

# Vector-borne diseases: a handbook for pharmacists

Disease prevention,  
control, management  
and treatment

2020



# Colophon

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## Foreword

Vector-borne diseases comprise a long list of illnesses caused by viruses, bacteria or parasites, transmitted to humans by a number of vectors, including insects. They account for nearly one fifth of all infectious diseases and cause over 700,000 deaths every year around the world. These diseases affect hundreds of millions of people worldwide and produce great suffering, long-term morbidity and disability, and stigmatisation with the associated distress and mental health problems.

In addition to the health burden of vector-borne diseases, the economic impact is enormous, especially so because they disproportionately affect the world's poorest countries, particularly Africa, the Americas and South-East Asia.

Malaria and dengue remain two of the most prevalent vector-borne diseases, and while the incidence and mortality of malaria have significantly reduced in the past decade, the opposite has happened with dengue, with global incidence increasing dramatically in recent decades. In 2019, the World Health Organization included dengue as one of the most important threats to global health, with half of the world's population now at risk of infection.

Different species of mosquito are responsible for the transmission of these two diseases. They are also responsible, alongside ticks, lice, other insect species and fresh water snails for the spread of other diseases such as chikungunya fever, Zika virus fever, yellow fever, West Nile fever, Japanese encephalitis, tick-borne encephalitis, Chagas disease, leishmaniasis, schistosomiasis and several others. Often, the same vector can transmit several diseases.

Many of these diseases have been largely confined to specific regions — especially in tropical and subtropical areas. This situation is now under profound change due to many factors including climate change, increased global travel, migration and refugee movements, global trade, deforestation and unplanned urbanisation to name but a few. These developments not only change the natural habitats of vectors but also promote their spread into new regions, exposing new populations to the diseases they carry.

Many of the vector-borne diseases are preventable through vector control and other measures, including effective vaccines, and community education and engagement. Pharmacists are ideally placed to support communities and patients in protecting themselves against vector-borne diseases through awareness-raising campaigns and advice, education on vector-control methods and disease prevention, vaccine administration and advocacy, treatment optimisation, supporting patients' physical and mental well-being, and reducing social stigma.

Combating vector-borne diseases is fundamental for achieving many of the United Nations' Sustainable Development Goals, from poverty eradication to quality education, from clean water and sanitation to action on climate change, and from reducing inequities to developing sustainable cities and communities — not to mention the most overtly linked goal of achieving good health and well-being for all.

Likewise, vector-borne diseases are a core element of FIP Development Goal 16 (Communicable diseases), aiming at the provision of services for the prevention, surveillance, management and therapeutic optimisation of communicable and vector-borne diseases, and it is directly linked to the majority of FIP DGs.

The Pharmaceutical Forum of the Americas (PFA) has previously published [guidelines](#) and organised [campaigns](#) for community pharmacists on the prevention, detection and control of arbovirus infections in 2018 with a grant from the FIP Foundation for Pharmacy Education and Research. Building on that expertise, FIP joined efforts with the PFA and is now publishing its first-ever handbook to support pharmacists in the area of vector-borne diseases. As the integration of the regional forums in FIP advances, such collaborative projects are tangible results of an increasingly regionally informed and regionally targeted work by FIP.

We hope this handbook will be of great value to pharmacists all around the world, and particularly to colleagues practising in countries where these diseases are endemic and represent a significant part of their daily practice.

**Dominique Jordan**  
President  
International Pharmaceutical Federation



**Eduardo Savio**  
President  
FIP Pharmaceutical Forum of the Americas



# 1 Introduction

Vector-borne diseases pose a significant risk to populations through widespread transmission to populations worldwide. It is estimated that 80% of the global population is at risk of developing at least one vector-borne disease. (1) These diseases bear the potential for harmful, debilitating, and life-threatening repercussions with over 700,000 deaths being caused by vector-borne diseases each year around the world. (1) According to the World Health Organization (WHO), vector-borne diseases account for more than 17% of all infectious diseases. (2) In addition, the burden of these diseases is highest in tropical and subtropical areas, and they disproportionately affect the poorest populations. Since 2014, major outbreaks of dengue, malaria, chikungunya, yellow fever and Zika have afflicted populations, claimed lives and overwhelmed health systems in many countries. (2)

Changes at the environmental, populational, and societal levels also contribute to the proliferation and dissemination of vectors and, consequently, of the diseases they carry and transmit. (1) Pathogens are not bound by national borders, and local and international movement of people can rapidly spread infections. Increasing urbanisation results in large, dense populations, raising the likelihood of infectious disease transmission and outbreaks. In addition, climate change may expand the habitats of some vectors to new regions, thus exposing new populations to the disease they transmit, and it may alter the patterns and intensity of seasonal diseases. Detecting, preventing and responding to infectious disease threats are therefore key to global health security. (3)

A crucial element in reducing the burden of vector-borne diseases is behavioural change, which can be achieved through education and by improving public awareness, so that people know how to protect themselves and their communities from mosquitoes and other flies, ticks, bugs and other vectors. Also, access to water and sanitation is a very important factor in disease control and elimination. (2)

In the fight against the burden of vector-borne diseases, member states of the WHO adopted a collective strategy to reinforce vector control across all regions. The Global Vector Response 2017–2030 serves as a global, comprehensive framework to strengthening countries' and territories' capacity to effectively manage vectors and vector-borne diseases. (1) Its main targets include reducing mortality by at least 75%, reducing case incidence by at least 60%, and preventing epidemics of vector-borne diseases worldwide by 2030. (1) This approach is also echoed in the recently adopted WHO Immunisation Agenda 2030, as vaccines are a critical component of the battle against emerging and re-emerging infections. (3)

To achieve these targets, accessible and effective prevention and treatment strategies, as well as collaborative efforts, are necessary. Pharmacists represent important key players in the multisectoral approach to effective vector control and the prevention and management of vector-borne diseases. Thanks to their accessibility, their proximity to patients and communities, their expertise in medicines, and their vital role within healthcare teams, pharmacists are well equipped to act as advocates, educators and providers in the collective endeavour of preventing and treating vector-borne diseases, especially in low- and middle-income countries, where such diseases are often more prevalent.

This handbook aims to strengthen pharmacists' capacities to comprehend many vector-borne diseases and their modes of transmission around the world, including the specific burden of the various diseases per region, and to describe and offer guidance on prevention and control strategies and treatment options. FIP seeks to address a gap in pharmacy resources pertaining to the impact of vector-borne diseases and the role that pharmacists must play in minimising their impact for patients and societies.



This important role by pharmacists is overtly linked to the **FIP Development Goal 16: Communicable diseases**. This goal specifically aims at the development of strategies and people-centred professional services for the prevention, surveillance, management and therapeutic optimisation of communicable and vector-borne diseases. However, this role is related to a total of 16 out of the 21 FIP Development Goals (highlighted in Figure 1), with a core role in seven of them in addition to FIP DG16.



**Goal 7: Advancing integrated services** — A people-centred and integrated health care provision that is based on an interprofessional and cross-setting seamless continuum including pharmacist-delivered professional services.



**Goal 8: Working with others** — Clearly identifiable elements of inter- and intra-professional collaboration and multidisciplinary healthcare, delivered through cohesive and interdependent teams working across interfaces and transitions of care.



**Goal 10: Equity and equality** — Clear strategies for equity and diversity in pharmaceutical services delivery, service access and service impact so that all people have access to quality pharmaceutical care. This is particularly relevant as vector-borne diseases disproportionately affect low- and middle-income countries and the poorer and most vulnerable members of society.



**Goal 11: Impact and outcomes** — Evidence of the impact of pharmaceutical services in terms of health outcomes and quality of life, improved efficiency of health systems and sustainability



**Goal 14: Medicines expertise** — Strategies and systems in place on pharmaceutical expert information and advice provision to patients, formal and informal caregivers, health care professionals and relevant agencies and stakeholders.



**Goal 17: Antimicrobial stewardship** — Develop and implement systems and structures to deliver antimicrobial stewardship services as a coordinated programme that promotes the appropriate use of antimicrobials, improves patient outcomes and decreases the spread of infections caused by multidrug-resistant organisms.



**Goal 18: Access to medicines, devices & services** — Systems in place to optimise access to effective medicines and pharmaceutical care services through appropriate supply chains, quality standards, self-care & prevention services, and affordability and fair pricing policies.

Figure 1. Links between the role of pharmacists in vector-borne diseases and the FIP Development Goals



## 1.1 What is a vector-borne disease?

A vector-borne disease is a human illness caused by the transmission of parasites, bacteria or viruses by vectors. Vectors are living organisms, such as ticks and mosquitoes or other flies that transmit disease-causing pathogens between humans, from animals to humans, from humans to animals, or between animals. (2) Vectors are responsible for causing acute diseases that can range from asymptomatic or mild presentations to severe, life-threatening illness, or chronic illness with the possibility of permanent disabilities. Such illnesses include dengue, malaria, yellow fever, and Japanese encephalitis among many others.

## 1.2 A glimpse at the global burden

Vector-borne illnesses are significant contributors to the global infectious disease burden; thus, they remain a threat to human health. Although it is difficult to fully estimate the global burden, dengue, the most common vector-borne illness, puts over half of the world's population at risk in nearly 130 countries alone. When considering all vector-borne illnesses, it is therefore clear that a tremendous threat exists. Disease burden is greatest in tropical and subtropical areas where many of these vectors thrive, because vector survival is influenced by temperature, rainfall patterns and humidity. (2)

Along with climate-related risk factors, vector-borne illnesses tend to affect a higher percentage of the poorer populations. These communities may struggle with access to clean water and proper sanitation techniques, and have poor infrastructure, which can contribute to favourable living conditions for vectors and pathogens. The consequences of infection may in turn also have economic impacts as illness, disability and death affect the workforce and productivity (2), leading to a circular relation between disease burden and economic prosperity.

## 1.3 Targeting prevention

As for many acute and chronic diseases, preventive methods for vector-borne illnesses have proven to be a successful method of disease control. Prevention methods include vector control, vaccines and medicines, early disease screenings, protection from bites, safe hygiene practices and increased community cooperation.

Of these various methods, vector control seems to be most responsible for containing and decreasing the regions impacted by vector-borne illnesses. And yet vector control is not used to its full potential. According to the WHO, it is imperative to prioritise vector control and the fundamental capacities that underpin it, including staff with technical expertise, stronger surveillance systems and better laboratory infrastructure. This would lead to saving many lives and averting much suffering. Vector control measures are especially important for diseases like Zika and chikungunya, which have neither a vaccine nor an effective treatment. For diseases that can be prevented by a vaccine or effectively treated, vector control works as a complementary measure that can reduce the disease burden faster. (4)

Vector suppression and control are also important because several vector-borne diseases are frequently endemic in the same regions and are often caused by a common vector. Also, some interventions may provide protection against several vectors. As such, vector control measures are a fundamental part of the strategy of reducing the burden of these diseases. (4)

Vector control is typically thought to be insecticide-based; however, with the rise of insecticide-resistance, it is also important to implement non-insecticide-based approaches as well, including removal of aquatic habitats, waste disposal, and door and window screening, as well as the use of natural insect predators. Regardless of the vector control method selected, it proves to be most effective when continuously applied in a dedicated manner and in synergy with other methods. (4,5) Vector control is only one component of disease prevention.

Other active forms of prevention include administration of vaccines, preventive medicines and personal protection techniques. These methods vary in applicability to each disease, but generally one or more of these methods of prevention exists for a vector-borne illness. By taking a proactive stance on prevention, entire communities can be protected and transmission can be curbed.

Health professionals play an important role in the promotion and implementation of preventive health measures. Pharmacists, specifically, have a special position as highly accessible healthcare professionals with a diverse skillset. Pharmacists are trained to counsel on appropriate medicines use, address patient concerns, educate on healthy lifestyles and disease prevention and, in many nations, administer vaccines. It is through

these actions that pharmacists develop relationships of trust with their patients, providing reliable advice to promote and encourage positive attitudes and healthy actions by patients.

In the case of vector-borne illnesses, pharmacists can provide accurate and appropriate advice on what patients can do to protect themselves and their communities. They can raise awareness of these diseases and take on the role of providing support to those affected with a vector-borne illness. It is part of pharmacists' role to keep communities informed and safe.

Another important component of prevention of vector-borne diseases is vaccination. Safe and effective vaccines are available against several of these diseases, including malaria, dengue, yellow fever and others. Pharmacists play a role in administering vaccines in an increasing number of countries (36, according to a FIP report from 2020). (6) Either by vaccinating people living in areas where such diseases are endemic or people who travel to those areas, pharmacists can contribute to the prevention of these diseases.

## 2 Vectors and the diseases they transmit

### 2.1 Mosquitoes — genus *Aedes*

#### 2.1.1 Chikungunya

Chikungunya fever is a viral disease transmitted to humans by mosquitoes of the genus *Aedes*. “Chikungunya” is a word of Kimakonde origin (an ethnic group in south-eastern Tanzania and northern Mozambique) which means “to bend], alluding to the hunched appearance of those infected due to joint pain. (1,2)

The disease is characterised by the sudden onset of fever, usually accompanied by joint pain. Other common signs and symptoms are muscle aches and headaches, nausea, fatigue and skin rashes. Joint pains are usually very debilitating and disabling; they usually disappear within a few days although they can last for weeks. (7)

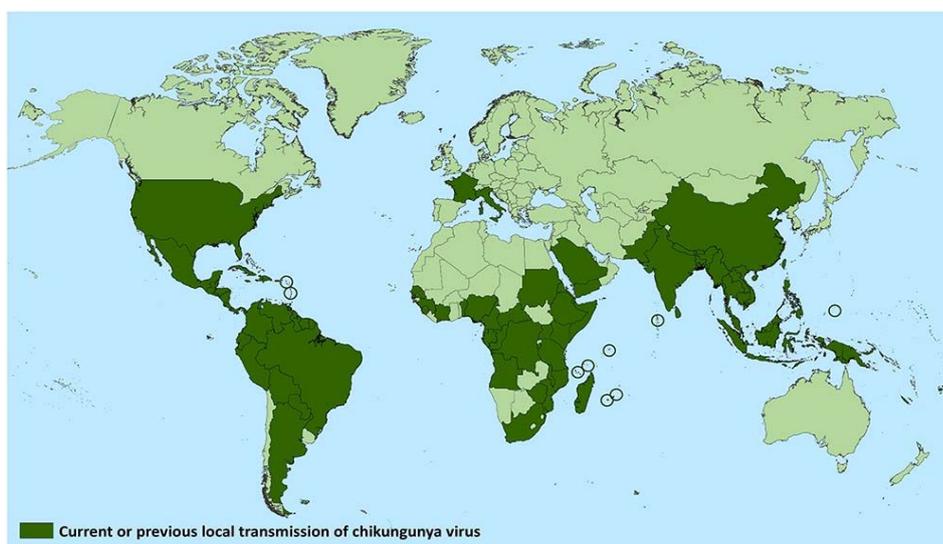
The chikungunya virus can cause acute, sub-acute and chronic disease. Often patients have only mild symptoms, and the infection may go unnoticed (28% of cases are asymptomatic) or be misdiagnosed as dengue fever in areas where that is common. Some studies report that up to 12% of those infected develop chronic arthritic disease even after the virus has been eliminated from the joints, as the inflammatory process may persist for more than a year after the initial symptoms. Occasional cases with ocular, neurological and cardiac complications, and also gastrointestinal discomfort, have been described. Serious complications are not frequent, although in older people with co-morbidities the disease can be fatal. (7,8)

To date there are no specific medicines that act against the chikungunya virus. Treatment consists mainly of relieving the symptoms with antipyretic and non-steroidal anti-inflammatory drugs. Rest and hydration are recommended. There is no vaccine against this virus. (7,8)

##### 2.1.1.1 Burden

First described during an outbreak in 1952 in southern Tanzania, chikungunya fever has now been detected in more than 60 countries in Asia, Africa, Europe and the Americas. It was not a common disease until 2004 when it began to reach epidemic proportions. It is mainly distributed in Africa, Asia, and the Indian subcontinent (Figure 2). (7,9)

Figure 2. Geographical distribution of chikungunya (as of 17 September 2019)<sup>1</sup>



Source: Centers for Disease Control and Prevention. Chikungunya virus. Geographic distribution. CDC, 2019. Available at: <https://www.cdc.gov/chikungunya/geo/index.html> (accessed 18 August 2020).

<sup>1</sup> Does not include countries or territories where only imported cases have been documented.

### 2.1.1.2 Transmission

Chikungunya is an RNA virus belonging to the *Alphavirus* genus of the family *Togaviridae*. There is a single serotype that appears to confer lifelong immunity to individuals recovering from infection. (7,8)

Both the *Aedes aegypti* and the *Aedes albopictus* species have been implicated in major outbreaks of chikungunya fever. While *Ae. aegypti* is confined to tropical and subtropical areas, *Ae. albopictus* is also present in temperate and even cold-temperate regions. In recent decades, *Ae. albopictus* has spread beyond Asia into parts of Africa, Europe and the Americas. These mosquitoes usually bite throughout the day, although their activity may be at its peak in the early morning and late afternoon. Both species bite outdoors, but *Ae. aegypti* can also bite indoors. Other mosquito vectors of the disease have been found in Africa, including species from the *Aedes furcifer-taylori* and *Aedes luteocephalus* groups. There are indications that some animals other than primates, such as rodents, birds and small mammals, may also act as reservoirs. (7)

The virus is transmitted from one person to another through the bite of infected female mosquitoes. It is introduced in the skin where it replicates in the fibroblasts of the dermis and spreads through the bloodstream to multiple tissues. Vertical transmission of the virus can also occur during birth, and is suspected of causing abortion if infection occurs in the first trimester of pregnancy. There is no evidence of transmission through breast milk. Viral replication occurs mainly in target tissues such as muscles, joints, skin, liver and spleen. It may also occur in the meninges of neonates. (7,8)

### 2.1.2 Dengue

Dengue fever is a flu-like viral disease that affects infants, young children and adults, but is rarely fatal. The infection may be asymptomatic or present with a broad clinical spectrum including non-serious and severe forms, where four phases are recognised: incubation (4–10 days after the bite of an infected mosquito), febrile period (2–7 days), critical or plasma leakage phase (3–7 days after the onset of symptoms) and recovery or fluid reabsorption period (7–10 days after the start of the leakage phase). (8,10)

A person should be suspected of having dengue fever when a sudden high fever (39–40°C), which may be biphasic, is accompanied by two or more of the following symptoms: severe headache, pain behind the eyeballs, muscle and joint pain, nausea, vomiting, enlarged lymph nodes or a rash. In the early febrile phase, it can be difficult to clinically distinguish dengue fever from other acute febrile diseases. In the case of children, they often have higher fevers, but generally experience fewer symptoms than adults, making differential diagnosis even more difficult. Clinical detection and appropriate treatment of dengue patients can significantly reduce mortality rates from severe dengue fever. (8,10)

Severe dengue (formerly called dengue haemorrhagic fever) is a potentially fatal development because it occurs with plasma leakage, fluid accumulation, respiratory distress, severe bleeding, or organ failure, and it must be treated urgently. Warning signs of this development, accompanied by a drop in body temperature (less than 38°C), include severe abdominal pain, persistent vomiting, tachypnoea, bleeding gums, fatigue, restlessness, and haematemesis. Individuals suffering from severe forms have been documented to have had a previous infection with a different serotype of the virus. (8,10)

There is no specific treatment for dengue fever. In the febrile phase, treatment is aimed at relieving symptoms with antipyretic drugs and painkillers. Hydration and rest are also recommended. A vaccine against dengue virus is available but is targeted for persons living in endemic areas, aged 9–45 years, who have had at least one documented dengue virus infection previously. (8,10)

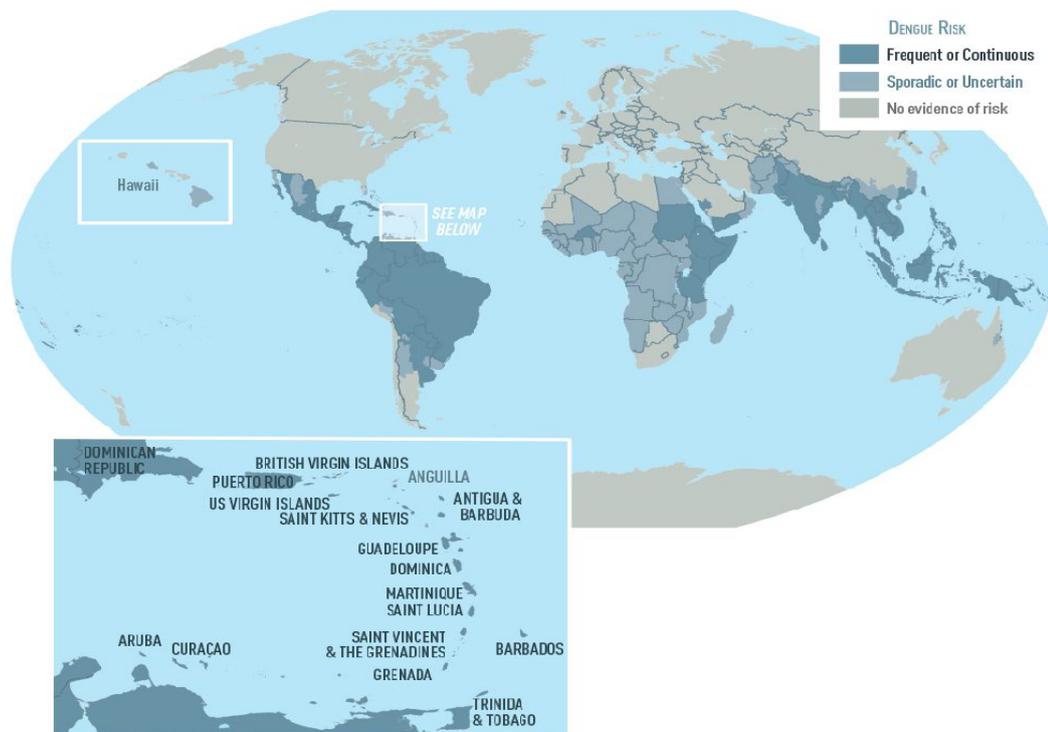
#### 2.1.2.1 Burden

The economic and social burden of dengue fever is significant and in recent decades its incidence greatly increased. A prevalence study estimates that 3.9 billion people in 128 countries are at risk of infection. The vast majority of cases are asymptomatic, so the actual number is underreported, and many are misclassified. According to recent estimates, there are 390 million dengue infections and 20,000 reported deaths each year. (8,10)

The dengue virus has ample potential to spread because *Ae. aegypti* can easily adapt to urban settings, across the tropical and subtropical regions. *Ae. albopictus*, the second most important dengue-related vector, has also spread rapidly to different areas in recent years. Another feature of the disease is its epidemiological pattern, in particular the hyperendemicity of the multiple serotypes of the virus in many countries, and the alarming impact on human health and national and global economies. The dengue virus is transported from one place to another by infected travellers. (8,10)

Severe dengue fever was first identified in the 1950s during a dengue epidemic in the Philippines and Thailand. Today, it affects most countries in Asia and Latin America and has become one of the leading causes of hospitalisation and death in children and adults in these regions (Figure 3). (10)

Figure 3. Geographical distribution of dengue fever



Source: Centers for Disease Control and Prevention. Dengue around the world. CDC, 2020. Available at: <https://www.cdc.gov/dengue/areaswithrisk/around-the-world.html> (accessed 25 August 2020).

### 2.1.2.2 Transmission

Dengue fever virus is transmitted by female mosquitoes, mainly those of the species *Ae. aegypti* and to a lesser extent by *Ae. albopictus*. These mosquitoes also transmit chikungunya, yellow fever and Zika virus infections. The disease is widespread in the tropics, with local variations in risk depending largely on rainfall, temperature and rapid unplanned urbanisation. (10)

Dengue fever is a flavivirus of which there are four related serotypes (DENV-1, DENV-2, DENV-3, DENV-4), each generating a unique immune response to infection in the host (they do not provide cross-immunity), distributed throughout tropical and subtropical regions and in some temperate regions around the world. These serotypes are transmissible to primates (wild form) and humans (human form) mainly by the *Ae. aegypti* mosquito. (8)

The *Ae. aegypti* mosquito lives in urban habitats and breeds mainly in artificial containers. Unlike other mosquitoes, it feeds during the day, early morning and evening, during which the female mosquito may bite many people. *Aedes* eggs can stay dry in their breeding sites for more than a year and hatch when they come into contact with water. *Ae. albopictus*, a secondary vector of dengue fever in Asia, has spread to Canada, the United States, and more than 25 countries in the European region due to the international trade in used tyres (which provide breeding grounds for the mosquito) and the movement of goods. *Ae. albopictus* is highly adaptable and can therefore survive in the coldest temperatures in Europe. Its tolerance of sub-zero temperatures, its ability to hibernate, and its ability to shelter in micro-habitats are factors in its spread. (8)

### 2.1.3 Lymphatic filariasis

Lymphatic filariasis, more commonly known as elephantiasis, is a disease of the lymphatic system. It can lead to the enlargement of limbs through severe swelling and tissue thickening. Most cases appear asymptomatic, although underlying damage to the kidneys and lymphatic system is occurring. (4) Unfortunately, because

there are no signs of disease, infected individuals contribute to the transmission cycle between humans and mosquitoes. (11)

Acute lymphatic filariasis is defined as episodes of local inflammation of the skin, lymph nodes and lymphatic vessels, which may be a response to the parasite or to a secondary infection. Acute episodes are often accompanied by the chronic form of the disease. (11)

In its chronic state, lymphatic filariasis causes lymphoedema, contributing to enlarged limbs and hydrocele. This form of the disease is painful and leaves behind distinct limb disfiguration (elephantiasis), which can cause permanent disability, loss of work, and social stigma. Chronic lymphatic filariasis can have major impacts on a patient's mental health. (11)

### 2.1.3.1 Burden

Although most individuals are infected during childhood, the disease does not typically present until adulthood, during which it then presents chronically. There is a higher burden of lymphatic filariasis among men than women. (4)

Globally, there are an estimated 15 million cases of lymphoedema, 25 million cases of men with hydrocele, and at least 36 million cases of limb disfiguration. (4,11) Nearly 65% of cases originate from the South East Asian region, and another 30% come from the African region. Remaining cases are found in tropical areas, including parts of the Americas and the Western Pacific. (4)

### 2.1.3.2 Transmission

Lymphatic filariasis is an infection caused by parasitic nematodes (roundworms) of the *Filariodidea* family. These worms live in the lymphatic vessels as adults, disrupting the normal function of the system. They produce larvae, also known as microfilariae, that develop in the blood vessels. Mosquitoes become infected when they ingest these microfilariae while feeding on blood of infected animals or humans. The microfilariae develop within mosquitoes and are transferred to human skin when mosquitoes feed. The transmission cycle continues as the worms make their way from the skin to the lymphatic vessels, mature into adults and produce more larvae. (11)

There are three types of worms responsible for infection: *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*. *Wuchereria bancrofti* causes about 90% of infections, with *Brugia malayi* causing most of the others. (4,11)

These worms are transmitted by several types of mosquitoes. *Aedes* mosquitoes are a vector in some Pacific islands where the disease is endemic. Other vectors include *Anopheles* mosquitoes, found in rural areas, and *Culex* mosquitoes, found in urban and semi-urban areas. The wide range of habitats where these mosquitoes are present contributes to the high burden of this disease. (4,11)

## 2.1.4 Rift Valley fever

Rift Valley fever (RVF) is a viral infection that can cause severe disease primarily in animals, but also in humans. There are both mild and severe forms of disease. (12)

In its mild form, RVF may be asymptomatic or may present with flu-like symptoms, such as sudden onset of fever, headache and muscle aches. Additionally, some patients may develop neck stiffness, photosensitivity, loss of appetite or vomiting. Mild RVF may be initially mistaken for flu or meningitis. (12)

The chances of developing severe RVF are rare, typically occurring in less than 5% of patients. If a patient does develop severe RVF it will develop as one or more of three distinct syndromes (12):

- The ocular form presents with mild RVF symptoms as well as retinal lesions which result in blurred or decreased vision. Spontaneous recovery may occur in 10 to 12 weeks with no lasting effects; however, half of patients that develop lesions on their maculae will become permanently blind. The risk of mortality is low for this form of severe RVF.
- The meningoencephalitis form is characterised by intense headache, memory loss, hallucinations, confusion, disorientation, vertigo, convulsions and coma. Neurological complications may develop after approximately 60 days and may have some lasting impacts, but the risk of mortality is low in this form.
- In the haemorrhagic fever form, symptoms appear much more suddenly and include severe liver injury evidenced by jaundice, haematemesis, haematochezia and epistaxis as well as bleeding from the

gums, within the skin, or from venepuncture sites. Death occurs quickly, about three to six days after onset of symptoms, in about half of patients.

#### 2.1.4.1 Burden

The virus responsible for RVF was first identified in the Rift Valley of Kenya, hence its name. The virus has since spread throughout the sub-Saharan region of Africa. It has also been introduced to Saudi Arabia and Yemen through livestock trading. The disease is more common in animals than humans, and therefore the risk of infection is higher for those working with animals, such as herders, farmers, slaughterhouse workers or butchers, and veterinarians. (12)

#### 2.1.4.2 Transmission

Transmission of RVF occurs mainly through direct or indirect contact with blood or organs of infected animals. This may include activities such as butchering an animal, birthing an animal, routine veterinary procedures, or disposal of dead animals. Beyond these direct contact activities, a human could also become infected through inhalation of air droplets produced during the slaughter of an animal or by inoculation through an accident with an infected knife or other broken skin. (12)

The other route of transmission is through mosquito vectors. The *Aedes* mosquito is most responsible for transmission, but the *Culex* mosquito is also thought to play a role. (12)

### 2.1.5 Yellow fever

Yellow fever is an acute, viral, haemorrhagic disease transmitted by infected mosquitoes and is endemic in tropical areas of Africa and Latin America. The term “yellow” arises from the jaundice present in some patients. (13)

The incubation period of the disease is three to six days. Its evolution can include three clinically evident periods: infection, remission and intoxication. Many cases are asymptomatic, but the most common symptoms are fever, myalgia, (especially in the back), chills, headaches, loss of appetite and nausea or vomiting. In most cases, symptoms disappear within three to four days. However, a percentage (between 15% and 25%) of patients go into a more severe and toxic phase within 24 hours of initial remission. High fever returns and several organs are affected, usually the liver and kidneys. Jaundice, dark coloured urine and abdominal pain with vomiting are common in this phase. There may be oral, nasal, ocular or gastric bleeding. Half of the patients who enter the toxic phase die within seven to 10 days. (8,13,14)

The diagnosis of yellow fever is challenging, especially in the early stages. In the most severe cases, it can be confused with severe malaria, leptospirosis, viral hepatitis (especially fulminant forms), other haemorrhagic fevers, other flavivirus infections (e.g., severe dengue fever) and some poisonings. (13,14)

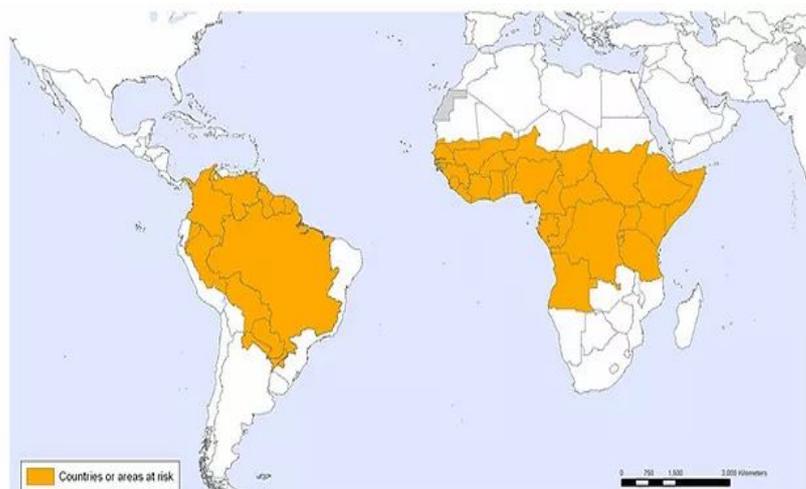
There is no specific treatment for yellow fever. The vaccine is the most important preventive measure and it is safe, affordable and highly effective. It provides effective immunity within 30 days for 99% of those vaccinated, and a single dose is sufficient to confer sustained immunity and protect against the disease for life. (13)

#### 2.1.5.1 Burden

There are 34 countries in Africa and 13 in the Americas (Central and South) where the disease is endemic throughout the country or in some regions (Figure 4). There are 200,000 cases of yellow fever and 30,000 deaths worldwide each year. Occasionally, travellers to countries where the disease is endemic may import it into countries or areas where there is no yellow fever. To avoid these imported cases, many countries require a vaccination certificate before issuing visas, especially when travellers come from endemic areas. (13,14)

The Eliminate Yellow fever Epidemics (EYE) strategy, aimed at eliminating epidemics of this disease that regularly afflict the African continent, was launched in April 2018 and aims to protect nearly one billion people in 27 high-risk African countries with the widespread use of yellow fever vaccine between 2018 and 2026. (15)

Figure 4. Geographical distribution of yellow fever



Source: Dirubbo N. Important update — yellow fever vaccine shortage. Available at: <https://www.travelhealthnh.com/single-post/2017/06/09/Important-Update--Yellow-Fever-Vaccine-Shortage> (accessed 22 August 2020).

#### 2.1.5.2 Transmission

The yellow fever virus is an RNA virus that belongs to the genus *Flavivirus*. The yellow fever virus is transmitted to people mainly through the bite of infected *Aedes* or *Haemagogus* species mosquitoes. The mosquitoes acquire the virus by feeding on infected primates (human or non-human) and can then transmit it. Different species of mosquitoes live in different habitats. Some breed near homes (domestic), some in the forest (wild) and some in both habitats (semi-domestic). (13,14)

There are three types of transmission cycles (13,15):

- **Jungle cycle:** In tropical rainforests, monkeys, which are the main reservoir of the virus, are bitten by wild mosquitoes, which then transmit the virus to other monkeys. People who live in, work in or visit the rainforest can be bitten by infected mosquitoes and get the disease.
- **Intermediate cycle:** Semi-domestic mosquitoes (which breed in the forest and near homes) infect both monkeys and humans who live in, work in or visit forest frontier areas. This type of cycle occurs in Africa and is the most frequent cause of disease outbreaks.
- **Urban cycle:** This involves the transmission of the virus between humans and urban mosquitoes, mainly *Aedes aegypti*. Widespread epidemics occur when infected people introduce the virus into densely populated areas with a high density of mosquitoes and where most of the population has little or no immunity due to lack of vaccination. Under these conditions, mosquitoes transmit the virus from one infected person to another.

#### 2.1.6 Zika

Zika infection is an emerging disease caused by the virus of the same name. It occurs mostly in the tropical regions of the Americas, Africa, Asia and the Pacific (Figure 5). (16)

The incubation period of the disease is three to 14 days. Most infected people are asymptomatic, and about 20% develop clinical manifestations, with mild symptoms lasting two to seven days, including sudden onset low-grade fever associated with an itchy maculopapular rash, arthralgias (mainly of small joints of hands and feet), conjunctivitis (not purulent), myalgia, retro-orbital pain, headache and general malaise. (8,16,17)

**Neurological complications:** The infection is a trigger for Guillain-Barré syndrome, neuropathy and myelitis, especially in adults and older children. Although less frequent, other manifestations are encephalitis, meningoencephalitis, cerebellitis, acute disseminated encephalomyelitis, inflammatory myelopathy and cranial nerve disorders. (8,16)

**Zika related congenital syndrome:** Infection during pregnancy causes microcephaly and other congenital malformations. It is also associated with pregnancy complications such as premature birth, miscarriage and intrauterine death as well as alterations of the central nervous system and of joints. (8,16)

To date, there are no specific medicines against the Zika virus. Treatment consists of relieving the symptoms with analgesic, antipyretic and antihistaminic medicines against pruritus. Rest and hydration are recommended. There is no vaccine against Zika virus currently available, although some are in clinical trials. (8,18)

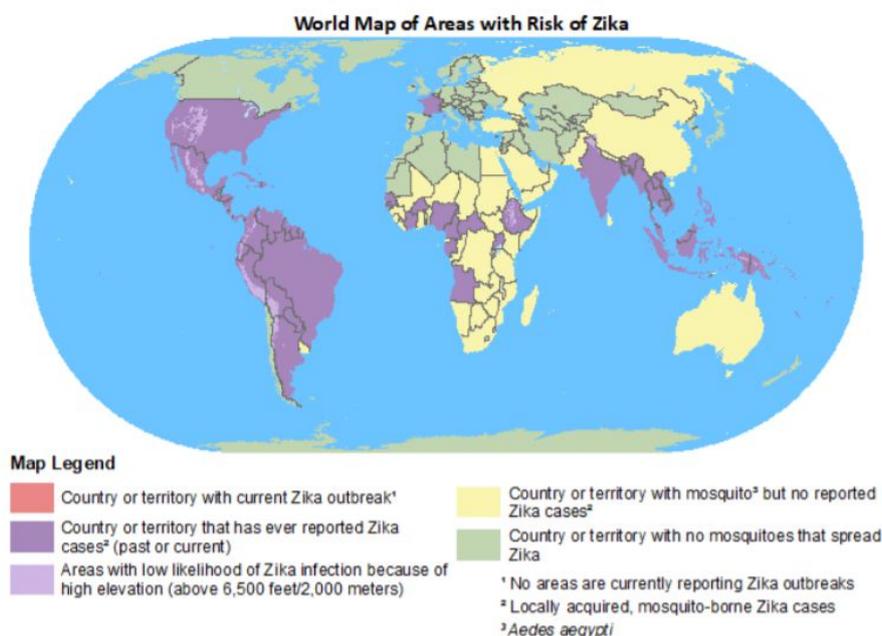
### 2.1.6.1 Burden

Zika virus disease was identified in 1947 in a Rhesus monkey used as a sentinel to monitor yellow fever in the Zika forest, Uganda, with cases reported in Africa and Asia in later years. In 2013 a large outbreak occurred in French Polynesia and, in 2014, the first indigenous case was identified in the Americas (Easter Island, Chile). During 2015, Brazil reported indigenous transmission of Zika virus in 18 states. Colombia, El Salvador, Guatemala, Mexico and Paraguay also reported indigenous transmission. (8,16,17)

In March 2015, Brazil reported a large outbreak of exanthematous disease that was quickly identified as a result of Zika virus infection and in July of the same year its association with Guillain-Barré syndrome was described. In September 2015, Brazilian researchers noted an increase in births of children with microcephaly in the areas where Zika virus had been reported and, in October 2015, they described the association between infection and microcephaly. (8,16)

From February to November 2016, the WHO declared the Zika virus infection a public health emergency of international concern after observing the rise of serious congenital anomalies in Brazil associated with the infection. Although no longer considered an emergency, it continues to represent a public health crisis that hits the poorest and most vulnerable communities hardest. Today, millions of people in 97 countries and territories located mainly in South-East Asia, the Americas and Africa are at risk of being infected by the Zika virus. (Figure 5) (16,19)

Figure 5. Geographical distribution of Zika



Source: Centers for Disease Control and Prevention. Zika travel information. Available at: <https://wwwnc.cdc.gov/travel/page/zika-information> (accessed 24 August 2020).

### 2.1.6.2 Transmission

Zika virus infection is transmitted through the bite of *Aedes* mosquitoes such as *Ae. aegypti*, *Ae. albopictus*, *Ae. polynesiensis* and *Ae. hensilli*. It is an arbovirus<sup>2</sup> of the family *Flaviviridae* that contains a single strand of RNA, and two main lineages (Asian and African) have been identified. Transmission happens in both jungle and urban environments, and it is suggested that it may have non-human primate reservoirs. *Aedes* mosquitoes usually bite during the day, especially at dawn and dusk. (8,16)

Zika virus can be transmitted from mother to fetus and produce microcephaly and other malformations that constitute the Zika virus congenital syndrome. Microcephaly is due to loss of brain tissue or abnormal brain development. Its consequences depend on the extent of the brain damage. Zika virus congenital syndrome includes other malformations, such as contractures of the limbs, muscular hypertonia, ocular alterations and deafness. The risk of congenital malformations following infection of pregnant women remains unknown, but it is estimated that 5–15% of infants born to such women have complications related to the virus. Congenital malformations can occur after symptomatic or asymptomatic infections. (16)

The Zika virus can be transmitted during sexual intercourse. In areas where there is active transmission of the virus, all infected persons and their sexual partners (particularly pregnant women) should receive information and counselling on this mode of transmission. Pregnant women should practise safer sex using appropriate methods of contraception or abstain from sex. In areas where there is no active transmission of the virus, it is recommended that men and women returning from areas where transmission of the virus is known to occur adopt safer sex practices or abstain from sex for at least six months after their return to avoid sexual transmission of the virus. Cases of transmission by blood transfusion have also been reported. (8,16,20)

## 2.2 Mosquitoes — genus *Anopheles*

### 2.2.1 Lymphatic filariasis

Lymphatic filariasis is known to be transmitted by *Anopheles* mosquitoes, as well as *Aedes* and *Culex* mosquitoes. See section 2.1.3. for more information on the disease presentation, burden and transmission.

### 2.2.2 Malaria

Malaria is one of the world's most serious public health problems. It is an acute febrile illness caused by parasites of the genus *Plasmodium* transmitted by female *Anopheles* mosquitoes. Infection with the malaria parasites can result in a wide variety of symptoms, ranging from absence or very mild symptoms to severe illness and death. In general, malaria is a curable disease if diagnosed and treated sufficiently quickly and appropriately. (21,22)

In malaria-endemic areas, people can develop partial immunity, allowing asymptomatic infections to occur. In a non-immune individual, symptoms usually appear 10–15 days after the bite of an infective mosquito. The first symptoms, which may be mild and difficult to recognise as malaria, are fever, chills, sweating, headache, nausea and vomiting, body aches and general malaise. If the disease is not treated immediately with effective medicines, it can progress to a severe condition that often leads to death. (21,23)

Manifestations of severe malaria include: cerebral malaria, with abnormal behaviour, impaired consciousness, convulsions, coma or other neurological abnormalities; severe anaemia and haemoglobinuria due to haemolysis; acute respiratory distress syndrome, which can occur even after the parasite count has declined in response to treatment; blood clotting abnormalities; hypotension caused by cardiovascular collapse; acute renal injury; hyperparasitaemia, where more than 5% of red blood cells are infected by parasites; and metabolic acidosis, often associated with hypoglycaemia. Severe malaria is a medical emergency and must be treated urgently and aggressively. (21)

Some population groups are at considerably higher risk of contracting malaria and developing a serious illness. These include infants, children under five years of age, pregnant women and HIV/AIDS patients as well as non-immune migrants, mobile populations and travellers. Early diagnosis and treatment reduce the disease, prevent deaths and help to reduce transmission. (21)

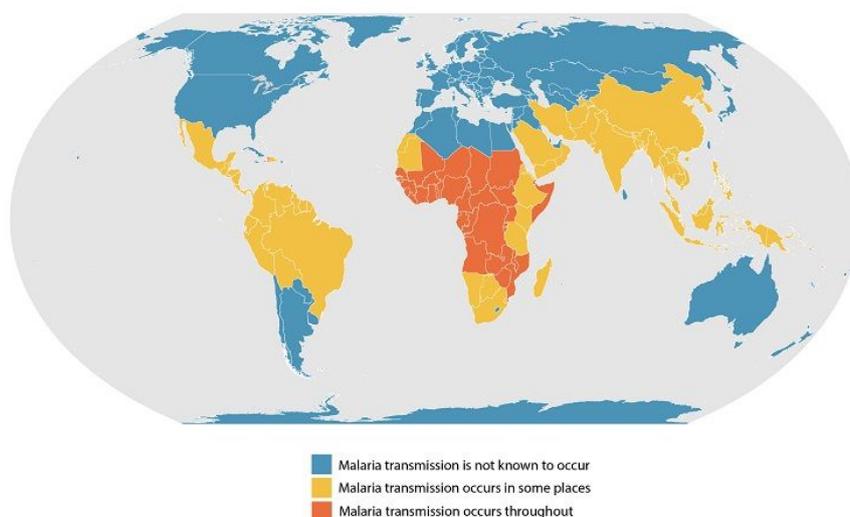
<sup>2</sup> 'Arbovirus' is an informal (non-taxonomical) name for the group of viruses transmitted by arthropods such as mosquitoes and ticks. The name is an acronym for **arthropod-borne virus**.

### 2.2.2.1 Burden

Malaria occurs mainly in the lower-income tropical and subtropical areas of the world. In 2018, almost half of the world's population in 91 countries and territories lived in areas at risk of malaria transmission (**Error! Reference source not found.**), and there were an estimated 228 million cases and 405,000 deaths worldwide due to the disease. Children under the age of five are the most vulnerable group, accounting for 67% of total global malaria deaths in 2018. (21,22)

Africa bears a disproportionately high share of the global burden of the disease. In 2018, 93% of the world's malaria cases and 94% of malaria deaths were recorded in that region. In the same year, and according to WHO established regions, *Plasmodium falciparum* was responsible for the majority of estimated cases in the African (99.7%), Eastern Mediterranean (71%), Western Pacific (65%), and South-East Asian (50%) regions. *Plasmodium vivax* is the predominant parasite in the region of the Americas, where it causes 75% of malaria cases. (1)

Figure 6. Geographical distribution of malaria



Source: Centers for Disease Control and Prevention. Where malaria occurs. Available at: <https://www.cdc.gov/malaria/about/distribution.html> (accessed 28 October 2020).

### 2.2.2.2 Transmission

Malaria is caused by *Plasmodium* parasites, which are transmitted to humans through the bites of infected female *Anopheles* mosquitoes. (21,22)

There are over 400 different species of *Anopheles* mosquitoes and about 30 of them are major vectors of malaria. There are five species of parasites that cause malaria in humans (*P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae* and *P. knowlesi*), with two of them (*P. falciparum* and *P. vivax*) being the most dangerous. All the important species of vectors bite between dusk and dawn. The intensity of transmission depends on factors related to the parasite, the vector, the human host and the environment. (21,23)

Malaria involves the cyclical infection of humans and female *Anopheles* mosquitoes. For malaria transmission to occur, conditions must be met that all three components of the malaria life cycle are present:

- Presence of *Anopheles* mosquitoes that can feed on humans and in which the parasites can complete half of their life cycle in an invertebrate host;
- Presence of humans that can be bitten by *Anopheles* mosquitoes and in whom the parasites can complete the other half of their life cycle in a vertebrate host; and
- Presence of malaria parasites. (22)

## 2.3 Mosquitoes — genus *Culex*

### 2.3.1 Japanese encephalitis

Japanese encephalitis is a viral disease affecting the central nervous system and represents the most important cause of viral encephalitis in the world. The first case was documented in Japan in 1871. Most infections are mild or without apparent symptoms, but about one in every 250 infections results in severe clinical illness. (24,25)

In people who develop symptoms, the incubation period is usually four to 14 days. Acute encephalitis is the most commonly recognised clinical manifestation. Milder forms of encephalitis, such as aseptic meningitis or non-specific febrile illness, can also occur. Initial symptoms often include fever, headache and vomiting. In children, gastrointestinal pain and vomiting may be the dominant initial symptoms. (24,26)

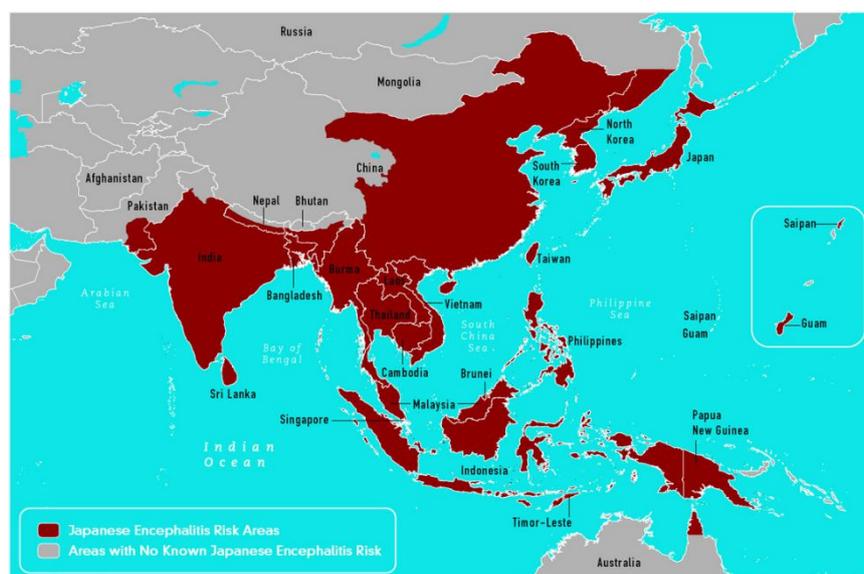
Severe illness is characterised by rapid onset of high fever, headache, stiff neck, disorientation, coma, convulsions, spastic paralysis and, eventually, death. The fatality rate can be as high as 30% among people with severe disease. Of those who survive, 20–30% suffer permanent intellectual, behavioural or neurological effects, such as paralysis, recurrent seizures or inability to speak. (24)

There is no specific antiviral treatment for this infection. Treatment is supportive to relieve symptoms and stabilise the patient, and is based on intensive care and prevention of post-disease disability. Several vaccines are available that are safe and effective for prevention. (24,26)

#### 2.3.1.1 Burden

The Japanese encephalitis virus is considered a public health problem in Asia, with 24 countries in the WHO South-East Asia and Western Pacific regions at risk of transmission, including more than three billion people (Figure 7). The three countries with the most reported cases are China, India and Vietnam. (24)

The annual incidence of clinical disease varies between and within endemic countries, ranging from less than one to greater than 10 per 100,000 population or more during outbreaks. According to estimates from a recent study, there are about 68,000 clinical cases worldwide each year with approximately 13,600 to 20,400 deaths. Japanese encephalitis mainly affects children. In countries where it is endemic, most adults are naturally immune through having had the infection in childhood, although the disease can affect people of any age. (24)

Figure 7. Geographical distribution of Japanese encephalitis<sup>3</sup>

Source: Centers for Disease Control and Prevention. Geographic distribution of Japanese encephalitis virus. Available at: <https://www.cdc.gov/japaneseencephalitis/maps/index.html> (accessed 18 August 2020),

### 2.3.1.2 Transmission

Japanese encephalitis virus, of the genus *Flavivirus* the family *Flaviviridae*, is closely related to West Nile and St Louis encephalitis viruses, as well as to dengue and yellow fever viruses. It is transmitted to humans through the bites of infected mosquitoes of the *Culex* species, especially *C. tritaeniorhynchus* and *C. vishnui*. (25,26)

The incidence of the disease is influenced by the abundance of the vector, which in turn is determined by various factors such as temperature, rainfall and agricultural practices. *Culex* mosquitoes persist in tropical climatic and temperature zones where they breed in slow-moving or stagnant water. Transmission occurs mainly in rural agricultural areas, often associated with rice production and flood irrigation. In some areas of Asia, these conditions may occur near urban centres. In temperate Asia, transmission of the virus is seasonal. Human diseases usually peak in summer and autumn. In the tropics and subtropics, transmission can occur year-round, often with a peak during the rainy season. (25,26)

The virus is transmitted between a wide variety of vertebrate hosts, including birds and mammals. Domestic animals, especially pigs, are implicated as a reservoir related to human infection. (26)

### 2.3.2 Lymphatic filariasis

Lymphatic filariasis is known to be transmitted by *Culex* mosquitoes, as well as *Aedes* and *Anopheles* mosquitoes. See section 2.1.3. for more information on the disease presentation, burden and transmission.

### 2.3.3 West Nile virus

West Nile virus (WNV) disease is a severe neurological disease which can be fatal to humans and other mammals. The disease is asymptomatic in nearly 80% of patients; the other 20% will develop West Nile fever. The disease is characterised by fever, headache, fatigue, body aches, nausea, vomiting, swollen lymph glands and, occasionally, skin rash. One case of severe disease will develop for every 150 infected persons. Severe disease presents with significantly worsened symptoms, such as headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness and paralysis, and death may occur. (27)

#### 2.3.3.1 Burden

The geographic distribution of WNV is extensive as it is present in Africa, Europe, the Middle East, North America and West Asia. Major outbreaks are often associated with the migratory patterns of birds because they are natural reservoirs of the disease. The biggest outbreaks have been in Greece, Israel, Romania, Russia and the United States. (27)

<sup>3</sup> As of February 8, 2019.

### 2.3.3.2 Transmission

Mosquitoes become infected by feeding on infected birds. They then pass on the infection when feeding on humans or other animals. (27)

Transmission has also occurred by blood transfusion, organ transplant, breast milk, or accidental needle stick injury. It may occur through contact with infected animals or their blood or tissues. (27)

## 2.4 Aquatic snails

### 2.4.1 Schistosomiasis (bilharzia)

Schistosomiasis (also known as bilharzia) is caused by parasitic trematode worms of the genus *Schistosoma*. It is considered to be both an acute and a chronic disease. There are two major forms of schistosomiasis, intestinal and urogenital, which arise from the host's reaction to the parasite's eggs as they are eliminated from the body. (28)

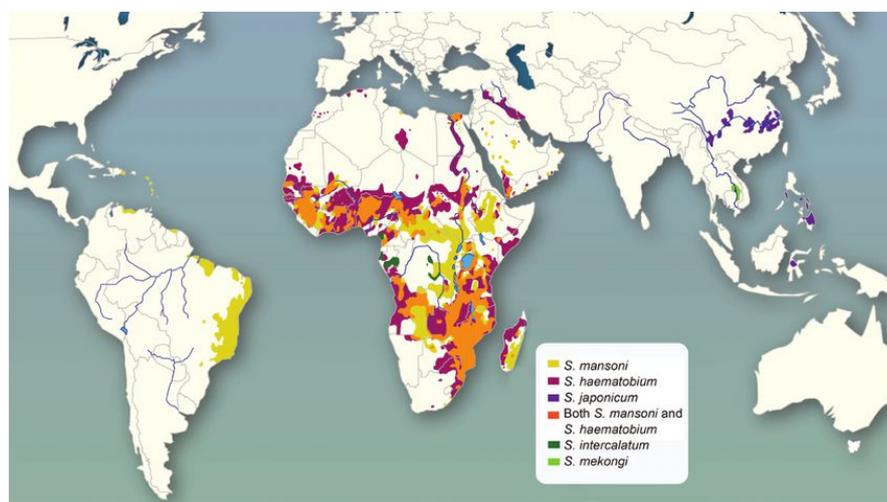
Intestinal schistosomiasis is characterised by abdominal pain, diarrhoea, blood in the stools, hypertension in abdominal blood vessels, and hepatomegaly and splenomegaly. (4,28)

Urogenital schistosomiasis is most notable for haematuria, but it may also cause lesions and fibrosis of the bladder and ureter, kidney damage and bladder cancer. Additionally, urogenital schistosomiasis is also considered to be a risk factor for HIV infection, especially in women, and may cause irreversible infertility. (4,28)

#### 2.4.1.1 Burden

Schistosomiasis is present in tropical and subtropical areas. Low-income communities, which rely on agriculture and fishing, and those without adequate water sanitation in place hold most of the burden. (28) These areas include more than 700 million people, mainly throughout sub-Saharan Africa (Figure 8). (4)

Figure 8. Geographical distribution of schistosomiasis



Source: Weerakoon K, Gobert G, Cai P, et al. Advances in the diagnosis of human schistosomiasis. *Clinical Microbiology Reviews* 2015;28:939–67. Available at: [https://www.researchgate.net/publication/280580610\\_Advances\\_in\\_the\\_Diagnosis\\_of\\_Human\\_Schistosomiasis](https://www.researchgate.net/publication/280580610_Advances_in_the_Diagnosis_of_Human_Schistosomiasis) (accessed 28 October 2020).

#### 2.4.1.2 Transmission

*Schistosoma mansoni*, *S. haematobium* and *S. japonicum* cause illness in humans; less commonly, *S. mekongi* and *S. intercalatum* can cause disease too. (29)

Transmission occurs when individuals come into contact with infested water, from which the larval forms of the parasite, released by aquatic snails, penetrate the skin. The larvae then develop into adults within the human body and live in the blood vessels, where females release eggs. The parasite's lifecycle continues when these eggs are passed out of the body through urine or faeces and contaminate more freshwater sources. The symptoms associated with schistosomiasis are reactions to the worms' eggs which get trapped in various tissues, not the worm itself. (4,28)

Aquatic snails, which act as the vector, are found in freshwater sources ranging from small, temporary bodies of water to long-standing lakes and rivers. The snails are found in shallow waters and most often in water with mild pollution, such as sewage. Because of the snails' ability to live in a variety of water sources, humans are likely to interact with the vector often through occupational, domestic, hygiene, or leisure activities, thus increasing the risk of infection. (4)

## 2.5 Blackflies

### 2.5.1 Onchocerciasis (river blindness)

Onchocerciasis, also commonly known as river blindness, is a disease caused by a parasitic worm transmitted through the bites of infected blackflies. It is a disease of the eyes and skin and presents with severe itching, skin depigmentation and eye lesions, which can lead to serious visual impairment and permanent blindness. (4,30)

#### 2.5.1.1 Burden

Onchocerciasis is endemic in many tropical areas. The vast majority of those infected live within sub-Saharan Africa, but the disease is also endemic in Yemen and in certain countries of the Americas, including Brazil, Venezuela, Guatemala and Mexico. Colombia and Ecuador have been successful in eliminating onchocerciasis from their countries. (4,30)

#### 2.5.1.2 Transmission

The parasite that causes onchocerciasis is the filarial worm *Onchocerca volvulus*, which is transmitted through repeated bites from infected blackflies. Within the human body, adult worms produce larvae, or microfilariae, which migrate to the skin, eyes and other organs. It is the inflammatory response to these invading microfilariae that causes the symptoms. The transmission cycle persists as female blackflies ingest the microfilariae when they bite an infected human. These then develop and are transmitted to a new human host. (4,30)

Blackflies breed and lay eggs in the waters of fast-flowing rivers and streams, which are often located near communities reliant on agriculture. Vector control measures can be taken to help prevent the spread of the disease and these will be discussed further on within this handbook. (4,30)

There is no vaccine or medicine to prevent infection with *O. volvulus*. (30)

## 2.6 Deerflies

### 2.6.1 Loiasis (African eye worm)

Loiasis, called African eye worm by most people, is caused by the parasitic worm *Loa loa*. Infection with the parasite can also cause repeated episodes of itchy swellings of the body known as Calabar swellings.

Knowing whether someone has a *Loa loa* infection has become more important in Africa because the presence of people with *Loa loa* infection has limited programmes to control or eliminate onchocerciasis (river blindness) and lymphatic filariasis (elephantiasis).

#### 2.6.1.1 Burden

The disease is endemic to certain rain forest areas of West and Central Africa. There may be more than 29 million people who are at risk of getting loiasis in the affected areas.

### 2.6.1.2 Transmission

The parasite is passed on to humans through the repeated bites of deerflies (also known as mango flies or mangrove flies) of the genus *Chrysops*.

There are no vaccines against loiasis. Diethylcarbamazine (DEC)—300mg taken once a week—can reduce the risk of infection. Avoiding areas where the deerflies are found, such as muddy, shaded areas along rivers or around wood fires, may also reduce the risk of infection. Other preventive measures include using insect repellents that contain DEET (N,N-Diethyl-meta-toluamide) and wearing long sleeves and long trousers during the day, which is when deerflies bite. Treating clothes with permethrin may also help.

There are two medicines that can be used to treat the infection and manage the symptoms. The treatment of choice is DEC, which kills the microfilariae and adult worms. Albendazole is sometimes used in patients who are not cured with multiple DEC treatments. (110)

## 2.7 Fleas

### 2.7.1 Plague

Plague is caused by a zoonotic bacterium, *Yersinia pestis*, typically transmitted by fleas living on small mammals, such as rats and other rodents. It is a very serious infectious disease with a high fatality rate if not detected and treated early. There are two forms of plague, which vary based on the route of infection. (31)

Bubonic plague, caused by the bite of an infected flea, is the most common form. In this form, the plague bacillus mainly impacts the lymph nodes causing inflammation, pain and sores filled with pus. Transmission from human to human is rare. In advanced cases, infection can spread to the lungs and become the second form, pneumonic plague. (31)

Pneumonic plague is the lung-based form of plague and is its most severe form. This form is transmittable through the spread of respiratory droplets to others. If left untreated or if not treated sufficiently early, pneumonic plague can be fatal. However, when detected and treated within 24 hours of onset, the chances of recovery are high. (31)

#### 2.7.1.1 Burden

Plague is found in all regions except Oceania. The risk for the disease exists wherever plague and humans co-exist. Africa, Asia and South America have all reported epidemics; however, Africa is the region where most cases have occurred in the past two decades. Peru, the Democratic Republic of Congo, and Madagascar are the most endemic countries, with Madagascar reporting an annual epidemic season from September to April. (31)

#### 2.7.1.2 Transmission

*Yersinia pestis* typically spreads from animal to animal via fleas. Unfortunately, the bacterium is able to infect humans through several mechanisms, including the bites of infected fleas, unprotected contact with infectious bodily fluids or other contaminated items, and inhalation of respiratory droplets from a person suffering from pneumonic plague. (31)

### 2.7.2 Tungiasis

Tungiasis is a skin infection caused by the burrowing of female *Tunga* sand fleas into the skin. The feet are the most affected site, due to fleas' jumping limitations. The resulting lesion is described as a white patch with a black dot and can restrict mobility due to the itching and local inflammation that occur. Repeated infections can result in foot disfiguration and long-term mobility challenges. (32,33)

#### 2.7.2.1 Burden

Like many vector-borne diseases, tungiasis largely burdens the tropical and subtropical areas of the Americas and Africa. It is estimated that more than 20 million people are at risk for infection in the Americas, mostly in South America, but also in Central America and the Caribbean. Much of sub-Saharan Africa is also at risk, which is the result of importing the sand flea in the 19<sup>th</sup> century. (32)

#### 2.7.2.2 Transmission

Tungiasis is acquired through unprotected contact with soil or floors where sandflies are present. The *Tunga* sand flea thrives in remote and rural areas. It likes warm, dry soil and sand as well as stables and stock farms. (32,33)

The female sand flea burrows into the skin permanently where it will feed on the human's blood. The toes, sole, lateral rim of the foot and heel are the most likely sites; 99% of all lesions occur on the feet. Itching and local irritation occur as the female fleas develop fully and increase their body volume by a factor of 2,000 within two weeks.

While burrowed, the female flea is fertilised by a male, and will develop and drop eggs, which fall onto the ground. The female will die in the host, but the eggs will continue to grow on the ground and develop into adult fleas. (32,33)

## 2.8 Lice

### 2.8.1 Typhus

Typhus is a disease caused by bacteria of the species *Rickettsia prowazekii* transmitted to humans by body lice. The disease is characterised by sudden onset of headache, chills, high fever, coughing, severe muscle pain and exhaustion. After five to six days, dark spots may develop on the body, excluding the face, palms, and soles. If untreated, death occurs in approximately 40% of cases. (34)

#### 2.8.1.1 Burden

Typhus fever most commonly occurs in the colder, mountainous, regions of Africa, South America, and Asia. Outbreaks typically occur in areas of overcrowding and poor hygiene, which may include prisons or refugee camps. (34)

#### 2.8.1.2 Transmission

The human body louse is responsible for transmitting typhus. These lice become infected by feeding on the blood of humans infected with acute typhus fever. While feeding on a second host, the lice excrete *Rickettsia* onto the host's skin. This host then rubs louse faecal matter or crushed lice into the bite wound, infecting themselves. (34)

### 2.8.2 Louse-borne relapsing fever

Louse-borne relapsing fever (LBRF) is a bacterial disease of sudden onset with symptoms of headache, chills, high fever, malaise, sweats, muscle aches and gastrointestinal upset. In some cases, it may also include scattered petechiae, erythematous rash, tachycardia, tachypnoea, non-productive cough, hepatomegaly, splenomegaly, and neurological and ocular complications. Symptoms tend to worsen over approximately five days, then subside as the pathogen is cleared from the blood. Without treatment, this disease has a fatality rate of 10–40%; this rate is significantly reduced with treatment to 2–5%. (35)

#### 2.8.2.1 Burden

LBRF is most common in areas of poverty, poor hygiene and overcrowding, such as prisons, refugee camps or slums. However, because of significant improvements made in living conditions, the disease burden has decreased substantially. LBRF was once found throughout Europe, the Balkans, Russia and Africa, but is now limited to a few countries, including Ethiopia, Somalia, and Sudan. There have also been cases reported in Peru and China. (35)

#### 2.8.2.2 Transmission

Transmission of LBRF occurs from human to human through the human body louse, which acts as a vector for the bacterium *Borrelia recurrentis*. An infected louse must be crushed on the surface of an individual's skin, releasing *B. recurrentis*, which can penetrate intact skin and mucosa. The transmission cycle continues when a new louse bites an infected human host and ingests *B. recurrentis*. This newly infected louse can then go on to infect other humans. (35)

## 2.9 Sandflies

### 2.9.1 Leishmaniasis

Leishmaniasis is a disease caused by over 20 species of protozoa parasites of the genus *Leishmania* transmitted to humans by sandflies. There are three forms of the disease: (36)

- Visceral leishmaniasis, also known as kala-azar, is the most serious form of the disease, and is fatal in over 95% of cases if left untreated. This disease is characterised by irregular bouts of fever, weight loss, hepatomegaly, splenomegaly and anaemia. (36)
- Cutaneous leishmaniasis is the most common type, with symptoms of skin lesions and ulcers, subjecting the infected individual to permanent scars, disability and social stigma. (36)
- Mucocutaneous leishmaniasis causes partial or complete destruction of the nose, mouth and throat mucous membranes. (36)

### 2.9.1.1 Burden

Sandflies are found throughout tropical and temperate climates, thus the range for potential disease is expansive. Within these regions, areas of poverty, poor housing and sanitation, and overcrowding are at higher risk due to sandfly breeding patterns and accessibility to blood-meals. (4,36)

Unfortunately, the burden of leishmaniasis is quite extensive, with an estimation of approximately one million new cases annually, affecting the regions of Africa, the Americas, Eastern Mediterranean, Europe, and South-East Asia. Several countries within each of these regions, including Algeria, Brazil, India, Iran, Somalia and Sudan, are considered highly endemic for visceral leishmaniasis. Cutaneous leishmaniasis is also prominent in each of these regions, with most cases appearing in the Americas and Eastern Mediterranean. More specifically, Afghanistan, Algeria, Brazil, Colombia, Iran and Syria carry the highest burden for cutaneous leishmaniasis. Mucocutaneous leishmaniasis mostly occurs in the Americas. (4,36)

### 2.9.1.2 Transmission

Leishmaniasis is transmitted through the bites of female sandflies infected with the parasite *Leishmania*. Female sandflies become infected when they feed on blood from infected individuals or animals. There are over 70 species of animals, including humans, which act as a reservoir for the parasite. (4,36)

Sandflies exist in tropical and temperate climates and prefer relatively cool and humid areas. They tend to live in the interior of houses, cellars, caves, cracks in walls, vegetation and tree holes, and household trash, near humans, dogs and other potential sources of blood meals. (4,36)

## 2.9.2 Sandfly fever

Sandfly fever, also known as phlebotomus fever, Pappataci fever and three-day fever, is an acute disease with a distinct set of symptoms. The illness begins about two to five days after exposure with symptoms of fatigue, gastrointestinal distress, dizziness and chills followed by the development of fever, muscle aches, flushing of the face and a quickened heart rate. After about two days, the fever will subside, and fatigue, weakness, a slow pulse and low blood pressure will set in and may persist for a few days or several weeks. Treatment is based on relieving symptoms, and recovery is expected. (37)

### 2.9.2.1 Burden

Sandfly fever is present in the subtropical areas of the eastern hemisphere, including the Mediterranean Sea, the Middle East, and parts of India. It is endemic during the summer season, just following sandfly breeding. The breeding sites of sandflies are difficult to find within thick vegetation, and thus difficult to control. (37)

### 2.9.2.2 Transmission

Transmission of sandfly fever occurs from the bite of an infected female sandfly. The sandfly may become infected after biting one of the many animals that can act as disease reservoirs, including warm-blooded vertebrates, cold-blooded vertebrates and humans. If a sandfly bites an infected human between 48 hours before until 24 hours after the onset of fever, the sandfly may become infected. Once the parasite is transmitted, the sandfly is infected for life and will act as a vector. (37)

## 2.10 Ticks

### 2.10.1 Crimean-Congo haemorrhagic fever

Crimean-Congo haemorrhagic fever (CCHF) is a severe viral disease of sudden onset. Symptoms of CCHF commonly include fever, headache, muscle aches, dizziness, neck stiffness and pain, sore eyes and

photosensitivity. Early on, some may experience nausea, vomiting, diarrhoea, sore throat or abdominal pain, followed by mood swings and confusion. After about two to four days, these symptoms may be replaced by fatigue, depression and abdominal pain in the upper right quadrant with hepatomegaly. Identifiable clinical signs of CCHF include tachycardia, enlarged lymph nodes and petechial rash. CCHF has a mortality rate of approximately 30%, with death occurring during the second week of the disease. (4,38)

#### 2.10.1.1 Burden

Unfortunately, CCHF is widespread around the world. The disease is endemic in Africa, the Balkans, the Middle East and Asia. (4,38)

#### 2.10.1.2 Transmission

CCHF is caused by a virus of the *Nairovirus* genus of the *Bunyaviridae* family. This virus is transmitted to humans and other animals through tick bites or to humans through contact with infected animal blood or tissues. When these animals, such as cattle, sheep, goats and other livestock, are bitten by an infected tick, the virus will survive in their blood for one week. During this time, the animal is infectious and the virus can be transmitted to other biting ticks or to humans working with the animal's body shortly after slaughter. Most people infected with CCHF work in close contact with animals, such as in agricultural, slaughterhouse or veterinarian settings. (4,38)

Transmission may also occur from human-to-human from contact with blood, secretions, organs or other bodily fluids of infected persons. Additionally, the disease may spread through medical equipment that is improperly sterilised, reused or contaminated. (4,38)

### 2.10.2 Lyme disease

Lyme disease is characterised by the unique rash left at the site of the tick bite, which gradually expands to a ring around the bite. Beyond this, Lyme disease causes symptoms of fever, chills, headache, fatigue, and muscle and joint pain. The infection can spread to the joints, heart and central nervous system, causing arthritis and other chronic health issues if left untreated. (4)

#### 2.10.2.1 Burden

Lyme disease is found in the forested areas of Asia, central and eastern Europe, and the United States of America. It is the most common tick-borne disease in the northern hemisphere. (4)

#### 2.10.2.2 Transmission

Deer ticks infected with the disease-causing *Borrelia* bacteria transmit Lyme disease to humans and other mammals through their bites. Deer and rodents act as reservoirs for the disease. Deer ticks tend to live in forested and rural areas, putting hikers and campers at higher risk of exposure. (4)

### 2.10.3 Tick-borne relapsing fever

Tick-borne relapsing fever (TBRF) is one of three types of relapsing fever caused by *Borrelia* bacteria. (39) This disease presents with high fever, headache, muscle aches and joint pain. As indicated by its name, this infection has a distinct pattern of fever for about three days, followed by seven days without fever, and followed again by fever for three days. (40)

#### 2.10.3.1 Burden

TBRF is found throughout the Americas, as well as the Mediterranean, central Asia, and Africa. It is commonly associated with forested areas and rodent-infested homes. (41)

#### 2.10.3.2 Transmission

So-called "soft ticks" of the genus *Ornithodoros* act as vectors to transmit *Borrelia* bacteria to humans through their bites. Soft ticks differ from hard ticks as their bites are usually very brief, and they inhabit rodent burrows and feed on rodents rather than grassy areas where they would have to search for prey. The infected ticks often come into contact with humans in homes or cabins that are infested with rodents. Because the bite is painless and these ticks feed at night, most individuals are unaware that they have been bitten, and may be unaware of the rodents' infestation. Ticks remain infectious for their entire life and continue the transmission cycle by infecting rodent offspring. A home usually remains at risk of infection until the rodent infestation is removed. (42)

## 2.10.4 Rickettsia diseases

Rickettsia diseases refers to a group of bacterial infections caused by bacteria of the Rickettsiales order. Such examples of diseases include spotted fever, typhus fever (see section 2.8.1), anaplasmosis and many others. Rickettsia diseases can be difficult to diagnose as they typically present one to two weeks after infection occurs with relatively ambiguous symptoms including fever, headache, fatigue, rash, nausea and vomiting. Some diseases may also present with maculopapular, vesicular or petechial rash, or an eschar at the site of the tick bite, which may help with disease diagnosis. (43)

### 2.10.4.1 Burden

Because Rickettsia diseases encompass several different vector-borne illnesses, there is a risk across the world that at least one form of Rickettsia disease exists in each region. (43) Check local guidelines and resources to find which Rickettsia diseases are present in your region.

### 2.10.4.2 Transmission

Rickettsia diseases are mostly spread by the bite of an infected tick; some may be transmitted by the bite or inoculation of infectious fluids, such as faeces or urine, into the skin from fleas, lice and mites. In rare cases, transmission can occur by contaminated blood products or organ transplant from an infected host. (43)

## 2.10.5 Tick-borne encephalitis

Tick-borne encephalitis (TBE) is an influenza-like disease which in some cases can progress to a severe disease that may result in paralysis or death. Initially, the disease presents with fever, severe headache, nausea, vomiting and back pain; approximately 30% of cases will progress to include the central nervous system, which may lead to paralysis or death. (4)

The disease is caused by a virus of the *Flaviviridae* family. There are three subtypes of TBE — European (also known as Western), Far Eastern and Siberian. (4,44)

### 2.10.5.1 Burden

The burden for TBE is highest in the Russian Federation, particularly in western Siberia. Other areas of burden include central Europe, the Balkans and parts of China. (4,44)

### 2.10.5.2 Transmission

The virus responsible for TBE is typically transmitted through the bites of infected ticks. In some cases, transmission can occur from the consumption of unpasteurised dairy products. (4,44) Human-to-human transmission does not occur. (44)

## 2.10.6 Tularaemia

Tularaemia is a bacterial infection that is often long and debilitating. The disease initially presents with fever, headache, chills and muscle aches, much like influenza. Following this, clinical presentation may change to reflect the form of disease the individual has, which is often based on the route of transmission (45):

- Oropharyngeal form: chronic pharyngitis
- Glandular and ulcero-glandular forms: local lymphadenopathy and skin inoculation ulcers
- Oculo-glandular form: conjunctivitis and local lymphadenopathy
- Pneumonic form: lung infection
- Typhoidal form: severe systemic symptoms

### 2.10.6.1 Burden

Tularaemia is mostly found in the northern hemisphere in forested, temperate and grassland areas. More specifically, it is found in North America, central Asia and throughout the European continent with the exceptions of Iceland, Ireland and the United Kingdom. (45)

### 2.10.6.2 Transmission

Tularaemia is an infection caused by the bacterium *Francisella tularensis*. As indicated above, the five forms of the disease are a result of five various routes of disease transmission, which include the consumption of contaminated food or water, handling of infected wild or domestic animals, bites from blood-feeding vectors such as ticks, aerosol from contaminated dust, and accidental transmission in a laboratory setting. (45)

*Francisella tularensis* is quite adaptable as it is able to survive in cold temperatures for weeks. It can survive in moist environments like swamps, in dry environments like hay, and in decaying animal carcasses. Additionally, its aerosolised form is highly infective. Overall, tularaemia has the potential to become an increasing threat to human health. (45)

## 2.11 Triatomine bugs

### 2.11.1 Chagas disease (American trypanosomiasis)

Chagas disease, more formally known as American trypanosomiasis, is caused by the *Trypanosoma cruzi* parasite transmitted mainly through triatomine bugs. It is a serious disease and is potentially fatal, if not properly detected and treated. The disease exists in two phases. (4,46)

The acute phase lasts for approximately two months after transmission occurs. During this phase, the parasite count is high within the blood, but it presents with mild, unspecific symptoms or may be asymptomatic. In some, a bite may be able to be identified early-on by the recognisable swelling and purple discoloration of one eyelid. Other symptoms that may present include fever, headache, enlarged lymph nodes, muscle aches, pallor, difficulty breathing, and abdominal or chest pain. (4,46)

The chronic phase of the disease is much more serious as the parasite has left the blood to inhabit the cardiac and digestive muscles. This phase of the disease can cause cardiac, digestive and/or neurologic disorders, which can later lead to death. (4,46)

#### 2.11.1.1 Burden

Chagas disease was once confined to the Americas; however, it has unfortunately spread worldwide. Interestingly, this disease which once impacted rural areas now affects many urban settings. It is estimated that nearly seven million people are at risk in the entire region of the Americas, many European countries, and select regions within Africa, the Eastern Mediterranean and the Western Pacific. (46)

#### 2.11.1.2 Transmission

The main route of transmission of Chagas disease is through contact with the faeces and/or urine of triatomine bugs infected with *Trypanosoma cruzi*. These bugs typically bite exposed skin areas, including the face, hence their common nickname of “kissing bug”, and defecate or urinate near the bite. Humans are then partially responsible for transmission as they unknowingly smear the faeces/urine into the bite, or their eyes, mouth or other broken skin, infecting themselves. (4,46)

Triatomine bugs live in the walls and roofs of poorly constructed structures in rural or suburban areas. They usually hide during the day and are active and feed at night. (4,46)

Other routes of transmission include the consumption of food contaminated with *Trypanosoma cruzi*, mother-to-foetus or new-born transmission, accidental transmission through needle stick injuries, and transmission through infected blood products or organ transplant. (4,46)

## 2.12 Tsetse flies

### 2.12.1 Sleeping sickness (African trypanosomiasis)

Sleeping sickness, more formally known as African trypanosomiasis, is both an acute and chronic disease caused by transmission of *Trypanosoma* parasites by tsetse flies. Depending on the parasite involved, the disease can take on two different forms. (47)

The more common form, accounting for 98% of cases, involves the parasite *Trypanosoma brucei gambiense*. This is the chronic form of the disease. However, a person may be unaware they are infected as it can be asymptomatic for months or even years. By the time symptoms appear, including fever, headaches, itching, enlarged lymph nodes and joint pain, the disease is often in its more advanced form and has likely begun to affect the central nervous system. Involvement of the nervous system is considered the second stage of chronic disease and causes changes in behaviour, confusion, poor coordination, sensory disturbances and sleep disturbances. (47)

The second form, accounting for only 2% of cases, involves the parasite *Trypanosoma brucei rhodesiense*. This acute infection presents with symptoms in a few weeks or months and transitions quickly to the second stage involving the nervous system. (47)

Without treatment, sleeping sickness is fatal. Treatment is available for both forms and stages of the disease. (47)

#### 2.12.1.1 Burden

Sleeping sickness is contained within the African region; it is endemic in 36 sub-Saharan African countries. Within this region, the chronic form of the disease is found in the west and central area, while the acute form is found in the east and south. Uganda is unique in that it has both forms of the disease, but in separate zones. (47)

#### 2.12.1.2 Transmission

Transmission of sleeping sickness occurs through the bite of the tsetse fly. These flies are found exclusively in sub-Saharan Africa, yet not every species of the fly transmits the disease. For unknown reasons, there are regions where the fly exists, but the disease does not. Additionally, disease may affect an entire region, with varying intensities in different villages, or just a single community. (47)

Populations most affected by sleeping sickness include rural communities that rely on activities such as agriculture, fishing and hunting. Exposure in these settings is higher as both wild and domestic animals may act as disease reservoirs. (47)

Although most transmission occurs by the bite from a tsetse fly, sleeping sickness has been known to transmit through other mechanisms. These alternative routes include mother-to-foetus transmission, transmission through sexual contact, accidental infection through needle stick injuries, and transmission through other blood-sucking insects. (47)

## 3 Strategies for prevention and control

### 3.1 Vector control

#### 3.1.1 Mosquitoes

Mosquitoes are responsible for many vector-borne illnesses, and some of the deadliest among them. Thus, there is a greater emphasis placed on the primary vector control strategy when it comes to mosquitoes. Vector control consists of intentional actions performed to modify a vector's habitat to make it less habitable, thus reducing vector exposure and reducing risk of infection. Several vector control strategies are undertaken at large-scale, at local, regional or country level. However, individual actions also contribute to the control of vectors in the home or workplace and immediate surroundings, and pharmacists have a role as health professionals to educate their communities to take precautions and adopt individual vector-control methods.

Several forms of chemical insecticides are utilised to interrupt the mosquito life cycle at different stages. Larvicides are applied at mosquito breeding sites, killing the larvae and pupae present in the water, and are more effective than adulticide products. However, adulticides are still utilised. Both larvicides and adulticides are derived from natural sources, such as plants or minerals, as well as synthetic chemicals including classes of carbamates, methoprene, organochlorines, organophosphates and pyrethrins. (48) Insecticides may be used either indoors or outdoors for control.

Insecticides have proven to be effective and generate desirable results, but they have several disadvantages. First, mosquitoes are shown to develop resistance to insecticides when they are used extensively. Because of this, existing forms will not be sufficiently effective in the future, and we have already been forced to explore other insecticide options. Secondly, there are high costs associated with the use of insecticides, which limits its implementation in some regions. Thirdly, many of these chemicals are considered highly toxic and pose a threat to human health. (48)

Many other forms of vector control exist which can be implemented on an individual basis.

A simple form of vector control involves eliminating breeding spaces by removing any free-standing water sources, such as pots, trash and tires. Even small concave objects such as plates or bottle caps can contain enough water for mosquitoes to lay their eggs in, and should be removed, dried or treated with insecticide. Equally important is to appropriately cover water containers used for storage. These methods are important for all mosquito-causing illnesses, but especially those with limited prevention and treatment options, such as Zika. (16)

Lastly, protection from mosquito bites is perhaps the best form of protection. Individuals can utilise several strategies to protect themselves.

Insect repellents do not kill mosquitoes but are effective at repelling mosquitoes to prevent them from biting. (49,50) Active ingredients that may be used include N,N-diethyl-m-toluamide (DEET), icaridin (also known as picaridin or KBR 3023), IR3535, oil of lemon eucalyptus (OLE), p-menthane-3,8-diol (PMD) and 2-undecanone (20). Pharmacists should instruct patients to correctly apply the product by following the directions printed on the product label, and avoid spraying the face, eyes, lips, sunburn or damaged skin. (49)

Mosquito nets are a commonly used physical barrier to prevent mosquitoes from biting while people sleep. Some nets are treated with insecticides and some are not; insecticide-treated nets are more effective, but both forms are recommended for use. (49)

Mosquito coils and aerosol sprays are forms of insecticides in vapour or aerosol form. Both forms act to kill mosquitoes and are considered safe for indoor use. (49)

Protective clothing is one of the easiest methods that can be employed. It is highly recommended that individuals in areas where mosquitoes pose a risk for transmission of vector-borne illnesses wear long trousers, long-sleeved shirts, appropriate foot coverage and socks that they can tuck their trouser legs into. Protective clothing is more effective when thicker materials are worn and when clothing is treated with insect repellents, such as permethrin or etofenprox. (49,50)

#### 3.1.2 Other vectors

Chemical insecticides, many of which are similar to mosquito-formulated products, are utilised for vector control, but their application method may vary. For example, indoor residual spraying is a preferred method

of application for sandflies, but outdoor sprays are preferred for blackflies. Chemicals effective in killing ticks, called acaricides, can be used in livestock production, if needed. (4)

Protection against sandflies, ticks and fleas also includes insect repellents and protection through protective clothing, just like as for mosquitoes. (4,33,51,52) However, for ticks there is an additional recommendation to always check the body for ticks after outdoor activities, looking thoroughly in hairy areas. Tick bites are painless and can often go unnoticed, but it is essential to remove the tick as soon as possible by pulling it straight out. (51) Early detection and removal of ticks from the body is something pharmacists should counsel on, especially if located in vector-borne illness-stricken areas.

Lastly, like for mosquitoes, it is important to drain standing water, which can serve as a habitat for aquatic snails. This may include draining pots, used tires, or other bodies of water, or planting trees to naturally drain aquatic environments where snails may thrive. (4) Protective boots or clothes should be worn when in contact with fresh water in schistosomiasis endemic areas.

## 3.2 Vaccines

Vaccines are a key form of prevention for many diseases. In fact, vaccines have proven to be so effective that several diseases, which used to be common, have now become eradicated (like smallpox) or nearly eradicated, like polio, measles, mumps and diphtheria. (53,54) Vaccines work by mimicking exposure to a disease through the delivery of the antigens that normally cause the disease, which leads to an immune response and subsequent antibody production. The antibodies remain in the body and provide protection from any subsequent attacks by the antigen, resulting in immunity. (53) In addition to personal immunity, mass vaccination within a large portion of a population can lead to herd immunity. Herd immunity occurs when the majority of a community is immune to a disease, either through vaccination or natural exposure and illness, which makes disease spread from person to person more difficult and unlikely. (55)

Vaccines that require a single dose may take anywhere from seven to 21 days for the immune response to occur and immunity to generate. (56) For other vaccines, several doses of the vaccine may be needed to generate immunity, or booster doses may be needed when immunity has been shown to wear off. (57)

While many forms of prevention prove to be effective in decreasing disease burden, vaccines prove to be the most cost-effective method. Unfortunately, vaccines are only available for a few vector-borne illnesses, which are dengue, Japanese encephalitis, malaria, tick-borne encephalitis and yellow fever. (58)

As described below, each vaccine has its own administration schedule, and its own set of criteria to indicate who is suitable for vaccination. Pharmacists can use their skillset to assist in the vaccination process in several ways. The most obvious way for pharmacists to contribute is by administering the vaccine(s), which has increasingly become part of pharmacists' expanded scope of practice. (6) In addition, pharmacists can address patient concerns regarding vaccination, educate patients on the importance of follow-up vaccinations, and counsel on other ways to protect themselves.

### 3.2.1 Dengue

Currently, one vaccine for dengue, Dengvaxia (CYD-TDV), has been licensed and approved in 20 countries, and several others are candidates in development. CYD-TDV is a live recombinant tetravalent dengue vaccine, which is administered as a three-dose series at six-month intervals. (8,59) The vaccine is recommended for those aged 9–45 years who are confirmed as dengue-seropositive. (59,60)

Vaccine efficacy varies among virus serotypes, with higher efficacy against serotypes 3 and 4. Overall vaccine efficacy varies by age and serostatus at baseline. Clinical data found that vaccine efficacy in those who are seropositive (78.2%) is nearly double that of those who are seronegative (38.1%) at baseline. (59) Evidence also found that patients seronegative at baseline are at higher risk of developing severe dengue if infected after receiving the vaccine. (59,60) Given the differences in safety and efficacy based on serostatus, it is recommended for countries considering vaccination to also implement a pre-vaccine screening strategy, in which only confirmed seropositive persons are vaccinated. Implementation of such a strategy will be up to the discretion of each country, based on assessments of sensitivity and specificity of screening, infection and hospitalisation rates, and affordability of the screening strategy and vaccine. (59)

The vaccine is administered subcutaneously.

It is contraindicated in:

- Patients with congenital or acquired immunodeficiency that impairs cell-mediated immunity including immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids;
- People with symptomatic HIV infection;
- Pregnant women; and
- Breastfeeding women. (8)

The vaccine can be offered to asymptomatic HIV-infected individuals with CD4+ counts  $\geq 200$  cells/mm<sup>3</sup> requiring vaccination. (8)

Regarding the vaccine's safety profile, the most frequent adverse reactions are reaction at the injection site (erythema, bruising, swelling, pruritus), headache, myalgia, general malaise, asthenia and fever. (8)

### 3.2.2 Japanese encephalitis

There are several vaccines for Japanese encephalitis that are both safe and effective for disease prevention. The WHO recommends integrating the Japanese encephalitis vaccine into immunisation schedules in areas where the disease is considered to be a public health issue. Furthermore, it is recommended that all people travelling to Japanese encephalitis-endemic areas be vaccinated before travelling. (24) There are four types of vaccines available, each with a unique administration protocol (61):

- Live attenuated vaccine (SA 14-14-2 strain): Administration schedules may vary based on country. In China, the first dose is given subcutaneously at eight months of age, with a booster dose at two years old. Some areas offer an additional booster at six to seven years of age. However, people in some countries achieve adequate protection from a single dose, with no additional booster. Check local protocols if using this vaccine.
- Inactivated, Vero cell-derived, alum-adjuvanted vaccine (SA 14-14-2 strain): Vaccination consists of two intramuscular doses given four weeks apart, with a recommended booster after one year. This vaccine is often given concomitantly with the hepatitis A vaccine, without significant issues in safety or immunogenicity.
- Inactivated, Vero cell-derived vaccines (Beijing-1 strain): Vaccination may be completed as a three-dose series administered at days 0, 7 and 28, or two doses given four weeks apart.
- Live chimeric vaccine (with yellow fever 17D as backbone): A single dose is recommended; the need for a booster is not yet determined.

### 3.2.3 Malaria

Many vaccine candidates are in trial for approval, but only one candidate, RTS,S/ASo1, is being introduced and tried in children for Phase 3 trials. (62) These trials are taking place in seven sub-Saharan African countries (Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique and Tanzania), which is the region where most malaria cases and deaths occur. (21,62) RTS,S/ASo1 is targeted against *Plasmodium falciparum*, the deadliest malarial disease, and has been the only vaccine candidate to significantly reduce malaria cases and life-threatening malaria. (21)

Questions of feasibility come into play as the vaccine series requires four separate vaccinations within 20 months. (21,62) The ability to implement a four-dose vaccine series as well as the risk-benefit analysis will be further evaluated in Phase 4 trials. (62)

### 3.2.4 Tick-borne encephalitis

Vaccines for tick-borne encephalitis are currently approved and available in Europe and Russia, but not yet in other regions. All vaccines currently available are inactivated and provide protection against all three virus subtypes. (63)

The routine vaccination process is lengthy, requiring at least six months to complete. Because of this time requirement, many travellers going to endemic areas prefer to avoid tick bites by other means rather than complete the vaccination series. Given the limited availability of the vaccine, those who are travelling to endemic regions for extended periods of time or those participating in activities such as camping, farming or adventure travel may want to consider being vaccinated in Europe. (63)

### 3.2.5 Yellow fever

There is a single highly effective and safe vaccine available for yellow fever, which provides effective immunity to 80–100 % of those vaccinated after 10 days and an immunity of 99% after 30 days. (8) A single dose of the vaccine, YF-Vax, provides life-long immunity with no need for a booster shot. (13)

Vaccination is a key form of yellow fever prevention, and thus several strategies of vaccination are recommended (13):

- Routine infant immunisation is recommended at age nine months or older.
- Mass vaccinations in at-risk regions is an important measure to increase coverage of the entire population. During an outbreak, it is recommended for at least 80% of the population in high-risk areas to be vaccinated to minimise disease transmission.
- Vaccination of travellers going to endemic areas in Africa or South America is recommended. In some countries, proof of vaccination is required or proof of medical grounds for not receiving the vaccine.

Vaccination against yellow fever has a few exclusions, including (13):

- Infants less than nine months old;
- Pregnant women — except during an outbreak when risk of infection is high;
- Those with severe allergies to egg protein; and
- Those with severe immunodeficiency, including symptomatic HIV/AIDS or other causes or who have a thymus disorder.

However, the vaccine can be offered to individuals with asymptomatic HIV infection with CD4 counts  $\geq 200$  cells/mm<sup>3</sup> who require vaccination.

The yellow fever vaccine is considered safe and beneficial; however, there have been rare reports of serious adverse effects following immunisations (AEFI), which include attacks on the liver, kidneys or nervous system. These effects are very rare, with fewer than 0.5 cases per 10,000 doses in populations where the disease is endemic and in populations not exposed to the virus. However, it is known that the risk for an AEFI is higher in those with immunodeficiency caused by HIV/AIDS or other causes, and those over the age of 60. Because of this, a risk-benefit assessment is recommended before vaccinating anyone over 60 years old. (13)

## 3.3 Preventive medicines

The strategy of administering medicines for the purpose of prevention is complex as it requires cooperation from most individuals within a population. Efficacy of such treatments are only effective when the medicines are properly taken. Thus, pharmacists play a central role in ensuring the safety and effectiveness of prescribed treatments as well as encouraging and optimising patient adherence.

Like vaccines, preventive medicines are a key method of warding off vector-borne illnesses but, unfortunately, they do not exist for all vector-borne illnesses.

### 3.3.1 Lymphatic filariasis

Through preventive chemotherapy, it is possible to reduce, or stop, the spread of lymphatic filariasis. This strategy for elimination requires large-scale administration of the medicine(s), also known as mass drug administration (MDA), and is recommended in at-risk populations. Typically, MDA must be repeated annually for several years to be effective. (11)

The medicines used in MDA work by interrupting the transmission cycle of the parasite to new mosquito hosts. Several MDA regimens are recommended by the WHO (11):

- Albendazole (400mg) alone twice per year for areas in which the disease is co-endemic with loiasis
- Ivermectin (200mcg/kg) with albendazole (400mg) in countries with onchocerciasis
- Diethylcarbamazine citrate (DEC) (6mg/kg) and albendazole (400mg) in countries without onchocerciasis

- New WHO recommended regimen in countries without onchocerciasis: ivermectin (200mcg/kg) together with diethylcarbamazine citrate (DEC) (6mg/kg) and albendazole (400 mg) in certain settings.

Evidence has shown that all three regimens can safely be given in combination, with results in a few weeks, as opposed to years with a two-medicine regimen. (11)

### 3.3.2 Malaria

Chemoprophylaxis for malaria is perhaps the most well-known preventive therapy for vector-borne diseases worldwide as it is widely recommended for travellers. In addition to travellers, the WHO also recommends chemoprophylaxis for infants and children under five years old and mothers in areas of high transmission rates. (21)

Antimalarial regimens used for chemoprophylaxis will vary based on the country and specific characteristics of the patient in need, such as age, weight and travel timeline. (49) Medicines that are commonly used include atovaquone/proguanil (Malarone), chloroquine, doxycycline, mefloquine, primaquine and tafenoquine (Arakoda). (64) Check local guidance for appropriate medication regimens for your patients.

It should be noted that no antimalarial prophylactic regimen can provide complete protection. However, it has been shown that informing a patient of the risk of infection often improves their adherence, therefore improving the efficacy of the regimen. (49)

### 3.3.3 Schistosomiasis

Disease control for schistosomiasis is focused on decreasing the spread of the disease through large-scale administration of preventive chemotherapy. It requires treatment of at-risk populations to occur regularly for several years. The at-risk populations that are most targeted include school-aged children and adults in endemic areas and people with occupations that put them in direct contact with potentially infectious waters, such as fishermen, farmers, irrigation workers and women transporting water for domestic use. (28)

The drug of choice for this large-scale population treatment is praziquantel because it is safe, effective and affordable. Praziquantel is effective against all forms of schistosomiasis. It reduces the risk of severe infection if there is reinfection after treatment, and has the capacity to reverse severe infection in some people. (28)

Control with praziquantel has been successful in many countries across several WHO regions, including Africa, the Americas, the Eastern Mediterranean, and the Western Pacific. (28)

## 3.4 Hygiene practices

Proper hygiene practices play a significant role in overall health as well as preventing the transmission of vector-borne diseases. Infected sources of water may put entire populations at risk through activities of direct contact such as farming, fishing, domestic chores such as clothes washing, children at play, or those using the water for bathing. (28) For those with lymphatic filariasis specifically, it is recommended to wash the affected limbs daily to prevent secondary bacterial infection. (65) Hence, there is a need for access to clean water and sanitation.

Access to clean water is also necessary when it comes to hygiene practices related to food safety. In areas burdened by Chagas disease, strict food preparation, transportation and storage must be practised due to the possibility of food contamination by triatomine bugs. (4)

Hygiene practices also come into play with Zika virus and sleeping sickness, which can be sexually transmitted. (47,16) In both cases, safer sex methods are recommended to prevent disease transmission and adverse outcomes with pregnancy. Proper and consistent use of contraceptives, including both barrier methods, e.g., condoms, and hormonal contraceptives reduce the risk of pregnancy. Emergency contraceptives may also be used when unprotected sex occurs. If a woman is already pregnant in an area with high risk of infection, safer sex practices, including proper and consistent use of condoms, or abstinence are encouraged for the duration of pregnancy. Lastly, if returning from areas of active Zika virus infection transmission, safer sex or abstinence is recommended for six months for men, two months for non-pregnant women, and for the entire duration of pregnancy in expectant mothers. (16)

Pharmacists in areas of active infection should counsel male and female patients on how they can help prevent disease transmission through sexual intercourse. By asking a few questions regarding the individual's or couple's reproductive goals, the pharmacist can educate on practices to fit a patient's lifestyle.

## 3.5 WHO Global Vector Control Response

In 2017, the WHO released guidance to strengthen vector control by means of preventing disease and treating outbreaks. This strategic plan is made up of four initiatives for countries to implement to achieve a holistic vector control programme. (2)

The first of the four initiatives, or pillars of action as deemed in the WHO Global Vector Control Response, is to strengthen inter- and intra-sectoral action and collaboration. This involves shared responsibility between health and non-health sectors by making the agents of these sectors stakeholders. The goal is to increase effective coordination and collaboration between hospitals, ministries, water hygiene and sanitation services, agriculture, infrastructure, etc. In addition to collaboration between these sectors, political commitment and national government support is required. (1)

The second pillar is engagement and mobilisation of communities. The WHO encourages communities to take the opportunity to start and promote dialogue, learn and share knowledge, self-assess, and identify strengths as a community. This approach will build community support and develop a solid foundation to build upon. (1) Community pharmacists and other health workers can greatly contribute to this pillar of action.

Enhanced surveillance and monitoring is the third pillar. This initiative requires implementing and maintaining methods for accurate surveillance, analysis and interpretation of vector data. The goal of this initiative is to identify outbreaks, monitor patterns of disease spread, identify areas of increased transmission risk and move resources to priority regions. (1)

Lastly, the fourth pillar is to scale up and integrate tools and approaches. This initiative involves the expansion of vector control interventions, which include the many preventive tactics already discussed. (1)

The WHO has developed this comprehensive plan for countries to work towards. Successful implementation requires ongoing efforts and individualisation based on each country's unique characteristics, with the hope of reducing the number of disease cases and mortality. (1)

## 4 Treatment

Prevention is the key to disease elimination. With regard to disease treatment, it is the unfortunate reality that many diseases do not have definitive treatments. Symptomatic relief, rehydration, rest and prevention of secondary infections is appropriate for all diseases, but it is currently the only treatment available for chikungunya, dengue, Japanese encephalitis, lymphatic filariasis, Rift Valley fever, sandfly fever, schistosomiasis, tick-borne encephalitis, West Nile virus, yellow fever and Zika. (5,8,11,12,13,14,17,24,27,28, 37)

Medicines and other therapies have been found to treat, and possibly cure, select vector-borne illnesses and have been proven safe and effective. In general, treatments are more effective if given as soon as possible after infection occurs.

Those diseases with treatment options beyond symptomatic relief and supportive care are summarised in Table 1 below. Check local guidelines for additional information on the availability and use of these regimens in your region.

Table 1. Treatment options for vector-borne diseases beyond symptomatic relief and supportive care

Vector-borne disease	Treatment	Reference
Chagas disease	Benznidazole and nifurtimox	(46)
Crimean-Congo haemorrhagic fever	Ribavirin	(38)
Leishmaniasis	Treatment options vary by the type of leishmaniasis, but common agents include liposomal amphotericin B, amphotericin B deoxycholate, miltefosine, pentavalent antimonial (Sb <sup>V</sup> ) therapy, pentamidine, paromomycin, ketoconazole, itraconazole or fluconazole	(66)
Louse-borne relapsing fever	Tetracycline, penicillin G, erythromycin or chloramphenicol	(35)
Lyme disease	Tetracycline antibiotic or derivatives Children can be treated with penicillin	(4)
Malaria	Treatment based on severity and causative agent of the disease: <ul style="list-style-type: none"> <li>Uncomplicated <i>Plasmodium falciparum</i> malaria: artemisinin-based combination therapy (ACT), such as artemether + lumefantrine, artesunate + amodiaquine, artesunate + mefloquine, dihydroartemisinin + piperaquine, or artesunate + sulfadoxine-pyrimethamine</li> <li>Uncomplicated <i>P. vivax</i>, <i>P. ovale</i>, <i>P. malariae</i>, <i>P. knowlesi</i> malaria: treat with ACT, chloroquine, or quinine, plus primaquine</li> <li>Severe malaria: IV or IM artesunate followed by ACT</li> </ul>	(67)
Onchocerciasis	Ivermectin	(30)
Plague	IV antibiotics followed by oral antibiotics as patient improves Recommended antibiotics: gentamicin, fluoroquinolones, streptomycin, chloramphenicol	(68)
Rickettsia diseases	Tetracycline antibiotic; doxycycline most recommended Alternatives: chloramphenicol, azithromycin or rifampicin	(43)
Sleeping sickness	Treatment is based on the stage of the disease:	(47)

Vector-borne disease	Treatment	Reference
	<ul style="list-style-type: none"> <li>• First stage: pentamidine, suramin or fexinidazole</li> <li>• Second stage: melarsoprol, eflornithine, nifurtimox or fexinidazole</li> </ul>	
Tick-borne relapsing fever	Tetracycline antibiotic or derivatives	(4)
Tularaemia	Streptomycin antibiotic	(4)
Tungiasis	<p>Treatment may be personalised and includes options of:</p> <ul style="list-style-type: none"> <li>• Extraction of fleas using sterile forceps or needles</li> <li>• Application of antiparasitic medications (ivermectin, metrifonate, thiabendazole)</li> <li>• Suffocation of fleas by application of wax or jelly</li> <li>• Localised freezing of lesions by cryotherapy</li> </ul>	(33)
Typhus	Doxycycline	(69)

## 5 Pharmacist intervention

Pharmacists have a unique role in healthcare and in the community as the most accessible healthcare professionals. They often develop relationships of trust with their patients, allowing them to engage in regular and meaningful conversations. Given their proximity to their communities, they serve as trusted educators.

A summary reference guide on vector-borne diseases, the vectors that transmit them, preventive measures, treatment options and vaccines is provided in Appendix 1.

### 5.1 Educating on prevention methods

Given the importance of vector control and protection from vectors, pharmacists should have a general understanding of prevention techniques that may be appropriate in their region and how to employ these techniques.

In regions where mosquitoes, for example, are a threatening vector, pharmacists should be aware of methods to help protect their community members and where to find the materials and/or resources to do so. Such methods would include the use of insecticide sprays, vaporisers or aerosols indoors, use of mosquito nets, and proper skin coverage to prevent bites. Furthermore, pharmacists can counsel on the proper application of mosquito repellents, making sure patients know to avoid the eyes, lips, and broken, damaged or sunburned skin (see sections below on advising on the use of repellents and on compounding mosquito repellents).

Pharmacists should encourage protective clothing including long sleeve shirts, long trousers, long socks and adequate foot coverage. (4)

Beyond personal protection from bites, pharmacists can advise patients to make their entire home as uninhabitable to vectors as possible by use of indoor-approved insecticides, use of properly fitting windows and screens, and drainage or coverage of water sources. (16)

Although we largely think of disease transmission occurring through vectors, in the case of Zika virus fever and sleeping sickness transmission can also occur through sexual intercourse. Community members may not be aware of this mode of transmission; thus, this gap in knowledge provides potential for pharmacist intervention. After interviewing an individual or couple and assessing their reproductive goals, a pharmacist can provide advice on the safer sex practices that would be the best fit for the individual(s). This may mean delaying pregnancy, use of contraceptives or abstinence. (16)

Given the variety of techniques available for protection, pharmacists should work with individuals to find prevention techniques that fit their lifestyle. Through pharmacist intervention, there is knowledge sharing and an increase in dialogue on the topic of vector-borne illnesses. If nothing else, a pharmacist is contributing to community support through these actions.

### 5.2 Advising on the use of repellents

Community pharmacists should advise every patient acquiring a repellent on the correct way to use it in order to achieve the desired effectiveness and safety, as well as their rational use.

Insect repellents are substances that, because of their smell or nature, offer protection against insect bites. They are applied on exposed areas of the body by means of different systems: lotions, creams, vaporisers, roll-ons, sticks, gels or impregnated wipes, by means of which the active principles are deposited on the skin. (8)

They generally ensure protection for four to eight hours after use. They do not kill the insect, but they keep it away from the area where the insect repellent has been applied. There are different types of insect repellents on the market. One of the most widely used is N,N-diethyl-m-toluamide (DEET). The concentration of DEET may vary from one product to another and in different forms of presentation. The duration of protection depends on the concentration. A product with 10% DEET protects for approximately two to three hours, whereas 25% DEET offers an average protection of six hours. (8)

Citronella is less effective than DEET and in situations of severe outbreaks, its use is discouraged. However, in a context not associated with a health contingency due to an outbreak of diseases, citronella is the choice for young children (under two years of age) and in pregnant women due to its low toxicity and high tolerance. Its

action consists of masking scents that are attractive to insects. It drives insects away, but it neither kills them nor poisons the environment. (8)

For optimal application of repellents, the biting activities of different mosquito species must be taken into account, and the recommendations for the times when they should be used should be adapted accordingly. For example, *Aedes aegypti* mostly bite in the morning, several hours after dawn and in the afternoon, hours before dark. However, it sometimes feeds during the day in indoor areas or in nearby areas protected from direct sunlight. Sometimes, it feeds indoors during the night if lights are on. (8)

It is important to take into account the following recommendations to avoid the appearance of adverse effects caused by the use of repellents:

- Check the product label to find information on how much DEET the repellent contains. Use products with concentrations that do not exceed 30%.
- Always follow the instructions on the product label.
- Do not apply the repellent under clothing.
- Do not apply the repellent on cuts, wounds or irritated skin.
- Do not spray products with DEET in closed areas.
- Do not spray products with DEET directly to the face. Spray the hands and then rub them carefully over the face, avoiding the eyes and mouth.
- Protect a baby's crib or stroller with mosquito nets when outside. When repellent is used on a child, the adult should apply it on their own hands and then spread it on the child's skin. Avoid applying it on the eyes and mouth of the child and use carefully around their ears.
- Do not apply the repellent on children's hands (children could put their hands in their mouths).
- Do not allow young children to apply the repellent themselves. Do not use repellents associated with sunscreens in the same formulation. (8)

The use of the following items or products is discouraged:

- Bracelets that contain chemical repellents;
- Garlic or vitamin B1 taken by mouth;
- Ultrasonic devices that issue sound waves designed to repel insects;
- Houses for birds or bats; and
- Garden devices that electrocute insects (in fact, they can attract insects to your garden). (8)

## 5.3 Compounding mosquito repellents

In areas or situations where there is a shortage or lack of access to industrially manufactured mosquito repellents, it may be necessary for pharmacists to compound such products for use in the community, provided that the appropriate authorisations have been obtained.

The Pharmacists Association of the Province of Buenos Aires (Argentina) produced technical guidance for the compounding of repellents. It is summarised in Table 2. (8)

Table 2. Guidance for compounding mosquito repellents

Citronella cream	Citronella lotion	N,N-diethyl-m-toluamide (DEET) lotion	N,N-diethyl-m-toluamide (DEET) gel
<p><b>Ingredients:</b></p> <ul style="list-style-type: none"> <li>- Essence of citronella q.s.</li> <li>- Non-ionic hydrophilic base cream qsp 10mg</li> </ul> <p><b>Concentrations:</b></p> <p>1.5%, 3.0% and 5.0%</p> <p><b>Preparation:</b></p> <p>In a suitable container weigh the entire base cream and add citronella in portions and with homogenisation. Pack and label</p> <p><b>Quality assurance:</b></p> <ul style="list-style-type: none"> <li>- Aspect: homogeneous white or lightly yellowish cream.</li> <li>- 10% pH in water: between 4 and 7</li> <li>- Content control and sealing of the closure.</li> </ul> <p><b>Storage:</b></p> <p>At a temperature not exceeding 40°C</p> <p><b>Expiry:</b></p> <p>3 months</p>	<p><b>Ingredients:</b></p> <ul style="list-style-type: none"> <li>- Essence of citronella q.s</li> <li>- Vehicle with enough quantity (qsp) for 1,000ml: isopropyl myristate 5g, polyethylene glycol 400 15g, isopropanol qsp 100ml</li> </ul> <p><b>Concentrations:</b></p> <p>1.5%, 3.0% and 5.0%</p> <p><b>Preparation:</b></p> <p>In a suitable container weigh the citronella and add the vehicle and shake until you have a clear solution, bring to volume and filter if necessary. Pack and label. It can be used as a spray lotion.</p> <p><b>Quality assurance:</b></p> <ul style="list-style-type: none"> <li>- Aspect: colourless or slightly yellowish liquid, free of foreign elements</li> <li>- Content control and sealing of the closure.</li> </ul> <p><b>Storage:</b></p> <p>At a temperature not exceeding 40°C</p> <p><b>Expiry:</b></p> <p>3 months.</p>	<p><b>Ingredients:</b></p> <ul style="list-style-type: none"> <li>- DEET q.s.</li> <li>- Glycerine 20g</li> <li>- Ethanol 70° qsp 100g</li> </ul> <p><b>Concentration:</b></p> <p>Up to 25%w/w</p> <p><b>Preparation:</b></p> <p>In a suitable container weigh the DEET and the glycerine. Dissolve with ethanol 70°. Glycerine and DEET are not soluble between them, but alcohol solubilises both. Filter if necessary. Pack and label. A plastic container of medium or high-density polyethylene is recommended due to the solvent effect of DEET.</p> <p><b>Quality assurance:</b></p> <ul style="list-style-type: none"> <li>- Aspect: colourless or slightly yellowish liquid, free of foreign elements</li> <li>- Content control and sealing of the closure.</li> </ul> <p><b>Storage:</b></p> <p>At a temperature not exceeding 40°C</p> <p><b>Expiry:</b></p> <p>12 months</p>	<p><b>Ingredients:</b></p> <ul style="list-style-type: none"> <li>- DEET q.s.</li> <li>- Carbomer 0.5g</li> <li>- Glycerine 20g</li> <li>- Triethanolamide (TEA) 50% q.s.</li> <li>- Ethanol 70° qsp 100g</li> </ul> <p><b>Concentrations:</b></p> <p>Up to 25%w/w</p> <p><b>Preparation:</b></p> <p>A. In a suitable container weigh the carbomer and glycerine. Homogenise and leave until the next day. A very viscous homogeneous material is left.</p> <p>B. Place the DEET in another container and mix it with 50g of 70° ethanol. Incorporate B over A with agitation. A slightly viscous, homogeneous liquid is obtained. Neutralise with 50% TEA by dripping and stirring until pH 6-7. Bring weight with 70° ethanol and homogenise. Pack and label. A plastic container of medium or high-density polyethylene is recommended due to the solvent effect of DEET.</p> <p><b>Quality assurance:</b></p> <ul style="list-style-type: none"> <li>- Aspect: homogeneous white or lightly yellowish cream.</li> <li>- 10% pH in water: between 4 and 7</li> <li>- Content control and sealing of the closure.</li> </ul> <p><b>Storage:</b></p> <p>At a temperature not exceeding 40°C</p> <p><b>Expiry:</b></p> <p>12 months</p>

## 5.4 Improving vaccination coverage

Pharmacists can contribute to improving vaccination coverage in several ways, including raising awareness about vaccines, addressing concerns through evidence-based advice, advocating for vaccination in their communities or administering vaccines, for example. They can make every contact count for promoting vaccination to people visiting the pharmacy.

A pharmacist's work begins by reviewing a patient's medical history through patient profiles, pre-vaccine paperwork and information reported through vaccine screening tools. Through these various channels of information, a pharmacist obtains a full picture of the patient's medical history and can often gauge the patient's health literacy. For example, if a patient is unable to fully complete pre-vaccine paperwork or cannot inform about the previous vaccines they received, it may be an indication that their health literacy is not well developed, and they may require more counselling time. In addition, patient history and immunisation screenings provide the pharmacist with enough information to decide whether a patient qualifies for a vaccine. Pharmacists can also explore other routine vaccines that may be missing. (70)

After gathering history and screening, a pharmacist should provide information about the vaccine and address any concerns the patient has. Patient counselling is especially important as patients can be hesitant to receive vaccines. It is the responsibility of the pharmacist to counsel on both the benefits and risks of the vaccine. Additionally, pharmacists should inform patients about the immunisation schedule, if applicable.

Where authorised to do so, pharmacists can then assist by administering the vaccine using the appropriate technique and ensuring the necessary monitoring and follow-up.

Lastly, pharmacists are responsible for documenting the vaccination in an appropriate manner, which may include the patient's electronic health record or an immunisation database, if available, or on a paper vaccination record. Documentation has the lasting benefit of providing more information to the pharmacist or other another health professional that provides the next immunisation. (70)

For details of pharmacists' role and advice on specific vaccines, see chapter 3.2.

## 5.5 Optimising adherence to treatments

Adherence to medication is an essential factor in effective treatments and is associated with improved patient outcomes, lower morbidity and mortality, and fewer hospitalisations. (49) There are many factors that contribute to adherence, making it more intricate than it seems. Health literacy, cost, transportation and other limitations can affect a patient's understanding of the medicine or their access to the medicine. Lack of adherence may not be an intentional choice, but a result of inadequate access to medicines, insurance coverage or funds, or unreliable transportation to the pharmacy. In situations like these, the pharmacist should search for possible solutions, such as identifying coupons or medication assistance programmes, sorting through insurance issues, dispensing a smaller quantity of product to help the patient meet costs, or providing medication delivery options.

If adherence issues are not related to cost or transportation, they may be related to the patient's health literacy and understanding of the medical issue and treatment at hand. In this case, it is the responsibility of the pharmacist to teach the patient about their medication regimen, including the medicines(s) prescribed, how they work, how and when to take them, and the possible side effects. Pharmacists should also take the time to address any specific questions or concerns from the patient. Another form of counselling that can have positive impacts on adherence is informing patients of the consequences of non-adherence.

A pharmacist's work does not have to end when medicines are dispensed. They also have the opportunity to follow up the patient and remind them of the importance of adherence via phone call or other communication channels, and at each pharmacy visit.

## 5.6 Reducing social stigma

Unfortunately, vector-borne illnesses can impact on a person's life beyond the initial infection. Many diseases pose the risk of becoming chronic and debilitating, which can lead to long-term disability. Some disabilities are more noticeable than others because of the effects on the body. For example, lymphatic filariasis and

leishmaniasis leave behind disfigured limbs and scars, respectively, which tend to be more associated with social stigma. (71)

Pharmacists can help reduce social stigma in several ways. First, pharmacists should offer their help and services to all patients, highlighting their availability to answer their concerns. Secondly, they should provide patients, especially those facing stigma, with empathy. Finally, pharmacists must treat patients with disabilities the same as any other patient. (72) Through these actions, pharmacists can improve a patient's treatment and overall mental health and well-being.

## 6 Disease burden per region

### 6.1 Africa

The burden of vector-borne diseases in the African region has been regarded as troublingly high by the WHO Regional Office for Africa, notably with malaria, yellow fever, chikungunya, dengue, and schistosomiasis significantly contributing to the global disease burden. Leishmaniasis, lymphatic filariasis, and Chagas disease have also been noted as significant contributors. (73)

It is estimated that the African region accounts for over 90% of malaria cases and malaria-associated deaths in the world, highlighting the extent of the burden within Africa, particularly in the sub-Saharan region. (21) This has been attributed to the mosquito vectors with increased survival as well as an increasing habit of biting humans rather than animals. (21) Vector control strategies used include insecticide-treated mosquito nets, indoor residual spraying, malaria prophylaxis for at-risk populations, and indoor larval source management. (21,73)

Moreover, the burden of yellow fever in the region is estimated to be up to 170,000 severe cases with up to 60,000 deaths each year. (74) A widespread campaign called the Yellow Fever Initiative was launched in 2006, and, to date, over 105 million individuals have been effectively vaccinated against the disease. (74) Dengue has also been reported as a significant vector-borne disease, spreading widely compared with previous years. Regarding schistosomiasis, 90% of cases are estimated to be found in the African region. (75)

Integrated vector management strategies have been put into place within the region, calling upon intra- and inter-sectoral approaches to developing optimal, efficient and effective vector control strategies on different levels, including policy-making, capacity building and on-the-ground initiatives. (73) At the WHO Regional Committee for Africa, a framework was recently endorsed by nations of the region as a collective push to halt the spread of vector-borne diseases in Africa. (76)

### 6.2 Eastern Mediterranean

Countries and territories in the Eastern Mediterranean region contribute 11% to the global burden of vector-borne diseases. (77) Climate imbalances, man-made changes to land and to the environment, and population movement shifts, especially in conflict situations, have been considered as contributing factors to the spread of the diseases. (77)

Out of all mosquito-borne diseases in the region, dengue is the most prevalent, with incident and epidemic reports dating back to the late 1990s. (78) A vaccine for each of the four dengue serotypes is available, although with varying levels of effectiveness. (78) Regarding malaria, different types of parasites causing the disease have been found across three designated eco-epidemiological zones within the region, with over three million cases reported in 2011. (79) Five countries (Afghanistan, Pakistan, South Sudan, Sudan and Yemen) made up more than 98% of confirmed cases. (79) Outbreaks of chikungunya have also been reported over the previous years, with tens of thousands of cases reported in nations, such as Pakistan, Saudi Arabia, Sudan and Yemen. (80) The different forms of leishmaniasis have also been reported as being endemic in several countries in the region. (81) Schistosomiasis, lymphatic filariasis, Crimean-Congo haemorrhagic fever, onchocerciasis, yellow fever, plague, relapsing fever, West Nile virus, and Rift Valley fever have also been reported in the region. (81)

The WHO Eastern Mediterranean Regional Office adopted a resolution in 2003 endorsing integrated vector management in the region by encouraging member states to allocate the necessary resources, foster intersectoral efforts, and develop nationwide policies and strategies to control vector-borne diseases. (77) Multiple member states reported progress in the objectives illustrated in the resolution. They revealed intersectoral work among ministries and institutions within their own borders, and described the methods used to limit the spread of vector-borne diseases, such as the implementation of long-lasting insecticidal nets and the proper management of insecticide resistance. (77) The continued efforts of member states within the region demonstrate that the control of vector-borne diseases remains a collective priority for the region.

### 6.3 Europe

The vector-borne illness burden in Europe is less severe relative to that in other WHO Regions. Several diseases have been detected within the region, but many are well-controlled. Because Europe has populations of

mosquitoes, wild rodents, sandflies and ticks, along with animals which help maintain the transmission cycles, the area is subject to vector-borne illnesses from these vectors, which include Chagas disease, chikungunya, Crimean-Congo haemorrhagic fever, dengue, leishmaniasis, Lyme disease, malaria, plague, tick-borne encephalitis, and West Nile fever. (82,4)

Mosquito-borne diseases are present in Europe and vector range may be expanding further into the region due to climate change. West Nile fever and chikungunya have been linked to outbreaks in 2000 and 2007, respectively, with the 2007 outbreak marking the first appearance of chikungunya in the continent. (83) Although the occurrence remains low, West Nile fever numbers increased between 2000 and 2010. (82)

Other mosquito-borne illnesses that have impacted Europe include dengue and malaria. Due to urbanisation and improved water safety, dengue infection is nearly negligible. (83) Increased efforts and support from the WHO European Regional Office led the region to reach its goal in 2015 of having zero occurrences of locally acquired indigenous cases of dengue infection. (84) Incidences of imported cases for both malaria and dengue are relatively low (82,84); however, given the risk of disease reintroduction to the region, efforts are being made to inform travellers of the risk and precautions they should take, and to screen and treat migrants, refugees, foreign students and travellers to Europe. (84)

Sandflies inhabit the region and may be expanding their range due to climate change. Sandfly distribution is largely in the southern half of the continent, affecting Spain, Portugal, France, Italy, Greece, Romania, Turkey and other countries. (83,85) Unfortunately, leishmaniasis is considered endemic in many of these countries, with poor control and under-reporting. (82) Leishmaniasis is neglected; however, the WHO supports leishmaniasis control through existing programmes and the development of reliable surveillance, case management services, and an outbreak response. (86)

Climate change is also influencing and expanding the range of habitats for ticks, which means an expansion of tick-borne diseases across the continent. These include tick-borne encephalitis, Lyme disease, Crimean-Congo haemorrhagic fever and Rickettsia diseases. (83) Tick-borne encephalitis has approximately 5,000–12,000 cases reported annually throughout Europe. While there is still room for better control, tick bite protection and vaccination are effective preventive measures. (82) Lyme disease, on the other hand, is the most prevalent vector-borne illness in Europe, and currently lacks an effective vaccine. Currently, research is aimed at understanding and predicting how socioeconomic change, climate change, and ecosystem change affect infected tick distribution, and therefore the risk of infection. (87) Lastly, given the vast spread of ticks across the continent, Crimean-Congo haemorrhagic fever and Rickettsia diseases have seen outbreaks in the past two decades, which may be linked to times of favourable climate conditions. Control for these diseases depends on prevention of tick bites and disease diagnosis and treatment. (83,88)

Europe hosts a variety of vector-borne diseases. However European efforts in disease prevention, detection and treatment have made great strides towards vector-borne disease control with elimination in some cases.

## 6.4 Pan American region

With the objective of strengthening regional and national capacity for the prevention and control of key vectors, the Pan American Health Organization (PAHO)/WHO is implementing the Action Plan on Entomology and Vector Control 2018–2023 in the region, in order to contribute to the reduction of the spread of vector-borne diseases. It is also developing the Regional Programme on Neglected Infectious Diseases that seeks the elimination of more than 30 of these diseases and related conditions by 2030. (92,93,94)

Vector-borne diseases transmitted by the *Aedes* mosquito represent a significant burden in the Americas. Dengue is the most widespread vector-borne viral infection in the world, but the highest number of cases is reported in the region of the Americas, making it a public health priority. However, the region also has the lowest dengue fatality rate compared with other WHO regions. The general trend of dengue indicates a steady increase in the number of cases and populations living in risk areas. (95) Furthermore, chikungunya, classified as a neglected disease in the Americas, has also been present in 48 countries and territories since the end of 2013. Seventy-three deaths were reported, all in Brazil, out of a total of 178,000 cases across the region.

Yellow fever has been present in 13 countries and territories in the Americas. In 2019, cases were reported in Brazil (82%), Peru (15%) and Bolivia (3%) whereas, during 2018, confirmed cases were reported in Bolivia, Brazil, Colombia, French Guyana and Peru. In 2020, an outbreak was reported in French Guyana. (96,97,98,99)

Zika virus infection has been reported in 47 countries and territories in the Americas. (100) Since the end of 2014, it has spread at an alarming rate throughout Latin America and the Caribbean, reaching the United States in 2016. The impact of Zika virus infection is disproportionate in the poorest countries of the region, as well as on the most disadvantaged and vulnerable groups, especially poor women in peri-urban communities. Rapid

urbanisation, accompanied by poor health conditions and poor infrastructure in some areas, provide favourable conditions for the *Aedes aegypti* mosquito to multiply and thus increase the risk of Zika virus transmission. (19)

Classified as a neglected disease in the Americas, malaria has been present in 21 countries and territories in the region. On one hand, from 2005 to 2014, the region showed a sustained trend towards a reduction in malaria, but since 2015 it has experienced an increase due to the rise in cases in Venezuela in the past three years, the rise in transmission in endemic areas, and outbreaks in countries that were making progress towards elimination. On the other hand, there was significant reduction in cases in other countries and territories. (101) In 2018, the Americas region reported 929,000 cases of malaria, of which 75% (700,000) were caused by the *Plasmodium vivax* parasite. (101)

Chagas disease is the most prevalent tropical communicable disease in Latin America. It is classified as neglected and is endemic in 21 countries. Some 70 million people currently live in areas exposed to the vector and are at risk of contracting the disease. The disease affects approximately six million people, with 30,000 new cases and 12,000 deaths being reported each year. (102)

Lymphatic filariasis, also classified as a neglected disease in the Americas, is endemic in four countries: Brazil, Dominican Republic, Guyana and Haiti. (103) It is estimated that 13.4 million people are at risk of infection, 90% of them in Haiti. (103) The PAHO/WHO considers this disease to be potentially eradicable and has therefore adopted measures to eliminate it as a public health problem in the Americas.

Schistosomiasis, a disease that is also classified as neglected in the Americas, is endemic in 10 countries and territories. (104,105) Approximately 25 million people are at risk of infection. The Americas could be the first WHO region to achieve interruption of disease transmission. (104,105)

Cases of other vector-borne diseases such as West Nile virus, onchocerciasis, plague, leishmaniasis, Lyme disease and tularaemia have been reported in the Americas in recent years (92). Efforts are being made both nationally and internationally to halt their spread and provide the necessary treatment.

## 6.5 South-East Asia

The WHO South-East Asia Region (SEAR) has specified malaria, dengue, Japanese encephalitis, chikungunya, lymphatic filariasis and leishmaniasis (kala-azar) as the vector-borne diseases of critical public health importance in the region. (89) At least one of these diseases can be found in all member states within the region at any time. (89) Other diseases, such as tick-borne diseases and Crimean-Congo haemorrhagic fever have also been reported. (90)

The region ranks second among all WHO regions with the greatest burden of malaria, reporting 3.4% of the global burden of 228 million cases in 2018. However, the South-East Asia region continued to see its malaria incidence rate fall – from 17 cases of the disease per 1,000 population at risk in 2010 to five cases in 2018 (a 70% decrease). (91) Nevertheless, the emergence of insecticide and drug resistance remains particularly concerning with regard to malaria prevention and treatment.

The SEAR contributes more than half of the global burden of dengue cases, with outbreaks being reported in various nations and with peak occurrences being associated with onset of monsoon storms. (89) To date, source reduction through clean-up programmes and insecticide use has been the primary method of dengue control, although the absence of an effective vaccine as well as a lack of specific treatments represent a significant challenge to combating dengue. (89)

Regarding Japanese encephalitis, close to 70,000 cases are reported each year. (89) Moreover, outbreaks of chikungunya have been reported in multiple nations, with close to two million cases having been reported in the region since 2005. (89) Lymphatic filariasis is also a vector-borne disease of significant concern as the region contributes more than half of the global disease burden. (89) Bangladesh, India and Nepal are among the six countries in which 90% of the cases of visceral leishmaniasis are found worldwide. (89) Resistance to medicines used to treat leishmaniasis has also been reported. (89)

Outbreaks of several of these diseases are thought to be associated with increasing population movement, trade globalisation and urbanisation without sufficient vector control and reduction strategies. (90) Integrated vector management, inter-country cooperation, and increased surveillance, in addition to community involvement, have been cited by the SEAR office in the fight against vector-borne diseases. (89,90)

## 6.6 Western Pacific

The incidence of vector-borne disease in the Western Pacific region has increased over the past few years, touching the countries, territories and island nations across the region. (106) Data from the WHO Western Pacific Regional Office (WPRO) show that efforts continue to be made to prevent and treat these diseases.

There are more than 700 million individuals in the region considered at risk of developing malaria, with Papua New Guinea, Cambodia, and Solomon Islands accounting for more than 90% of more than 350,000 confirmed cases in 2015. (107) Other countries and territories have reported a decrease in number of cases, and deaths due to malaria in the region are also decreasing. (107) Surveillance data show that malaria disproportionately affects ethnic minorities, migrant workers and other mobile populations. (107) Multidrug resistance as well as challenges pertaining to the financing and capacity of health systems have also been regarded as barriers to overcome in appropriately managing malaria. (107) A regional action framework was endorsed with the WPRO with the objective of eliminating malaria in the region by 2030. (107)

Regarding dengue, the total number of cases has more than doubled in recent years, with reports of more than 375,000 cases in the region in 2016 (10), corresponding to approximately 75% of all dengue cases in the world. (10) Despite the increase in cases, the mortality rates for dengue have decreased by 50%. (108) Following the regional strategic plan from previous years, a regional action plan was adopted in 2016 to reduce dengue-associated mortality, increase research and strengthen evidence on the disease, and ultimately decrease the disease burden within the region. (108)

Furthermore, outbreaks of chikungunya and Zika virus have also been reported in recent years, and Japanese encephalitis remains a disease of concern in the region. (106)

The WPRO has officially advocated for integrated vector management in the fight against vector-borne diseases. (109) By providing country-level support to assess vector control needs and develop the necessary strategies to overcome them, the region is utilising a collective approach to manage these diseases. (109)

## 7 Conclusion

Vector-borne diseases remain a major public health concern given their vast geographical burden and the distressing illnesses they inflict. For all health professions, it is imperative to consider the global impact of vector borne diseases, and to contribute to their control and management. Vector control techniques require commitment and engagement from many parties but remain the most effective method for preventing disease spread. For those diseases for which a vaccine is available, health professions, including pharmacists, have a role to play in improving vaccination coverage at population level. Also, in parallel with large-scale vector-control and vaccination strategies, individual actions and attitudes can go a long way to protect individuals, families and communities against the impact of such diseases.

We hope this handbook has provided an overview of vector-borne diseases and will encourage pharmacists to take a more active role in their prevention and management in the community. By understanding these diseases and the prevention and treatment methods available, pharmacists can work directly with community members to increase their safety and well-being.

With the expansion of several vectors and the diseases they carry due to climate change, population movements and several other factors, pharmacists in all countries are called to be knowledgeable and proactive in advising people who live in endemic areas, as well as travellers, on how to protect themselves and others from these diseases.

Pharmacists have vital roles in patient and community education, disease prevention and vector control, vaccine advocacy and administration, compounding and advising on the use of repellents, optimising the use of medicines and reducing the social stigma often associated with vector-borne diseases. Additionally, pharmacists provide a reliable support system and are making an important contribution to mitigating the impact of such diseases and to their eventual eradication around the world.

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## Appendix 1. Summary reference guide on vector-borne diseases

Legend: AFR, African Region; EMR, Eastern Mediterranean Region; PAR, Pan American Region; EUR, European Region; SEAR, South-East Asian Region; WPR, Western Pacific Region;

Vector-borne disease	Vector	WHO Regions in which it is endemic	Key preventive measures							
			Vaccine?	Preventive medicines?	Insecticides? Pesticides? Acaricides?	Repellents?	Mosquito nets?	Protective clothing?	Hygiene practices?	Treatment?
Chagas disease	Triatomine bugs	AFR, EMR, EUR, PAR, WPR							Yes	Yes
Chikungunya	Mosquitoes ( <i>Aedes</i> )	AFR, EMR, PAR, SEAR, WPR			Yes	Yes	Yes	Yes		
Crimean-Congo haemorrhagic fever	Ticks	AFR, EMR, EUR, PAR, SEAR, WPR			Yes	Yes		Yes		Yes
Dengue	Mosquitoes ( <i>Aedes</i> )	AFR, EMR, EUR, PAR, SEAR, WPR	Yes		Yes	Yes	Yes	Yes		
Japanese encephalitis	Mosquitoes ( <i>Culex</i> )	SEAR, WPR	Yes		Yes	Yes	Yes	Yes		
Leishmaniasis	Sandflies	AFR, EMR, EUR, PAR, SEAR			Yes	Yes		Yes		Yes
Loiasis (African eye worm)	Deerflies	AFR		Yes	Yes	Yes		Yes		Yes
Louse-borne relapsing fever	Lice	EMR								Yes
Lyme disease	Ticks	EUR, PAR, SEAR, WPR			Yes	Yes		Yes		Yes
Lymphatic filariasis	Mosquitoes ( <i>Aedes</i> , <i>Anopheles</i> , <i>Culex</i> )	AFR, PAR, SEAR, WPR		Yes	Yes	Yes	Yes	Yes	Yes	
Malaria	Mosquitoes ( <i>Anopheles</i> )	AFR, EMR, EUR, PAR, SEAR, WPR	Yes	Yes	Yes	Yes	Yes	Yes		Yes
Onchocerciasis	Blackflies	AFR, EMR, PAR			Yes					Yes

Vector-borne disease	Vector	WHO Regions in which it is endemic	Key preventive measures							
			Vaccine?	Preventive medicines?	Insecticides? Pesticides? Acaricides?	Repellents?	Mosquito nets?	Protective clothing?	Hygiene practices?	Treatment?
Plague	Fleas (transmitted by rats)	AFR, EMR, EUR, PAR, SEAR, WPR				Yes		Yes		Yes
Rickettsia diseases	Ticks	AFR, EMR, EUR, PAR, SEAR, WPR			Yes	Yes		Yes		Yes
Rift Valley fever	Mosquitoes ( <i>Aedes</i> )	AFR, EMR			Yes	Yes	Yes	Yes		
Sand-fly fever	Sandflies	AFR, EMR, SEAR			Yes	Yes		Yes		
Schistosomiasis	Aquatic snails	AFR		Yes						
Sleeping sickness	Tsetse flies	AFR							Yes	Yes
Tick-borne encephalitis	Ticks	EUR, WPR	Yes		Yes	Yes		Yes		
Tick-borne relapsing fever	Ticks	AFR, EMR, PAR, SEAR			Yes	Yes		Yes		Yes
Tularaemia	Ticks	EUR, PAR, SEAR			Yes	Yes		Yes		Yes
Tungiasis	Fleas	AFR, PAR						Yes		Yes
Typhus	Lice	AFR, PAR, SEAR								Yes
West Nile virus	Mosquitoes ( <i>Culex</i> )	AFR, EMR, EUR, PAR, WPR			Yes	Yes	Yes	Yes		
Yellow fever	Mosquitoes ( <i>Aedes</i> )	AFR, PAR	Yes		Yes	Yes	Yes	Yes		
Zika	Mosquitoes ( <i>Aedes</i> )	AFR, PAR, SEAR, WPR			Yes	Yes	Yes	Yes	Yes	

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