized and blotchy and lasting for about 4 days. The rash may lead to skin desquamation. Sometimes pathognomonic small gray-white lesions (Koplik spots) appear on the posterior buccal mucosa.

Diagnosis. Measles often occurs in epidemics; therefore, recent episodes in the area should raise the suspicion of measles. A diagnosis of measles should be readily made if the mother clearly reports that the child has had a typical measles rash or if the child has the following symptoms:

- fever;
- generalized rash; and
- one of
 - cough,
 - runny nose, or
 - red eyes.

In children with HIV these symptoms and signs may not be present, and the diagnosis of measles may be difficult.

Severe complicated measles. A child with measles who presents with the following symptoms should be diagnosed as having severe measles:

- Inability to drink or breast-feed
- Vomiting all foods and liquids
- Convulsions

On examination, signs of late complications after the rash has disappeared should be looked for, including the following:

- Lethargy or unconsciousness
- Corneal clouding
- Deep or extensive mouth ulcers
- Pneumonia
- Dehydration from diarrhea or inability to drink
- Stridor caused by measles croup
- Severe malnutrition

Treatment. All children with severe or complicated measles require admission and management in a hospital. Vitamin A therapy should be given to all children with measles unless the child has had adequate vitamin A treatment for this illness as an outpatient or had received a preventive vitamin A supplement within 1 month. Two doses should be given: the first dose immediately upon diagnosis; the second dose, the next day. The dose varies according to the age of the child (**Table 1**).

Table 1. Dose of vitamin A

Age	Dosage (IU)
<6 mo	50,000
6-11 mo	100,000
12 mo-5 yrs	200,000

Those children who show eye signs compatible with vitamin A deficiency (xerophthalmia with corneal scarring) or are severely malnourished should receive a third dose of vitamin A 2-4 weeks after the second dose when the child comes for follow-up.

Supportive care for fever. If the temperature is $\geq 39^{\circ}\text{C}$ or $\geq 102.2^{\circ}\text{F}$, the child should be given paracetamol at a dose of 15 mg/kg up to four to six times a day to relieve the fever. If the fever persists for more than 3-4 days, a secondary infection should be considered. Antimalarial medications should be given in areas of high malaria endemicity if the malaria smear is positive or if there is high clinical suspicion of malaria.

Nutritional support. Nutritional status should be determined by weighing the child and plotting on a growth chart (rehydrate before weighing). The mother should be encouraged to breast-feed and to give the child frequent, small meals. The mouth should be examined for ulcers that might discourage the child from eating or drinking. National Guidelines on nutritional management should be followed depending on the degree of malnutrition.

Complications. Eye problems such as conjunctivitis and corneal damage may occur because of infection, vitamin A deficiency, or harmful local remedies. In addition to vitamin A, any infection should be treated

with an appropriate antibiotic such as tetracycline or gentamicin eye ointment three times a day. If there is no improvement after 7 days of treatment, the child should be referred to an ophthalmologist. A steroid eye ointment should never be used.

Neurologic complications. Convulsions, excessive sleepiness, drowsiness, or coma may be a symptom of encephalitis or severe dehydration. The child should be assessed for dehydration and treated accordingly (see the diarrhea chapter). The chapter on neurologic complications of HIV discusses management of convulsions. Other sections in this publication describe the management of other complications such as pneumonia, otitis media, and diarrhea.

Monitoring. The child's temperature should be checked twice a day and there should be daily assessment for the preceding complications. In uncomplicated measles the temperature usually returns to normal within about 4 days after the appearance of the rash. The child should be weighed daily to monitor hydration and nutritional status.

Follow-up. Recovery after acute measles is often delayed for many weeks or even months, especially in malnourished children. Recovery may be complicated by failure to thrive, recurrent infections, and persistent pneumonia and diarrhea. The death rate during this phase is high. Upon discharge mothers should be advised of potential problems and asked to return if they arise. A third dose of vitamin A should be arranged before discharge.

Public health measures. Measles is preventable with use of measles vaccine. Measles vaccine should be encouraged to all children according to the national vaccine schedule. Whenever possible, a child with measles should be isolated for at least 4 days after the onset of the rash. In malnourished and immunocompromised children, the isolation should be continued throughout the duration of the illness. When there are children with measles in the hospital, immunize all other children older than 6 months. If children receive their measles vaccination at 6-9 months, ensure that they receive a second dose as soon as possible after 9 months. Check the immunization status of the staff and vaccinate accordingly.

Measles (nonsevere)—diagnosis. Nonsevere measles should be diagnosed in children whose mothers clearly report measles rash or if the child has

- fever;
- a generalized rash; and
- one of
 - cough,
 - runny nose, or
 - red eyes, but
- none of the features of severe or complicated measles.

Measles (nonsevere)—treatment. Nonsevere measles should be treated on an outpatient basis. The treatment is largely supportive and symptomatic. The supportive treatment is outlined in the management of severe measles. Vitamin A therapy should also be given as described earlier.

Malaria

In malaria-endemic regions, the diagnosis of malaria should be considered in any patient presenting with fever, particularly if no other source for the fever can be identified. Malaria is responsible for an estimated 300 million-500 million infections and 1 million-3 million deaths per year. In areas of high malaria transmission, children younger than 5 years are most at risk of severe malaria and death. Children with HIV/AIDS are more likely to be infected with malaria, and the infection is more likely to be symptomatic, more severe, and less responsive to treatment. HIV infection is associated with increased susceptibility, higher parasitemia, and an increased risk for recurrent malaria infections, especially in patients with CD4 counts less than 200 cells/ μ L.

Malaria is caused by infection of red blood cells (RBCs) with protozoan parasites of the genus *Plasmodium*. Human malaria is caused primarily by four species of plasmodia: *Plasmodium falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*. A fifth species, *P. knowlesi*, was previously confined to infections in nonhuman primates but has also been implicated in human disease.

In humans, malaria parasites grow and multiply first in the liver cells and then in RBCs. Successive broods of parasites grow inside the RBCs and destroy them, releasing daughter parasites that continue the cycle by invading other RBCs. When certain forms of blood stage parasites are picked up by a female *Anopheles* mosquito

during a blood meal, they start another, different cycle of growth and multiplication in the mosquito. The parasite eventually ends up in the mosquito's salivary glands, ready to be injected into another human host.

Diagnosis. In stable high-transmission settings, malaria is usually the most common cause of fever in children younger than 5 years. For severe malaria, accurate prereferral diagnosis and treatment are imperative to prevent illness and death associated with delays in the initiation of effective therapy. As immunity is acquired, however, malaria becomes less likely as a cause of fever. Thus, in children older than 5 years and in adults, the diagnosis of malaria should be based on parasitological confirmation.

The typical presentation of malarial infection may be nonspecific and be similar to that of a minor systemic viral illness. The prodrome often includes headache, coughing, malaise, fatigue, abdominal discomfort, and muscle and joint pain. These symptoms are followed by paroxysms of fever, shaking chills, and perspiration. Nausea, vomiting, diarrhea, abdominal pain and worsening malaise may accompany the fever. Physical examination may reveal splenomegaly and mild jaundice, but there is usually no lymphadenopathy.

Severe malaria is a medical emergency. Severe disease is life threatening and is manifested by the presence of one or more of the following conditions:

- Coma
- Metabolic acidosis
- Severe anemia
- Hypoglycemia
- Acute renal failure
- Acute pulmonary edema

In older children and adults, malaria diagnosis should be based on parasitological confirmation. Parasitological diagnostic techniques are important in confirming the diagnosis of malaria, quantifying the degree of parasitemia, and identifying the species of the parasite and confirming treatment failures. If the diagnosis of malaria is excluded by careful parasitologic diagnostics, then unnecessary exposure to antimalarial medications can be prevented, thereby reducing side effects, drug interactions, and selection pressure. Parasitological diagnosis should also be promoted in pregnant women to improve the differential diagnosis of fever and to

reduce the unnecessary use of antimalarial medications in pregnancy. Parasitological diagnosis is also important in settings with a high prevalence of HIV/AIDS because of the high incidence of febrile disease that is not malaria.

Light microscopy of Giemsa-stained thick or thin blood smear remains the mainstay of the diagnosis of malaria. Light microscopy has the advantage of low cost and high sensitivity and specificity when used by well-trained staff. The thick smear is more sensitive in diagnosing malaria. Examination of thin films allows the examination of the morphologic features of the parasites and the host RBC, which is useful for identifying the particular malaria species. The thin smear also allows quantification of the percentage of parasitized RBCs.

Rapid diagnostic tests for the detection of parasite antigens are available and generally more expensive than light microscopy. These tests may also be vulnerable to ambient conditions, such as heat and humidity, that might compromise their accuracy. These tests may be of benefit in allowing the diagnosis of malaria in settings where light microscopy is not possible.

Treatment. In uncomplicated infections, if prompt and effective treatment is provided, recovery is complete and case fatality is low. If treatment is delayed or if ineffective drugs are given, the parasite burden continues to increase and severe malaria may result. A patient can progress from having minor symptoms to having severe disease within a few hours. In severe malaria, if untreated, mortality approaches 100%. Even with treatment, risk of mortality remains as high as 15%-20%. Thus, it is imperative to consider malaria as a cause of fever of children in endemic regions and to provide prompt treatment to decrease associated illness and death. Delays in the recognition and treatment of malaria are directly associated with increases in morbidity and mortality.

If the patient presents only with fever but no danger signs, stiff neck, or signs of severe malaria, and if the patient has no cough with rapid breathing, then he is presumed to have uncomplicated malaria. This patient should receive oral antimalarial medications. If there is concern for pneumonia with cough and rapid breathing, then the patient should also be treated with an appropriate antibiotic.

To counter the threat of resistance of *P. falciparum* to single antimalarial medications and to improve treatment outcomes, treatment for malaria is based on the use of combinations of two or more antimalarial medications, each with independent modes of action and thus unrelated biochemical targets in the parasite. The potential disadvantage in the use of combinations of drugs is the possibility for increased risk of adverse effects and the increased cost of using multiple drugs.

Artemisinin-based combination therapy (ACT) is a preferred treatment option for malaria. Artemisinin and its derivatives (artesunate, artemether, artemotil, and dihydroartemisinin) produce rapid clearance of parasitemia and rapid resolution of symptoms. See Tables A1-A4 (in the appendix) for information of currently recommended ACTs. The choice of ACT in a country or region will be based on the level of resistance of the partner medication in the combination. Important features of ACT include the following:

1. The artemisinin derivative components of the combination must be given for at least 3 days for an optimum effect.
2. Sulfadoxine-pyrimethamine should be avoided for malaria treatment in HIV-infected patients receiving cotrimoxazole prophylaxis.
3. Artemether-lumefantrine (Coartem) should be used with a six-dose regimen.
4. Amodiaquine plus sulfadoxine-pyrimethamine may be considered as an interim option in situations where ACTs cannot be made available.

Because the initial symptoms of malaria may include isolated cough or rapid breathing associated with metabolic acidosis, the caregiver must be advised to return promptly if the patient's condition worsens (including the development of any of the danger signs or signs of severe malaria) or fails to improve.

If there are any of danger signs, neck stiffness, or any of the preceding signs of severe malaria, the patient is classified as having severe malaria. Young children and nonimmune adults may deteriorate quickly. Severe malaria is a clinical emergency. The physician or health care worker should use his clinical judgment and treat any patient suspected of having severe malaria appropriately. The risks of undertreating severe malaria greatly outweigh those of giving emergent treatment to a patient who does not need it.

The patient should be immediately given full doses of IV or IM antimalarial treatment with whichever effective antimalarial is first available for treatment of severe malaria as well as the first dose of appropriate broad-spectrum antibiotics for bacterial causes of fever.

For children in high-transmission areas, one of the following antimalarial medications is recommended for emergency prehospital use:

- Artesunate 2.4 mg/kg IV or IM given on admission (time = 0) and then at 12 h, 24 h, and then once daily.
- Artemether 3.2 mg/kg IM given on admission and then 1.6 mg/kg/day.
- Quinine 20 mg salt/kg on admission IV or divided IM injection and then 10 mg/kg every 8 h. IV infusion rate should not exceed 5 mg salt/kg/h.

Also, the patient should be treated to prevent or treat low blood sugar and treated with paracetamol if temperature is greater than 38.5°C. After these measures have been taken and the patient is stable, the patient should be referred urgently to the hospital, where he or she can be managed in an intensive care unit where clinical monitoring can be assured.

Public health measures. Prevention of malaria transmission remains a key measure to reduce the morbidity and mortality associated with malaria infection. Prevention of malaria in HIV-infected people living in endemic areas is increasingly regarded as part of basic HIV care. A combination of cotrimoxazole, antiretroviral therapy, and insecticide-treated bednets substantially reduces the frequency of malaria and thus the morbidity and mortality of malaria infection.

Septicemia

Septicemia should be suspected in any seriously ill child with fever and no apparent focus of the infection. Where meningococcal disease is common, a clinical diagnosis of meningococcal septicemia must be made if petechiae or purpura are present. Antibiotic therapy should be started promptly.

Table 2. Estimated minimal incidence of bacteremia by causative organism among children in the catchment area of a rural Kenyan hospital

Pathogen	Incidence of bacteremia per 100,000 for age (yrs)		
	<1 (N = 26,968)	<2 (N = 50,804)	<5 (N = 136,444)
Any organism	1457	1080	505
<i>Streptococcus pneumoniae</i>	241	213	111
<i>Staphylococcus aureus</i>	89	57	27
Group A streptococci	96	63	29
Group B streptococci	74	39	15
Nontyphoidal salmonella species	170	175	88
<i>Haemophilus influenzae</i>	159	120	60
<i>Escherichia coli</i>	204	136	54

A recent study by Berkley et al. reported the following estimated minimal incidence of bacteremia by causative organism among children in the catchment area of a rural Kenyan hospital (**Table 2**).

The following differential diagnoses must be ruled out.

- Malaria: do a blood film. Malaria can kill children quickly. In malaria-endemic areas, or if there is any suspicion of malaria, give antimalaria treatment as soon as possible. Do not wait for the result of the blood film. It is better to err on the side of caution.
- Meningitis: look for a stiff neck, Kernig sign, or Brudzinski sign; do a lumbar puncture.

Laboratory investigations. Wherever feasible, perform the following:

- Blood for microscopy, culture, and sensitivity
- Urine for microscopy, culture, and sensitivity
- Lumbar puncture for Gram stain, India ink, and CSF culture
- Malaria blood slide in malaria-endemic areas or if there is a history of travel to a malaria-endemic area

Treatment. Treatment options include the following:

- Benzylpenicillin 500,000 U/kg IV or IM every 6 h plus chloramphenicol 25 mg/kg IV or IM every 8 h for 7 days.

- If there is no improvement on the preceding regimen, switch to chloramphenicol 25 mg/kg IV or IM every 8 h plus ampicillin 50 mg/kg IV or IM every 6 h.
- Often, especially where there is known or suspected microbial resistance to the preceding antibiotics, the best antibiotic may be a third-generation cephalosporin such as ceftriaxone 80 mg/kg IV or IM once daily for 7 days.

Complications. Common complications of septicemia may include the following:

- Shock (septicemic shock)
- Cardiac failure
- Disseminated intravascular coagulation
- Anemia
- Convulsions
- Confusion
- Coma

Death from septicemic shock is common. A thorough history and physical examination and appropriate investigations should result in recognition of the preceding complications, and prompt appropriate treatment should be initiated to reduce the associated mortality.

Public health measures. Children should receive all the WHO-recommended childhood vaccinations to reduce the morbidity and mortality from preventable childhood illnesses.

Respiratory Infections

Respiratory infection may involve the upper or lower respiratory tract. The upper tract includes the nose, middle ear, and pharynx. The lower tract includes the trachea, bronchi, bronchioles, and lungs. Signs and symptoms of respiratory infection include cough, difficulty breathing, sore throat, runny nose, and ear pain or ear drainage. Fever is also common in children with respiratory infections.

Respiratory infections involving both the upper and lower respiratory tracts are common in children. Most respiratory infections in children are caused by viruses. The most frequently isolated viruses are respiratory syncytial virus, rhinoviruses, influenza viruses, and adenoviruses. Human metapneumovirus, identified in 2001, also has been associated with otitis media (ear infections) in children. Bacterial causes of respiratory

infection in children include *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Other bacterial causes include group A β -hemolytic streptococci, staphylococci, *Chlamydia trachomatis*, and mycoplasma.

Younger children are more susceptible to more severe infection because of anatomic differences. Young children's airways are narrower and more easily obstructed by edema and secretions. The eustachian tube, the tube between the nasopharynx and middle ear, is shorter in infants and young children, which leads to increased susceptibility to otitis media.

In the early stages of HIV infection, before immune suppression develops, an older child with a respiratory infection involving both the upper and lower respiratory tracts should be evaluated as an immunocompetent host. It is not until the older child develops severe immunosuppression (CD4⁺ count of <15%) that he or she becomes more susceptible to opportunistic infections. However, young infants tend to be susceptible to opportunistic infections (especially pneumocystis jirovecii [previously pneumocystis carinii] pneumonia) even with high CD4 counts.

A child with a mild respiratory infection or cold may be treated symptomatically at home. A child with a more severe infection, such as pneumonia, may need to be treated in the hospital. According to the WHO, lower respiratory infections are responsible for 18% of all deaths in developing countries. Many of these deaths occur among children who are younger than 2 months. Early recognition and appropriate treatment of pneumonia can greatly reduce the number of deaths.

Most cases of pneumonia can be identified by checking for the most common signs of pneumonia, fever, fast breathing, and retractions. In this module, the student will learn how to differentiate between a cold and pneumonia and how to determine which cases of pneumonia can be treated in an outpatient clinic and which require admission to a hospital.

Assessment of a child with a respiratory infection should include both subjective data and objective data. Subjective data include the following:

1. Which signs/symptoms are present? Does the child have a cough? Is the child having difficulty breathing? Parents may describe such breathing as "fast," "noisy," or "interrupted."

2. Does the child have fever? If yes, how high is the temperature, and how long has it been elevated?
3. Does the child have a sore throat or runny nose? Is there ear pain or ear drainage? How long have these symptoms been present?
4. Is the child complaining of chest pain? Is the pain localized or generalized, dull or sharp, deep or superficial, associated with rapid, shallow respirations or grunting?
5. Can the child drink and is he or she interested in drinking? When was the child's last urine output?
6. What is the child's activity level?
7. Has the child had convulsions?
8. Is the child abnormally sleepy or difficult to rouse?

Correct interpretation of objective findings will depend on the child's age. Younger children normally have higher respiratory rates than those of older children. The respiratory rate should be counted for an entire minute, especially in infants, for whom variations in rate are normal. Respiratory rate should be counted while the child is quiet, where this is possible (See **Table A5** [in the appendix] for normal vital signs.) gives age-specific vital signs. Objective data should include the following:

1. The child's respirations should be observed for rate, depth, ease, and rhythm of breathing.
 - a. Rate. Is the rate normal, rapid, or slow for the child?
 - b. Depth. Is the depth of the respiration normal, too shallow, or too deep?
 - c. Ease. Are the respirations effortless or labored? Does the child need to be upright to breathe? Are there intercostal or substernal retractions (sinking in of the chest with respiration)? Does nasal flaring or head bobbing accompany the child's breathing? Is the child grunting or wheezing?
 - d. Rhythm of breathing. Is there variation in rate and depth of respiration?
2. Is the chest movement symmetrical? Asymmetry may indicate pneumonia, pneumothorax (air in the normally closed pleural space between two membranes on the exterior of the lungs), atelectasis (collapse of a lobe of the lung), or foreign-body obstruction.
3. The lungs should ideally be auscultated (listened to) throughout all lung fields while the child is quiet. The stethoscope should be placed directly on the child's skin. Are any abnormal sounds present? Chest auscultation usually reveals some of the following:
 - a. Decreased breath sounds
 - b. Bronchial breathing
 - c. Crepitations (crackles)
 - d. Increased vocal resonance (over consolidated lung tissue) or decreased vocal resonance (over a pleural effusion)
 - e. Pleural rub
4. Is there other evidence of infection, such as enlarged cervical lymph nodes, inflamed nasal mucous membranes, or discharge from the nose (rhinorrhea) or lungs (sputum)?
5. Does the child have a cough? When is the cough most frequent (e.g., morning or night)? How frequent is the cough? Is the cough productive or nonproductive? If the cough is productive, note volume, color, viscosity, and odor of sputum. How does the cough sound—moist, dry, or croupy? Is the cough accompanied by wheezing or stridor?
6. Are there changes in skin color, such as mottling, pallor, or cyanosis? What is the distribution of the discoloration (peripheral, circumoral, central)? What is the capillary refill time? Is cyanosis associated with activity or present at rest?
7. Is clubbing present? Clubbing is an abnormal growth of tissue about the terminal phalanges (bones of the fingers and toes). Clubbing is usually associated with chronic hypoxia (decreased oxygen to body tissues) and in HIV-infected children is a common sign of lymphocytic interstitial pneumonitis or bronchiectasis.
8. Wherever possible, a chest radiograph should be obtained, which may clearly define the following:
 - a. Consolidation
 - b. Interstitial infiltrates
 - c. Pleural effusion
 - d. Empyema thoracis
 - e. Pneumothorax or pneumatocele

Severe Pneumonia

A child is classified as having severe pneumonia if he or she has cough or respiratory distress plus at least one of the following:

- Central cyanosis
- Inability to drink or breast-feed or vomiting everything
- Convulsions, lethargy, or unconsciousness

The child's respiratory rate needs to be adequately assessed to determine whether the child is in respiratory distress or faces impending respiratory failure. Cardinal signs of respiratory failure are restlessness, tachypnea (rapid respiration), tachycardia (rapid heart rate), and diaphoresis (profuse sweating). Early signs of respiratory failure include altered depth and pattern of respirations, shortness of breath, nasal flaring (**Figure 3**), chest wall retractions (**Figure 4**), expiratory grunt, and wheezing and/or prolonged expiration. See also **Table 3**.

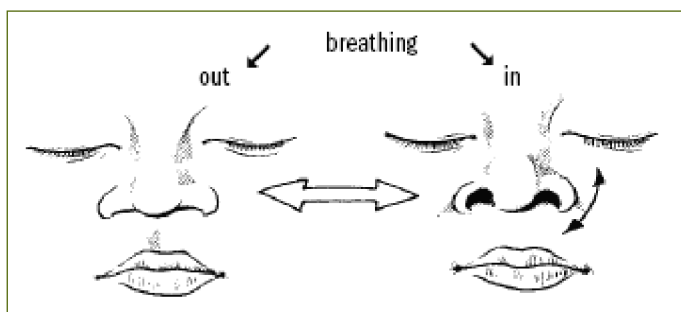


Figure 3. Nasal flaring: with inspiration, the sides of the nostrils flare outward. (World Health Organization. Management of the child with a serious infection or severe malnutrition. Guidelines for care at the first-referral level in developing countries, 2000.)

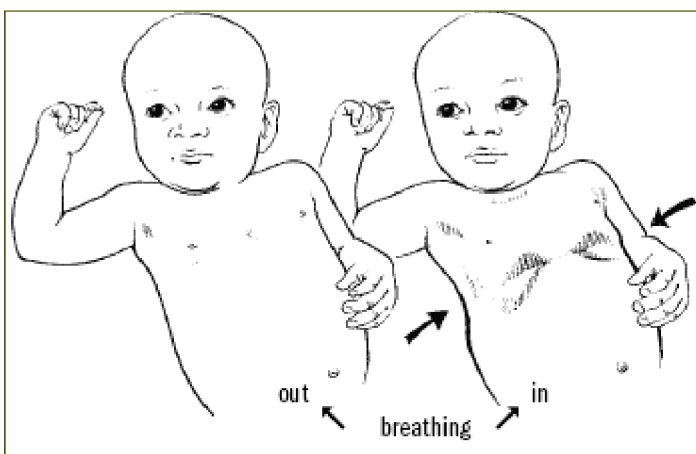


Figure 4. Lower chest wall indrawing: with inspiration the lower chest wall moves inward. (World Health Organization. Management of the child with a serious infection or severe malnutrition. Guidelines for care at the first-referral level in developing countries, 2000.)

Table 3. Differential diagnosis of a child presenting with cough and respiratory distress*

Diagnosis	In Favor
Pneumonia	<ul style="list-style-type: none"> • Cough with fast breathing • Lower chest wall indrawing • Fever • Coarse crackles on auscultation • Nasal flaring • Grunting • Head nodding
Malaria	<ul style="list-style-type: none"> • Fast breathing in febrile child • Blood smear: high parasitemia • Lives in or travelled to a malarious area • In severe malaria: deep (acidotic) breathing/lower chest wall indrawing • Chest clear on auscultation
Severe anemia	<ul style="list-style-type: none"> • Severe palmar pallor • Hemoglobin <6 g/dl
Cardiac failure	<ul style="list-style-type: none"> • Gallop rhythm • Raised jugular venous pressure • Basal fine crackles • Apex beat displaced • Enlarged palpable liver • Heart murmur
Congenital heart disease	<ul style="list-style-type: none"> • Central cyanosis • Difficulty in feeding or breastfeeding • Enlarged liver • Heart murmur
Tuberculosis	<ul style="list-style-type: none"> • Chronic cough (more than 30 days) • Poor growth/wasting or weight loss • Positive contact history with tuberculosis patient • Diagnostic chest x-ray such as primary complex or miliary tuberculosis
Pertussis	<ul style="list-style-type: none"> • Paroxysms of cough followed by whoop, vomiting, cyanosis or apnea • No fever • No history of DPT immunization
Foreign body	<ul style="list-style-type: none"> • History of sudden choking • Sudden onset of stridor or respiratory distress • Focal areas of wheeze or reduced breath sounds
Empyema	<ul style="list-style-type: none"> • Stony dullness to percussion
Pneumothorax	<ul style="list-style-type: none"> • Sudden onset • Hyper-resonance on percussion on one side of the chest • Shift in mediastinum
Pneumocystis pneumonia	<ul style="list-style-type: none"> • 2-6-month-old child with central cyanosis • Hyper-expanded chest • Fast breathing • Finger clubbing • Chest x-ray changes, but chest clear on auscultation • Enlarged liver, spleen, lymph nodes • Wasting • HIV test positive

*World Health Organization. Management of the child with a serious infection or severe malnutrition. Guidelines for care at the first-referral level in developing countries, 2000.

Treatment. All children with severe pneumonia should be urgently transferred to a hospital for inpatient management with IV antibiotics and oxygen therapy. Whenever feasible, the child should be given the first antibiotic dose and placed on oxygen therapy if an oxygen cylinder is available prior to transfer.

Empiric antibiotic therapy should be guided by locally prevailing susceptibility patterns. Usually, however, benzylpenicillin 50,000 IU/kg IM or IV can be given prior to hospital transfer.

Nonsevere Pneumonia

Most pneumonia cases in children aged 2 months to 5 years will be characterized by rapid respirations without retractions. A child with pneumonia can be treated on an outpatient basis with oral antibiotics. The child's caregiver should be instructed on how to administer the antibiotics; if feasible, the first dose should be given in the clinic to demonstrate proper administration. A child treated at home should return to the clinic in 2 days to be reassessed. The caregiver should be instructed to return to the clinic sooner if the child continues to have rapid respirations, develops retractions, continues to have fever, or does not improve on oral antibiotics. If any of these outcomes occurs, the child should be referred to a hospital. If the child improves on oral antibiotics, the antibiotics should be continued to complete at least 5 days of treatment. If the child's signs and symptoms have not improved and the caregiver has been giving the antibiotics correctly, a different antibiotic should be given for 5-10 days, or an alternative etiology should be considered.

No Pneumonia (Upper Respiratory Tract Infection or Cold)

A child with cough or difficulty breathing but without any general danger signs is determined to have a cold. Young children average six to eight colds per year, each lasting about 2 weeks. Purulent nasal discharge is characteristic, and fever is common in children during the first 3 days of the illness. Other symptoms may include sore throat, cough, irritability, difficulty sleeping, and decreased appetite. Physical signs are nonspecific but may include erythema and swelling of the nasal mucosa, as well as moderate anterior cervical lymphadenopathy. The symptoms of the common cold can be caused by a variety of viruses. Rhinoviruses, respiratory syncytial virus, influenza viruses, parainfluenza viruses, and adenoviruses are commonly responsible for colds in preschool children.

Such a child does not require treatment with antibiotics. The child can be cared for at home. The caregiver should be instructed to watch for signs of respiratory distress (e.g., nasal flaring, abdominal or intercostal retractions, cyanosis, grunting) and to bring the child back immediately if any of these signs occur. If coughing has persisted for more than 30 days, the child should be referred to a hospital for assessment.

Upper Respiratory Tract Infections, Otitis Media, and Sore Throat

Otitis media, or infection of the middle ear, can be classified into four categories to help identify proper treatment:

- acute ear infection,
- chronic ear infection,
- mastoiditis, and
- no ear infection.

Acute Ear Infection (Acute Otitis Media)

A child with an ear infection may have ear pain, ear drainage, and/or fever. On physical examination, the child will have an erythematous (abnormally red), bulging, dull, immobile eardrum and/or pus draining from the ear. If the signs and symptoms have been present for less than 2 weeks, the child is classified as having acute otitis media. Acute otitis media is treated with oral antibiotics at home for 5 days. If the child has fever for more than 48 h on antibiotics, consider a change in the antibiotics and consider looking for other possible causes of the fever.

Chronic Ear Infection (Chronic Otitis Media)

Chronic suppurative otitis media is common in HIV-infected children. A child who has had ear drainage for longer than 2 weeks is considered to have chronic otitis media. The ear should be dried by a method known as wicking. This procedure should be done for the first time in the clinic to demonstrate the technique to the child's caregiver. To dry the ear, roll a clean, soft, absorbent cotton cloth into a wick. Place the wick in the child's ear, and remove it when it is wet. Repeat this step until the wick no longer gets wet; this indicates that the drainage has stopped. This treatment should be done at home at least three times per day. Antibiotics generally have no place in the management of chronic suppurative otitis media because they are usually ineffective and do not alter the course or the outcome.

Mastoiditis

Mastoiditis is a complication of otitis media. A child with mastoiditis will have a tender, swollen, erythematous, warm area behind the ear. Mastoiditis requires treatment with IV antibiotics and possible surgery. A child with mastoiditis should be referred to a hospital. The first dose of antibiotics should be given in the clinic, if feasible. The same antibiotics used to treat pneumonia are used in the treatment of mastoiditis.

Management. If antibiotics are given for an ear infection, the caregiver should be instructed to complete the full course of antibiotics even if the child is feeling better and to return for follow-up as instructed. The caregiver should be instructed not to put oil or any other fluid into the child's ear, and the child should avoid getting water into the ear. Recurrent, chronic ear infections can cause deafness.

Sore Throat

Sore throat is one of the most common symptoms of an upper respiratory infection. Most cases of sore throat are caused by viruses, can be treated symptomatically, and resolve in a few days. Occasionally a child with a sore throat will require antibiotics. Antibiotics are necessary if the sore throat is caused by a throat abscess or streptococcal infection. A child with a throat abscess will not be able to swallow secretions, fluids, or food and should be referred to a hospital for drainage of the abscess. A child with a streptococcal throat infection will have tender, enlarged lymph nodes in the front of the neck and white exudate in the posterior oropharynx and/or on the tonsils.

Management. Most children with a sore throat get better in a few days with symptomatic treatment. Caregivers should be encouraged to offer frequent liquids to keep the mucosal surface of the throat moist. Paracetamol may be given by mouth at a dose of 15 mg/kg/dose every 4-6 h to relieve discomfort or fever. Caregivers should be instructed not to exceed six doses per day of paracetamol because an overdose can cause liver failure. The child's temperature should be rechecked 30-60 min after the dose to confirm the effectiveness of the medication. If the child has a streptococcal infection, the best treatment is one injection of benzathine penicillin. If this is not available, the child should be treated with oral amoxicillin, ampicillin, or penicillin for 10 days. If

oral antibiotics are given, the caregiver must understand the importance of completing the antibiotics to prevent complications such as rheumatic fever or a relapse of the illness.

FEVER IN INFANTS AGED 1 WEEK TO 2 MONTHS

Fever in a young infant represents a special clinical situation. Most young infants with fever will have a benign viral infection, but serious bacterial infections include pneumonia, sepsis, urinary tract infection, and meningitis. In young infants, these diseases may all present similarly; thus, clinical signs cannot reliably distinguish between these diagnoses. Therefore, the goal of the evaluation in the prehospital setting is to recognize that young infants are at high risk for serious illness. It is therefore imperative that the infant be promptly evaluated, that appropriate antibiotic treatment be initiated promptly, and that the infant be referred to the hospital even before a specific diagnosis is confirmed. In the referral hospital, laboratory investigations can be carried out and the infant can receive parenteral antibiotics and be monitored pending results of laboratory investigations and cultures.

History

In young infants, the symptoms of serious bacterial infection are often nonspecific and may include lethargy, poor feeding, vomiting, and/or convulsions. Other historical details to elicit might include the following:

- Associated symptoms
- Exposures to sick contacts
- Any previous illness or antibiotic use
- Birth history
 - Maternal fever
 - Maternal history of infections
 - Duration of rupture of membranes prior to delivery
 - Delivery at home or in hospital
 - Infant's neonatal course

Objective

General appearance. The infant's general appearance is a vitally important observation. Toxic-appearing infants are pale or cyanotic, lethargic, or inconsolably irritable. They may also have tachypnea and tachycardia with poor capillary refill.

Other physical findings include the following:

- Alterations in body temperature
 - Fever (axillary temperature $\geq 37.5^{\circ}\text{C}$ or $\geq 99.5^{\circ}\text{F}$)
 - Hypothermia (axillary temperature $\leq 35.5^{\circ}\text{C}$ or $\leq 95.9^{\circ}\text{F}$)
- Alterations in color
 - Pallor
 - Cyanosis
 - Jaundice
- Signs of respiratory distress
 - Fast or irregular breathing
 - Lower chest wall indrawing/retractions
 - Nasal flaring
 - Grunting
 - Apnea
- Abdominal distension
- Hepatosplenomegaly

Physical findings that might indicate the source of fever include

- Pus draining from the ear
- Painful joints, joint swelling, reduced movement and irritability if these parts are handled
- Umbilical redness extending to the periumbilical skin

Meningitis might be suspected if the following signs are present:

- Tense or bulging fontanel
- Neck stiffness
- High-pitched cry
- Apneic episodes
- Convulsions

All young infants must be assessed to determine if they should be classified as having possible serious bacterial infection or a local bacterial infection. Young HIV-infected infants tend to be susceptible to opportunistic infections (especially pneumocystis jirovecii [previously pneumocystis carinii] pneumonia, even with high CD4 counts.

Severe Disease

An infant is classified as having severe disease if any of the following danger signs are present: lethargy, decreased intake, wheezing, fever ($>37.5^{\circ}\text{C}$) or low body temperature ($<35^{\circ}\text{C}$), or severe malnutrition.

In this age group, all pneumonia is considered severe. A child is diagnosed as having pneumonia if the respiration rate is greater than 60 breaths per minute or the infant is having chest wall retractions. A young infant with pneumonia should be treated with IV antibiotics and referred to a hospital for inpatient management.

Meningitis should be suspected if the infant presents with general illness such as irritability, vomiting everything, abnormal cry, or lethargy. Physical examination might reveal bulging or tense fontanel, stiff neck, apneic episodes, or convulsions. A young infant with severe disease should be transferred immediately to a hospital where there is access to laboratory tests including a full blood count, blood culture, urinalysis and urine culture, chest radiograph, lumbar puncture, and CSF examination.

If possible, give one dose of one of the following antibiotic regimens before the transfer.

For sepsis when the precise diagnosis is not yet established:

- Ampicillin 50 mg/kg IV or IM every 6-8 h plus gentamicin 7.5 mg/kg IV or IM once daily
- Benzylpenicillin 50,000 U/kg IV or IM every 6-8 h plus gentamicin 7.5 mg/kg IV or IM once daily

For meningitis:

- Ampicillin 50 mg/kg IV or IM every 6-8 h plus gentamicin 7.5 mg/kg IV or IM once daily
- Benzylpenicillin 50,000 U/kg IV or IM every 6-8 h plus chloramphenicol 25 mg/kg IV or IM every 6 h

Chloramphenicol should not be given to premature infants (<37 weeks' gestation) and should be avoided in all infants in the first week of life. For infants aged 1 week to 1 month, chloramphenicol should be given every 12 h.

No Pneumonia (Upper Respiratory Tract Infection or Cold)

A young infant without fever; without any danger signs (lethargy, decreased intake, wheezing, or low body temperature, severe malnutrition); and without fast breathing, retractions, or wheezing is determined to have a cold. The infant can be cared for at home. The caregiver should be encouraged to offer frequent fluids and to clear the infant's nose prior to feeding. The caregiver should be instructed to watch for signs of respiratory distress (e.g., nasal flaring, retractions, cyanosis, grunting) and to take

the infant to the nearest clinic or hospital immediately if any of the signs occur.

CONCLUSION

Children with HIV present commonly for evaluation and treatment of illness. The integrated approach to management of childhood illness remains the most effective method for managing sick children. The health care provider must consider the subjective data revealed by taking a thorough history and the objective data obtained by performing a complete physical examination. These data allow the health care provider to accurately classify the condition and to identify the appropriate treatment actions.

Fever is a symptom of many conditions, some simple and others serious. It is imperative for the health care provider to rapidly assess the patient so that the appropriate treatment plan can be promptly initiated. Because malaria can evolve quickly into serious disease, malaria should be considered as a possible diagnosis in malaria-endemic areas. Young infants are susceptible to febrile infections and when ill, often show less specific clinical signs. Thus, if any danger signs are present, young infants should be referred emergently to the hospital for further management.

Many upper respiratory tract infections can be treated at home with oral antibiotics and/or simple treatments for symptoms. Children presenting with cough and/or difficulty breathing might be referred urgently to the hospital, treated with oral antibiotics, or treated only for symptoms depending upon whether they were assessed as having severe disease or severe pneumonia, uncomplicated pneumonia, or no pneumonia. Caregivers for the child should be given clear follow-up instructions. They should be educated on how to recognize symptoms that might indicate progression or complication of the condition. They should be instructed to urgently get the child to the nearest health facility upon earliest suspicion of deterioration in the child's condition or development of danger signs.

APPENDIX: DOSING SCHEDULES FOR ANTIMALARIAL MEDICATIONS

Artemether-Lumefantrine (Coartem)

Currently available as coformulated tablets containing 20 mg of artemether and 120 mg of lumefantrine. The total recommended treatment is a six-dose regimen of artemether-lumefantrine twice daily for 3 days.

Table A1. Dosing schedule for artemether-lumefantrine (Coartem)

Body wt (kg)	Age (yrs)	No. of tablets at approximate timing of dosing (h)					
		0	8	24	36	48	60
5-14	<3	1	1	1	1	1	1
15-24	≥3-8	2	2	2	2	2	2
25-34	≥8-14	3	3	3	3	3	3
>34	≥14	4	4	4	4	4	4

Artesunate Plus Amodiaquine

Currently available as separate scored tablets containing 50 mg of artesunate and 153-mg base of amodiaquine. The total recommended treatment is 4 mg/kg of artesunate and 10 mg/kg of amodiaquine given once daily for 3 days.

Table A2. Dosing schedule for artesunate plus amodiaquine

Age	Dose, mg (No. of tablets)					
	Artesunate (50 mg)			Amodiaquine (153 mg)		
	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
5-11 mo	25 (1/2)	25	25	76 (1/2)	76 (1/2)	76 (1/2)
≥1-6 yrs	50 (1)	50	50	153 (1)	153 (1)	153 (1)
≥7-13 yrs	100 (2)	100	100	306 (2)	306 (2)	306 (2)
≥13 yrs	200 (4)	200	200	612 (4)	612 (4)	612 (4)

Artesunate Plus Sulfadoxine-Pyrimethamine

Currently available as separate scored tablets containing 50 mg of artesunate and tablets containing 500 mg of sulfadoxine and 25 mg of pyrimethamine. The total recommended treatment is 4 mg/kg of artesunate give once a day for 3 days and one administration of sulfadoxine-pyrimethamine (25/1.25 mg of base/kg) on day 1.

Table A3. Dosing schedule for artesunate plus sulfadoxine-pyrimethamine

Age	Dose, mg (No. of tablets)					
	Artesunate (50 mg)			Sulfadoxine-pyrimethamine (500 mg/25 mg, respectively)		
	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
5-11 mo	25 (1/2)	25	25	250/12.5 (1/2)	—	—
≥1-6 yrs	50 (1)	50	50	500/25 (1)	—	—
≥7-13 yrs	100 (2)	100	100	1000/50 (2)	—	—
≥13 yrs	200 (4)	200	200	1500/75 (3)	—	—

Artesunate Plus Mefloquine

Currently available as separate scored tablets containing 50 mg of artesunate and 250-mg base of mefloquine. Total recommended treatment is 4 mg/kg artesunate given once daily for 3 days and 25 mg of base/kg of mefloquine usually split over 2 or 3 days. Two different doses of mefloquine have been evaluated, 15 mg of base/kg and 25 mg of base/kg. The lower dose is associated with inferior efficacy and is not recommended. To reduce acute vomiting and optimize absorption, the 25 mg/kg dose is usually split and given as 15 mg/kg (usually on the second day) followed by 10 mg/kg 1 day later, or as 8.3 mg/kg per day for 3 days. Mefloquine is associated with an increased incidence of nausea, vomiting, dizziness, dysphoria, and sleep disturbance in clinical trials, but these symptoms are seldom debilitating and mefloquine is generally well tolerated.

Table A4. Dosing schedule for artesunate plus mefloquine

Age	Dose, mg (No. of tablets)					
	Artesunate (50 mg)			Amodiaquine (153 mg)		
	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
5-11 mo	25 (1/2)	25	25	76 (1/2)	76 (1/2)	76 (1/2)
≥1-6 yrs	50 (1)	50	50	153 (1)	153 (1)	153 (1)
≥7-13 yrs	100 (2)	100	100	306 (2)	306 (2)	306 (2)
≥13 yrs	200 (4)	200	200	612 (4)	612 (4)	612 (4)

Table A5. Normal pediatric vital signs

Age	Wt (kg)	Pulse/min	Respirations/min	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)
Premature	1	145	<40	42 ± 10	21 ± 8
Newborn	2-3	125	—	60 ± 10	37 ± 8
1 mo	4	120	24-35	80 ± 16	46 ± 16
1 yr	10	120	20-30	96 ± 30	66 ± 25
2-5 yrs	12-14	115	—	99 ± 25	64 ± 25
6-9 yrs	20-26	100	12-25	100 ± 20	65 ± 15
10-12 yrs	32-42	75	—	112 ± 20	68 ± 15
>14 yrs	>50	70	12-18	120 ± 20	75 ± 15

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