

# Childhood Infectious Diseases in Pediatric Refugee Populations

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#### Prologue

Walking with my team in one of the informal tent settlements of Syrian refugees in Lebanon we were intercepted by a worried father. He wanted us to go into his tent and see his baby, a 1-year-old girl who had been having diarrhea and vomiting for the last 3 days and was now quite drowsy and dehydrated. There were two other children in the family who had diarrhea. While talking to the father we found out that it was very hard for them to go out of the settlement to look for medical assistance because of police blockades and transportation difficulties. It had been raining and the scarce latrines were flooding, there were puddles and mud everywhere and it was difficult to walk around. Drinking water was brought by truck every 2 weeks and it was often dirty. At the end of our visit we had seen around 20 children with diarrhea and many adults were also reported sick.

When large groups of people are displaced, due to war, violence, food insecurity, poverty, or any other situation, living conditions become harsh and inadequate. In Lebanon, for example, there are no refugee camps; people are scattered around in informal test settlements. This makes it difficult for agencies and NGOs to assist the population with water and sanitation interventions. Because the number of tents are limited, many families live and sleep in the same spaces, which favors overcrowding. These are ideal conditions for viral, bacterial, and parasitic infections to spread easily and cause diseases, individual deaths, and ultimately outbreaks.

Communicable disease control is a challenge in most contexts where refugees live. Prevention and preparedness to recognize and manage an outbreak is essential. Infectious diseases can be brought by the refugees from their places of origin or from places they passed along their journeys. Refugees can acquire communicable disease in the host country, or they can be caused by the conditions encountered once the populations are settled.

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In this chapter, we will talk about infectious diseases in the context of children of refugee populations.

# Introduction

According to the UNCHR there are five diseases that have the most immediate impact on large-scale mortality, causing 60–80% of deaths among refugees [1]. They are:

- 1. Measles
- 2. Diarrheal diseases (see Gastrointestinal Diseases chapter)
- 3. Acute respiratory infections (see Respiratory chapter)
- 4. Malaria
- 5. Malnutrition (see Nutrition chapters)

In this chapter of the book we will go over some infections that have not been reviewed in depth in other chapters of the book. We will also talk about other infectious diseases that cause significant morbidity in children. Please note that all drug dosages provided in this chapter should be confirmed with local providers and national dosing guidelines.

#### Measles

#### **Overview**

Measles is a particularly important disease to discuss in the context of refugee populations since it is extremely contagious. It is one of the main killers in displaced populations and refugees. When people live in overcrowded and unhygienic conditions it spreads rapidly and in higher infectious doses, resulting in more severe clinical disease, especially in malnourished children. If we look at history, measles accounted for 53% of deaths in refugee children in eastern Sudan and 42% in Somalia in 1985, after this it was clear to everyone that this particular infection should always be addressed in refugee populations [2].

#### **Know Your Bugs: The Infectious Agent**

Measles is caused by a virus called *Measles morbillivirus* of the genus morbillivirus and the family *Paramyxoviridae*. The only host of measles virus is humans [2].

#### Epidemiology, Incidence, and Mortality

Measles is a widespread problem around the globe. It caused 140,000 deaths in 2018 [3]. When caring for displaced populations, it is important to understand their

risk of measles in order to have a clear picture of where measles outbreaks are happening in the local communities.

In developed countries, there are occasional outbreaks which usually start from imported cases that infect people who are not vaccinated. In low-income countries, where measles is endemic, it causes recurrent large-scale epidemics with very high death tolls.

#### Transmission

Measles is one of the most contagious microbes in the world. Nine out of ten vulnerable people will become infected if exposed to the virus [4].

Transmission occurs person-to-person through infected respiratory droplets (nose and throat) that go from a patient with measles to a healthy person's mucosa (nose, eyes, and mouth). These droplets can become airborne when a sick person talks, sneezes, or coughs, and they can remain in the air for up to 2 h, so it can be transmitted in public spaces, even in the absence of contact with someone who is ill. This is why large outbreaks can occur in areas of crowding.

The incubation period is 6–21 days. Contagiousness is estimated to be from 5 days before the appearance of rash to 4 days afterward; however, a malnourished or immunocompromised child can transmit the infection for much longer. The period of maximum contagiousness is thought to be during the late prodrome phase when the patient is febrile and has respiratory symptoms [4].

### **Clinical Features**

Stages of infection [5, 6]:

Incubation period	Prodrome	Enanthem (involvement of the mucosa)	Exanthem (rash)	Recovery
6–21 days	2–4 days	48 h prior to the onset of rash Lasts 12–72 h	2–4 days after onset of fever	
Virus enters the respiratory mucosa or conjunctivae, replicates locally, spreads to lymphatic tissues, and disseminates through the bloodstream (viremia).	Fever (as high as 40 °C), malaise and anorexia, conjunctivitis (with lacrimation or photophobia), coryza (runny nose), and cough.	Koplik spots: 1–3 mm whitish, grayish, or bluish elevations with an erythematous base, on the buccal mucosa opposite the molar teeth. Does not appear in all patients.	Erythematous, maculopapular rash. Spreads cephalocaudally and centrifugally. Lymphadenopathy and splenomegaly, high fever, respiratory signs, pharyngitis, non-purulent conjunctivitis.	Clinical improvement typically ensures within 48 h of the appearance of the rash. Cough may persist 1–2 weeks.

#### The Rash

- Blanching in early stages (the skin becomes white after you put pressure and then release), after it becomes non blanching (stays red, even if you put pressure).
- Begins on the face and spreads downwards: cephalocaudal.
- Goes from the center of the body, outwards, to involve the neck, upper trunk and extremities: centrifugal.
- Petechia (tiny hemorrhages that look like less than 1 mm red dots) may be seen and in severe cases rash appears hemorrhagic.
- Palms and soles are rarely involved (very important point if you are suspecting a different diagnosis).
- After 3–4 days the rash darkens to a brownish color and begins to fade. Followed by fine desquamation.
- Rash lasts 6–7 days and fades in the order it appeared (head to toe).

# Complications

As other viruses do, the measles virus can cause inflammation in various organs such as the brain, the lungs, and the liver. It can also affect the immune system, making a child more susceptible to other infections. In fact, measles-associated immune suppression can last up to 3 years after the infection, increasing morbidity and mortality from other infections. One or more complications occur in 30% of cases.

- Gastrointestinal complications: The most common is diarrhea in 8% of cases, caused by intestinal inflammation. Together with gingivostomatitis (painful mouth ulcers) can cause difficulty eating and drinking and high water loss, which leads to dehydration, electrolyte imbalance, and worsening malnutrition. It can also cause hepatitis (elevated liver enzymes), mesenteric lymphadenitis, and appendicitis [6].
- Respiratory complications: the virus on its own can cause laryngotracheobronchitis (croup), bronchiolitis, and severe pneumonitis associated with respiratory distress. Pneumonia is present in 6% of cases and it is the main cause of mortality. Bacterial superinfection is also likely and occurs in 5% of cases. Bronchiectasis has also been reported, which predisposes the child to recurrent respiratory infections [6].
- Otitis media occurs in 5–10% of cases [6].
- Coinfections:
  - Viruses: parainfluenza virus, adenovirus, cytomegalovirus, enterovirus, influenza, and respiratory syncytial virus.
  - Bacteria: *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Steptococcus pyogenes*. Tuberculosis reactivations [7].

- Neurologic: encephalitis, acute disseminated encephalomyelitis, and subacute sclerosing panencephalitis [6].
  - Encephalitis: Occurs in 1 per 1000 cases. It can appear from day 1 to 14 of the rash. Characterized by persistent fever, headache, vomiting, stiff neck, meningeal irritation, drowsiness, irritability, seizures, and coma. Twenty-five percent will have neuro-developmental sequelae. Cerebrospinal fluid will show elevated lymphocytes, proteins, and normal glucose.
  - Acute disseminated encephalomyelitis (1 per 1000 cases): caused by post-infectious autoimmune response. Presents during the recovery phase, usually 2 weeks after the rash. It can show as fever, headache, neck stiffness, seizures, and mental status changes. Any abnormal neurological finding should be suspected (sensory loss, muscle weakness, paraplegia, etc). CSF shows the same findings as encephalitis. It has 10–20% mortality. Residual neurological abnormalities are common, including behavior disorders, mental retardation, and epilepsy.
  - Subacute sclerosing panencephalitis: Is a fatal progressive degenerative disease. Appears 7–10 years after measles infection. More common if measles presented at an early age (<2 years of age). It can start with personality changes, somnolence, and evolve progressively to dementia, motor or sensory deficit, vegetative state, and death. Patients may live weeks to years but it is almost always fatal.</p>
- Ocular: xerophthalmia, keratitis, Bitot's spots (dry conjunctival lesion), keratomalacia, corneal ulceration, and blindness, especially in children with malnutrition and vitamin A deficiency [7].
- Cardiac: myocarditis and pericarditis [7].
- Death: the case fatality rate in developing countries can vary from 4% to 10% [2].

# **Immunity and Vulnerability**

Contracting and surviving measles infection provides lifelong immunity. Children born to mothers who were vaccinated before pregnancy have immunity until the age of 3–6 months, after this anti-measles antibodies begin to fade. Immunocompromised children such as those with severe malnutrition, HIV/AIDS, blood malignancies, or affected cell-mediated immunity due to medications can develop severe measles and all its complications [6]. Pregnant women are at risk for severe complications. There can also be the risk of low birth-weight, abortion, intrauterine fetal death, and congenital measles which can present as a broad spectrum of illness from mild to severe. In addition, Vitamin A deficiency due to malnutrition contributes to delayed recovery and to the high rate of post measles complications. Measles infection can also precipitate acute vitamin A deficiency and xerophthalmia [7].

### Diagnosis

The first way to diagnose measles is with compatible clinical signs and symptoms, plus a history of recent exposure or travel to a place with high measles prevalence, especially in the absence of previous measles immunity. It can be confirmed with reverse transcriptase-polymerase chain reaction tests (RT-PCR) on respiratory secretions (throat swab is preferred), blood, bronchial lavage, or urine samples, detecting measles specific immunoglobulin M (IgM) and IgG in blood serum or through isolation of measles virus in cell culture [5].

Usually in the context of an outbreak, not every patient can be tested. Diagnosis is done with clinical signs and symptoms that are specified in by a case definition (see outbreaks section below). Depending on the situation, some patients will be tested—usually the first ones to be suspected to have measles [8].

# Treatment

There is no specific antiviral treatment for measles but in order to avoid complications, the focus should be on the following management:

- Early recognition/triage of patients with clinical signs of severity.
- Supportive care: good nutrition, adequate fluid intake, and treatment for dehydration with oral rehydration solution or intravenous fluids.
- Vitamin A: can reduce morbidity and mortality rates as well as blindness due to kerato conjunctivitis. Administer orally once daily for 2 days at the following doses [9]:

Less than 6 months: 50,000 IU

6–11 months: 100,000 IU

Older than 12 months: 200,000 IU

Children with clinical signs and symptoms of vitamin A deficiency: give the third dose 4–6 weeks later

- Close follow-up and continual assessment to detect infections and sepsis in a timely manner. Antibiotics to treat associated bacterial infections. Antibiotic prophylaxis is not recommended.
- Immune globulin (IG) can be considered for exposed susceptible individuals who are severely immunocompromised and for pregnant women. It can be given within 6 days of exposure to prevent or modify the diseases. Recommended dose: IV 400 mg/kg, IM 0.5 mL/kg (maximum 15 mL) [5].

## Vaccination

Measles vaccination resulted in a 73% drop in measles deaths between 2000 and 2018 worldwide. It prevented an estimated 23.2 million deaths. It can provide herd immunity, but to stop broad transmission 85–90% of the population must be vaccinated [10].

The measles vaccine is often incorporated with rubella and or mumps vaccines. It is equally safe and effective in single or combined form. Adding rubella to the measles vaccine increases the cost only slightly and allows for shared delivery and administration costs. It is a live attenuated vaccine. Antibodies will develop in 94% of immunized children. The second dose is to ensure that children who had no response with the first dose, do develop antibodies [2].

General recommendations for measles immunization:

- Children 6–11 months in epidemic situations: they should receive one dose of vaccine. This dose is not considered valid and two valid doses should be administered after the first birthday.
- Children older than 12 months: two doses of vaccine, separated by 28 days minimum.
- All nonimmunized people: should receive two doses of vaccine, separated by 28 days to ensure protection.
- Exposed susceptible individuals: if the vaccine is administered within 72 h of exposure, it will provide protection or disease modification in some cases. Consider an individual as susceptible if they have not received any doses of measles vaccine or they have only received one dose [7].

# **Measles Outbreaks**

A measles outbreak is defined as a two or more laboratory-confirmed measles cases that are temporally related (with dates of rash onset occurring 7–23 days apart) and epidemiologically or virologically linked or both (being a known contact or being in the same physical setting as the case during their infectious period for any length of time).

The main preventive measure for a measles outbreak is routine measles vaccination for children, combined with mass immunization campaigns in countries with high case and death rates [2]. All suspected cases of measles should be reported to public health authorities according to each country's protocol. Communication with public health authorities is very important. Health care systems should have guidelines for infection control measures and rapid response protocols for measles cases, including a clear case definition (see chapter on outbreaks for more information).

All health care personnel should have evidence of measles immunity. Give two doses with 28-day interval if there is no evidence of vaccination.

In case of outbreaks prioritize hospital admission for patients with clinical warning signs. Non-severe cases should receive outpatient treatment and be isolated at home. All patients should receive vitamin A as recommended [11].

Infection control:

- Airborne transmission precautions (see Appendix on precautions) for 4 days after the onset of rash in healthy patients and for the duration of illness in immunocompromised patients.
- Susceptible individuals should not be in contact with suspected or confirmed cases.
- Exposed individuals should be placed on airborne precautions and excluded from social contact or work from day 5 through day 21 after exposure. Even those who were vaccinated within 72 h of exposure.
- Patients with febrile rash illness should be in a separate waiting area or placed immediately in an isolated room.
- Patients should wear appropriate masks to prevent generation of droplets, and staff should wear respirators to filter airborne particles.
- If the patient goes home, he/she should remain in isolation at home for 4 days after rash onset.
- A room occupied by a suspected case should not be used for 2 h after the patient's departure [11].

# **Other Viral Infections Associated with Skin Rashes**

There are many infectious diseases that present with skin erythema or other lesions. They can be caused by bacteria, rickettsias (a special kind of bacteria), fungi, and parasites. Many of them are associated with specific regions of the world. A thorough description of all of them is beyond the scope of this chapter; here we will focus only on the most common viral rashes of childhood [5, 12].

ngitis, ressive es- sts. sts. tages on mities. n stops fall lleave lleave pain and pain ful ruritic, ul. ruritic, il. appular, appular, ighs, and	Signs and symptoms	Treatment and precautions Complications	Complications	Vaccine
From naso- -Zoster     from naso- bharyngeal     loss of appetite.       -Zoster     pharyngeal     Rash: appears in successive crops, pruritic, macules- brirect contact with vesicle fluid       ZV)     Direct contact with vesicle fluid     Rash: appears in successive crops, pruritic, macules- trace, trunk, and extremities.       IO-21 days     Lesions in different stages on face, trunk, and extremities.       IO-21 days     New vesicle formation stops within 4 days. Crusts fall within 1-2 weeks and leave hypopigmentation.       ot-mouth     Fecal—oral route.     -       Contact with vesicle     <7 years.		Antihistamines for	- Skin and soft tissue bacterial	Vaccine: Live
<ul> <li>Zoster pharyngeal</li> <li>Zoster pharyngeal</li> <li>ZV) secretion</li> <li>Direct contact with papules-pustules-crusts.</li> <li>Direct contact with papules-pustules-crusts.</li> <li>Vesicle fluid</li> <li>Io-21 days</li> <li>Vesicle fluid</li> <li>face, trunk, and extremities.</li> <li>New vesicle formation stops within 4 days. Crusts fall within 1-2 weeks and leave hypopigmentation.</li> <li>Dread—oral route.</li> <li>Incubation period.</li> <li>Incubation period.</li> <li>Incubation stops within 1-2 weeks and leave hypopigmentation.</li> <li>Incubation period.</li> <li></li></ul>		pruritus.	infection: cellulitis, myositis,	attenuated virus
ZV)       secretion       crops, pruritic, macules-         Direct contact with       papules-pustules-crusts.         Vesicle fluid       Lesions in different stages on         Incubation period:       face, trunk, and extremities.         10-21 days       New vesicle formation stops         within 4 days. Crusts fall       within 1-2 weeks and leave         hypopigmentation.       hypopigmentation.         nouth       Fecal—oral route.       -         Contact with vesicle       <7 years.	Rash: appears in successive	Antipyretics.	necrotizing fasciitis, and toxic vaccine	vaccine
Direct contact with vesicle fluid     papules-pustules-crusts.       Incubation period:     Lesions in different stages on face, trunk, and extremities.       10-21 days     New vesicle formation stops within 4 days. Crusts fall within 1-2 weeks and leave hypopigmentation.       ot-mouth     Fecal—oral route.       contact with vesicle     - Infants and children       respiratory     - Mouth and throat pain and mild fever       s, most     secretions.       s, most     - Oral enanthem:       respiratory     mild fever       respiratory     - Oral enanthem:       fivito of 6 weeks to     erythematous macules that respiratory tract up       respiratory     - Dral enanthem:       for 6 weeks to     progress to vesicles that rubers.       incubation period:     - Exanthem: Non pruritic, uuens.       3-5 days.     - Exanthem: Non pruritic, uuceks, upper thighs, feet, buttocks, upper thighs, feet, buttocks, upper thighs, feet, buttocks, upper thighs, and arms.		At-risk hosts: Acyclovir	shock syndrome.	2 doses:
vesicle fluid     Lesions in different stages on Incubation period:       10-21 days     face, trunk, and extremities.       10-21 days     New vesicle formation stops within 4 days. Crusts fall within 1-2 weeks and leave hypopigmentation.       0t-mouth     Fecal—oral route.     -       10-21 days     New vesicle formation stops within 1-2 weeks and leave hypopigmentation.       0t-mouth     Fecal—oral route.     -       10-21 days     -     Infants and children       10-21 days     -     Ornact with vesicle       11-2 weeks and leave     -     Nouth and throat pain and mild fever       11-2 weeks in stools     -     -       11-2 weeks to     -     -       11-2 weeks to     -     -       11-1-2 weeks to     -     -       11-1-1-2 weeks to     -     -       11-1-1-2 weeks     -     -       11-1-1-1-2 weeks     -     -       11-1-1-2 weeks     -     -       11	papules-pustules-crusts.	Oral: 20 mg/kg/dose in 4	<ul> <li>Encephalitis: acute</li> </ul>	Minimum age
Incubation period:       face, trunk, and extremities.         10-21 days       New vesicle formation stops within 4 days. Crusts fall within 1-2 weeks and leave hypopigmentation.         0t-mouth       Fecal—oral route.       - Infants and children         0t-mouth       Fecal—oral route.       - Infants and children         10-21 days       within 1-2 weeks and leave hypopigmentation.         nouth       Fecal—oral route.       - Infants and children         contact with vesicle       - Mouth and throat pain and mild fever         respiratory       - Oral enanthem:         with rescilencies.       - Oral enanthem:         virus stays in stools       erythematous macules that rupture and form painful respiratory tract up         respiratory tract up       - Exanthem: Non pruritic, usually not painful.         adays.       - Exanthem: non pruritic, usually not painful.         adays.       - Exanthem: more pays, feet, puttocks, upper thighs, and arms.	s on	doses for 5 days.	cerebellum ataxia, diffuse	12 months,
10-21 days     New vesicle formation stops within 1-2 weeks and leave hypopigmentation.       0t-mouth     Fecal—oral route.     - Infants and children       0t-mouth     Fecal—oral route.     - Infants and children       1-mouth     Fecal—oral route.     - Oral enanthem:       1-mouth     respiratory     mild fever       1-mouth     - Oral enanthem:     - Oral enanthem:       1-mouth     Ferencions.     - Oral enanthem:       1-mouth     erythematous macules that     - Oral enanthem:       1-mouths, in     rupture and form painful     - Infants       1-mouths, in     rupture and form painful     - Infants       1-mouths, in     - Exanthem: Non pruritic,     - usually not painful.       1-mouths, in     - Use usually not painful.     - Maculary, maculopapular,       1-mouth     - Nesicular on hands, feet,     - puttocks, upper thighs, and	face, trunk, and extremities.	IV: 1500 mg/m <sup>2</sup> or 30 mg/	encephalitis.	Second dose
the intervent of the intervent intervent     within 1-2 weeks and leave hypopigmentation.       the intervent intervent intervent     hypopigmentation.       the intervent intervent intervent intervent     - Infants and children       the intervent interve		kg/day in 3 doses.	<ul> <li>Pneumonitis and pneumonia</li> </ul>	minimum interval
tr-mouth     Fecal—oral route.     Infants and children       tr-mouth     Fecal—oral route.     Infants and children       contact with vesicle     -7 years.       fluid or oral and     - Mouth and throat pain and       respiratory     - Oral enanthem:       s, most     secretions.     - Oral enanthem:       virus stays in stools     - Oral enanthem:     erythematous macules that       respiratory     - Oral enanthem:     erythematous macules that       respiratory tract up     - Exanthem: Non puritic,     ulcers.       10:30 days.     - Exanthem: Non puritic,     usually not painful.       3–5 days.     or vesicular on hands, feet,     buttocks, upper thighs, and	_	Precautions:	- Hepatitis	1–3 months.
tr-mouth     Fecal—oral route.     -     Infants and children       ot-mouth     Fecal—oral route.     -     Infants and children       Contact with vesicle     <7 years.		In hospital: Isolation	<ul> <li>Reye syndrome associated</li> </ul>	Outbreaks:
termouth     Fecal—oral route.     -     Infants and children       contact with vesicle     -7 years.       fluid or oral and     -     Mouth and throat pain and       respiratory     -     Mouth and throat pain and       us     respiratory     -     Oral enanthem:       s.most     secretions.     -     Oral enanthem:       virus stays in stools     -     Oral enanthem:       respiratory     -     Oral enanthem:       virus stays in stools     erythematous macules that       revirus     for 6 weeks to     erythematous macules that       respiratory tract up     -     Dral enanthem:       rogoress to vesicles that     rupture and form painful       respiratory tract up     -     Exanthem: Non puritic,       lncubation period:     -     Macular, maculopapular,       3-5 days.     or vesicular on hands, feet,       buttocks, upper thighs, and		<ul> <li>Standard</li> </ul>	with salicylates.	Common.
ot-mouth     Fecal—oral route.     -     Infants and children       otr-mouth     Fecal—oral route.     -     Infants and children       Contact with vesicle     <7 years.		<ul> <li>Contact</li> </ul>		
<ul> <li>t-mouth Fecal—oral route.</li> <li>Contact with vesicle</li> <li>Mouth and throat pain and</li> <li>respiratory</li> <li>Nirus stays in stools</li> <li>Virus stays in stools</li> <li>Virus stays in stools</li> <li>Virus stays in stools</li> <li>Virus stays in stools</li> <li>Nirus stays in stools</li> <li>Nirus stays in stools</li> <li>Nirus stays in stools</li> <li>Nirus stays in stools</li> <li>Virus stays in stools</li> <li>Virus stays in stools</li> <li>Virus stays in stools</li> <li>Nirus stays in to baintoil.</li> <li>Nacular, maculopapular, or vesicular on hands, feet, buttooks, upper thighs, and arms.</li> </ul>		- Airborne		
Contact with vesicle<7 years.fluid or oral and respiratory-Mouth and throat pain and mild feverusrespiratory secretionsOral enanthem:virus stays in stools stor 6 weeks to respiratory tract up for 30 daysOral enanthem:3-5 daysDral enanthem:-3-5 daysDral enanthem:3-5 daysNot enanthem:0 virus stays in stools0 virus stays in stools0 virus stays in stools-0 virus stays-0 virus stays- <td>I</td> <td>Good oral intake and</td> <td><ul> <li>Dehydration due to refusal to</li> </ul></td> <td>No vaccine.</td>	I	Good oral intake and	<ul> <li>Dehydration due to refusal to</li> </ul>	No vaccine.
fluid or oral and respiratory-Mouth and throat pain and mild fevercusrespiratory secretionsOral enanthem:s, mostsecretionsOral enanthem:virus stays in stools-Oral enanthem:virus stays in stools-Oral enanthem:virus stays in stools-Oral enanthem:for 6 weeks to several months, in respiratory tract up for 30 daysOral enanthem:3-5 daysExanthem: Non pruritic, usually not painful.3-5 days.Macular, maculopapular, or vesicular on hands, feet, buttocks, upper thighs, and arms.	<7 years.	ydration.	drink.	Good hand hygiene
tus respiratory s, most secretions. Virus stays in stools for 6 weeks to several months, in respiratory tract up to 30 days. Incubation period: 3–5 days.		<ul> <li>Pain and fever control.</li> </ul>	<ul> <li>Palmar and plantar</li> </ul>	in the home
<ul> <li>s, most secretions.</li> <li>Virus stays in stools for 6 weeks to several months, in respiratory tract up to 30 days.</li> <li>3-5 days.</li> </ul>		No specific antiviral	desquamation 1-3 weeks	(especially when
Virus stays in stools for 6 weeks to several months, in respiratory tract up to 30 days. Incubation period: 3–5 days.		therapy available.	after.	changing diapers).
for 6 weeks to several months, in respiratory tract up to 30 days. Incubation period: 3–5 days. 3–5 days. macular, maculopapular, or vesicular on hands, feet, buttocks, upper thighs, and arms.		recautions in hospital:	<ul> <li>Nail dystrophy or shedding of Outbreaks:</li> </ul>	Outbreaks:
rupture and form painful – ulcers. – Exanthem: Non pruritic, usually not painful. Macular, maculopapular, or vesicular on hands, feet, buttocks, upper thighs, and arms.	progress to vesicles that	Standard	nails 1–2 months after.	Common.
<u> </u>		Contact	<ul> <li>Rhombencephalitis, acute</li> </ul>	
period:			flaccid paralysis, aseptic	
period:	<ul> <li>Exanthem: Non pruritic,</li> </ul>		meningitis.	
			<ul> <li>Pulmonary edema and</li> </ul>	
or vesicular on hands, feet, buttocks, upper thighs, and arms.	Macular, maculopapular,		hemorrhage.	
buttocks, upper thighs, and arms.	or vesicular on hands, feet,		<ul> <li>Myocarditis</li> </ul>	
arms.	buttocks, upper thighs, and		<ul> <li>Pancreatitis</li> </ul>	
	arms.		<ul> <li>Conjunctival ulceration</li> </ul>	
			- Fetal loss	

Vaccine No vaccine widely available. Outbreaks: Unlikely.	Vaccine: Usually in combination with measles. Schedule 2 doses. In children >12 months, with an interval of at least 28 days between doses. Outbreaks: Likely in unvaccinated population.
Complications - Complications are rare. - Seizures. - Aseptic meningitis. - Encephalitis. - Thrombocytopenic purpura.	<ul> <li>Post-infectious encephalitis.</li> <li>Congenital rubella syndrome (not described in this chapter, more information on: https:// www.who.int/news-room/ fact-sheets/detail/rubella)</li> </ul>
Treatment and precautionsComplications- Good oral intake and- Complicati- Hydration Seizures Fever control- Aseptic mePrecautions:- Aseptic meHand hygiene ThrombocyChildren are not to be- Thrombocyexcluded from normalactivities. Not consideredcontagious considered	Supportive. Precautions: – Standard – Contact – Droplet For 7 days after the onset of the rash. *Avoid contact with women of child-bering age and pregnant women.
Signs and symptomsTreatment and precaut-Children <2 years.	<ul> <li>and extremities (can be confused with drug allergy).</li> <li>Low-grade fever and lymphadenopathy (Characteristic: posterior cervical, posterior auricular, and suboccipital)</li> <li>L-5 days before the rash.</li> <li>Rash: pinpoint, pink maculopapules. Appears on the face and spreads down and becomes generalized in 24 h. Due to the risk of congenital rubella and international efforts for vaccination coverage rubella should be confirmed by measuring IgM antibodies.</li> </ul>
Transmission HHV-6: HHV-6: transmission not clear, possibly through saliva from mother to infant and perinatal. Shedding is thought to be lifelong. Incubation period: not certain, but thought to be 9–10 days.	Inhalation of respiratory droplets and aerosols. Shedding: 1–2 weeks before symptoms and stops 7 days after rash appears. Incubation period: 14–18 days.
TransmissionRoseola infantumHHV-6:(Exanthemtransmission nosubitum or sixthclear, possiblydisease)through saliva fHumanmother to infanHerpesvirus 6perinatal. Shedd(HHV-6)is though to beOther: HHV-7,lifelong.enteroviruses,not certain, butadenovirus es, andnot certain, butparainfluenza9–10 days.	Rubella Rubella virus

Erythema	Inhalation or	- Fever, malaise, myalgias, Supportive.	Supportive.	<ul> <li>Arthralgia and chronic</li> </ul>	Vaccine: No
infectious or fifth	nfectious or fifth mucosal contact	watery eyes, headache, nausea, Precautions:	Precautions:	arthritis.	Outbreaks: common
disease	with respiratory	diarrhea.	<ul> <li>Standard</li> </ul>	<ul> <li>Papular purpuric gloves and in school-aged</li> </ul>	in school-aged
Parvovirus B19	droplets and saliva.	droplets and saliva. – Rash: appears 2–5 days	<ul> <li>Droplet (if</li> </ul>	socks syndrome, in teenagers.	children.
	Vertical	later, distinctive malar	immunocompromised	<ul> <li>Transient aplastic crisis</li> </ul>	
	transmission during	ransmission during erythema with pallor around	children)	<ul> <li>Myocarditis</li> </ul>	
	pregnancy and	the mouth (slapped cheek	Children with rash are no	Children with rash are no - Pregnant women: miscarriage,	
	through blood	rash). Sometimes followed by	longer contagious, no need	rash). Sometimes followed by  longer contagious, no need intrauterine fetal death, hydrops	
	products.	a pruritic, symmetric, macular, to be isolated or excluded fetalis.	to be isolated or excluded	fetalis.	
	Incubation period:	lace-like rash on trunk that from normal activities.	from normal activities.		
	4-21 days.	spreads peripherally to arms,			
		buttocks, and thighs.			

# **Diarrhoeal Diseases**

Displaced children are at great risk of infectious diarrheal diseases. In this chapter, we will focus on the organisms that can cause severe diarrhea with high morbidity and mortality rates in refugee children. Less severe causes of diarrhea such as amebiasis and giardiasis will be reviewed elsewhere.

Rotavirus

- Virus.
- Leading cause of diarrhea in children <5 years [13].
- Incubation period: 1–3 days.
- Transmission: fecal-oral route between people. Ingestion of contaminated water or food and contact with contaminated surfaces or objects.
- Clinical features:
  - Acute onset fever, usually high
  - Projectile vomiting
  - Profuse watery diarrhea that leads to rapid dehydration
- Complications: dehydration, electrolyte abnormalities, acidosis.
- Diagnosis: clinical, antigen-detection immunoassay, or RT-PCR on stool for surveillance purposes or research.
- Treatment: self-limited, oral rehydration therapy, and fever control.
- In hospital: standard precautions, contact precautions for children with diapers or incontinence for the duration of the illness.
- Surfaces should be washed with soap and water; bleach can also be used.
- · Outbreaks common in child care centers and pediatric wards.
- Vaccine available: 4 oral, live attenuated [14].

#### Shigella

- Bacteria, gram-negative bacilli. *Shigella dysenteriae* serotype 1 (Sd1) produces shiga toxin and causes more severe illness.
- Most frequent cause of dysentery.
- Incubation period: 1–7 days.
- Transmission: humans are the only host. Fecal-oral route, contaminated objects, food and water, and sexual contact. Houseflies are also a vector.
- Causes large-scale and prolonged dysentery epidemics. It is highly contagious because the infective dose is very low (ingesting 10 organisms is enough). Risk factors: overcrowded areas with poor sanitation and water supplies.
- Clinical features:
  - Ranges from watery or loose stools with minimal constitutional symptoms to high fever, abdominal cramps or tenderness, tenesmus, and mucoid bloody stools.
  - Sd1 causes more severe illness in children <5 years, especially neonates, malnourished children, and children recovering from measles [15].
- Complications: dehydration, electrolyte abnormalities, generalized seizures, sepsis, pseudomembranous colitis, toxic megacolon, intestinal perforation, rectal prolapse, hemolysis, and hemolytic-uremic syndrome (HUS) [5].
- Diagnosis: Culture of feces or rectal swab specimens or PCR assays. Determining antibiotic susceptibility is essential in areas where Shigella is endemic and in case of an outbreak.
- Treatment: mild infection is self-limited oral rehydration salts, zinc supplementation. No antibiotics and anti-motility agents should be given. If severe disease or risk factors:
  - Essential to investigate regional resistance to antimicrobials.
  - Due to high resistance ampicillin, Trimethroprim/sulfametoxazol (co-trimoxazol) and nalidixic acid are no longer recommended.
  - First-line: Ciprofloxacin (irrespective of age) 15 mg/kg/dose 2 times a day for 3 days.
  - Second-line: Ceftriaxone 50–100 mg/kg/dose IM/IV once a day for 2–5 days or Azithromycin 20 mg/kg/dose once a day for 1–5 days (resistance is rapidly developed) [15].
- Case fatality rate is 15% in hospitalized children.
- Outbreaks:
  - Cases of dysentery and deaths due to bloody diarrhea should always be recorded and reported every week in order to rapidly detect and increase in cases.
  - At least one laboratory within the country should be able to isolate and identify Shigella, including Sd1, and perform antimicrobial susceptibility testing.
  - Establish rapid preventive measures and health education: water and sanitation (hand hygiene, clean water, adequate food preparation, appropriate disposal of human waste), support breastfeeding, control of flies.
  - Clear case definition and accessible care facilities.
  - Isolate patients on in an independent area of the care facility, use standard and contact precautions [15].
- No vaccine available.

E. coli

- There are five types of diarrhea producing *Escherichia coli*: Shiga toxin-producing (STEC), enteropathogenic (EPEC), enterotoxigenic (ETEC), enteroinvasive (EIEC), and enteroaggregative (EAEC) [12].
- STEC, serotype O157-H7 are the organisms associated with outbreaks in at-risk populations, we will focus only on this type. Although other types of *E. coli* can cause important diarrhea in children.
- Transmission: food or contaminated water, fecal-oral route, contact with infected animals, and contaminated objects [16].
- Incubation period: 3-8 days.
- Clinical features: begins with non-bloody diarrhea, that becomes bloody after 2–3 days. Severe abdominal pain, low-grade fever. Can mimic intussusception, appendicitis, ischemic colitis.
- Complications: hemorrhagic colitis, hemolytic-uremic syndrome, coagulopathy [5].
- Diagnosis: Stool culture and PCR assays. Rapid enzyme immunoassays and immunochromatographic assays for detection of shiga toxin in stool.
- Treatment: oral rehydration salts. Anti-motility agents should not be given. Antimicrobials are not recommended in case of STEC. In case of outbreaks, it is essential to differentiate between shigella and STEC. Strict hand hygiene measures while taking care of children with dysentery [15].
- Precautions in hospitalized patients: standard and contact.
- No vaccine available.

#### Salmonella

- Bacteria, gram-negative bacilli.
- Two kinds of Salmonella infection:
  - Gastroenteritis caused by nontyphoidal Salmonella (serovars Typhimurium, Enteritidis, and all other non Typhi or Paratyphi serovars): Diarrhea, abdominal cramps, and fever. Affects distal small intestine and colon. Bacteremia and focal infection, such as meningitis, brain abscess, and osteomyelitis. More common in infants and children with hemoglobinopathies (Sickle cell) and immunocompromising conditions.

Reservoirs include humans, birds, mammals, reptiles, and amphibians (turtles). Food vehicles like poultry, beef, eggs, and dairy, as well as fruits, vegetables, peanut butter, powdered infant formula, cereal, and bakery products. Contaminated water and contact with infected animals can be another mode of transmission [12]. Incubation period: 6–72 h.

Enteric fever caused by *Salmonella* serovars *Typhi*, *Paratyphi* A, B, and C [8].
 Fever, headache, malaise, anorexia, lethargy, abdominal discomfort and tenderness, hepatomegaly, splenomegaly, dactylitis, rose spots, and changes in mental status.
 Either diarrhea (stool tends to have pea soup appearance) or constipation.
 There can be bacteremia, invasive infection with severe clinical symptoms, and meningitis.

Characteristic: Relative bradycardia (slower heart rate than expected for a given temperature).

Only human hosts, usually chronic carriers that contaminate food and water. Incubation period: 7–14 days.

- Diagnosis: Culture of stool, blood, urine, bile, and other tissues. Test to detect salmonella antigens such as enzyme immunoassay, latex agglutination, and monoclonal antibodies. Gene-bases PCR [5].
- Treatment:
  - Antibiotics are not indicated for asymptomatic or mild infections (prolongs duration of fecal excretion).
  - Antibiotics for children with a high risk of invasive disease.
  - Recommended agents depend on local resistance patterns. Amoxicillin, ampicillin, and trimethoprim-sulfamethoxazole used to be the treatments of choice but resistance is common thus fluoroquinolones or azithromycin can be used.
  - If resistant to fluoroquinolones (usually in Southeast Asia) empiric treatment can be started with ceftriaxone.
- Precautions: in hospitalized patients use standard and contact precautions for diapered and incontinent children for the duration of illness.
- Outbreaks are rare in children, except for Salmonella serovar Typhi or Paratyphi.
- Vaccines: only for *S. Typhi*, there are 3: live oral Ty21a, injectable typhoid conjugate vaccine (Vi polysaccharide antigen), injectable unconjugated polysaccharide vaccine. For more information [8].

Campylobacter

- Bacteria, comma-shaped, gram-negative bacilli. Twenty-five species, most common. *C. jejuni* and *C. coli*. Reservoirs can be domestic and wild birds and animals.
- Transmission due to contaminated food and water, unpasteurized milk or contact with feces of infected animals or people.
- One of the main causes of diarrhea in children <5 years.
- Incubation period: 2-5 days. Excretion of bacteria continues for 2-3 weeks [12].
- Clinical features:
  - Diarrhea, abdominal pain (can be severe, mimicking appendicitis or intussusception), malaise, and fever. Stool can contain visible or occult blood.
  - In neonates and young infants, bloody diarrhea without fever is common.
  - Fever can be high and can result in febrile seizures.
- Complications:
  - Prolonged, relapsing, or extraintestinal infection in immunocompromised children.
  - Acute idiopathic polyneuritis: Guillain-Barré syndrome.
  - Reiter syndrome (arthritis, urethritis, and bilateral conjunctivitis).
  - Myocarditis, pericarditis, and erythema nodosum.
  - Outbreaks are rare but can be a cause of healthcare-associated diarrhea, especially in neonates [5].
- Diagnosis: culture from feces, antigenic enzyme immunoassay, and multiplex nucleic acid amplification tests.
- Treatment:
  - Rehydration salts.
  - Azithromycin (10 mg/kg/day, for 3 days) or erythromycin (40 mg/kg/day, divided in 4 doses, for 5 days). They shorten the duration of illness and excretion of susceptible organisms and prevents relapse.
- Precautions: In hospitalized patients, standard and contact precautions are recommended for children with diapers or incontinence for the duration of illness.
- · No vaccine available.

#### Cholera

- Bacteria Vibrio cholerae. Gram-negative comma-shaped rod. Humans are the only host but free-living bacteria can stay in bodies of water [17].
- Only toxin-producing serogroups O1 and O139 cause epidemic cholera.
- Endemic area: area where bacteriologically confirmed cholera cases, resulting from local transmission, have been detected in the last 3 years.
- There have been massive outbreaks around the world, associated with inadequate access to clean water and sanitation [18].
- Incubation period 12 h to 5 days.
- Contaminated food and water, particularly raw or undercooked shellfish, raw or partially dried fish, or moist grains or vegetables.
- Bacteria can be present in asymptomatic people from 1 to 10 days, infecting others.
- Clinical features:
  - Severe acute watery diarrhea that can kill within hours.
  - Stool has rice-water appearance, white-tinged, and contains small flecks of mucus.
  - No fever, no abdominal pain [5].
- Complications: Hypovolemic shock, hypokalemia, metabolic acidosis, hypoglycemia.
- Diagnosis: rapid diagnostic test (WHO has authorized this type of test only for detection purposes), PCR, or culture on stool samples.
- Treatment:
  - Prompt administration of oral rehydration salts or isotonic intravenous fluids.
  - Breastfeeding should be promoted.
  - Zinc supplement.
  - Antibiotics decrease duration and volume of diarrhea and shedding of viable bacteria. Choice of therapy depends on the severity of disease, age, and patterns of antibiotic resistance. Possible options [17]:
    - Doxycycline 4–6 mg/kg, single dose. Not recommended for children <8 years. Ciprofloxacin 15 mg/kg, 2 times a day for 3 days.
    - Azithromycin 20 mg/kg, single dose.
    - Erythromycin 12.5 mg/kg, 4 times a day for 3 days.
    - Tetracycline 12.5 mg/kg, 4 times a day for 3 days [17].
- A surveillance system is very important in a humanitarian crisis such as displacement of populations and overcrowded refugee camps. One or more positive tests should trigger a cholera alert.
- Outbreak management:
  - Surveillance system.
  - Information for population: disinfection of drinking water (chlorination or boiling), thorough cooking of food, appropriate hand hygiene after defecating and before preparing or eating food, safe disposal of feces, identification of symptoms, location of treatment sites, and adequate funeral practices.
  - Ensure access to clean water and appropriate sanitation.
  - Rapid detection and treatment: trained health personnel, clear disease definition, appropriate treatment centers, and protection equipment.
  - All patients: standard and contact precautions for the duration of the illness [19].
- Vaccine: there are three oral, WHO-approved vaccines that require two doses [20].

# Malaria

# Overview

Malaria or Paludismo is a life-threatening disease caused by a parasite that spreads to people through the bite of the female *Anopheles* mosquitoes. It can be preventable and curable if treated on time.

# **Know Your Bugs: The Infectious Agent**

Malaria is caused by the parasite *Plasmodium*, there are five species:

- *Plasmodium falciparum:* The most deadly. Causes 99.7% of malaria in Africa, 50% in Southeast Asia, 71% in the Eastern Mediterranean region, and 65% in the Western Pacific.
- *Plasmodium vivax:* Second most deadly. It is found in central and south America (75% of cases), India, and Southeast Asia.
- The less dangerous *Plasmodium ovale, Plasmodium malariae, Plasmodium kowlesi* (comes from monkeys, rarely affects humans) [5].

# **Epidemiology, Incidence, and Mortality**

Children under 5 years are the most vulnerable group, accounting for 67% of deaths of malaria worldwide. According to the WHO 2019 Malaria Report, in 2018 there were an estimated 228 million cases of malaria (405,000 deaths) of which 93% occurred in the African region (and 94% of deaths), followed by the South East Asia region with 3.4% and Eastern Mediterranean region with 2.1%. The six countries most affected were: Nigeria (25%), the Democratic Republic of the Congo (12%), Uganda (5%), Côte d'Ivoire (4%), Mozambique (4%), and Niger (4%). For specific information by country review the WHO World Malaria report 2019 [21].

# Transmission

In most cases, malaria is transmitted by the bites of female Anopheles mosquitoes. They bite between dusk and dawn. They like to lay their eggs in water, that is why malaria transmission is higher during the rainy season in tropical countries. It can also be transmitted from the mother to the fetus during pregnancy and through blood transfusions that contain parasites [12].

#### **Immunity and Vulnerability**

The people most at risk of contracting malaria and developing severe disease are infants, children under 5 years, pregnant women, and people with HIV/AIDS and anatomical or functional asplenia, (children with sickle cell anemia), as well as nonimmune migrants, mobile populations, and travelers who have never been in contact with the disease. In areas with intense transmission partial immunity is developed over years of exposure and can reduce the risk of severe diseases; however, if a person leaves the area, immunity will be lost [21].

# **Clinical Features**

If working with refugees in a malaria-endemic area, always think of malaria if a child comes with fever. This also applies to newborn babies born to mothers with a positive malaria test. The sooner a child starts treatment, the better the outcome. In susceptible people, if treatment is delayed death can occur within hours [22].

There are two clinical presentations:

- 1. Uncomplicated malaria: confirmed parasitic diagnosis plus general malaise, high fever, chills, rigor, sweats, headache, anorexia, nausea, vomiting, diarrhea, abdominal pain, arthralgia, myalgia, and pallor from anemia.
- 2. Severe malaria: confirmed parasitic diagnosis plus organ dysfunction with one or more of the following clinical or laboratory signs [22]:

Hemoglobin <5 g/dL, hematocrit <15%
Hypoglycemia Hypoglycemia Metabolic acidosis (bicarbonate <15 mmol/L) Hyperlactataemia (lactate >5 mol/L) Urine positive for blood Hyperparasitaemia (>10% of Red blood cells or 500,000 parasites/ mcl) Thrombocytopenia Renal failure Pulmonary edema (confirmed with X-ray) Disseminated intravascular coagulation

Associated infection such as sepsis, pneumonia, and meningitis should always be considered and rapidly treated, since clinic and laboratory signs are impossible to differentiate.

# **Malaria in Newborns**

Congenital malaria presents in the first 7 days of life. It can be acquired vertically (from mother to child through the placenta) or at the time of birth (mother without malaria). Neonatal malaria presents from day 8 to 28. It can be acquired from mosquito bites or infected blood. Clinical signs and symptoms can be indistinguishable from neonatal sepsis [22].

# Complications

- Severe anemia
- Renal failure
- Shock
- Disseminated intravascular coagulation
- · Cerebral edema and increased intracranial pressure
- Neurological sequel
- Hypersplenism: with danger of splenic rupture
- Relapse of infection: for as long as 3–5 years after primary infection, attributed to latent hepatic stages (hypnozoites) with *P. vivax* and *P. ovale*, or as long as decades with *P. malariae*
- Associated bacterial infection
- Pregnancy: maternal anemia, fetal loss, premature delivery, intrauterine growth retardation, delivery of low birth-weight infants, early neonatal death [22]

# Diagnosis

- Microscopy: thick blood film to detect and count parasites (even if scarce) and thin blood film to detect species and determine the degree of parasitemia. If no parasites are seen, but there are clinical signs, microscopy should be repeated every 12–24 h for at least 3 days [5].
- Rapid diagnostic test (RDT) for antigen-detection. This test should be confirmed with microscopy because low-level parasitemia may not be detected. There are different brands that detect different species. You should refer to each test's manufacturer guidelines [5].

# Treatment

Malaria treatment is based on the infecting species, possible drug resistance, and severity of the disease.

The recommended management by WHO is as follows [9]: Severe Malaria:

- If child is unconscious, protect the airway and minimize risk for aspiration pneumonia: open airway, place in recovery positions, and place nasogastric tube.
- Check for hypoglycemia and correct.
- Treat seizures with rectal or IV diazepam. Do not give prophylactic anticonvulsants.
- Antipyretics for fever (paracetamol or ibuprofen).
- Check for dehydration and treat appropriately and after it is corrected, ensure proper IV fluids or nasogastric feeding.
- Ensure close follow-up, vital signs, alertness, and urine output.
- Treat complications: hypoxia, hypoglycemia, severe anemia, seizures, and associated or suspected infection.
- Antimalarial treatment [9]:
  - Rectal artesunate should be given to all children before referral from a health center to a hospital.
  - Parenteral artesunate is the drug of choice for severe *P. falciparum* malaria. If not available use parenteral artemether or quinine, until the child can take oral medication or for a minimum of 24 h.
  - Artesunate: 2.4 mg/kg IV or IM on admission, then at 12 and 24 h, then daily until the child can take oral medication but for a minimum of 24 h even if the child can tolerate oral medication earlier.
  - Quinine: loading dose of quinine dihydrochloride salt at 20 mg/kg by infusion in 10 mL/kg of IV fluid over 2–4 h. Then, 8 h after the start of the loading dose, give 10 mg/kg quinine salt in IV fluid over 2 h, and repeat every 8 h until the child can take oral medication. The infusion rate should not exceed a total of 5 mg/kg/h of quinine dihydrochloride salt. Never as a bolus injection. It can be given as a diluted divided IM injection. Loading dose split into two as 10 mg/kg of quinine salt into the anterior aspect of each thigh. Then, continue with 10 mg/kg every 8 h until oral medication is tolerated.
  - Artemether: 3.2 mg/kg IM on admission, then 1.6 mg/kg daily until the child can take oral medication.
  - After 24 h and when the child can tolerate oral medication, complete treatment with a full course of Artemisin-based combination therapy. See uncomplicated malaria.

Uncomplicated Malaria:

- Treat with a first-line antimalarial agent. Refer to national guidelines [9].
- Treat for 3 days with one of the following artemisin-based combination therapies:

Combination	Presentation	Dose
Artemether– lumefantrine	Tablets 20 mg artemether, 120 mg of lumefantrine	5-<15 kg: 1 tablet twice a day 15-24 kg: 2 tablets twice a day for 3 days >25 kg: 3 tablets twice a day for 3 days
Artesunate plus amodiaquine	Tablets containing 25/67.5 mg, 50/135 mg, or 100/270 mg of artesunate/ amodiaquine	4 mg/kg/day artesunate and 10 mg/ kg/day amodiaquine: 3-<10 kg: 1 tablet (25/67.5 mg) twice a day for 3 days 10-18 kg: 1 tablet (50/135 mg) twice a day for 3 days
Artesunate plus sulfadoxine– pyrimethamine	Separate tablets of 50 mg artesunate and 500 mg sulfadoxine–25 mg pyrimethamine	4 mg/kg/day artesunate once a day and 25 mg/kg sulfadoxine—1.25 mg/ kg pyrimethamine on day 1.         Artesunate:         3-<10 kg: half tablet once daily for 3 days         ≥10 kg: one tablet once daily for 3 days         Sulfadoxine-pyrimethamine:         3-<10 kg: half tablet once on day 1
Artesunate plus mefloquine	Separate tablets of 50 mg artesunate and 250 mg mefloquine base	4 mg/kg/day artesunate once a day for 3 days and 25 mg/kg of mefloquine divided into two or three doses.
Dihydroartemisinin plus piperaquine	Tablets containing 40 mg dihydroartemisinin and 320 mg piperaquine	4 mg/kg/day dihydroartemisinin and 18 mg/kg/day piperaquine once a day for 3 days. 5–<7 kg: half tablet (20/160 mg) once a day for 3 days 7–<13 kg: one tablet (20/160 mg) once a day for 3 days 13–<24 kg: one tablet (320/40 mg) once a day for 3 days

- Children with HIV infection: if on treatment with zidovudine or efavirenz should avoid amodiaquine-containing artemisinin-based combination therapy, and those on cotrimoxazole (trimethoprim plus sulfamethoxazole) prophylaxis should avoid sulfadoxine–pyrimethamine.
- Uncomplicated *P. vivax, ovale,* and *malariae* malaria: still responsive to 3 days' treatment with chloroquine, followed by primaquine for 14 days.
- For *P. vivax*:
  - Give a 3-day course of artemisinin-based combination therapy as recommended for *P. falciparum* (with the exception of artesunate plus sulfadoxine–pyrimethamine) combined with primaquine at 0.25 mg base/kg, taken with food once daily for 14 days.

- Give oral chloroquine at a total dose of 25 mg base/kg, combined with primaquine: initial dose of 10 mg base/kg, followed by 10 mg/kg on the second day and 5 mg/kg on the third day plus Primaquine at 0.25 mg base/kg, taken with food once daily for 14 days.
- Chloroquine-resistant vivax malaria should be treated with amodiaquine, mefloquine, or dihydroartemisinin plus piperaquine as the drugs of choice [9].

# Prevention

- 1. Reduce the number of bites [16]:
  - Reducing mosquitoes: indoor residual spraying with insecticides once or twice a year. This should be implemented at a high coverage level.
  - Avoiding mosquitoes: if a refugee area can be selected, special care should be taken to avoid proximity to vector breeding sites, such as ponds, streams, or swamps. Attempt to get rid of unnecessary collections of water or using larvicides.
  - Reducing contact with mosquitoes: sleeping under an insecticide-treated net provides a physical barrier from bites and also kills mosquitoes. This also needs to be consistent within the population in order to work.
- 2. Kill the parasite before the person develops the disease (drug prophylaxis): suppresses the blood stage of malaria infection. It can be given continuously or intermittently. This program can be difficult to implement but can have a big impact.
  - IPT (intermittent preventive treatment): administration of a curative dose of an effective antimalarial drug (Sulfadoxine–pyrimethamine (SP)).
    - Pregnant women: IPTp at each antenatal care visit, starting in the second trimester, at least twice during pregnancy.
    - Infants: IPTi: one dose of SP at each contact through the expanded program on immunizations (EPI), usually 10 weeks, 14 weeks, and 9 months of age [23, 24].
    - Children: IPTc: seasonal malaria chemoprevention.

# **HIV/AIDS**

This is a very complex topic that cannot be covered to its full extent in this chapter; therefore, we will only talk about essential information for first contact with a child in whom HIV is suspected. For children already diagnosed, please refer to national guidelines.

#### **Overview**

An estimated 1.8 million children aged 0–14 were living with HIV at the end of 2019, 150,000 children were newly infected and 95,000 died of AIDS-related illnesses. Infants and children have an immature immune system and are less able to suppress HIV viral replication. Because of this, without prompt diagnosis and treatment 50% will die by the age of 2 and 80% by the age of 5.

Countries in Sub-Saharan Africa have been the hardest hit by the global HIV epidemic, but there can be infected people in every country. Each country's HIV prevalence should be reviewed in order to organize services for displaced or refugee populations.

HIV infection is a serious problem in refugee populations during humanitarian crises for a number of reasons. HIV/AIDS positive people may be subject to violation of human rights. Health care systems are unable to provide appropriate testing and treatment. Antenatal care may not be easily available and therefore there may be no testing available and no prevention of mother-to-child transmission (PMTCT) programs. Drugs and follow-up may not be easily available. There is no epidemiological evidence that refugee or displaced persons have a higher risk of contracting or transmitting AIDS; however, host countries may engage in discriminatory measures such as mass testing. The risk is the same as for other populations; however, sexual abuse and sex work may be increased and there may be less availability of condoms. Culturally appropriate programs to prevent HIV transmission should be implemented [16].

# Transmission

- In children 90% of HIV infections are acquired through mother to child transmission during pregnancy, labor, and delivery, or later through breastfeeding.
- Transfusion with contaminated blood.
- Sexual abuse.
- Injury with contaminated objects such as razors, needles, or non-sterile surgical instruments.
- In adolescents risk factors are the same as adults [25].

### Prevention of Mother to Child Transmission (PMTCT)

All pregnant women should be tested for HIV at the beginning of antenatal care and in the third trimester. Partners should also get tested. All HIV testing (child or adult) must be confidential, be accompanied by counseling, and conducted only with informed consent so that it is both informed and voluntary. HIV serological antibody test (ELISA or rapid tests) should be used [25].

All HIV positive pregnant women need to be properly evaluated (CD4, viral load if possible, screening for TB and sexually transmitted diseases) and proper

treatment started. She should continue treatment after delivery and during breast-feeding. Counseling is essential to avoid loss to follow up [25].

Babies born to HIV positive mothers or abandoned babies with a positive rapid HIV test should be started on Nevirapine (NVP) once a day for 6 weeks (according to national guidelines). At 6 weeks NVP can be stopped, and cotrimoxazole syrup started (which should continue until a confirmed negative HIV test is obtained). Exclusive breastfeeding for at least 6 months is recommended [9].

The best way to diagnose HIV in infants is to look for evidence of the virus in the blood, rather than looking for antibodies or antigens (because they may be acquired from the mother, lasting for up to 18 months). This may require sending a blood sample (whole blood, serum, or dried blood spots on paper) to a specialized laboratory that can perform this test [9, 25]:

- HIV RNA or DNA PCR testing (which detects viral DNA) should be performed at 6 weeks, and if positive, perform a confirmatory PCR.
- If breastfeeding stops, perform a rapid test 6 weeks after cessation. If positive, do a confirmatory PCR.
- If breastfeeding at 9 months, perform a rapid test. If positive, do a confirmatory PCR. If negative and continues to breastfeed, do a rapid test 6 weeks after breastfeeding cessation and if positive, do a PCR test.
- If exclusively formula-fed do a confirmatory rapid test at 18 months.
- If clinical features of HIV at any age a PCR test should be done.

### **Clinical Features**

Clinical presentation of HIV infection in children is highly variable. They can show severe signs and symptoms in the first year of life (rapid progression, 25–30%); they can slowly develop symptoms early in life, then follow a downhill course and die at the age of 3–5 years (50–60%); or, they can be long-term survivors, who live beyond 8 years of age (5–25%).

Signs that indicate possible HIV infection include [12]:

- Recurrent infection: >3 severe episodes of a bacterial infection (pneumonia, meningitis, sepsis, cellulitis, chronic otitis media, tuberculosis) in the past 12 months.
- Persistent diarrhea (>14 days).
- Severe acute malnutrition that does not respond to therapy or persistent failure to thrive.
- Oral candidiasis or thrush: especially if it lasts >30 days despite antifungal treatment, recurs, extends beyond the tongue, or presents as oesophageal candidiasis.
- Chronic parotitis: unilateral or bilateral parotid swelling ≥14 days, with or without associated pain or fever.
- · Generalized lymphadenopathy with no apparent cause.

- Hepatomegaly with no apparent cause.
- Persistent and/or recurrent fever.
- Progressive neurological impairment, microcephaly, developmental delay, hypertonia, or mental confusion.
- Herpes zoster (shingles).
- HIV dermatitis: erythematous papular rash. Typical skin rashes include extensive fungal infections of the skin, nails, and scalp and extensive molluscum contagiosum.
- Chronic suppurative lung disease.
- Lung infection consistent with Pneumocystis jiroveci (PCP).
- Lymphocytic interstitial pneumonia.
- · Kaposi sarcoma.
- Acquired recto-vaginal fistula (in girls).

For clinical staging see national guidelines or WHO Pocketbook of Hospital Care for Children: guidelines for the management of common childhood illnesses–second ed. 2013 [9].

## Diagnosis

- All testing should be done after age-appropriate counseling.
- Children with HIV positive parents and with HIV siblings should be tested.
- Adolescents with risk factors should always be offered testing.
- Children younger than 18 months should be tested with a PCR and confirmed with a second one if positive.
- For children above 18 months two positive rapid HIV tests confirm the diagnosis [9, 25].

#### Treatment

All HIV positive children under 5 years should be started on antiretroviral drugs (ARV) immediately. If over 5, start ARV in CD4 count is less than 500 cells/mcl or with severe or advanced disease [25]. Once started children must take their medicine regularly. Supply must be assured for all children. Advocacy for pediatric formulations to facilitate treatment should continue. Adolescents should be accompanied and counseled in specific adolescent clinics. Children with HIV should be immunized unless specific contraindications. For specific guidelines on treatment options and follow up see national guidelines or WHO Pocketbook of Hospital Care for Children: guidelines for the management of common childhood illnesses–second ed. 2013 [9].

# **Appendix: Precautions for Infection Control**

Infections may be passed from one person to another, especially in hospital settings. Patients can transmit the infection to other patients, health care personal and even the hospital environment. Depending on the way a microbe is transmitted it needs different preventions or precaution methods. They are described here.

Type of precaution	
Standard	<ul> <li>All patients no matter what disease they have.</li> <li>Respect the 5 moments of hand hygiene.</li> <li>Gloves, gowns and eye protection if in contact with blood or body secretions.</li> <li>Follow respiratory hygiene/cough etiquette principles.</li> <li>Ensure appropriate patient placement according to isolation needs.</li> <li>Properly handle and clean and disinfect patient care equipment and instruments/devices.</li> <li>Clean and disinfect the environment appropriately.</li> <li>Handle textiles and laundry carefully.</li> <li>Follow safe infection practices. Wear a surgical mask when performing lumbar punctures.</li> <li>Ensure healthcare worker safety including proper handling of needles and other sharps.</li> </ul>
Contact	<ul> <li>Use contact precautions for patients with known or suspected infections that represent an increased risk for contact transmission.</li> <li>Standard precautions PLUS:</li> <li>Put on gloves before room entry. Discard gloves before room exit.</li> <li>Put on gown before room entry. Discard gown before room exit.</li> <li>Do not wear the same gown and gloves for the care of more than one person.</li> <li>Use dedicated or disposable equipment. Clean and disinfect reusable equipment before use on another person.</li> </ul>
Droplet	<ul> <li>Use droplet precautions for patients known or suspected to be infected with pathogens transmitted by respiratory droplets that are generated by a patient who is coughing, sneezing, or talking.</li> <li>Standard precautions PLUS:</li> <li>Use an appropriate mask to cover nose and mouth.</li> <li>Use eye protection.</li> <li>Remove face protection after leaving the room.</li> </ul>
Airborne	<ul> <li>Use airborne precautions for patients known or suspected to be infected with pathogens transmitted by the airborne route (e.g., tuberculosis, measles, chickenpox, disseminated herpes zoster).</li> <li>Standard precautions PLUS:</li> <li>Put on a fit-tested N-95 or higher level respirator before room entry.</li> <li>Remove respirator after exiting the room and closing the door.</li> <li>Door to room must remain closed.</li> </ul>

# 5 Moments for Hand Hygiene:

#### Your 5 Moments

#### for Hand Hygiene

- BEFORE TOUCHING A PATIENT
- 2 BEFORE CLEAN / ASEPTIC PROCEDURE
- 3 AFTER BODY FLUID EXPOSURE RISK
- **4** AFTER TOUCHING A PATIENT
- 5 AFTER TOUCHING A PATIENT SURROUNDINGS



# **More Information:**

- 5 Moments for Hand Hygiene: https://www.who.int/gpsc/5may/background/ 5moments/en/.
- Tools on infection prevention and control: https://www.who.int/infectionprevention/tools/en/.
- Infection control CDC: https://www.cdc.gov/infectioncontrol/basics/ transmission-based-precautions.html.

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