Management of Prevalent Infections in Children Following a Disaster

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INTRODUCTION

Morbidity and mortality resulting from an acute humanitarian emergency in developing countries are related to the excessive childhood mortality that existed prior to the disaster. According to the World Health Organization (WHO), children living in low-income countries are 10 times more likely to die before reaching age 5 than children in the industrialized world (Black, 2003; WHO, 1999; Murray, 1996), the main causes of death being pneumonia, diarrhea, measles, malaria, and malnutrition.

During acute humanitarian emergencies, mortality related to those common childhood infections increases due to crowded living conditions; displacement to areas with higher disease prevalence; and compromised personal hygiene resulting from inadequate water supplies, contaminated water, and poor sanitation. The pre-existing nutritional status (particularly micronutrient and vitamin A deficiencies) and immunization rates of children, as well as the pre-existing primary care infrastructure and the degree of damage caused by the disaster, also affect childhood morbidity and mortality after a disaster. Figure 1 summarizes the causes of death in two refugee camps and illustrates the significance of various illnesses following a disaster.

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**FIGURE 1. Mortality in two refugee camps**

**Malawi, 1990**
- Malaria: 25%
- Malnutrition: 23%
- ARI: 9%
- Diarrhea: 11%
- Measles: 10%
- Other: 22%

**Sudan, Wad Kowli Camp, 1985**
- Diarrhea: 30%
- Measles: 53%
- ARI: 9%
- Malaria: 7%
- Other: 1%

ARI: acute respiratory infection

From Famine-affected, refugee, and displaced populations: Recommendations for Public Health issues. MMWR 1992(RR-13); 1-76.
OBJECTIVES

- Describe the rationale for the WHO evidence-based syndromic approach to case management as described in the IMCI.
- List the clinical illnesses included in the IMCI program and their relevance in situations associated with disasters.
- Assess and classify the condition of a child to determine its severity and establish the relationship between this classification and the subsequent management.
- List the danger signs that should be routinely checked in all children.

What is IMCI?

The strategy for the IMCI was designed by PAHO and WHO to enhance children’s health and reduce the mortality and morbidity due to the most prevalent diseases in developing countries. This strategy includes the early diagnosis, treatment and timely referral of children under 5 years of age with the most common diseases. It also contributes to improving parental skills and practices associated with the home care of children. A community-based approach is essential for childhood health, because it promotes healthy habits in the family, ade-

CASE 1

A 15-month-old boy presents at the emergency department with a fever. He had been healthy until 3 days ago, when he developed symptoms of upper respiratory airway infection. His mother reports giving ibuprofen to her son the day before, because of the fever. The child continues to be febrile with reduced food and fluid intake, urine output, and activity level. There is no history of vomiting, diarrhea, cough, or rash. He is not receiving any medication. You note fatigue and irritability when the child is stimulated during the physical examination. Respiratory rate is 50 breaths/min, pulse rate 162 beats/min, blood pressure 92/70 mm Hg, and axillary temperature 38.9°C. He has dry lips but wet oral mucosa without lesions. His neck is flexible. Lung and heart examination are unremarkable with no significant findings. A few isolated petechiae are noted over the abdomen and lower limbs. Peripheral pulse is normal and capillary refill time is 3 seconds.

- What is your global clinical impression for this boy?
- What is the most probable diagnosis?
- What treatment strategies you should adopt initially?
quate care of children (feeding, clothing, stimulation, etc.), disease prevention, and prompt seeking of medical care when alarming signs and symptoms are noted.

The IMCI strategy also helps healthcare professionals take advantage of opportunities for prevention, promote childhood development, and encourage the rational use of drugs and medications. This strategy is not meant for chronic or less frequent diseases or acute emergencies. As a complement to ambulatory care, this strategy includes procedures and practices at different referral levels and types of hospitals.

The IMCI strategy is based on the importance of simple clinical signs and symptoms, the proper classification of the disease, timely treatment, and interventions for prevention and follow-up. It is particularly useful in the first level of care, i.e., camps, medical offices, health care centers or hospital primary care departments. It includes a series of procedural algorithms and standardized forms to record the patients’ care. Figure 2 shows the algorithm describing the care processes.

**IMCI guidelines**

The practical IMCI guidelines are based on the following principles:

- All sick children must be assessed for general danger signs, which indicate the need for immediate referral or admission to a hospital.
- All sick children must be routinely assessed for major symptoms (for children from 2 months to 5 years old: cough or difficult breathing, diarrhea, fever; ear problems; for infants age 1 week to 2 months: bacterial infection and diarrhea). They must also be assessed for nutritional and immunization status, feeding disorders, and other potential problems.
- Only a limited number of carefully selected clinical signs are used, based on evidence of their sensitivity and specificity to detect diseases. These signs were selected also considering the available resources in first-level health care facilities.
- The combination of individual signs leads to a child’s classification rather than a diagnosis. This classification indicates the severity of the condition and calls for specific actions based on whether the child (a) should be urgently referred to a higher level of care, (b) requires specific treatments, or (c) can be safely managed at home. The classification is color-coded: red requires hospital referral or admission; yellow indicates the need to initiate treatment; and green indicates home management.
- The IMCI strategy addresses most, but not all, of the major reasons why a sick child is brought to a clinic. A child with a chronic condition or a less common illness may require special care. The guidelines do not describe the management of trauma or other acute emergencies due to accidents or injuries.
- IMCI management strategy uses a limited number of essential drugs and encourages the active participation of caregivers in the treatment of children.
- A basic component of the IMCI strategy is the counselling of caretakers about home management issues, such as feeding, fluids, and when to return to a health facility (Box 1).
Assessment of sick children

The assessment procedure for this age group includes a number of important steps that must be taken by the health care provider: (1) Take a history and talk with the caregiver about the child’s problem; (2) check for general danger signs; (3) assess major symptoms; (4) evaluate nutritional status, immunization status, feeding disorders, and other potential problems; (5) assess the child’s feeding; (6) check the child’s status; and (7) look for other problems.

Danger signs that should be routinely checked in all children

Seizures during the current illness. Seizures may result from fever. Febrile seizures do little harm beyond frightening the parents. But seizures may also be associated with meningitis, cerebral malaria, or other life-threatening conditions. All children with seizures during the current illness should be considered seriously ill.

Unconsciousness or lethargy. An unconscious child is likely to be seriously ill. A lethargic child who is awake but does not take any notice of his/her surroundings or does not respond normally to sounds or movement may also be very sick. These signs can be associated with many conditions, including severe dehydration, severe hypoxia, sepsis, or meningitis.

Inability to drink or breastfeed. An infant may be unable to drink if he/she is too weak or cannot swallow. Observe the child while the mother breastfeeds or gives him/her something to drink.

Persistent vomiting. Vomiting itself may be a sign of serious illness. This symptom may also prevent the child from taking medications or fluids for rehydration.

A child with one or more of these signs must be considered seriously ill and will require hospital referral. To start treatment for severe illnesses without delay, quickly assess the child for the most important causes of serious illness and death, including acute respiratory infection (ARI), diarrhea and dehydration, sepsis, malaria, and measles.

BOX 1. Key aspects of the IMCI strategy

- Evaluates general danger signs
- Assesses major symptoms
- Assesses nutritional status, immunization status, feeding disorders, and other potential problems
- Includes a limited number of carefully selected clinical signs
- Combines clinical signs to define the classification for the evaluated child
- Addresses most, but not all, of the major reasons why a sick child is brought to a clinic
- Uses a limited number of essential drugs
- Encourages active involvement of adult caretakers in the children’s management
- Offers counselling to caretakers
FIGURE 2. Summary of the process of integrated care of children

For all sick children age 1 week up to 5 years who are brought to a first-level health facility

**ASSESS** the child: Check for danger signs (or possible bacterial infection). Ask about main symptoms. If a main symptom is reported, assess further. Check nutrition and immunization status. Check for other problems.

**CLASSIFY** the child’s illnesses: Use a color-coded triage system to classify the child’s main symptoms, and his or her nutrition or feeding status.

**IF URGENT REFERRAL** is needed and possible

**IDENTIFY URGENT PRE-REFERRAL TREATMENT(S)** needed for the child’s classifications

**TREAT THE CHILD:** Give urgent pre-referral treatment(s) needed

**REFER THE CHILD:**
- Explain to the child’s caretaker the need for referral.
- Calm the caregiver’s fears and help solve any problems.
- Write a referral note addressed to the hospital.
- Give instructions and supplies needed to care for the child on the way to the hospital.

**IF NO URGENT REFERRAL** is needed or possible

**IDENTIFY TREATMENT** needed for the child’s classifications: Identify specific medical treatments and/or advise

**TREAT THE CHILD:** Give the first dose of oral drugs in the clinic and/or advise the child’s caregiver. Teach the caretaker how to give oral drugs and how to treat local infections at home. If needed, give immunizations.

**COUNSEL THE MOTHER:**
- Assess the child’s feeding, including breastfeeding practices, and solve feeding problems, if present.
- Advise about feeding and fluids during illness and when to return to a health facility.
- Counsel the mother about her own health.

**FOLLOW-UP CARE:** Give follow-up care when the child returns to the clinic and, if necessary, reassess the child for new problems.
FIGURE 3. IMCI strategy for case management in the outpatient health care facility, first-level referral service, and at home for the sick child from age 2 months to 5 years

THE INTEGRATED CASE MANAGEMENT PROCESS

OUTPATIENT HEALTH CARE FACILITY

Check for DANGER SIGNS
- Seizures
- Lethargy/unconsciousness
- Inability to drink/breast-feed
- Vomiting

Assess MAIN SYMPTOMS
- Cough/difficult breathing
- Diarrhea
- Fever
- Ear problems

Assess NUTRITION, IMMUNIZATIONS and POTENTIAL FEEDING PROBLEMS

Check for OTHER PROBLEMS

CLASSIFY CONDITIONS and IDENTIFY TREATMENT ACTIONS
According to color-coded treatment

RED
Urgent referral
OUTPATIENT HEALTH CARE FACILITY
- Pre-referral treatments
- Counsel parents
- Refer child

YELLOW
Treatment at outpatient health care facility
OUTPATIENT HEALTH CARE FACILITY
- Treat local infection
- Give oral drugs
- Counsel and teach caretaker
- Follow-up

GREEN
Home management
HOME
Caregiver is counselled on:
- Home treatment(s)
- Feeding and fluids
- When to return immediately
- Follow-up

REFERRAL FACILITY
- Emergency Triage and Treatment (ETAT)
- Diagnosis
- Treatment
- Monitoring and follow-up
What is Influenza?
Influenza is a segmented, single-stranded enveloped RNA virus classified into influenza A, B and C based on antigenic differences. Influenza A is a potentially severe illness, causes epidemics and pandemics, is rapidly changing, and infects birds, swine, horses, seals, and humans. Influenza B is more uniform, causes epidemics and only infects humans. Influenza C is of minimal public health impact and infects humans and swine. Further subtyping of influenza A virus is based on the neuraminidase and hemagglutinin proteins on the viral surface. There are 16 different hemagglutinins and 9 different neuraminidase subtypes. Hemagglutinin proteins allow the virus to stick to cells by binding to a specific receptor. The neuraminidase protein helps newly formed viral particles get released from the cell surface so that they have the potential to infect other cells. Only H1N1, H2N2, H3N2 subtypes are associated with widespread epidemics in human. Since 1997, rare but severe infections in humans with influenza A subtype H5N1 viruses have been identified in Asia, Africa, Europe, and the Middle East where these viruses are present in domestic or wild birds.

Repeated seasonal influenza epidemics persist because the type A and type B viruses undergo constant and rapid change due to antigenic drift. Antigenic drift refers to a gradual change in the virus that occurs through a slow series of amino acids changes in the hemagglutinin or neuraminidase surface antigens. Occurring only after a particular viral strain has become established in humans, antigenic drift represents an adaptation to the development of host antibodies. Newly developed antigenic strains of influenza then prevail for a period of 2 to 5 years, only to be replaced by the next emerging strain. This new strain can then trigger a new epidemic, since it is now unfamiliar to the antibody repertoire of the population. The development of yet another set of host antibodies eventually protects the population—at the same time it puts pressure on the virus to drift yet again. Ongoing change caused by antigenic drift requires ongoing reformulation of influenza vaccines usually on an annual basis. The World Health Organization and the Centers for Disease Control and Prevention continually track these changes to better recommend strains to be contained in the next seasonal influenza vaccine.

In contrast to the gradual evolution of strains subject to antigenic drift, antigenic...
shift occurs as soon as a type A influenza virus with a completely novel hemagglutinin or neuraminidase moves into humans from another host species. The primary source is birds, certain species of which carry a reservoir of 15 influenza A subtypes. These subtypes either genetically reassort themselves with circulating human influenza virus or are transmitted directly into humans, typically via intermediate hosts such as swine. Antigenic shift of type A influenza viruses occurs less frequently than antigenic drift, but with more dramatic impact that can lead to a pandemic. A pandemic is defined by the emergence and global spread of a new influenza A virus subtype to which the population has little or no immunity and that spreads rapidly from human to human. Pandemics, therefore, can cause increased morbidity and mortality rates compared with seasonal influenza. During the 20th century, there have been four influenza pandemics, in 1918 (H1N1), 1957 (H2N2), 1968 (H3N2), and 2009-10 (H1N1). The recent influenza pandemics of 2009 H1N1 (“swine flu”) was caused by genetic reassortment between human, two avian and one swine influenza viruses. Avian influenza (H5N1) continues to cause outbreaks among poultry and wild birds worldwide but has caused relatively few cases of human H5N1 infection although case fatality rates are greater than 50 percent.

**Epidemiology**

Influenza is spread from person to person primarily by respiratory droplets created by coughing or sneezing. Contact with respiratory droplet-contaminated surfaces or fomites is another possible mode of transmission. During community outbreaks of influenza, the highest attack rates occur among school-aged children. Secondary spread to adults and other children within a family is common. Incidence and disease severity depend, in part, on immunity developed as a result of previous experience (by natural disease) or recent influenza immunization with the circulating strain or a related strain. In temperate climates, seasonal epidemics usually occur during winter months. Peak influenza activity in the United States can occur anytime from November to May but most commonly occurs in January and February. Community outbreaks can last 4 to 8 weeks or longer. Circulation of 2 or 3 influenza virus strains in a community may be associated with a prolonged influenza season of 3 months or more and bimodal peaks in activity. Influenza is highly contagious, especially among semi enclosed institutionalized populations.

Attack rates in healthy children generally have been found to be 10% to 40% each year, but illness rates as low as 3% also have been reported. Children younger than 5 years of age visit clinics or emergency departments for influenza illness at the rate of 1 to 2 children per 100 annually. Influenza and its complications have been reported to result in a 10% to 30% increase in the number of courses of antimicrobial agents prescribed to children during the influenza season. These medical care encounters for children with influenza result in considerable costs and
likely are an important cause of inappropriate antimicrobial use.

**Influenza Pathogenesis and Symptoms**

Influenza in adults typically begins with the sudden onset of fever, often accompanied by chills or rigors, headache, malaise, diffuse myalgia, and nonproductive cough. Subsequently, respiratory tract signs including sore throat, nasal congestion, rhinitis, and cough become more prominent. Conjunctival injection, abdominal pain, nausea, vomiting, and diarrhea are less commonly associated with influenza illness. Influenza symptoms may be different among different age populations with older children and adolescents having more classic adult influenza like symptoms. Neonates may present with fever and a sepsis like picture and toddlers may have few respiratory signs but have vomiting and diarrhea as their predominant symptom. The usual incubation period between the time someone is exposed and infected with influenza virus to the time that they experience symptoms of illness ranges from 18 hours to 5 or more days with an average of 2-3 days. Once infected with influenza the principal site of replication is the columnar epithelium in the back of the throat. Viral shedding in respiratory secretions occurs for 1 day before illness and 5-10 days after illness onset. Viral titers are generally higher in young children with shedding lasting 10 days or longer. Peak shedding of virus generally occurs during the first 3 days of illness and correlates with the presence of fever.

**Complications of Influenza**

Post-influenza complications are common. Influenza is an important cause of otitis media. Acute myositis characterized by calf tenderness and refusal to walk has been described especially with influenza type B. In infants, influenza can produce a sepsis-like picture and occasionally can cause croup, bronchiolitis, or pneumonia. Although the large majority of children with influenza recover fully after 3 to 7 days, previously healthy children can have severe symptoms and complications. Neurologic complications associated with influenza range from febrile seizures to severe encephalopathy and encephalitis with status epilepticus, with resulting neurologic sequelae or death. Reye syndrome has been associated with influenza infection and salicylate exposure. Death from influenza-associated myocarditis has been reported. Invasive secondary infections or coinfections with group A streptococcus, Staphylococcus aureus (including methicillin-resistant S. aureus [MRSA]), Streptococcus pneumoniae, or other bacterial pathogens can result in severe disease and death.

Hospitalization rates among children younger than 2 years of age are similar to hospitalization rates among people 65 years of age and older. Children younger than 24 months of age consistently are at substantially higher risk of hospitalization than are older children, and the risk of hospitalization attributable to influenza infection is highest in the youngest chil-
increased likelihood of false-positive results during periods of low influenza activity. Direct fluorescent antibody (DFA) and indirect immunofluorescent antibody (IFA) staining for detection of influenza A and B antigens in nasopharyngeal or nasal specimens are available at most hospital-based laboratories and can yield results in 3 to 4 hours. Reverse transcriptase-polymerase chain reaction (RT-PCR) testing of respiratory tract specimens may be available at some institutions and offers potential for high sensitivity and specificity in particular with the 2009-2010 H1N1 pandemic strain.

Treatment of Influenza
Treatment is mostly supportive with rest, fluids, and antipyretics such as acetaminophen or ibuprofen. Aspirin and other salicylate-containing products should be avoided as it is associated with a rare severe complication called Reye Syndrome. Antivirals administered within 2 days of illness onset may have the greatest benefit to reduce the duration of uncomplicated influenza illness and should be considered for those who are at increased risk of severe or complicated influenza infection. Other candidates for antiviral therapy include healthy children with moderate to severe illness and people with special environmental, family, or social situations where ongoing influenza illness would be detrimental. Antiviral treatment should be continued for 5 days and be discontinued approximately 24 to 48 hours after symptoms resolve. Children with severe influenza
In the United States, two classes of antiviral medications are available for treatment or prophylaxis of influenza infections: neuraminidase inhibitors (oseltamivir and zanamivir) and adamantanes (amantadine and rimantadine). Treatment has been shown to decrease the duration of flu-related symptoms by 1 to 1.5 days. Oseltamivir has been approved for chemoprophylaxis and treatment of patients older than one year old. Zanamivir has been approved for treatment in patients 7 years and older and chemoprophylaxis of patients age 5 years and older.

Influenza B viruses intrinsically are resistant to adamantanes and since 2005 all H3N2 strains in the United States have been resistant to adamantanes. During the 2008–2009 influenza season, virtually all H1N1 influenza strains were resistant to oseltamivir but remained susceptible to zanamivir, amantadine, and rimantadine. The most recent pandemic 2009-2010 H1N1 strain was once again susceptible to oseltamivir.

These resistance patterns among circulating influenza A virus strains present challenges in selecting antiviral medications for treatment and chemoprophylaxis of influenza and provide additional reasons for clinicians to test patients for influenza virus infection and to consult surveillance data in their community when evaluating people with acute respiratory tract illnesses during the influenza season. Specific drug recommendations for treatment and chemoprophylaxis may vary by season, geographic location, and level of circulating viral resistance. The CDC website provides current recommendations for treatment and chemoprophylaxis of influenza: www.cdc.gov/flu/professionals/antivirals/index.htm.

Zanamivir (Relenza®) is available as a dry powder administered via oral inhalation with a plastic device. The dose is two breath-activated inhalations (one 5 mg blister per inhalation = 10 mg) bid for 5 days. Zanamivir is not recommended for use in patients with underlying airway disease including asthma or COPD, because of a lack of safety and efficacy data in these patients. Oseltamivir (Tamiflu®) is available as pills or liquid and is given twice daily for 5 days, with dose adjustments required in renal impairment. Pediatric dosing of oseltamivir for 1 – 12 years is 2 mg/Kg/dose bid x 5 days (max. dose = 75 mg) and for 13 years and older: 75 mg bid x 5 days.

Chemoprophylaxis
Chemoprophylaxis or prolonged administration of antiviral medications during the periods of highest risk for transmission is an adjunct for control and prevention of influenza in specific situations and is not a substitute for immunization. Chemoprophylaxis should be considered for protection of children at increased risk of severe infection or complications who are unable to receive influenza vaccine due to contraindications and for immunocompromised children who may not respond to
vaccine. Other considerations include the protection of unimmunized high-risk children or children who were immunized less than two weeks before influenza circulation and who may not have developed an adequate immune response, protection of unimmunized close contacts of high-risk children, protection of immunized high-risk children if the circulating influenza strain is a poor match to the strain in the vaccine and for the control of influenza outbreaks in some institutional closed settings.

Prevention of Influenza
Good infection control maintenance is a well known cornerstone of disease management and needs to be the focus of general practice management of all respiratory outbreaks including seasonal and pandemic influenza. Infection control refers to all policies, procedures and activities that aim to prevent or minimize the risk of transmission of infectious diseases. This includes simple measures such as adequate hand hygiene by hand washing or hand rubs, and cough etiquette to more involved measures such as personal protective equipment (PPE).

Hospitalized patients with influenza should be placed on droplet precautions (mask, gown and glove). Respiratory hygiene/cough etiquette (placing masks on patients with a cough when outside of their room) should be incorporated into infection control practices. Visitors who have any respiratory illness symptoms should be discouraged from visiting patients. Health care workers who are ill should be restricted from working until they are healthy.

The primary measure to prevent influenza is vaccination of both patients and families, and healthcare workers. The rapid evolution of new strains of influenza necessitates annual reformulation of the vaccine strains and annual vaccination of vaccine recipients to maintain immunity to current influenza strains. All currently available inactivated and live attenuated influenza vaccines are trivalent, meaning they contain 3 strains that represent the most recent circulating wild-type strains in a given year: A (H3N2), A (H1N1), and B. Initiation of influenza vaccination programs should start as soon as influenza vaccine is available from manufacturers and should be continued throughout the influenza season.

Surveillance and Surge Planning
During the pre-pandemic intervals, healthcare providers and healthcare facilities play an essential role in surveillance for suspected cases of infection with novel strains of influenza and should be on the alert for such cases. Novel strains may include avian or animal influenza strains that can infect humans such as avian influenza A H5N1 or novel influenza A H1N1 and new or re-emergent human viruses that cause cases or clusters of human disease. For detection of cases during the Pre-Pandemic and Pandemic Intervals, hospitals should have predetermined thresholds for activating pandemic influenza surveillance plans.
Influenza pandemics are different from many of the threats for which public health and the healthcare system are currently planning. The pandemic will last much longer than most other emergency events and may include “waves” of influenza activity separated by months (in 20th century pandemics, a second wave of influenza activity occurred 3 to 12 months after the first wave). The numbers of healthcare workers and first responders available to work can be expected to be reduced; they will be at high risk of illness through exposure in the community and in healthcare settings, and some may have to miss work to care for ill family members. It is reasonable to assume that absenteeism may exceed 25%. Resources in many locations could be limited because of how widespread an influenza pandemic would be.

The goal of a pandemic surge plan for an emergency department or other outpatient setting is to provide safe and effective care in the event of an influenza pandemic or similar event, and to optimize resources and mitigate throughput issues in order to provide for maximum surge capacity for pediatric patients presenting to the emergency department for care. Utilizing the all-hazards approach to develop plans for epidemic and pandemic respiratory illness is based on the concept that most disaster-response functions are common to all disaster types, and unified planning provides the strongest basis for effective response.

Critical components of comprehensive plans must address the following: 1) Screening, surveillance, and tracking of exposed individuals; 2) controlled access to the healthcare facility; 3) prevention strategies (isolation and cohorting, PPE use, vaccination, antiviral prophylaxis, modification of environmental controls (i.e., separate areas for ill and non-ill patients); 4) disease-specific admission criteria, treatment, and triage algorithms; and 5) enabling the continuity of limited clinical operations.

In all healthcare settings, patients with symptoms of influenza or influenza-like illness (ILI) should be segregated from non-influenza patients as rapidly as possible, especially in a triage setting. When possible, consider having different teams of staff should care for influenza and non-influenza patients. In acute care settings, triage non ILI patients promptly to specific non-ILI waiting and examining areas, physically separate from the ILI assessment area to prevent their exposure to ILI if possible. Additionally separate entrances and exits should be established for those who believe they may have been exposed to ILI or those that are in need of other types of medical attention if feasible.

Admission policies and testing and treatment algorithms should also be created for determining if a patient needs to be admitted to the hospital or if an alternate care facility may be more appropriate if altered standards of care are being used. If possible, hospitals triage protocols for phone triage may help to educate patients and families and provide help with illness management without accessing the clinic, emergency department or
hospital setting. The diagnosis and treatment algorithms used at the Children’s Hospital Colorado can be found in this module appendix.

**Special Issues in Developing Countries**

Several factors may be involved in the high mortality rates pandemics cause in developing countries. These include lack of access to adequate medical care, weak public health infrastructures, social factors such as housing conditions and population density, and host factors such as nutritional status and co-existing medical conditions. Core interventions to control or mitigate the effects of an influenza pandemic include pharmaceutical interventions such as vaccines and antiviral agents, and nonpharmaceutical interventions such as quarantine, isolation, social distancing, and personal hygiene.

Antiviral agents are particularly useful in the early stages of a pandemic when there is shortage of vaccines. Stockpiling of neuraminidase inhibitors is part of many industrialized countries pandemic preparedness plans however stockpiles of antiviral agents available in developing countries is small and limited. The most critical limiting factor for stockpiling neuraminidase inhibitors in developing countries is their high cost and allocating scarce resources to stockpile sufficient quantities of oseltamivir for an unpredictable influenza pandemic. Because only a limited number of vaccines will be initially available, particularly in the early stages of a pandemic, and most of them would likely be supplied to industrialized countries, developing countries will need to focus initially on nonpharmaceutical interventions. Maintaining a balance between pharmaceutical and nonpharmaceutical interventions is necessary to achieve the best use of limited resources.

During an influenza pandemic, additional essential medical supplies such as gloves, masks, syringes, antipyretics, and antimicrobial agents will also be required. These supplies are insufficient in healthcare facilities in developing countries, even in nonemergency situations. Lack of these supplies may hamper provision of adequate medical care for patients with pandemic influenza. Basic PPE such as disposable gloves and surgical masks are needed for protecting healthcare workers. Anti-microbial agents are expected to be effective for secondary bacterial pneumonia, which can be a major cause of death for patients with pandemic influenza.

Providing better medical care during a pandemic is essential to reduce the health consequences of the pandemic including death. Since the availability of pharmaceutical interventions in developing countries is less likely, nonpharmaceutical interventions such as social distancing and personal hygiene may be the only available interventions. Essential medical supplies such as masks, gloves, and antimicrobial agents should be available in hospitals and clinics. The stockpiles of these basic supplies can be more cost-effective in developing countries than stockpiles of more expensive antiviral agents. Healthcare personnel
should be trained for infection control measures, especially hand hygiene and use of personal protective equipment. The overarching goal is to maintain the current healthcare and public health systems need to minimize the impact of a pandemic. The link to PAHO’s Pandemic Influenza A (H1N1) 2009 manuals that describe preparedness planning, infection prevention and control, nonpharmaceutical strategies and IMCI diagnosis, treatment and management protocols in Spanish, English, Portuguese and French is http://new.paho.org/hq/index.php?option=com_content&task=view&id=2914&Itemid=1084&lang=en.

Lessons Learned from 2009-2010 H1N1 Pandemic
The WHO plans to continue to strengthen influenza surveillance and the early warning system, build capacity to cope with a pandemic, and further coordinate global scientific research and development activities. The current novel influenza A (H1N1) pandemic confirms the need for preparedness plans that focus on both nonpharmaceutical strategies (social distancing, infection control and quarantine), and pharmaceutical strategies (antiviral drugs use for the treatment and prophylaxis of influenza, and the use of influenza vaccines) to mitigate the effect of the pandemic. The importance of building human surge capacity allows the allocation of health resources including the provision of essential health services and determination of the roles each institution plays in the response. Infection prevention and control activities have been critical to protect healthcare workers and to prevent the nosocomial spread of influenza infections.

Additionally, there is an urgent need to have better detection methods for influenza viruses, including the creation or strengthening and scaling-up of laboratory capacity for influenza diagnosis in most settings (low-, middle-, and high-income countries), through international networks of collaboration, technology transfer, and capacity-building efforts. Pharmacologic interventions including the use of antiviral drugs and medical interventions such as antimicrobials to treat secondary bacterial pneumonias, along with the use of supportive medical care such as oxygen, anti-inflammatory drugs, and antipyretics, have also shown to be a critical component of the overall response activities during the current influenza pandemic. Finally, all countries should develop pandemic influenza vaccine deployment or antiviral deployment plans, regardless of the current absence of availability of pandemic influenza vaccine or adequate supplies of antiviral medications.
measles infections are less than 0.1% in developed countries, in developing countries the rates exceed 1% to 2%. CFRs for hospitalized cases have been reduced by the use of vitamin A treatment.

In developing countries, mortality from measles is related to the intensity of the exposure and host's nutritional and immunologic status. Secondary cases within a household are at greater risk than index cases. Knowing the level of measles vaccination coverage in the affected community and the frequency of measles cases diagnosed within the past few years is helpful. If measles cases have been diagnosed in the community within the past several years, plan a measles immunization campaign, regardless of the immunization coverage level.

Give measles vaccination high priority in a large displaced or refugee population because there may be enough susceptible children to cause an epidemic. Malnourished children living in crowded shelters following a disaster are especially vulnerable and at high risk for severe disease. Implement a surveillance system to identify possible measles cases in the camp or area. Educate medical staff about the clinical signs that suggest measles, such as fever, cough, conjunctivitis, and rash. Respiratory syndromes are often nonspecific; measles cases can be easily overlooked and other respiratory infections can be mistaken for measles.

**What is the impact of measles?**

A measles outbreak is potentially devastating in displaced populations. In many parts of the developing world measles is one of the leading causes of childhood morbidity and mortality: it is highly contagious and spreads through aerosolized particles from respiratory secretions containing the virus. Measles fatalities vary from 200,000 to 800,000 per year in developing countries (Black 2003; WHO 1999 and 2001; Murray 1996). While case fatality rates (CFR) for all
**SECTION III / MEASLES**

**Importance of vaccination**

Unfortunately, isolation of patients is not an effective preventive measure since individuals are most contagious in the prodromal period, before a diagnosis can be made. The only effective approach is to vaccinate the population as soon as possible. Give measles vaccination the highest priority early in disaster situations. Do not delay until cases of measles have been reported (Box 2) (CDC, 1992).

Consider vaccinating children presenting with acute illness, such as fever, diarrhea, and ARI, as well as malnourished children and those with tuberculosis or HIV infection.

**Vitamin A and measles**

Vitamin A deficiency increases measles-associated morbidity and mortality.

Moreover, measles infection increases the severity of the complications resulting from vitamin A deficiency. Vitamin A is important in maintaining epithelization of the respiratory tract and in the recovering process after infection. It also plays a key role in the body's immune defenses.

Children deficient in vitamin A who become infected with measles have higher corneal ulceration and fatality rates. Develop a plan to administer prophylactic vitamin A in conjunction with a measles immunization program. However, when measles vaccine is not yet available and a delay is anticipated, administer vitamin A. This vitamin by itself reduces morbidity and mortality during measles outbreaks. The prophylactic dose of vitamin A according to World Health Organization current recommendations is 100,000 IU for infants and 200,000 IU for children older than 12 months. Pregnant women should receive only 30,000 IU of vitamin A.

**Measles diagnosis**

Following an incubation period of 10 to 12 days from exposure, measles prodrome is characterized by 2 to 4 days of fever, cough, coryza, and conjunctivitis. During this period, Koplik spots can be seen as tiny blue-white spots on an intensely reddened oral mucosa. These lesions disappear within 3 days. The mac-
ulopapular erythema or morbilliform rash of measles first appears on the hairline and forehead, then moves downward to involve the face, neck, and the rest of the body. Initially the lesions are discrete and then become confluent. If no complications occur, fever disappears within 2 to 3 days after the onset of rash.

The rash persists for 4 to 6 days. It becomes brownish in color for a few days before desquamating. Many children have anorexia, and some have mild stomatitis. Generalized lymphadenopathy can occur, but it is uncommon.

Measles complications
Measles is a highly catabolic disease, associated with reduced food intake, increased gastrointestinal losses, and rapid weight loss. Complications occur in approximately 30% of cases; complication rates are even higher in developing countries. The most frequent acute complications are pneumonia, croup, otitis media, and diarrhea. Measles virus is immunosuppressive and predisposes to secondary viral and bacterial infections, as well as to the reactivation of tuberculosis.

Malnourished children often have atypical presentations that may vary from hemorrhagic lesions associated with mucosal bleeding and disseminated intravascular coagulation (called black measles), to a less intense rash because of compromised cell mediated immunity. These children may also have a deeper desquamation resulting in extensive areas of depigmentation. Providing nutritional support continued feeding, even if diarrhea is present, is crucial. If the child refuses feeding, consider using a nasogastric tube. Give additional fluids to prevent or treat dehydration. When acute infection has resolved, enroll malnourished children in a feeding program, if available.

Most measles-related deaths are associated with pneumonia, croup, and diarrhea. Rare acute complications include encephalitis and endocarditis. Major longterm sequelae in developing countries include measles-related blindness, malnutrition, and chronic lung disease. The immunosuppressive effect of measles may delay recovery for many months and cause recurrent infections and later death.

Classification
Measles is classified according to the severity of the illness. Refer severe or very severe cases to a hospital (Hussey and Berman, 2003).

Mild: Fever resolves within 4 days and rash within 8 days with no sign of complications.

Moderate: There are signs of secondary bacterial upper respiratory infection: acute otitis media, sinusitis, or cervical adenitis.

Severe: Signs of respiratory distress emerge with tachypnea, indrawing, reduced oxygen saturation, or stridor. Other possible signs are heart murmurs or electrocardiographic changes, ophthalmologic signs of vitamin A deficiency or corneal ulcerations, deep or
extensive mouth ulcers, bloody diarrhea, jaundice, abdominal pain, moderate to severe dehydration, or purpura (hemorrhagic measles). Patients with severe malnutrition, immunodeficiency disorders, cardiopulmonary disorders, or pre-existing tuberculosis are most at risk.

**Very severe**: Patient exhibits any of the following symptoms: altered mental status with coma, seizures, or focal neurologic signs; shock with poor peripheral perfusion; upper airway obstruction or signs of respiratory failure; signs of congestive heart failure; or acute abdominal pain with peritoneal signs.

**How can complications of measles be prevented?**
Administer vitamin A 100,000 IU to infants and 200,000 IU to children older than 12 months. Repeat the dose in 24 hours. For patients with ophthalmologic signs of vitamin A deficiency (xerosis, Bitot's spots, keratomalacia, corneal ulceration, or clouding) repeat the dose in 4-6 weeks to prevent corneal ulceration.

Severe mouth ulceration can be a consequence of herpes infection and may contribute to reduced fluid and food intake. Promote oral hygiene with regular mouth washes using clean water and the application of local antiseptic solutions. Consider gentian violet to treat mouth ulcers.

Prevent secondary eye infections through regular cleansing of the eyes with water and topical antibiotics, such as tetracycline. Consider a protective eye pad to prevent secondary infection.

If dysentery is present, treat with an appropriate antibiotic therapy for *Shigella*. 
Acute Respiratory Infections: The Patient with Cough or Difficult Breathing

All types of respiratory infections are more common among people living in overcrowded conditions in developing countries. Most cases of acute respiratory infections (ARI) are viral upper respiratory tract infections that should not be managed with antibiotics. The IMCI strategy uses 3 key clinical signs to assess children with cough or difficult breathing:

- **Respiratory rate (RR)** distinguishes the presence or absence of pneumonia.
- **Lower chest wall indrawing** indicates severe pneumonia.
- **Stridor** in a calm child indicates severe upper airway obstruction and the need for hospital admission.

CASE 2

A 3-month-old infant presents with fever, restlessness, and poor food intake. He is irritable and it is difficult to soothe him. He is breathing normally. His vital signs include respiratory rate 36 beats/min, heart rate 120 beats/min, blood pressure 90/58 mm Hg, temperature 102°F (39.2°C), and oxygen saturation 98%. The fontanelle looks full and the neck is flexible. Capillary refill time is 2 seconds.

- Which of these findings are consistent with the diagnosis of meningitis?
- Which is the most important therapeutic measure to be implemented?
- Which complications could possibly occur?
Respiratory rate
No single clinical sign has a better combination of sensitivity and specificity to detect pneumonia in children under 5 years than RR. Even auscultation by an expert is less sensitive as single sign. Cutoff rates for fast breathing (tachypnea) depend on the child’s age. Normal RR is higher in children aged 2 to 12 months than in children from 12 months to 5 years (Table 1).

The specificity of RR for detecting pneumonia depends on the prevalence of bacterial pneumonia among the population. In areas with high levels of viral pneumonia, RR has relatively modest specificity. Nevertheless, even if the use of RR leads to some over-treatment, this will still be small compared with the use of antibiotics among all children with an ARI, as frequently occurs.

Lower chest wall indrawing
Lower chest indrawing is defined as the inward movement of the bony structure of the chest wall with inspiration. It is a useful marker of severe pneumonia. It is more specific than “intercostal indrawing,” which includes the soft tissue between the ribs without affecting the bony structure of the chest wall. Chest indrawing should only be considered present if it persists in a calm child. Agitation, a blocked nose, or breastfeeding can all cause temporary chest indrawing.

Stridor
Stridor is a harsh noise made when the child inhales. Children who present with stridor when calm are at substantial risk of upper airway obstruction and should be referred. Some children with mild croup manifest stridor only when they are crying or agitated.

Wheeze
Sometimes a wheezing noise is heard at exhalation. Wheezing is usually associated with asthma or viral bronchiolitis. With fast breathing, no distinction is made between children with bronchiolitis and those with pneumonia.

In some cases, especially when a child has wheezing at exhalation, the final decision on presence or absence of fast breathing can be made after a test with a rapid-acting bronchodilator (if available). Experience suggests that even where asthma rates are high, mortality from asthma is relatively uncommon.

<table>
<thead>
<tr>
<th>Child’s age</th>
<th>Cutoff rate for fast breathing (tachypnea)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months to 12 months</td>
<td>50 breaths per minute or more</td>
</tr>
<tr>
<td>12 months to 5 years</td>
<td>40 breaths per minute or more</td>
</tr>
</tbody>
</table>

TABLE 1. Respiratory rate
Classification of children with cough or difficult breathing
Based on a combination of the aforementioned clinical signs, children presenting with cough or difficult breathing can be classified into 3 categories: those who require referral for possible severe pneumonia or very severe disease, those who require antibiotics as outpatients, and those who do not require antibiotic treatment (Box 3).

The group requiring referral for possible very severe disease includes children with any general danger sign, lower chest indrawing, or stridor when calm. Children with severe pneumonia or very severe disease are more likely to have life-threatening invasive bacterial infections. This indicates the need to use injectable antibiotics. Give outpatient antibiotics to children with a fast RR for their age to treat bacterial pneumonia when they do not have additional danger or severe signs. Fast breathing, as defined by WHO, detects about 80% of children with pneumonia who need antibiotic treatment. Treatment based on this classification has been shown to reduce mortality.

Patients with cough and no signs suggesting pneumonia or severe disease do not require antibiotics. Such children may require a safe agent to relieve cough. A child with cough will normally improve in 1 to 2 weeks. However, a child with chronic cough (more than 30 days) needs to be further assessed (and, if needed, referred) to rule out tuberculosis, asthma, whooping cough, or another respiratory problem (Mulholland et al., 1992).

**Antibiotics**
First-line oral antibiotics for suspected pneumonia will typically be amoxicillin or cotrimoxazole (trimethoprim-sulfamethoxazole). Intramuscular (IM) antibiotics used to treat severe pneumonia or very severe disease include chloramphenicol, benzylpenicillin, and ceftriaxone. IM chloramphenicol (40 mg/kg every 12 hours) is commonly used for serious infections when oral agents cannot be administered. Bear in mind that there is no pharmacologic value to giving IM or intravenous (IV) chloramphenicol instead of the oral agent in terms of achievable blood levels (Sazawal and Black, 1992).

**BOX 3. Classification of children with cough or difficult breathing according to clinical signs**

<table>
<thead>
<tr>
<th>Very severe respiratory disease or pneumonia (RED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Any general danger sign</td>
</tr>
<tr>
<td>– Chest indrawing</td>
</tr>
<tr>
<td>– Stridor in a calm child</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pneumonia (YELLOW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Fast breathing</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cough without pneumonia (GREEN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>– No signs of pneumonia or other severe disease</td>
</tr>
</tbody>
</table>
**Ear problems**

Ear problems are the next condition that should be checked in all children brought to the outpatient health care facility. A child presenting with an ear problem should first be assessed for general danger signs, cough or difficult breathing, diarrhea, and fever. Although otitis is rarely a cause of death, it is the main cause of deafness in low-income areas, which in turn leads to learning problems.

**Clinical assessment**

When otoscopy is not available, examine the child for the following clinical signs:

- **Tender swelling behind the ear.** The most serious complication of an ear infection is an infection in the mastoid bone (mastoiditis). It usually manifests with swelling behind one of the ears. In infants, this swelling may also be above the ear. When present, this sign is considered positive and should not be mistaken for swollen lymph nodes.

- **Ear pain.** In the early stages of acute otitis, a child may suffer ear pain, which usually causes the child to cry and become irritable.

- **Ear discharge.** This is another sign of an ear infection.

**Classification of ear problems**

Based on the presence and duration of clinical signs (swelling behind the ear, ear pain or ear discharge), the child’s condition can be classified as mastoiditis, acute otitis, or chronic otitis (Box 4).

Children presenting with swelling of the mastoid bone are classified as having mastoiditis and should be referred to a hospital for treatment. Before referral, these children should receive a dose of antibiotics and a single dose of paracetamol for pain. Children with ear pain or ear discharge for less than 14 days are classified as having acute otitis. Treat them for 5 days with the same first-line antibiotic as for pneumonia. If there is ear discharge for more than 14 days, the child’s classification is chronic otitis. Attempt to wick or dry up the ear. In this case antibiotics are not recommended because they are expensive and their efficacy is not proven.

If no signs of ear infection are found, children are classified as having no ear infection and do not require any specific treatment.
OBJECTIVES

- Recognize the public health importance of febrile illnesses, such as malaria and dengue, in the context of acute emergency settings.
- Understand the role of the clinician in malaria identification, prevention, and treatment using the IMCI strategy.
- List the factors that lead to malaria and differentiate the species that cause benign (uncomplicated) and malignant (complicated) malaria.
- Describe which individuals are more prone to suffer morbidity and mortality from malaria infection and the causes that determine the higher risk.
- Describe the features of severe/complicated malaria and distinguish these features from those associated with typical uncomplicated malaria.
- Diagnose and develop a treatment plan (medications, supportive care, and monitoring) using available resources for patients with:
  - Severe/complicated malaria
  - Typical uncomplicated malaria
  - Severe dengue fever
  - Dengue fever

Characteristics and incidence of malaria

Malaria is caused by a protozoan blood parasite (Plasmodium) transmitted by the Anopheline mosquito as a vector. The infection produces a clinical syndrome that ranges in severity depending on the species of the parasite and the immune status of the individual. Malaria caused by Plasmodium vivax, P. malariae, and P. ovale usually results in mild or moderate disease. P. falciparum often results in a life-threatening disease and severe anemia. The emergence of multidrug-resistant P. falciparum is a global problem.

Worldwide there are 300 million new cases of malaria each year and 1 to 2 million deaths. Most deaths occur in children under 5 years of age. Most susceptible individuals to severe, fatal malaria include infants and young children, malnourished children, and pregnant women.

Children who have been recently treated for malaria can contract malaria again. Malaria immunity following an infection is at best partial, and protects only against the species causing the initial infection. Children can therefore be infected with a different malaria species in regions having more than one prevalent species or they can be reinfected with the same species. A relapse or recrudescence of an existing infection can be related to a failure to eradicate a parasite that has become drug-resistant or to a patient’s failure to adhere to a therapeutic regimen.

Malaria occurs in areas of Southeast Asia and Latin America where transmission is seasonal or limited to specific focal
areas, so the general population does not have a high level of acquired immunity. Both children and adults in these areas are at high risk for severe disease. Malaria also occurs in areas of Africa where the disease is widespread and endemic. It generates high levels of acquired immunity in adults, but young children are at higher risk for severe disease. Most Anopheline mosquitoes are not well adapted to urban environments or places about 3,900 ft (1,200 m) above sea level. Consequently, individuals living within a malaria endemic country may be nonimmune if they live within one of these malaria-free “pockets.” When these nonimmune people are displaced from their communities to areas with high malaria transmission, the consequences can be devastating.

Malaria diagnostic tests
Malaria infection is diagnosed by identifying the parasite in stained (Giemsa or Wright) blood smears. A blood sample is easily obtained from a finger prick. After a drop is placed on a clean labeled glass slide, spread it with another glass slide into a thin blood smear. Thick smears are obtained by placing some drops of blood on a glass slide and spreading the drops with the corner of another glass slide. Dry the resulting smear without fixation. Since thick smears allow the examination of more blood than thin smears, they facilitate the detection of the parasite in cases of low-grade parasitemia. New rapid diagnostic tests for malaria have been developed and will become more widely available in the future.

Children suspected of having malaria should have thick and thin smears of peripheral blood done whenever possible. Serial samples at 6- to 12-hour intervals for 48 hours may be necessary to identify the parasite. Species identification in the field setting is important only for discriminating between *P. falciparum* and other species because the treatment can be different. *P. vivax*, *P. ovale*, and *malariae* are all sensitive to chloroquine and produce less severe disease than *P. falciparum*.

The quantitative level of parasitemia is a prognostic marker; >5% of parasitized red blood cells is associated with high mortality. Low-grade parasitemia related to partial immunity or treatment can result in a negative smear. Even patients with cerebral malaria can be smear-negative at presentation.

Therefore, when the clinical history and presentation suggest malaria, begin treatment regardless of the presence of parasites on the smears. If experienced laboratory technicians and equipment are not available, then the diagnosis and treatment of malaria must be based on the presence of clinical signs and symptoms consistent with malaria and the knowledge of local malaria prevalence.

However, it is also important to acknowledge that malaria can coexist with other conditions that cause fever. In the absence of specific diagnostic tests, empiric treatment of any serious febrile illness should include coverage for malaria, as well as other pathogens. Remember: fever in a malaria endemic area should be
considered caused by malaria unless another cause is identified.

**Surveillance**
In areas with endemic malaria, determine the proportion of febrile illness in a camp or settlement attributable to malaria by comparing thick (and thin, if possible) blood smears from a sample of patients under 5 years of age who have a history of recent fever with an equal number of patients without fever. Comparing the prevalence of malaria parasites in the blood of these two groups gives an indication of how much malaria is contributing to acute febrile illness in the general population. This will be useful for the empiric management of other patients.

**Chemoprophylaxis**
Chemoprophylaxis for malaria is rarely feasible in the acute emergency setting. It has been used to limit epidemics in groups without immunity that are relocated to a high malaria transmission area and to reduce mortality among targeted populations, such as malnourished children under 5 years of age.

Adequate infrastructure and resources must be available to implement a preventive chemoprophylaxis program for a targeted population. Efforts must be coordinated with local and national public health authorities.

**Clinical presentation**
There are two distinct clinical malaria presentations: typical uncomplicated malaria and severe, complicated malaria.

Typical uncomplicated malaria presents with fever, chills, headaches, myalgias, diarrhea, and anemia. Classic malaria fever has been described as paroxysms of fevers and shaking chills lasting 8 to 12 hours, every 2 to 3 days. During the afebrile period, fever disappears and the subject feels relatively well (depending on the species). The febrile paroxysms coincide with the cyclical release of parasites from ruptured red blood cells; the afebrile period coincides with the quiet growth of the parasite in a new population of red blood cells. Partially immune individuals may have a non-specific fever pattern.

Malaria is considered to be very severe if parasitemia is >5% or any of the following complications is present: severe anemia associated with hemoglobinemia, bleeding diathesis, hypotension and shock, renal failure, hypoglycemia, acidosis, or encephalopathic signs (cerebral malaria). Cerebral malaria is associated with signs of acute encephalopathy (coma and seizures), normal cerebrospinal fluid (CSF), and no other identifiable cause (meningitis, viral encephalitis, metabolic abnormalities). Cerebral malaria mortality varies from 15% to 50% (Table 2).

**Treatment of typical uncomplicated malaria**
The treatment of malaria depends on the likelihood of a malaria infection and the risk of chloroquine-resistant *P. falciparum* or *P. vivax*, the severity of the infection, the setting, and the availability of drugs. In high-risk areas, treat all forms of typical uncomplicated malaria not caused by
### TABLE 2. Degree of illness in malaria

<table>
<thead>
<tr>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache, malaise, irritable (can be soothed)</td>
<td>Irritable and not easily soothed, poor eye contact (lethargic), feeds poorly</td>
<td>Unresponsive, too weak to feed, or extreme weakness or seizures</td>
</tr>
<tr>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>Parasitemia &lt;2%</td>
<td>Signs of mild or moderate dehydration but good peripheral perfusion</td>
<td>Signs of severe dehydration with shock, poor peripheral perfusion with cold, mottled extremities, capillary refill &gt;2 seconds, low blood pressure</td>
</tr>
<tr>
<td>WITHOUT SIGNS OF</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>• Dehydration</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>• Respiratory distress or pulmonary edema</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>• Severe anemia</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>• Bleeding or a metabolic disorder</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td></td>
<td>Parasitemia &gt;2% and &lt;5%</td>
<td>Signs of respiratory distress or pulmonary edema with respiratory rate &gt;60, cyanosis, or respiratory failure</td>
</tr>
<tr>
<td></td>
<td>But</td>
<td>or</td>
</tr>
<tr>
<td></td>
<td>No signs of respiratory distress, pulmonary edema, severe anemia, or a metabolic disorder</td>
<td>Severe normocytic anemia, hemoglobinuria, or bleeding associated with disseminated intravascular coagulation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metabolic disorder, hypoglycemia, metabolic acidosis, or renal failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parasitemia ≥5%</td>
</tr>
</tbody>
</table>

**Plasmodium falciparum** with oral or nasogastric chloroquine phosphate (except for chloroquine-resistant parasites). Primaquine is effective at preventing relapses because it eradicates the liver stages of *P. vivax* and *P. ovale* that persist in patients who have experienced the acute illness. This drug is not normally used in disaster situations.

In low-risk areas or areas with seasonal malaria, only treat children presenting with fever with no other identified cause (acute respiratory infection, ear infection, pharyngitis, measles, etc.). However, the persistence of fever longer than 5 days requires reassessment and, if possible, laboratory testing for malaria.

The management of all forms of *Plasmodium falciparum* now recommended by the WHO since 2008, given the increasing resistance to chloroquine shown by these organisms, is a new first-line therapy that replaces classical chloroquine phosphate: artemisinin-based agents. There are combination therapies and non-combination therapies, but the first are recommended. They are given orally for 3 days.

1. **Combination therapies**
   (2 drugs in one tablet)
   - artemether-lumefantrine (Coartem®) (Table 3)
   - artemesunate + mefloquine
   - artemesunate + amodiaquine

2. **Non-combination therapies**
   (Table 4)
   - artemesunate (4 mg/kg once a day for 3 days) + mefloquine (25 mg/kg base divided in 2 doses on the second and third days)
   - artemesunate (4 mg/kg once a day for 3 days) + SP (sulfadoxine 25 mg/kg + pirimetamine 1,25 mg/kg as a single dose on day 1) in areas where cure rate with SP is higher than 80%
   - artemesunate (4 mg/kg once a day for 3 days) + amodiaquine (10 mg base/kg/day for 3 days) in areas where cure rates with amodiaquine as single therapy are higher than 80% If the abovementioned drugs are not available, recommended therapy continues to be chloroquine phosphate. For children, a total dose of 25 mg/kg of chloroquine over a 3-day

**TABLE 3. Dosage schedules for artemether-lumefantrine**

<table>
<thead>
<tr>
<th>Weight (approx. age)</th>
<th>Number of tablets at approximate timing (hours) of dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 h</td>
</tr>
<tr>
<td>5-14 kg (&lt;3 years)</td>
<td>1</td>
</tr>
<tr>
<td>15-24 kg (&gt;3-8 years)</td>
<td>2</td>
</tr>
<tr>
<td>25-34 kg (&gt;9-13 years)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;34 kg (&gt;14 years)</td>
<td>4</td>
</tr>
</tbody>
</table>

### TABLE 4.

#### Dosage schedules for artesunate + mefloquine

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of artesunate tablets (50 mg) per day</th>
<th>Number of mefloquine tablets (250 mg base) per day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>5-11 months</td>
<td>1/2</td>
<td>1/2</td>
</tr>
<tr>
<td>&gt;1-6 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&gt;7-12 years</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>&gt;13 years</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

#### Dosage schedules for artesunate + SP

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of artesunate tablets (50 mg) per day</th>
<th>Number of SP tablets (25 mg S + 500 mg P base) per day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>5-11 months</td>
<td>1/2</td>
<td>1/2</td>
</tr>
<tr>
<td>&gt;1-6 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&gt;7-12 years</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>&gt;13 years</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

#### Dosage schedules for artesunate + amodiaquine

<table>
<thead>
<tr>
<th>Age</th>
<th>Artesunate tablet (50 mg)</th>
<th>Amodiaquine tablet (153 mg base)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>5-11 months</td>
<td>1/2</td>
<td>1/2</td>
</tr>
<tr>
<td>&gt;1-6 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&gt;7-12 years</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>&gt;13 years</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>


...period; 10 mg base/kg (maximum 1 g = 600 mg base), then 5 mg base/kg 6 hours later; 5 mg base/kg/dose at 24 and 48 hours. For adults, 1 g (600 mg base), 500 mg (300 mg base) 6 hours later; then 500 mg (300 mg base) at 24 and 48 hours.

Chloroquine-resistant strains of *P. falciparum* are common throughout many regions of the world. When the proportion of chloroquine-resistant *P. falciparum* is less than 25%, it may be reasonable to use chloroquine as first-line treatment in less severe patients and assess the response. Failure to respond in 48 to 72 hours indicates infection with a resistant strain. Treat children with chloroquine-resistant *P. falciparum* uncomplicated
malaria with quinine sulfate 25 mg/kg/day tid for 3 to 7 days (depending on resistance patterns to quinine) plus one of the following:

- Doxycycline 2.2 mg/kg/day for 7 days (adult dose 100 mg bid for 7 days)
- Tetracycline 25 mg/kg/day qid for 7 days (adult dose 250 mg qid for 7 days)
- Clindamycin 20 mg/kg/day tid for 7 days (adult dose same as for children)

Treat children who may have acquired malaria in Southeast Asia (Thailand) and East Africa with quinine for 7 days, because of the presence of multiple resistant strains in these areas. Additional alternative therapies for resistant *P. falciparum* include atovaquone-proguanil, mefloquine, halofantrine (associated with heart-related side effects), and artesunate. See appendix for Centers for Disease Control and Prevention (CDC) actual recommended treatment options.

Chloroquine is effective and safe for treating pregnant women. This is important because malaria during pregnancy is more severe and can be fatal. Ideally, use supervised therapy. Observe administration of at least the first dose to be sure that it is not vomited.

If chloroquine phosphate is not available, hydroxychloroquine sulfate is also effective, but in this case 400 mg of hydroxychloroquine are equivalent to 500 mg of chloroquine phosphate.

In several regions mixed infection with species of *P. falciparum* and *P. vivax* commonly occurs. If diagnosis of infection is based solely on clinical data, therapy must cover both types of parasites. In the acute phase of an emergency, the detection of a *P. falciparum* infection is a priority and artemisinin-based agents (except artesunate SP) are effective against both organisms.

Supportive management of uncomplicated malaria includes antipyretics, oral rehydration solution (ORS), assessment, and possible referral to a feeding program for malnutrition. Successfully treated patients should improve by 48 hours and be symptom-free by 72 hours. If symptoms persist after 3 days, obtain a new blood smear and consider the possibility of chloroquine-resistant malaria or an alternative cause for the fever.

**Treatment of severe and complicated malaria**

Assume that all severe, complicated malaria infections are caused by resistant *P. falciparum* strains unless proven otherwise. Children with severe, complicated malaria can deteriorate rapidly, so initiate treatment with the best available drug and, if possible, arrange a transfer to a hospital for intravenous (IV) therapy (see appendix).

As from 2008, given the increasing chloroquine resistance mentioned above, the first line treatment for severe malaria recommended by the WHO is based on artemisinin derivatives, such as:

- IM artemether

Intramuscular (IM) loading dose (3.2 mg/kg) as a single dose on day 1
Maintenance dose (1.6 mg/kg) IM until the child tolerates oral therapy
- Intravenous (IV) or IM artesunate
  IV loading dose (2.4 mg/kg) over 3 minutes as a single dose on day 1, at 0, 12 and 24 hours
  Maintenance dose (2.4 mg/kg) over 3 minutes, starting on day 2, once a day, until the child tolerates oral therapy
- Rectal artesunate, only if IV or IM routes are not feasible
  Administer rectal artesunate 10 mg/kg in a suppository. Repeat the dose if the drug is eliminated within the first hour. Repeat the dose in 24 hours if the patient can not be transferred to the hospital. Artesunate suppositories remain stable at temperatures of up to 40 degrees and, therefore, require warm, not cold, temperatures for transportation and storage.
  After IM or IV therapy, the patient should be switched to oral therapy; the recommended agent in this case is artemetherlumefantrine (Coartem®) during three days.
  If first-line drugs were unavailable, an option is quinine dihydrochloride. A loading dose of 20 mg/kg in 10 mL/kg of 5% dextrose should be administered IV over 4 hours, followed by 10 mg/kg over 4 hours (maximum 1,800 mg/kg) until oral therapy can be started (see Appendix). Blood glucose monitoring for hypoglycemia is recommended every 4 hours after each loading and maintenance infusion. If IV quinine is required for more than 48 hours, maintenance dose should be reduced to 7 mg/base/kg. It is extremely important to bear the infusion volume into account. In order to avoid volume overload due to the IV administration of liquid, the quinine infusion volume should be included in the estimation of daily liquid requirements.
  Quinine can be diluted in 5% glucose solution, 10% glucose, 4% glucose, 0.18% saline or 0.9% normal saline. It should be diluted to a total volume of 10 mL/kg (the same volume should be used both for the loading dose and the maintenance dose) and infused over 4 hours. After a minimum of three IV doses of quinine, the patient should be switched to oral therapy. Therapy options by this route include: artemetherlumefantrine (Coartem®) over 3 days, or oral quinine 10 mg base/kg, every 8 hours, until a 7-day course is completed. In areas of multiple resistant malaria, quinine should be combined with oral clindamycin, 5 mg/kg 3 times a day, during 7 days. Mefloquine should be avoided in children that have been in coma, since it increases the risk of neuropsychiatric complications.
  A third choice is administering an initial dose of quinine sulfate by oral route or nasogastric tube until IV therapy is available. If the patient vomits, repeat the dose within 30 minutes. If vomits persist, start IM quinidine 10 mg/kg every 4 hour until the patient is transferred to a hospital for IV therapy. At the hospital, treat very severely ill patients with an IV loading dose of quinine gluconate 10 mg/kg administered over 1 to 2 hours, then with a 0.02 mg/kg/min continuous infusion until oral therapy can be given. If possible, measure hemoglobin, blood sugar, and
perform blood and cerebrospinal fluid (CSF) cultures.

Treat children with severe complicated malaria with antibiotics for potential bacteremia or meningitis pending the results of blood and CSF cultures. If possible, monitor the patient for electrocardiographic changes (QT interval, arrhythmias), cinchonism (tinnitus, nausea, headache, and visual changes), and hypoglycemia. Discontinue IV quinidine as soon as the child has improved and switch to oral or nasogastric quinine to complete a 3 or 7 day course (varies by region).

Indications for exchange transfusion vary according to the quality of intensive care facilities and availability and safety of blood products. The theoretical benefits of an exchange transfusion are parasitemia reduction, correction of anemia, improved oxygenation, and enhanced capillary blood flow. It is recommended when children have signs of very severe illness with parasitemia >10%.

Supportive treatment of severe, complicated malaria includes antipyretics and oral rehydration solution (ORS). Monitor signs that suggest fluid overload causing pulmonary or cerebral edema. Additional sugar may be added to the ORS because of the risk for hypoglycemia.

Initial treatment of seizures with 50% dextrose is recommended, followed by phenobarbital (10 mg/kg IM) if seizures persist.

**Dengue**

Dengue infections occur worldwide but are most prevalent in Southeast Asia, although an important outbreak has occurred in Central and South America. In Southeast Asia, outbreaks of hemorrhagic fever occur cyclically every 4 to 5 years. It is caused by an arbovirus, usually acquired by the bite of Aedes mosquitoes. There are 4 closely related serotypes of dengue virus, all of which can cause severe disease.

Dengue fever is a mild, self-limited febrile episode that is associated with rash. It begins with fever, respiratory symptoms (sore throat, coryza, cough), anorexia, nausea, vomiting, and headache. Back pain, myalgias, arthralgias, and conjunctivitis are less frequent symptoms. The initial fever resolves within approximately 1 week, and a generalized morbilliform or maculopapular rash develops a few days later. Fever often returns with the rash (Table 5).

**Dengue hemorrhagic fever (DHF grades I and II)** is characterized by hemoconcentration, thrombocytopenia, and coagulation abnormalities.

**Dengue shock syndrome (DHF grades III and IV)** is the most severe form of the disease (approximately 25% of cases) and is characterized by severe hypovolemia and shock. Fatality rates range from 1% to 5%, although much higher rates have been reported. Complications include severe bleeding, pleural effusions, shock, pneumonia, liver dysfunction or failure, encephalopathy, and pulmonary hemorrhage.

The underlying immunopathology of severe dengue infection involves host and viral factors and possibly sequential infections with different virus serotypes. Cardinal features are a marked increase in

The underlying immunopathology of severe dengue infection involves host and viral factors and possibly sequential infections with different virus serotypes.
### TABLE 5. Degree of illness in dengue infection

<table>
<thead>
<tr>
<th>Mild/Moderate (Dengue fever)</th>
<th>Severe (DHF grades I and II)</th>
<th>Severe (Dengue shock syndrome, DHF grade III)</th>
<th>Very Severe (DHF grade IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental status: headache, malaise, irritable (can be soothed)</td>
<td>Mental status: headache, malaise, irritable (can be soothed)</td>
<td>Mental status: irritable (easily soothed), poor eye contact (lethargic), feeds poorly</td>
<td>Mental status: unresponsive, too weak to feed, extreme weakness, or seizures</td>
</tr>
<tr>
<td>No signs of dehydration</td>
<td>Signs of dehydration</td>
<td>Signs of moderate dehydration with hemoconcentration</td>
<td>Signs of severe dehydration with shock</td>
</tr>
<tr>
<td>Good peripheral perfusion</td>
<td>Good peripheral perfusion</td>
<td>Good peripheral perfusion</td>
<td>Poor peripheral perfusion</td>
</tr>
<tr>
<td>Normal blood pressure</td>
<td>Normal blood pressure</td>
<td>Pulse pressure &lt;20 mm Hg</td>
<td>Pulse pressure &lt;10 mm Hg, Capillary refill &gt;2 seconds</td>
</tr>
<tr>
<td>No signs of respiratory distress or pulmonary edema</td>
<td>No signs of respiratory distress or pulmonary edema</td>
<td>Signs of respiratory distress (pneumonia or pulmonary edema)</td>
<td>Signs of severe respiratory distress (pneumonia, pulmonary edema or CHF) with RR &gt;60</td>
</tr>
<tr>
<td>Tourniquet test: negative</td>
<td>Tourniquet test: positive Low platelet count &lt;100,000 Raised hematocrit &gt;20% No signs of severe anemia or bleeding</td>
<td>Tourniquet test: positive Low platelet count &lt;100,000 Raised hematocrit &gt;20% Signs of severe anemia or bleeding</td>
<td>Tourniquet test: positive; Low platelet count &lt;100,000; Raised hematocrit &gt;20%; Life threatening anemia, bleeding associated with DIC</td>
</tr>
<tr>
<td>No signs of metabolic or end-organ failure</td>
<td>No signs of metabolic or end-organ failure</td>
<td>No signs of metabolic or end-organ failure</td>
<td>Metabolic disorder, including hypoglycemia, metabolic acidosis, or liver or renal failure</td>
</tr>
</tbody>
</table>


DIC: Disseminated Intravascular Coagulation. DHF: Dengue Hemorrhagic Fever. RR: Respiratory Rate. CHF: Congestive Heart Failure.
capillary permeability and a bleeding disorder. Increased capillary permeability predisposes to pulmonary edema, pleural effusion, and ascites, as well as intravascular involvement and hemoconcentration. Bleeding (epistaxis, purpura, petechiae, gastrointestinal hemorrhage, menorrhagia) is related to disseminated intravascular coagulation (DIC), with thrombocytopenia and liver damage.

Leukopenia and neutropenia are characteristic findings. In dengue hemorrhagic fever and dengue shock syndrome, most common laboratory findings include hemoconcentration, thrombocytopenia, increased prothrombin time, and abnormalities in fibrinogen and other coagulation factors. Liver function may be impaired (in particular with elevated transaminases). Virus isolation and serologic tests confirm the diagnosis.

Treatment of dengue
For patients with grades III and IV DHF, administer an isotonic fluid (Ringer’s lactate or normal saline solution) at 10 to 20 mL/kg/hour for hemodynamic stabilization. To prevent fluid overload, reduce the rate of infusion to 1 to 5 mL/kg/hour as soon as the hemodynamic condition stabilizes. If there is no improvement (perfusion, pulse pressure, or hematocrit) within 1 hour, consider changing to a colloid solution.

Hospitalize grade IV DHF patients in an intensive care unit whenever possible. In these cases monitor fluid replacement. If pulse pressure on admission is <10 mm Hg, consider initial resuscitation with a colloid solution starting at 10 mL/kg/hour. Also consider transfusion with whole blood or packed red cells and fresh frozen plasma to correct severe anemia and to replace clotting factors. Heparin should be used with caution only when DIC persists despite hemodynamic stabilization, correction of acidosis, and good oxygenation. Systemic steroids do not appear to be effective. Diuretics may be required in the recovery phase to prevent sustained fluid overload.
OTHER CASES THAT REQUIRE ATTENTION AT THE SCENE OF THE DISASTER

OBJECTIVES

- Distinguish other clinical entities that can present at the scene of the disaster, such as tuberculosis.
- Consider meningitis in emergency settings and assess the clinical findings.

**Tuberculosis**

Even though tuberculosis (TB) is the leading infectious cause of death in some parts of the developing world, TB treatment and control programs are not part of an emergency relief response. TB is a chronic infection and effective treatment is very resource-intensive. Treatment programs need to include resources to identify and monitor true cases by sputum smears exam, a stable population for at least 6 months (to complete shortcourse therapy), enough available drugs to treat all cases, and enough personnel to supervise all therapy in the first 2 to 3 months. Administration of anti-TB drugs to persons who will not adhere to or complete treatment is likely to contribute to drug resistance in the community.

**Meningitis**

Meningitis is the inflammation of the membranes (meninges) that surround the brain and spinal cord. Encephalitis is the inflammation of the cerebral cortex. Meningoencephalitis involves both the meninges and the cerebral cortex.

Meningitis may be due to viral, bacterial, or fungal infections. Approximately two thirds of diagnosed cases are viral and one third are bacterial. The most common viral infections are caused by enteroviruses and herpes simplex virus.

The most common bacterial pathogens that cause meningitis during the first 3 months of life include group B Streptococcus (GBS), *Escherichia coli*, *Listeria monocytogenes*, *enterococi*, *Staphylococcus aureus*, and gram-negative enteric organisms. The viral pathogens in this age group are herpes simplex virus, enterovirus, and cytomegalovirus.

Pathogens infecting infants older than 3 months of age and children are most often *S. pneumoniae*, *Haemophilus influenzae* type b (Hib) and Neisseria meningitidis. Other organisms such as *M. tuberculosis*, *Salmonella*, and *Mycoplasma pneumoniae* are rare.

The frequency of *Haemophilus* infection has dramatically decreased with immunization. However, in areas of the world where
conjugate Hib vaccine is not administered, this organism remains a common cause of meningitis. Viral pathogens most prevalent in this age group include enterovirus, arbovirus, herpes simplex virus, herpes virus, influenza, and Epstein-Barr virus.

**Clinical findings of meningitis**

Look for changes in mental status and level of activity, including irritability, changes in feeding and sleeping patterns, unresponsiveness, and seizures.

Check for signs of meningeal irritation: nuchal rigidity, bulging fontanelle, paradoxical irritability, and Brudzinski and Kernig signs.

Evaluate hydration status and signs of shock, such as mottled skin, slow capillary refill, increased pulse, and decreased blood pressure. Perform a neurologic examination and document focal neurologic signs, paresis, or ataxia. Measure the head circumference and look for exanthem, purpura or petechiae, or soft-tissue, bone, or joint infections.

Signs associated central nervous system complications include focal neurologic findings, prolonged seizures, persistent changes in mental status, enlarging head circumferences, or ataxia. Complications include subdural effusion or empyema, cerebral edema, cerebral abscess, cerebral infarction, or hydrocephalus.

**Treatment of meningitis**

Suspected cases of severe sepsis or meningitis need to be treated promptly with the best available drugs. Report such cases to health authorities and make attempts to obtain appropriate samples for identification of the causative agent.

Identification of *Neisseria meningitidis* is particularly important because of its epidemic potential and the fact that a reasonably effective vaccine is available.

During confirmed *N. meningitidis* outbreaks, implement vaccination and chemoprophylaxis of household contacts.

*N. meningitidis* remains susceptible to penicillin all over the world. A long-acting suspension of chloramphenicol in oil, called tifomycin, could be an alternative to penicillin. When other antibiotics are available, the initial antibiotic therapy depends on the age of the patient. Treat newborn infants with ampicillin and an aminoglycoside (gentamicin) or cefotaxime. Ampicillin is needed to cover *Listeria* and enterococci. Treat infants 1 to 3 months of age with ampicillin and ceftriaxone, or cefotaxime to cover enterococcus, *Listeria*, and *H. influenzae*. Treat older children with vancomycin and ceftriaxone if the rate of penicillin-resistant *S. pneumoniae* in the area is high.

When non susceptible organisms are identified, consider the recommended high doses of cefotaxime and ceftriaxone, and add rifampin when the minimum inhibitory concentration (MIC) of the nonsusceptible pneumococci is $>2.0 \mu g/mL$. If possible, obtain serum creatinine levels before giving vancomycin and repeat weekly during treatment, because vancomycin excretion depends on glomerular filtration.

Use penicillin G, ampicillin, cefotaxime,
or ceftriaxone for *N. meningitidis*. The duration of intravenous therapy varies with the pathogen. Treat gram-negative enteric organisms for 21 days; *S. pneumoniae* for 10 to 14 days; *H. influenzae* for 7 to 10 days, and *N. meningitidis* for 4 to 7 days.

When using aminoglycosides or chloramphenicol, monitor blood levels if possible (therapeutic levels for gentamicin or tobramycin are 4 to 8 µg/mL; for kanamycin or amikacin, 15 to 25 µg/mL). Adequate blood chloramphenicol levels can be achieved with oral administration. Whenever possible, avoid administering aminoglycosides in patients with renal disease and chloramphenicol in patients with hepatic dysfunction.
The only vaccine that must be routinely administered during immediate emergency relief efforts is measles. A routine immunization program for other vaccines should only be considered if the population is expected to stay in the area for longer than 3 months, if it is possible to keep appropriate records, and if other assistance efforts are not disrupted or compromised by the activities needed for vaccination.

Tetanus

Tetanus immunization is not routinely recommended in disaster situations, but if the vaccine is available, it is reasonable to apply it prophylactically to individuals who have tetanus-prone wounds if the time of the last tetanus immunization is unknown or greater than 5 years, or when the child has not received the primary 3-dose vaccination series. The characteristics of tetanus-prone wounds are a wound that was first cleaned more than 6 hours after its occurrence; irregular wounds; wounds from bullets, crushing, burns, or frostbite; and presence of devitalized tissue or wound contaminants.

Specific situations requiring prophylaxis

Pertussis

The vaccine. It is well established that pertussis vaccine provides clinical protection after exposure to the disease in most people. The effectiveness of the vaccine with a regimen of 3 or more doses is around 80% to 90%. Appropriately immunized children who acquire the disease have milder symptoms and fewer complications.

Management of outbreaks. When an increase in the number of cases is suspected, mass immunization is a priority in children under 7 years old. If disease rates are higher among children over 7 years old and adolescents, use of acellular vaccines may be considered.

Household contacts—vaccination. Household contacts and other close contacts of patients under 7 years old who have had at least 4 previous doses of diphtheria-tetanus-pertussis vaccine (DTP or DTaP) must receive a booster injection of DTP or DTaP, unless they have received a dose.
Management of outbreaks. When cases of diphtheria are suspected, mass vaccination is indicated, taking into account the rates of incidence by age groups.

Household contacts—vaccination. Asymptomatic contacts whose immunization regimen is complete and who have received their last dose more than 5 years ago must receive a DTP or dT booster according to their age. Close asymptomatic contacts whose immunization regimen is incomplete (<3 doses of diphtheric toxoid) or whose immunization status is unknown must receive a dose and complete the schedule.

Chemoprophylaxis. All household contacts and other close contacts, regardless of their age or immune status, should receive erythromycin (40-50 mg/kg/day orally, divided in 4 doses), for 14 days because immunity after vaccination is not total and infection may not be prevented. It has been proven that erythromycin eliminates the carrier state and is effective in limiting secondary spread. For patients who are intolerant to erythromycin, clarithromycin (15 mg/kg/day orally divided in 2 doses, for 1 week) may be administered; other options are azithromycin and trimethoprim-sulfamethoxazole.

Diphtheria
The vaccine. In diphtheria, as in tetanus, immunity relies only on the presence in blood and interstitial fluids of antitoxin IgG antibodies with titers ≥0.01 IU/mL. These antibodies work locally, where the toxin is released by the bacteria, and in blood against the toxin that reaches the circulation. After primary immunization with 3 doses of toxoid, antitoxin titers above 0.01 IU/mL can be found for 5 or more years, and after one or more booster injections they persist for 10 years. In clinical practice, vaccination has shown an efficacy rate above 99%.

Meningococcal disease
Few infectious diseases cause as much concern among the general population and health workers as meningococcal infection. The estimated attack rate for household contacts is 4 cases per 1,000 exposed persons. This is 500 to 800 times higher than rates in the general population.
Chemoprophylaxis is indicated for those individuals who meet the criteria for close contacts. The goal is to eradicate *N. meningitidis* carriers and prevent the occurrence of secondary cases.

- Close contacts: household members, attendees at child care centers, nursery schools, schools, universities, and members of closed communities that are in contact with any individual with meningococcal disease for more than 4 hours daily, 5 days a week; any other person directly exposed to oral secretions of the patient (e.g., sharing tableware, drinks, kisses; sneezing or coughing).

- Secondary case: any case occurring in a close contact 24 hours or more after onset of the disease in the primary case. Because there is a high rate of secondary disease during the 5 days following contact, give chemoprophylaxis within the first 24 hours. It is not indicated beyond 14 days. A nasopharyngeal culture to determine the need for chemoprophylaxis is not warranted. If the patient was treated with third generation cephalosporins, chemoprophylaxis before discharge is not needed. Rifampin is the first choice agent for chemoprophylaxis in children, but there are alternatives for adults (Table 4).

Chemoprophylaxis is indicated for household members and contacts (Box 5). Monitor exposed individuals and assess if they have a febrile disease.

The vaccine: immunogenicity and effectiveness. With unconjugated polysaccharide vaccines, protection is achieved 7 to 10 days after immunization. Bivalent A + C vaccine is safe and effective (85% to 90%) in children older than 2 years old and in adults. The A component induces an immune response from 3 months of age on, with a seroconversion rate of 88% after the second dose, applied in children between 7 and 12 months old.

Management of outbreaks. An outbreak of meningococcal disease is defined when the attack rate is higher than 10 cases in

<table>
<thead>
<tr>
<th>TABLE 4. Recommended agents for chemoprophylaxis</th>
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<tbody>
<tr>
<td><strong>Agent</strong></td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>Rifampin</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
</tr>
</tbody>
</table>

IM: Intramuscular.
100,000 persons, in a specific area, with an epidemiologic relation among cases, and with a predominating serogroup. With active epidemiologic surveillance, an outbreak is also considered when the incidence rate by age is doubled.

Where can outbreaks occur? Outbreaks can occur in an institution or an organization. In this case, an outbreak is defined by 3 or more confirmed, presumptive, or probable cases occurring in a period of 3 months or less within the same institution or organization, but without close contacts (e.g., schools, universities, military organizations, jails).

Community outbreaks are defined by 3 or more confirmed, presumptive, or probable cases that occur in 3 months or less among people who live in the same area and are not close contacts (e.g., small towns, cities, countries).

Guidelines for evaluation and management of a meningococcal disease outbreak

1. Reinforcement of active surveillance

In areas where surveillance for meningococcal disease is passive, case reports may be incomplete or delayed. When an outbreak is suspected, alert public health authorities and request immediate report of new cases.

2. Case detection and bacteriologic confirmation

Establish the diagnosis of meningococcal disease considering confirmed, presumptive, or probable cases.

a. Confirmed case: isolation of \(N.\ menin-gitides\) from a usually sterile site (blood, CSF) in an individual with clinically consistent findings.

b. Presumptive case: observation of Gram-negative diplococci in any usually sterile site, with negative cultures and symptoms of disease.

c. Probable case: positive antigen test for \(N.\ meningitidis\) (latex agglutination

**BOX 5. Indications for chemoprophylaxis**

**Contacts who should receive chemoprophylaxis**

- Household members
- Individuals who often sleep or eat with the patient, and meet the definition of contact
- Contacts in child care centers and nursery schools (including staff members) for more than 4 hours during 5 days of the previous week
- Individuals who have been directly exposed to the patient’s secretions through kissing or sharing food, drinks, toothbrushes, etc.
- Individuals administering mouth-to-mouth resuscitation
- Individuals who experience unprotected contact during endotracheal intubation in the 7 days prior to the onset of the disease

**Situations where chemoprophylaxis is NOT indicated:**

- Casual contact: no direct exposure to the patient’s oral secretions (classmates or coworkers)
- Indirect contact: no contact with the patient, only with his/her contact
- Health care workers with no direct exposure to the patient’s oral secretions
test, immunoelectrophoresis), with negative cultures and consistent symptoms.

Information about serogroup is essential. Laboratories not performing this test routinely should forward the sample to referral laboratories of higher complexity to identify the serogroup. If possible, investigate *N. meningitidis* subtype by pulsed-field gel electrophoresis or multilocus enzyme electrophoresis to determine if the strains of a group of cases are interrelated and whether they represent an outbreak.

3. Appropriate treatment of patients, according to management guidelines

4. Chemoprophylaxis and careful observation of contacts
Chemoprophylaxis and careful observation are recommended for close contacts. Chemoprophylaxis for individuals who are not close contacts is ineffective in preventing community outbreaks; therefore, it is not recommended. Exposed individuals must be carefully monitored and evaluated in case of any febrile illness.

5. Investigation of relationships between cases
In addition to demographics, obtain the following information for each affected individual: history of close contact with another primary case; participation in social activities or sports; attendance at child care centers, kindergartens, schools, universities, or clubs. This information will help identify cases as co-primary or secondary, reveal relationships between cases, and define the population at risk.

6. Assessment of the relationship of the suspected outbreak with the community or with an institution or organization

7. Definition of at-risk population
In outbreaks related to an institution or organization, cases are linked with a shared affiliation, such as attending the same day care center, kindergarten, school, or university or belonging to the same sports team. In such cases, the population at risk is everyone in those places. On the other hand, in community outbreaks patients do not share an affiliation, only a geographically defined location, such as a neighborhood, small town, city, or country. The risk group includes every individual living in those places.
8. Estimation of attack rate

Attack rate can be estimated by the following formula:

\[
\text{Attack rate} = \frac{\text{Number of probable and confirmed cases (over a 3-month period)}}{\text{Population at risk}} \times 100,000
\]

With a global attack rate higher than 10 cases in 100,000, consider vaccination of at-risk population. Consider the incidence rates by age groups. If the incidence rate doubles in a population with adequate epidemiological surveillance, immunization may be considered.

9. Selection of the target group for vaccination

Consider the guidelines from public health authorities regarding the serogroup involved and the age group affected. In that case, it is necessary to have adequate vaccine supplies.
OBJECTIVES

- Identify and establish the treatment for sick infants 0 to 2 months of age.

Assessment of the sick infant 0 to 2 months of age

As mentioned previously, newborn and infants under 2 months of age are very vulnerable to infections, with high morbidity and mortality rates associated with very severe clinical conditions including sepsis, meningitis, and pneumonia. Thus, if an infant under 2 months is suspected of having a severe neonatal illness or a possible severe bacterial infection, there is no time to lose in laboratory studies. It is extremely important to start antibiotic therapy immediately and to refer the patient to a hospital if needed resources are not available.

Infants weighing less than 2,000 g who are brought to the primary health care facility with a possible infection should be referred to a hospital for specialized treatment, regardless of the severity of the condition, because they are more vulnerable due to their immaturity. The assessment of the infant 0 to 2 months old should include the following questions:

- What is your baby doing?
- Is he/she feeding well or poorly?
- Has he/she vomited / Is he vomiting all he eats?
- Has he/she had diarrhea?
- Has he/she difficulty breathing?
- Has he/she had fever or hypothermia?
- Has he/she had seizures or shivering?

In addition, look for clinical signs that indicate the severity of the illness, from subtle signs such as “he doesn’t look good” to neurologic signs (e.g., seizures) or difficult breathing. Assessment of body temperature, hydration status, capillary refill, and fontanelle characteristics are also important, as well as looking for other problems (congenital anomalies, surgical disorders). Figure 3 shows the algorithm used by the Integrated Management of Childhood Illness (IMCI) for assessment of sick infants 0 to 2 months of age.

Classification of the infant 0 to 2 months of age with severe illness or possible severe bacterial infection

Based on general danger signs, infants can be classified into four different categories as shown in Table 5.

Children presenting with any sign in the upper row of Table 5 are classified as having a severe illness or possible severe bacterial infection. In infants younger than 2
### TABLE 5. Classification of the infant 0 to 2 months with severe illness or possible severe bacterial infection

<table>
<thead>
<tr>
<th>SIGNS</th>
<th>CLASSIFY AS</th>
<th>TREATMENT</th>
</tr>
</thead>
</table>
| **(RED)** One out of the following signs:  
• “Doesn’t look good”  
• Cannot be breastfed  
• Lethargic/unconscious or flaccid  
• Vomiting  
• Seizures  
• Intense pallor  
• Weight <2,000 g  
• RR > 60 or <30 per min  
• Temperature <36.5ºC or >37.5ºC  
• Bulging fontanelle  
• Apnea  
• Nasal flaring  
• Grunting  
• Severe lower chest wall indrawing  
• Central jaundice  
• Jaundice below the umbilicus  
• Petechiae, pustules or vesicles in the skin (many or extended)  
• Pus drainage from ear  
• Umbilicus redness extending to skin  
• Poor capillary refill (>2 sec)  
• Abdominal distension | **(RED)** SEVERE ILLNESS OR POSSIBLE SEVERE BACTERIAL INFECTION | **(RED)**  
• URGENTLY refer to hospital, according to the guidelines for stabilization and transportation  
• Give the first IM dose of recommended antibiotics  
• Prevent hypoglycemia  
• Keep the child warm  
• Advise the mother/caregiver not to stop breastfeeding  
• Clarify any doubt and give support to the mother/caregiver  
• Advise mother to accompany the child and show how to keep the infant warm on the way to the hospital |
| **(YELLOW)**  
• Ocular pus discharge  
• Red umbilicus or draining pus  
• Skin pustules (few or localized) | **(YELLOW)** LOCAL BACTERIAL INFECTION | **(YELLOW)**  
• Give an appropriate oral antibiotic for 7 days  
• Teach the mother/caregiver how to treat local infections at home  
• Apply local treatment (topical antibiotic)  
• Teach the mother/caregiver to recognize signs of danger  
• Clarify doubts and give support to the mother/caregiver  
• Follow up 2 days later |
| **(GREEN)**  
• Normal activity  
• Feeding well  
• Normal physical examination results  
• White plaques in the mouth | **(GREEN)** NO BACTERIAL INFECTION | **(GREEN)**  
• Counsel the mother to continue breastfeeding  
• No additional treatment  
• Teach the mother to recognize signs of danger and to implement hygienic measures  
• Tell the mother when to come back to the clinic  
• Check immunization status  
• Clarify doubts and give support to the mother/caregiver  
• Consider applying Nistatin locally 100,000 units in the mouth, 4 times a day |

Look for clinical signs that assess the severity of the presentation, from very subtle signs such as “he doesn’t look good” to neurologic signs or severe difficulty breathing.
It is difficult to distinguish between a very severe illness and a severe infection, such as sepsis or meningitis, since clinical findings are usually similar. For this reason, the classification gives both possibilities.

If the infant is suffering from a local but extensive bacterial infection, he or she should also be classified as having a possible severe bacterial infection because the local infection can disseminate and result in sepsis, due to the immaturity of the immune system. He or she needs to be referred urgently to a specialized hospital to receive different kinds of treatments, such as oxygen or parenteral antibiotics. Before transfer, administer the first dose of the adequate antibiotic. Transfer according to the guidelines for stabilization and transport. Counsel the mother or caregiver in order to clarify possible doubts and provide support. Infants with no general danger signs but who have purulent discharge from the umbilicus or eyes, pustules in the skin (limited in number or localized), are classified as having a local bacterial infection. Children who exhibit no danger signs are classified as having no bacterial infection.

**Treatment of infants 0 to 2 months of age with infection**

Infants 0 to 2 months old who need to be transferred to a hospital more than 5 hours away should receive an intramuscular (IM) dose of an adequate antibiotic.

Possible antibiotic combinations include:

- gentamicin + ampicillin
- gentamicin + G penicillin procaine

Avoid oral feeding if the infant presents with altered consciousness or difficult breathing, and administer a 5% dextrose solution through nasogastric tube to prevent hypoglycemia.

If there is no incubator available for the transfer, the “mother kangaroo” technique is advisable in order to prevent hypothermia. If available, also administer supplemental oxygen during the transfer to prevent hypoxemia.

Infants 0 to 2 months of age with a local bacterial infection should receive an adequate oral antibiotic as well as topical antibiotic therapy according to the site of infection.
SUMMARY

The morbidity and mortality associated with infectious diseases are very high in developing countries. During acute humanitarian emergencies, morbidity and mortality increase significantly. Deterioration of the nutritional status associated with such situations increases the risk of infectious diseases among the affected children.

The IMCI strategy, designed for primary care management of children and based on a number of clinical signs at presentation, is an ideal tool for the effective management of people affected by disasters, particularly in situations with limited resources, both material and human. This tool allows a quick and simple distinction between children who require referral to the hospital and those with less severe illness that can be managed in a less complex setting.

Measles, acute respiratory infections, malaria, dengue, and acute diarrhea are the infections that cause more concern in an emergency setting. Take also into consideration sepsis and meningitis. It is important to recognize these diseases as early as possible in order to give appropriate therapy and prevent a possible outbreak among people displaced by a disaster.

SUGGESTED READING


Case resolution

Case 1.
The child is ill-appearing, febrile, tachycardic, and tachypneic with a physical exam remarkable for scattered petechiae on the abdomen and lower extremities. The primary concern is whether this child is in shock. Tachycardia and decreased capillary refill are consistent with compensated shock.

Since the child is febrile and has a history of an upper respiratory disease, the most likely etiology of the shock is sepsis. The fever and the presence of petechiae suggest a severe bacterial infection, most likely meningococcemia. While many other conditions such as viral infection— influenza, enterovirus, adenovirus, infectious mononucleosis, or group A Streptococcus infection—can present with fever and petechiae, meningococcal infection is rapidly progressive and life-threatening.

Initial management begins with 100% oxygen. An IV line was placed and a blood sample was sent for complete blood count, serum electrolytes, coagulation studies, and culture. Rapid blood glucose determination was 120 mg/dL. As the child was tachypneic and had signs of shock, the lumbar puncture was deferred and IV antibiotics were administered immediately. An IV bolus of normal saline was given because of poor oral intake and decreased urine output, with no signs of cardiac or pulmonary disease.

His initial laboratory tests showed a white blood cell count of 21,000. Serum bicarbonate was 11, prothrombin time 15 seconds, and partial thromboplastin time 28 seconds.

Over the next several hours the child developed purpura, had increasing respiratory distress, and labile blood pressure. He was intubated and ventilated. His blood culture grew N. meningitidis.

Case 2.
The infant is manifesting many of the classic features of an acute presentation of bacterial meningitis. The patient is irritable, febrile, and has a bulging fontanelle. The fact that the patient has a supple neck should not dissuade the examiner from the overall impression of meningitis. Children younger than 18 months frequently lack sufficient neck musculature to manifest nuchal rigidity.

Because the patient is well oxygenated and has stable vital signs, the most pressing intervention is the rapid delivery of IV antibiotics. Antibiotics should cover all possible organisms, especially S. pneumoniae. Treatment should begin with cefotaxime or ceftriaxone and vancomycin (if resistant S. pneumoniae is in the community). Possible complications of meningitis include seizures, syndrome of inappropriate antidiuretic hormone (SIADH), and intracranial hypertension.

MODULE REVIEW

SECTION I - INTEGRATED MANAGEMENT OF CHILDHOOD ILLNESS (IMCI)
1. What is IMCI?
2. What are the IMCI steps for the assessment of sick children?
3. What are the general danger signs that must be routinely checked in all children?

SECTION II - INFLUENZA
1. What are the risk factors for having a more severe Influenza infection?
2. What methods can be used to prevent the spread of H1 N1 Influenza infections in the hospital and community?

SECTION III - MEASLES
1. How should measles immunization be implemented?
2. What is the relationship between vitamin A and measles?
3. How is a measles diagnosis made?
4. Which are the most common complications of measles?

SECTION IV - ACUTE RESPIRATORY INFECTIONS
1. What are the clinical signs that should be assessed in children with cough or respiratory problems?
2. What are the antibiotics used for lower respiratory infections?
3. How should ear problems be assessed?

SECTION V - FEBRILE ILLNESSES: MALARIA, DENGUE
1. How is a malaria diagnosis made?
2. What is the clinical presentation of malaria?
3. What is the treatment for classic malaria and for complicated malaria?
4. How is dengue infection classified?
SECTION VI - OTHER CASES THAT REQUIRE ATTENTION AT THE SCENE OF THE DISASTER

1. What clinical signs raise the suspicion of meningitis?
2. What must be taken into consideration for the treatment of meningitis?

SECTION VII - VACCINATION IN DISASTER SITUATIONS

1. What interventions are recommended when tetanus is suspected?
2. What are the situations that require prophylaxis?
3. How should a meningitis outbreak be evaluated and managed?

SECTION VIII - INFECTIONS IN INFANTS 0 TO 2 MONTHS OF AGE

1. What are the clinical signs that suggest a severe illness in infants 0 to 2 months of age?
2. What immediate action should be taken with an infant 0 to 2 months of age with severe illness?
Currently Influenza A-H1 (Swine), susceptible to oseltamivir (Tamiflu), is the only strain circulating in Colorado. Recommendations will change as strains change in the community – for most current information go to “Planetch/Quicklinks/Influenza info”

Patient presenting to ED/NOC/outpatient clinic

Patients presenting with symptoms consistent with Influenza

1. Place immediately in and rigorously enforce DROPLET PRECAUTIONS
2. Give information sheet that recommends notification of high-risk contacts

Patient requiring hospitalization

Patient NOT requiring hospitalization

Rapid Flu IA* with backup PCR

Respiratory Flu IA* with backup PCR

Treat presumptively (even if symptoms >48 hrs) until both tests are influenza negative. Use Oseltamivir or Zanamivir while prevalence of seasonal influenza is low. (See tables)

High-Risk Child\textsuperscript{x}

Low-Risk Child

No Test Recommended

No treatment recommended

\textsuperscript{x}High Risk Child per CDC suggestion = Children < 2 yrs (CDC includes those 2-5 yrs but many experts feel that is excessive); children with any of the following medical conditions: chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), neurologic, neuromuscular, or metabolic disorder (including diabetes mellitus); immunosuppression including that caused by medications or by HIV; pregnant women; persons who are receiving long-term aspirin therapy; residents of chronic-care facilities; or children who present with a severe illness.

\textsuperscript{\textregistered}Nasopharyngeal Aspirate – Observe droplet precautions + N95 mask and eye protection. Get a good specimen – the quality of the result is directly proportional to the quality of the specimen! Immunoassay (IA) sensitivity alone = 70%.

Note to ordering physicians – Due to the increased number of samples being tested, the microbiology lab will only call physicians for respiratory virus results if positive for Influenza. It is the ordering physician’s responsibility to follow up for all other testing results.

Recommendations will change when seasonal influenza and/or RSV become more widespread in the community.
## INFLUENZA ANTIVIRALS

### Table 1. Influenza A-H1 (Swine) Oseltamivir dosing recommendations

<table>
<thead>
<tr>
<th>Agent, group</th>
<th>Treatment</th>
<th>Chemoprophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>75-mg capsule twice per day for 5 days</td>
<td>75-mg capsule once per day</td>
</tr>
<tr>
<td>Children (age, 12 months or older), weight:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 kg or less</td>
<td>60 mg per day divided into 2 doses</td>
<td>30 mg once per day</td>
</tr>
<tr>
<td>16-23 kg</td>
<td>90 mg per day divided into 2 doses</td>
<td>45 mg once per day</td>
</tr>
<tr>
<td>24-40 kg</td>
<td>120 mg per day divided into 2 doses</td>
<td>60 mg once per day</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>150 mg per day divided into 2 doses</td>
<td>75 mg once per day</td>
</tr>
</tbody>
</table>

### Table 2. Dosing recommendations for antiviral treatment of children younger than 1 year using oseltamivir

<table>
<thead>
<tr>
<th>Age</th>
<th>Recommended treatment dose for 5 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 months</td>
<td>12 mg twice daily</td>
</tr>
<tr>
<td>3-5 months</td>
<td>20 mg twice daily</td>
</tr>
<tr>
<td>6-11 months</td>
<td>25 mg twice daily</td>
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</tbody>
</table>

### Table 3. Summary of Antiviral Resistance, U.S. 2008-09

<table>
<thead>
<tr>
<th>Antiviral</th>
<th>Influenza viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A-H1 (Swine)</td>
</tr>
<tr>
<td>Amantadine</td>
<td>Resistant</td>
</tr>
<tr>
<td>Rimantadine</td>
<td></td>
</tr>
<tr>
<td>Oselfamivir (Tamiflu)</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Zanamivir (Relenza)</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>