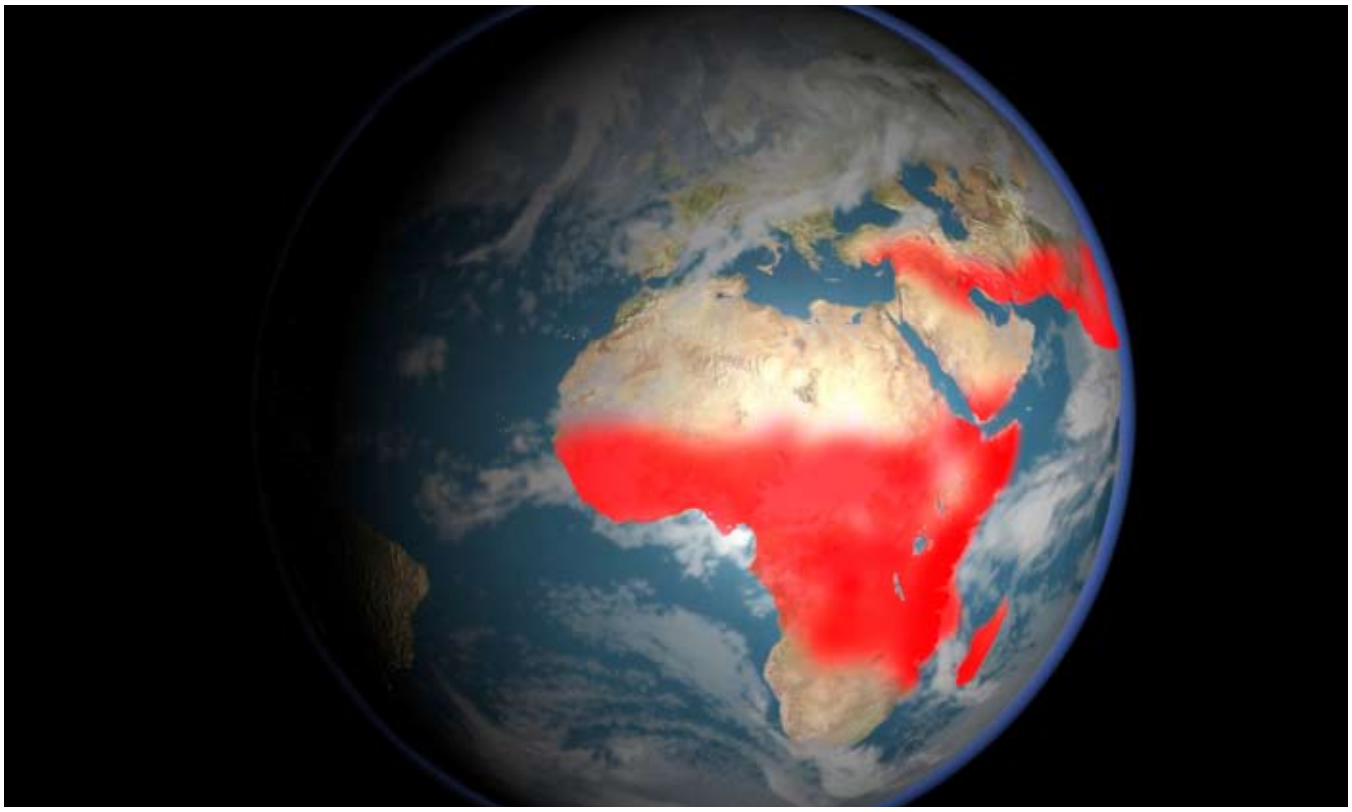
Vector-Borne Disease
Primary Examples



INTRODUCTION

Vector-borne infections, diseases caused by pathogens transmitted by insects and ticks, have long impacted human affairs. Alexander the Great, conqueror of many nations, was vanquished by the bite of a tiny mosquito bearing malaria parasites in the marshes of what is now called Iraq. The Black Death, decimator of Europe, killer of tens of millions worldwide is the work of a tiny flea vectoring the bacilli that cause bubonic plague from rats to people. Vector-borne infections remain influential to this day, filling the hospitals of sub-Saharan Africa with malaria victims, suppressing the economies of nations and interrupting industrial operations where it remains endemic. Some less common agents cause blindness and horrible disfigurement. Together they form a fearsome array of potential threats to the health and livelihood of those who visit, work, or live in the tropics where they exert their greatest impact.

Companies working in emerging markets face a unique set of challenges. One such challenge is keeping employees and contractors safe from life-threatening vector-borne diseases. Business leaders and managers are often instinctively aware of these threats but uncertain of the means and measures that must be taken to assess the risks and impact of vector-borne diseases on the workforce. An integrated vector control program that involves assessment, ongoing surveillance, targeted treatment and on-site training and education is necessary. Customized vector control programs help corporations mitigate the risks associated with the spread of disease to employees and contractors across business operations. **By preventing disease, corporations are also preventing the threat of employee and contractor fatalities, operational downtime, lost productivity and reputational damage that can hinder corporate ability to attract workers to a project.**

This article reviews the basic mechanisms by which arthropod vectors transmit pathogens and some of the vector/pathogen combinations of importance to industries.

Examples of Integrated Vector Control Activities

Identification

Clothing Treatment

Source Reduction

Spraying

Larval Surveillance

The World's Deadliest Animal – the female Anopheles mosquito

Vectors, in General

Pathogens transmitted by arthropod (insect) vectors are some of the most dangerous and unpredictable on earth. They are also the most difficult to prevent or control because they are so resilient to intervention and so deeply embedded in the ecologies and landscapes of the regions they infest. Vectors make all the difference in this equation because they exponentially increase the range and transmissibility of pathogens over those that would depend on transmission by direct human contact. Vectors help pathogens bridge the gap from a diverse array of host animals (mice, rats, monkeys, birds, prairie dogs, pigs, etc.) to humans. Some harbor reservoirs of pathogens over periods less conducive to transmission (winters, dry seasons). Vectors are facilitators of many dangerous disease-causing organisms, the prevention and treatment of which cannot be effective for long without addressing the vector directly.

The defining characteristic of a vector-borne infection is its high transmissibility. Directly transmitted infections like colds and influenza depend on one-to-one contact between people or contaminated surfaces. Transmission of vector-borne infections is facilitated by multitudes of mobile, intelligent carriers who disperse from the source of an infection then home in like guided missiles on new victims.

Vectors generally don't become "ill" from carrying their various viral, protozoan and nematode infections. They might accrue some damage to their tissues, but in some cases this "damage" actually makes them more likely to transmit and infect. A mosquito with problems in its feeding apparatus will need to take additional bites to complete a blood meal. A flea with a gut clogged with plague bacteria will regurgitate more.

Vectors remain infected for their entire lives, which are longer than most people think. A mosquito, for instance, doesn't have a fixed lifespan. Many die

Characteristics of Vector-Borne Diseases

- High disease transmissibility
- Explosive, unpredictable spread of disease
- Resilient to control and prevention because of vector's small size and sheer numbers
- Larger range vs diseases that require direct contact

within their first week of life, but some can persist almost indefinitely. They are limited by the damage that accumulates on their non-repairable wings and appendages and do not age as much as they wear out. Predation, desiccation and entrapment in water probably kill more mosquitoes than any other cause. West Nile vectors on the East Coast of the United States that emerge in August of one-year can over winter and become active in May of the following year for a lifespan of at least nine months.

Vectors shouldn't be thought of as mere dumb vessels or flying hypodermic needles. It is helpful to think of them as tiny, well-programmed robots. They have a limited set of responses to particular stimuli. Their programming can be sophisticated. They can detect minute quantities of insecticides on the breeze and refuse to enter a home that has been sprayed with pyrethroids or DDT. Some like salt water. Some never bite before midnight. Some are indoor feeders and others prefer to bite and feed outdoors.

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This becomes troublesome when we realize that their programming is also diverse and adaptable. Because the programs of individual mosquitoes differ slightly from each other and only the best programs survive long enough to produce progeny, their programs are always getting better and adapting to changing conditions. Like the Red Queen's race in Alice in Wonderland, just to keep up, vector control operators must similarly adapt their methods, changing insecticides, surveillance strategies and timing of operations to achieve the maximum effect.

Vectors, Specifically

Mosquitoes and ticks account for the majority of transmissions of the most important vector-borne diseases, although some close relatives of mosquitoes also get involved, including sand flies and black flies. Each of these organisms has unique habitat requirements and feeding behaviors, which can vary greatly, even within a closely related group. For example, dozens of species of *Anopheles* mosquitoes can transmit malaria around the world. Some bite at night, others only at dawn and dusk. Some breed in bright sunlight. Others never venture from the deep shade of forests. Salt water is lethal to some. Others thrive in water with saline content approaching that of seawater. Generalization, when it comes to vector biology, typically fails. The specific habits of vectors provide the keys to controlling them and preventing them from spreading infection. Some of the most common types of vectors are described in *Figure A*.

Figure A: Disease carrying insects of industrial importance

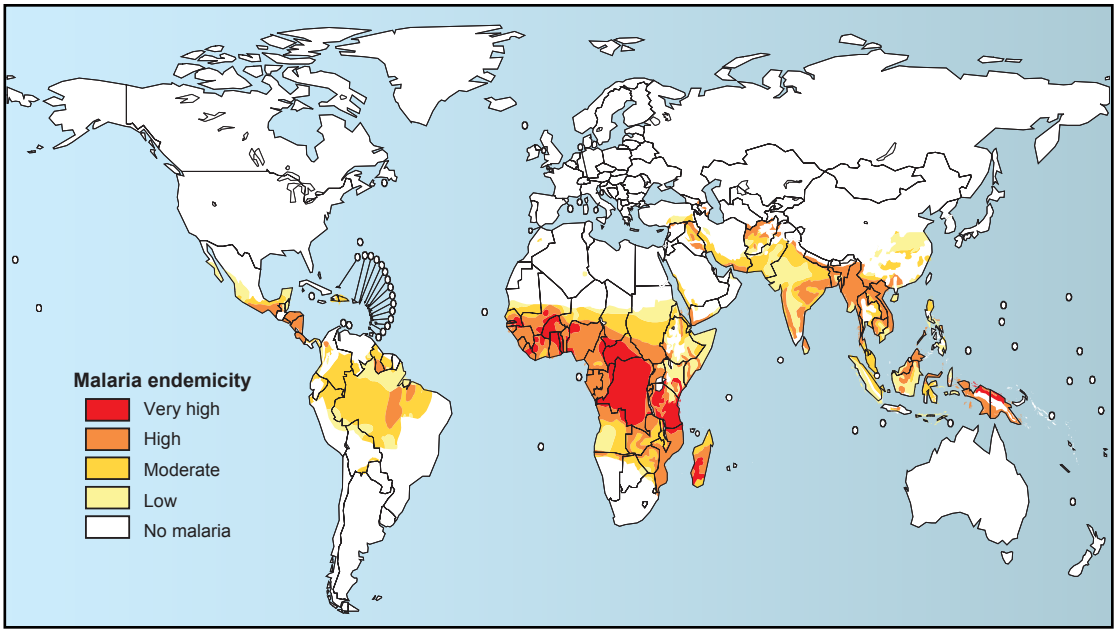
Mosquitoes	
	Mosquitoes, by far the most important of the disease vectors, number over 3,000 species worldwide. Only the female mosquito can transmit disease because only she, and not the male, has the knife-like mouthparts needed to extract blood from her victims. She needs the blood meal to provide protein for egg formation. **AKA:** *Mossies, Nippers, Skeeters* **Diseases vectored:** Malaria, Yellow Fever, Dengue Fever, West Nile virus, Rift Valley Fever, Chikungunya, Japanese Encephalitis, Venezuelan Equine Encephalitis, Murray Valley Encephalitis
Sand Flies	
	Closely related to mosquitoes, sand flies are blood-feeders and breed in caves, rodent burrows, manure piles and other dark places that retain humidity and are rich in organic matter. They are weak fliers, tending to move from host to host in short "hopping" flights. Their bodies are so small (3 mm) they are hard to detect until after they begin biting. Their bite generates intense discomfort for several days. **AKA:** *Punkies, Black Gnats, No-see-ums, Biting Midges, Chitras,* **Diseases vectored:** Leishmaniasis, Sand Fly Fever
Black Flies	
	Black flies are yet another relative of mosquitoes that are specialized for breeding in running water from small trickles to large rivers. Unlike mosquitoes, black flies feed by slashing through the skin, and they never feed indoors. They can attack in such large numbers that their salivary fluids alone can cause a person to become ill, causing a condition called "black fly fever." They also vector a nematode that can live in the human body for up to fifteen years destroying tissue in internal organs, most notably in the eye thereby causing blindness. **AKA:** *Buffalo Gnat, Turkey Gnat, White Socks* **Diseases vectored:** River Blindness/Onchocerciasis, Black Fly Fever
Kissing Bugs	
	Triatomines are large insects with nocturnal habits. They are typically found in structures with thatched roofs that offer hiding places during the daytime. They are called "kissing bugs" due to their predilection for feeding on the soft skin of people's faces, including lips. Although these can be large insects, their bites are generally painless. After feeding on the victim's blood this insect releases its infected feces near the bite wound. The victim by scratching the bite causes the infection to enter its body. **AKA:** *Conenose bugs, Assassin Bugs, Benchuca, Vinchuca, Chipo, Pito, Chupanca, Barbeiro* **Diseases vectored:** Chagas
Ticks	
	Ticks in general have a much longer life cycle than a mosquito. Hard ticks feed only a few times during their lifespan, which tends to limit their odds of acquiring an infection. Nevertheless, the longevity and host selectivity of hard ticks allows them to be relatively efficient vectors. Soft ticks are long-lived nest and burrow dwellers. Like mosquitoes they can feed many times during their lifespan. **Diseases vectored:** Tick-borne Encephalitis, Lyme Disease, Tick-borne Relapsing Fever

Important Vector-borne Diseases

1. Malaria

Malaria exists in every tropical and subtropical landscape across the globe, sometimes making seasonal excursions into temperate areas as well. The protozoan parasites that cause it have more complex genomes, metabolisms and life cycles than almost any other vector-borne threat. This complexity makes them a difficult target for interventions such as drugs and vaccines because the parasite's shape-shifting ways allow it to evade chemical and immunological defenses. They pose a moving target as well, intentionally changing their outer coating during each phase of their life cycle, and creating a diverse antigenic and metabolic wardrobe through sexual recombination, an engine of diversity creation unavailable to simpler microbes such as viruses and bacteria.

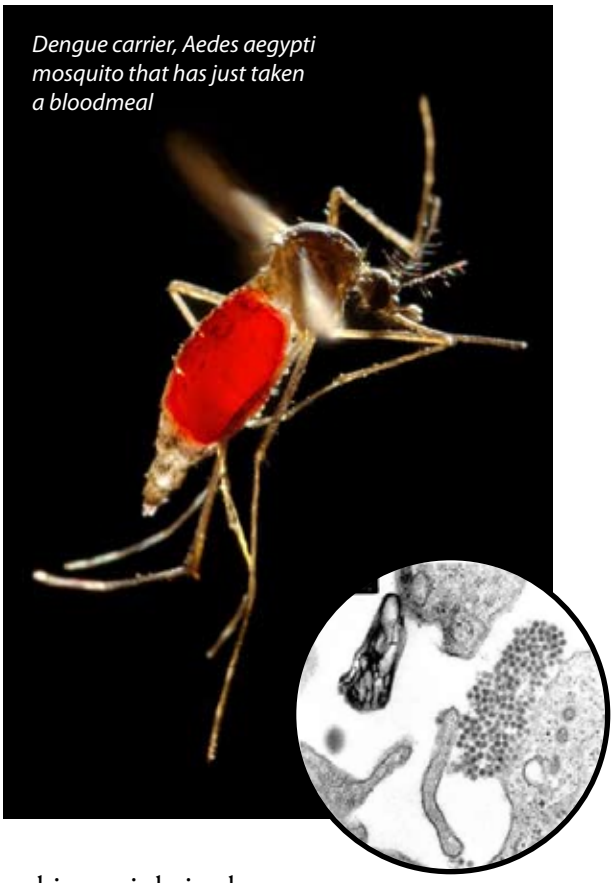
Malarious Regions of the World



Malaria is present in more than 100 countries, and imposes an economically significant burden on the populations of at least 80. Malaria kills at least 1.1 million people per year, and probably more due to incomplete reporting in many of the countries on which it imposes the greatest burdens. Four species of parasites affect humans, but two of them, *Plasmodium falciparum* and *P. vivax* account for more than 95% of cases. *P. falciparum*, the most dangerous of the pair, ranges throughout the deep tropics from Africa to Asia and South America. *P. vivax*, which can develop in mosquitoes at cooler temperatures, has a wider range, extending beyond the fringes of *P. falciparum* distribution and often coexisting with *P. falciparum* in many areas.

P. falciparum malaria poses the greatest threat to industry of any vector-borne disease, as it can kill an unprotected individual very quickly and can reinfect and repeatedly debilitate even those who develop semi-protective immunity. In local populations most deaths occur in children between 6 months and 2 years old. Their vulnerability derives from a lack of immunological protection. The immune evasiveness of malaria parasites prevents complete immunity from developing, but older children and adults who have experienced multiple infections, enjoy some level of protection from the most severe manifestations of the illness.

Expatriates, tourists and urban dwellers share the immunological experience of an infant and thus remain particularly vulnerable to the life threatening aspects of this disease. Certain complications, such as cerebral malaria, strike quickly, clogging small blood vessels in the brain to produce coma. Stories of expatriates falling ill on a Friday, putting off treatment till Monday and dying over the weekend are not uncommon. Thus, malaria prevention requires serious attention when visiting areas where it is transmitted. Although no vaccine is currently available, prophylactic drugs and measures that reduce exposure to night-biting *Anopheles* mosquitoes, such as bed nets and repellents can be very effective. Unlike some infections, victims of malaria often never get a second chance.



Dengue carrier, Aedes aegypti mosquito that has just taken a bloodmeal

2. Dengue Fever

Dengue virus in many ways seems to be the obverse of malaria. While malaria transmission occurs most frequently in rural areas, Dengue is a city disease. While the *Anopheles* vectors of malaria bite mainly at night, the *Aedes* vectors of dengue bite mainly in the daytime. While an initial malaria infection generally produces the most severe symptoms, a second infection of dengue can be much more dangerous than the first, when it involves a different serotype of the virus.

Dengue fever can be painful (hence its nickname of "breakbone fever") and debilitating but is generally not life threatening when first acquired. However, severe manifestations arise in areas where more than one of the four main strains of the virus coexist. Becoming exposed to a second, different strain of the virus can provoke a severe immunological reaction called Dengue Hemorrhagic Fever (DHF), which can carry a significant risk of death, especially in children and younger adults. Presently, about five percent of the hundreds of thousands of people who acquire DHF die, although prompt and effective medical care can greatly reduce this case fatality rate.

Dengue is caused by one of four virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4). Infection with one of these serotypes provides immunity to only that serotype for life. Subsequent dengue infections carry significant risk of death.

Approximately 2.5 billion people live under the threat of dengue transmission. Like malaria, dengue fever exists throughout the tropics, and seems particularly prevalent in Asia, the Middle East and Latin America, although poor reporting in Africa may obscure its true prevalence there. Dengue in Africa appears to be mainly concentrated in the eastern half of the continent.

No prophylactic drugs or vaccines are available to prevent dengue, but measures that limit or prevent biting such as repellents or removal of water-bearing containers in which the mosquito vectors can breed does help.

3. Arboviruses

Dengue is not the only arthropod-borne virus (arbovirus) of concern in the world. A wide variety of often-dangerous viruses exist almost anywhere on the globe where mosquitoes are found. Although each of these individual viruses generally have restricted ranges and many affect relatively small populations, we consider them here as a group because of their collective importance.

The following "rogues gallery" is far from exhaustive, but illustrates some of the more notorious pathogens as well as those that are currently in the news due to resurgence or expansion of their boundaries. In many areas these infections may account for the poorly documented "fevers of unknown origin" (FUOs) that commonly arise in seasons when mosquitoes are most active.

A. Chikungunya

Rash caused by Chikungunya

Chikungunya tops this list because of its recent resurgence in places like India, Sri Lanka, Mauritius and countries in Europe involved in frequent tourism to these destinations. Concern has recently arisen that it will soon increase its range in Europe due to the spread of Asian Tiger mosquitoes (*Aedes albopictus*), which can act as significant vectors for this infection. The traditional range for this virus also includes Africa and Southeast Asia.

Infection with chikungunya can be severe and temporarily debilitating but is generally not life threatening in otherwise healthy people. No vaccine or curative drug treatment is currently available. Prevention must rely entirely on measures that reduce exposure to mosquito bites.

B. Yellow Fever

Yellow Fever is a dangerous infection whose prevalence around the world has been greatly reduced due to the availability of an effective vaccine. It is mainly transmitted by day-biting *Aedes* mosquitoes and can cycle in both urban and rural areas. In its rural incarnation, monkeys serve as maintenance hosts and tree-hole and bromeliad breeding mosquitoes transmit it. No one should travel to an area

where Yellow Fever remains endemic without being vaccinated. Some countries still require proof of vaccination for entry.

C. West Nile Virus (WNV)

West Nile virus, formerly limited to Africa, the Middle East and parts of Southern Europe (Romania), has now spread to the New World. It has become a ubiquitous fixture on the summer landscape of North America and continues to make incursions into South America. While most people who become infected don't experience anything more than flu-like symptoms, a small percentage go on to develop a potentially fatal cerebral hemorrhage and permanent neurological damage. Transmission occurs primarily through urban vectors because the mosquito (*Culex pipiens*) most responsible for amplifying the virus in bird populations prefers relatively polluted habitats. No vaccine or curative drug treatment is currently available.

Culex pipiens mosquito

D. Eastern Equine Encephalitis (EEE)

EEE is a relatively uncommon, but deadly, mosquito-borne infection that ranges up the Atlantic Coast from South America (Venezuela) to New England. It causes the most severe disease in children (<15 years old) and older people (>50 years old). Those who survive generally suffer permanent, debilitating brain damage. Birds provide the primary source of infection. Several types of daylight/twilight biting mosquitoes transmit it to people. No vaccine or curative drug treatment is currently available.

E. Japanese Encephalitis (JE)

Pigs are an important maintenance host for this virus, which is mainly transmitted by night-biting mosquitoes in the *Culex tritaeniorhynchus* group. JE is found from India and Southeast Asia to Japan and has a similar risk for fatality and permanent debilitation as EEE, except JE affects a wider range of age groups. It has recently expanded its range to northern Australia. Thirty percent of those who exhibit JE symptoms die and another 30% develop serious and permanent neurological damage. Between 30,000-50,000 clinical infections are reported each year throughout Asia. Most infections, however, are asymptomatic. An effective vaccine is available for preventing this infection.

F. Rift Valley Fever (RVF)

RVF is transmitted to animals and humans in sub-Saharan and North Africa by day-biting *Aedes* mosquitoes. Humans can also acquire infections through con-

tact with the blood of infected animals during slaughter. Many cases of RFV are relatively mild, but the hemorrhagic form of this disease has a case fatality rate of over 50%. The overall case fatality rate associated with human infection is probably less than 1%. RFV is one of the few viral pathogens that can be transmitted to the eggs of infected mosquitoes, thus some mosquitoes can be infected before they ever bite a host. No vaccine or curative drug treatment is currently available.

G. Tick-borne Encephalitis (TBE)

TBE differs from all of the other arboviruses thus far discussed in that ticks rather than mosquitoes transmit it. TBE is found in temperate regions from China to Europe. Although infections can often be mild, permanent or long-lasting neurological damage can occur in about 10-20% of patients. Only 1-2% of cases are fatal. Rodents are the primary maintenance hosts for this infection and hard ticks in the genus *Ixodes* serve as the primary vectors. No vaccine or curative drug treatment is currently available.

H. Others

Venezuelan Equine Encephalitis, St. Louis Encephalitis, Western Encephalitis, Lacrosse Encephalitis, Powassan Encephalitis, Murray Valley Encephalitis, etc.

Many other, highly localized arboviruses exist throughout the world, some of which can be deadly. Companies should help their travelers become familiar with the particular threats they may face. Few arboviruses other than some of those mentioned have vaccines available. Basic preventive measures that reduce exposure to mosquito bites are recommended to avoid infection.

4. Lyme Disease

Bull's Eye Rash – Lyme Disease

The same kinds of hard ticks that transmit TBE also transmit Lyme Disease, although Lyme Disease has a wider range that includes North America. Lyme Disease has never killed anyone but can nevertheless be debilitating if left untreated. Once the spirochete bacteria (*Borrelia*) that cause it reach the synovial (joint) fluid or penetrate the central nervous system, routine antibiotics can no longer reach it and the pathogen can cause such problems as arthritis, memory loss and other neurological problems.

Prevention involves reducing exposure to tick bites with repellents, insecticide-treated clothing and simple awareness of tick habitats and their presence on the body. LD spirochetes require at least two days to become activated and if an attached tick can be removed before that time, the risk of infection will be negligible. A vaccine had formerly been available but is no longer on the market because of incomplete efficacy.

5. Tick-borne Relapsing Fever (TBRF)

Tick-borne Relapsing Fever is caused by a spirochete bacteria (*Borrelia*) closely related to the ones that cause Lyme Disease. Where its range overlaps with malaria, the fevers this persistent infection causes are often mistaken for malaria. It is a much more dangerous infection that Lyme Disease. In Africa, this illness sometimes kills 30-70% of those who become infected during outbreaks. Illness can last for up to two weeks. No vaccine or curative drug treatment is currently available.

Soft ticks transmit TBRF in Africa (and in remote cabins in the Western USA). Soft ticks are generally nest-dwellers (both mammals and birds). Relapsing Fever most often occurs where human habitations and nest-dwelling organisms overlap. Unlike hard ticks, which feed only once per life stage, soft ticks can feed multiple times similar to mosquitoes, thus are much more prolific transmitters of pathogens. No vaccine or curative drug treatment is currently available.

6. Leishmaniasis

Leishmaniasis includes a diverse group of protozoan infections that can cause anything from skin sores (in its mildest form) to severe organ damage. Some forms of leishmaniasis can be found in nearly every part of the tropics and subtropics, but the primary areas of concern include North Africa, the Middle East (it is a big problem in Iraq) and southwest Asia. Infections are difficult to treat and the drugs generally used can be quite toxic to humans and produce many side effects. No vaccine or curative drug treatment is currently available.

Leishmaniasis skin sore

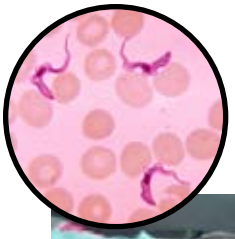
Sand Flies, a relative of mosquitoes, that breed in caves, animal burrows and manure piles serve as the vectors. Weak, nocturnal fliers, they will not be active when the wind is strong. Preventive measures include bed nets and repellents. Some commercial insecticide-treated bed nets have been found not as effective in preventing sand fly bites as they are in protecting against mosquitoes.

7. Chagas' Disease

This disease, while limited to Latin America can have a large impact on rural communities. A large, home-dwelling insect known as a "kissing bug" (*Reduviidae: Tratominae*) transmits the protozoon pathogen that causes it (*Trypanosoma cruzi*) to people while they sleep. This disease mainly threatens those who live in homes with thatched roofs, and can be combated through indoor residual spraying or housing improvements (tin roofs). The pathogen causes

"Kissing bugs" often bite near the eye

chronic organ damage and can kill by affecting the function of the heart over many years. Although its short-term effects on workers would be minimal, on-the-job exposure can cause many years of declining health.



8. African Trypanosomiasis (Sleeping Sickness)

African trypanosomes resemble those found in Latin America but are transmitted by Tsetse flies, which are found only in Africa. This pathogen causes "African Sleeping Sickness" which can induce coma by invading the central nervous system. Tsetse flies are particularly common in mixed savannah/woodland environments. *Trypanosoma brucei gambiense* ranges mainly through West and Central Africa, while *Trypanosoma brucei rhodesiense* is found in East and southern Africa. The Rhodesian form produces a more quickly progressing and acute infection, but both can kill people if left untreated. No vaccine or curative drug treatment is currently available.

9. Lymphatic Filariasis (Elephantiasis)

Filariasis generally doesn't kill but it can cause considerable disability. Several forms of this mosquito-borne infection are caused by nematode worms that invade the lymphatic system causing swelling and tissue buildup in various parts of the body, but particularly affecting the legs. In its most serious manifestation, this disease causes grotesque distortion of appendages known as "elephantiasis." Major surgery and extensive tissue removal provides the only cure for infections that reach this level of severity. The more severe symptoms require many years of repeated infection to develop, thus would not present a significant problem to workers in the short-term. However, on-the-job exposure can cause many years of declining health and suffering.

Filariasis is found throughout Africa, India and parts of Southeast Asia and Oceania. Most cases are caused by *Wuchereria bancrofti* or *Brugia malayi*. Night-biting mosquitoes in the genus *Culex* serve as the primary vectors so bed nets are an effective means of limiting exposure to this parasite. No vaccine or curative drug treatment is currently available.

10. Onchocerciasis (River Blindness)

Onchocerciasis is also caused by nematodes, but its vectors are black flies, relatives of mosquitoes that breed in clean, running water. The adult worms that cause onchocericasis cause the body to form hard lumps or nodules of fibrotic tissue under the skin. Clinically, the biggest problem derives from the millions of pre-larval microfilarial worms that are shed from these nodules and migrate into the skin, causing itchy skin reactions and in some cases, blindness, when they invade the eyes (thus the term "river blindness"). A well-tolerated drug, ivermectin, can kill the microfilaria and temporarily inhibit the ability of the adult female worms to reproduce. Black flies bite only outdoors and during daylight hours, so bed nets are not useful in preventing exposure. The repellents that work on mosquitoes, however, are generally effective against black flies.

Onchocerciasis is limited to Africa and Latin America. River-dwelling black flies (*Simulium damnosum)* serve as the primary vectors in Africa. In Latin America black flies called *Simulium ochraceum* and *metallicum* are the important vectors. No vaccine is currently available.

Eye lesions from worm invasion

Glossary

Arthropod

Arthropods are animals belonging to the Phylum Arthopoda and include insects, spiders, centipedes, shrimp and crayfish. They are characterized by the possession of a segmented body with appendages on at least one segment. They are the largest phylum in the Animal Kingdom with more than a million described species making up more than 80% of all described living species.

Arbovirus

Arboviruses (i.e., Arthropod-borne viruses) are viruses that are maintained in nature through biological transmission between blood feeding arthropods (mosquitoes, flies, ticks) and susceptible vertebrate hosts such as humans. Vertebrate infection occurs when the infected arthropod takes a blood meal.

Endemic

Relating to a disease or pathogen that is found in or confined to a particular location, region, or people. Malaria, for example, is endemic to tropical regions.

Semi-immune

A person is considered semi-immune if they have developed a certain degree of immunity against malaria either by birth in an infested country and/or by repeated exposure over their lifetime to the malaria parasite on a regular basis without interruption.

Non-immune

Non-immune people have never had a malaria infection. Typically, these are considered to be any expatriate, even if such people have spent a significant amount of time in a particular malaria high-risk country. These types of people are considered as a high risk population for malaria. For a non-immune person, if malaria is not diagnosed and/or effectively treated, malaria can be fatal in less than one week.

Vector

A carrier. In parasitology, the vector carries the parasitic agent. For example, in malaria, a mosquito serves as the vector that carries and transfers the infectious agent (Plasmodium), injecting it with a bite.

MosquitoZone™

MosquitoZone provides turnkey vector-borne disease control and educational programs for industries that operate in areas of the world where worker health, safety and operations efficiency may be adversely affected by infections.

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