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Mosquito-borne diseases, January 2012-March 2022 in Japan

Table 1. Characteristics of key mosquito vectors

Genus	<i>Aedes</i>		<i>Culex</i>		<i>Anopheles</i>	
Species	<i>Aedes albopictus</i>	<i>Aedes aegypti</i>	<i>Culex tritaeniorhynchus</i> *	<i>Culex pipiens pallens</i>	<i>Anopheles sinensis</i>	<i>Anopheles minimus</i>
Distribution in Japan	Nationwide excluding Hokkaido	Not established	Nationwide	Nationwide	Nationwide	Miyako and Yaeyama Islands
Disease	• Dengue fever • Chikungunya fever • Zika virus infection • West Nile fever • Yellow fever	• Yellow fever • Dengue fever • Chikungunya fever • Zika virus infection • West Nile fever	• Japanese encephalitis	• West Nile fever • Bancroftian filariasis • Dirofilariasis • Japanese encephalitis	• <i>Plasmodium vivax</i> malaria • Bancroftian filariasis • Dirofilariasis	• <i>Plasmodium falciparum</i> malaria
Feeding behavior	Daytime, outdoors	Daytime, indoors	Nighttime, outdoors	Nighttime, outdoors/indoors	Nighttime, outdoors	
Preferred hosts	Human, other animals	Human	Swine, cattle, human, birds	Human, birds	Cattle, horse, human (large mammals)	
Key larval habitats	Small water puddles outdoors • Flowerpot trays • Cemetery flower vases • Rainwater catch basins	Artificial containers indoor and outdoors • Flower vases • Fish bowls/tanks • Water jars • Flowerpot trays	Rice fields, lakes and marshes	Stagnant wastewater • Sewage ditch • Cesspool • Rainwater catch basins	Rice fields, wetlands, canals/waterways	Creeks, springs
Flight distance	200-500 m	≤ 200 m	> 10 km	2-4 km	1-2 km	

* see p.133 of this issue

Mosquitoes are classified in the family Culicidae, and approximately 3,600 species have been recorded worldwide, with 112 in Japan (as at 2014). Many species are bloodsucking (limited to females). Of these diverse mosquito species, some are responsible for the transmission of pathogens that affect humans (Table 1). If the blood sucked by a mosquito and taken into the digestive tract contains a pathogen that is capable of infecting the mosquito, the pathogen infects the mosquito and proliferates in the gastrointestinal epithelial cells, and the infection spreads to tissues and organs in the body cavity, or, it moves to the body cavity without proliferation. In either case, the pathogen reaches the mosquito's salivary glands from the digestive tract through the body cavity within two days to three weeks, and the mosquito becomes capable of transmitting the pathogen. When mosquitoes in this state suck blood from vertebrates, the pathogen, together with the saliva, enters the blood vessels of the animal.

Characteristics of major mosquito vectors

The ability of mosquitoes to transmit a pathogen is determined not only by the type of mosquito, but also by the type of pathogen and the amount of pathogen ingested by the mosquito from the blood meal. The growth rate of the pathogen inside the mosquito varies by pathogen, and it is generally considered that the shorter the time period required for a pathogen to proliferate, the more likely it is to spread. Chikungunya virus, for example, multiplies rapidly inside the mosquito and can be detected in the salivary glands of mosquitoes within 2 days of ingestion, while West Nile virus takes 7-10 days. Factors thought to affect the magnitude of epidemics include the population density and host preferences of the mosquito, frequency of contact with the host (s), and air temperature, which affects the growth and physiology of mosquitoes. For example, *Aedes albopictus*, which inhabits urban environments and has a high incidence of occurrence with frequent contact with and/or opportunities for bloodsucking from humans, has a high likelihood of pathogen transmission. In contrast, *Anopheles* spp. mosquitoes, which have few suitable productive habitats in urban environments, is thought to have a low likelihood of spreading infectious diseases in urban areas of Japan. In addition, the growth of insects basically depends on the external environment (air temperature, length of day, etc.), and it is known that the developmental period of the larvae and the lifespan of adults change when the air temperature changes. The time it takes for *Aedes albopictus* to develop from a larva to an adult is 10 to 12 days in the summer (average daily temperature of around 27°C), but in early spring (April) and late autumn (October) when the temperature is lower (average daily temperature 15-20°C), it may take 30 to 50 days.

Mosquito habitats change depending on the external environment. *Aedes albopictus* requires an average annual temperature of

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11°C or higher to establish itself, and its geographic distribution in Japan has been expanding northward with global warming. The northern limit was confirmed to be Tochigi Prefecture around 1948, Akita to Miyagi Prefectures around 1996, Iwate Prefecture in 2009, and Aomori Prefecture in 2015 (IASR 41: 92-93, 2020). *Aedes aegypti*, globally the main vector of dengue fever, once inhabited the Ryukyu Islands and the Ogasawara Islands of Japan, which belong to the subtropical climate zone. In Kyushu and areas north of there, which belong to the temperate climatic zone, it had been confirmed that it inhabited the Amakusa region of Kumamoto Prefecture for 9 years from 1944 to 1952. However, since the 1970s, *Aedes aegypti* has not been collected in Japan (including the Ryukyu Islands and the Ogasawara Islands), and its domestic distribution has not been confirmed. On the other hand, *Aedes aegypti* and their offspring from overseas are frequently captured at international airports in Japan. Based on the temperature at which the larvae of this species can grow, there is a possibility that it will become established in subtropical climate zones such as Tanegashima Island and southwards (IASR 41: 91-92, 2020). For other mosquitoes, natural disasters, such as tsunamis, typhoons, and floods, increase areas with stagnant water, which may become mosquito breeding grounds. After the Great East Japan Earthquake, multiple species of mosquitoes were collected from new grounds in the Tohoku region, suggesting that they were related to the tsunami disaster. There is concern for an increase in mosquito-borne diseases due to the global expansion of mosquito habitats as a result of climate change.

Subnational level health governments continuously monitor the occurrence of mosquito vectors (see p.129 of this issue). For areas considered to be suitable habitats for mosquitoes, monitoring sites are determined based on factors such as the influx of people from endemic areas, and the density, species identification, and seasonal trends of the adult mosquitoes flying into the area are investigated. Investigations of pathogen carriage in adult mosquitoes and larvae (species, specimen counts, source) may also be conducted in some cases. In addition, quarantine stations monitor international airports and seaports for mosquitoes that are not established in Japan (see p.130 of this issue).

Mosquito-borne diseases in the National Epidemiological Surveillance of Infectious Diseases system

To date, there are at least 20 known mosquito-borne diseases, of which 11 are monitored as a notifiable disease under Category IV through the national surveillance system, based on the Infectious Diseases Control Law (Table 2 on p.127). The report status of the six diseases notified thus far is as follows (Figure on p.127).

In recent years, the maximum annual number of Japanese encephalitis case notifications has been about 10, all of which have been domestic infections (IASR 38: 151-152, 2017). Most of the areas where the infection was acquired have been in western Japan, which is consistent with the population density distribution of *Culex tritaeniorhynchus*, the main mosquito vector. Infected pigs are confirmed every year, and Japanese encephalitis virus infection continues to be possible in Japan.

The number of dengue fever cases is increasing worldwide, and this has been attributed to the concentration of human populations in urban areas in tropical and subtropical regions where dengue fever is endemic. Before 2020, the number of travelers from endemic countries to Japan and the number of travelers from Japan to endemic countries was on the rise, and the number of dengue fever cases infected abroad and diagnosed and reported in Japan (imported cases) increased, reaching a record high of 462 case notifications in 2019 (Figure on p.127, IASR 36: 33-35, 2015 & 41: 89-90, 2020). The number of notified cases of dengue fever has decreased since 2020, with 44 cases in 2020 and 7 cases in 2021. This may be due to the impact of international travel (entry/exit) restriction measures enacted against the COVID-19 pandemic. Examples of cases that spread through domestic infections include an epidemic in the 1940s attributed to importations by veterans from the Southeast Asian region that resulted in a total of 200,000 cases and an outbreak of about 160 cases in parks in Tokyo in 2014.

The endemic area of chikungunya fever is expanding globally (Table 3 on p.128). The first imported case in Japan was confirmed in 2006. Since chikungunya fever was designated as a notifiable disease in 2011, 4-17 cases were reported annually from 2012 to 2018. In 2019, a chikungunya fever epidemic occurred in Myanmar, and 32 imported cases from Myanmar were notified. The number of reported cases of chikungunya fever was 3 in 2020 and 0 in 2021.

Since the late 2000s, Zika virus infection has been expanding worldwide with reports of large-scale epidemics. In Japan, the first imported case of the disease was confirmed in 2013, and 21 cases have been reported since it was designated as a notifiable disease in 2016.

The malaria parasite was once present in Japan, and it is estimated that 20,000 cases occurred annually in the 1940s. No domestic transmission has been observed since around 1960, and in recent years all reports have been imported cases (IASR 39: 167-169, 2018). The number of reported cases of malaria from 2012 to 2019 was about 40-70 per year, with 19 cases in 2020 and 29 cases in 2021.

In 2005, one imported case of West Nile fever was notified.

Imported cases of mosquito-borne diseases are expected to increase again with the relaxation of international travel restrictions put in place during the COVID-19 pandemic (see p.132 of this issue). Dengue fever, chikungunya fever, and Zika virus infection may spread domestically from imported cases and cause outbreaks. This is because mosquito vectors are widely distributed in Japan, including in urban areas, with high contact frequency with humans. On the other hand, the likelihood of such autochthonous transmission is low for malaria and West Nile fever. Mosquitoes that can transmit malaria do not live in urban areas of Japan and have low contact frequency with humans. In addition, because the viral load in human blood is low for West Nile virus, a human-to-mosquito-to-human infection cycle cannot be established. The route of infection for West Nile fever is assumed to be wild birds → mosquitoes → humans.

The following measures are important for routine responses to mosquito-borne diseases: surveillance of mosquito vectors and human cases, elimination of adults and larval sources in high-risk areas, individual prevention measures (mosquito control, vaccines), and situational awareness of overseas epidemics. Early detection and treatment of patients with mosquito-borne diseases also contribute to preventing the spread of infections. In the event of mosquito-borne disease occurrence, it is important to rapidly share information among prefectures, the national level, and residents; determine the route (s) of infection through active epidemiological investigations; and, if necessary, to conduct mosquito density surveys or control activities in areas presumed to be the source of infection.

The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Environmental Health and Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

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(特集つづき) (THE TOPIC OF THIS MONTH-Continued)

表2. 感染症法に基づき4類感染症に規定されている蚊媒介感染症

Table 2. Mosquito-borne infectious diseases designated as category IV notifiable disease based on the Infectious Diseases Control Law, Japan

国内感染例*の届出あり Diseases with notifications of domestic infection*		海外感染例の届出のみ (国内感染例の届出なし) Diseases with a notification(s) of infection from overseas only (No notifications of domestic infection)		届出なし Diseases without any notifications	
日本脳炎 (1999年)	Japanese encephalitis (1999)	マラリア (1999年)	Malaria (1999)	黄熱 (1999年)	Yellow fever (1999)
デング熱 (1999年)	Dengue fever (1999)	ウエストナイル熱 (2002年)	West Nile fever (2002)	西部ウマ脳炎 (2007年)	Western equine encephalitis (2007)
		チクングニア熱 (2011年)	Chikungunya fever (2011)	東部ウマ脳炎 (2007年)	Eastern equine encephalitis (2007)
		ジカウイルス感染症 (2016年)	Zika virus infection (2016)	ベネズエラウマ脳炎 (2007年)	Venezuelan equine encephalitis (2007)
				リフトバレー熱 (2007年)	Rift Valley fever (2007)

() : 感染症法上の届出対象となった年

() : The year specified as a notifiable disease

*日本脳炎は国内感染例が継続して届出されている。一方デング熱は輸入例が大半を占め、輸入例を発端に国内で感染が伝播したと推定される症例の届出がある

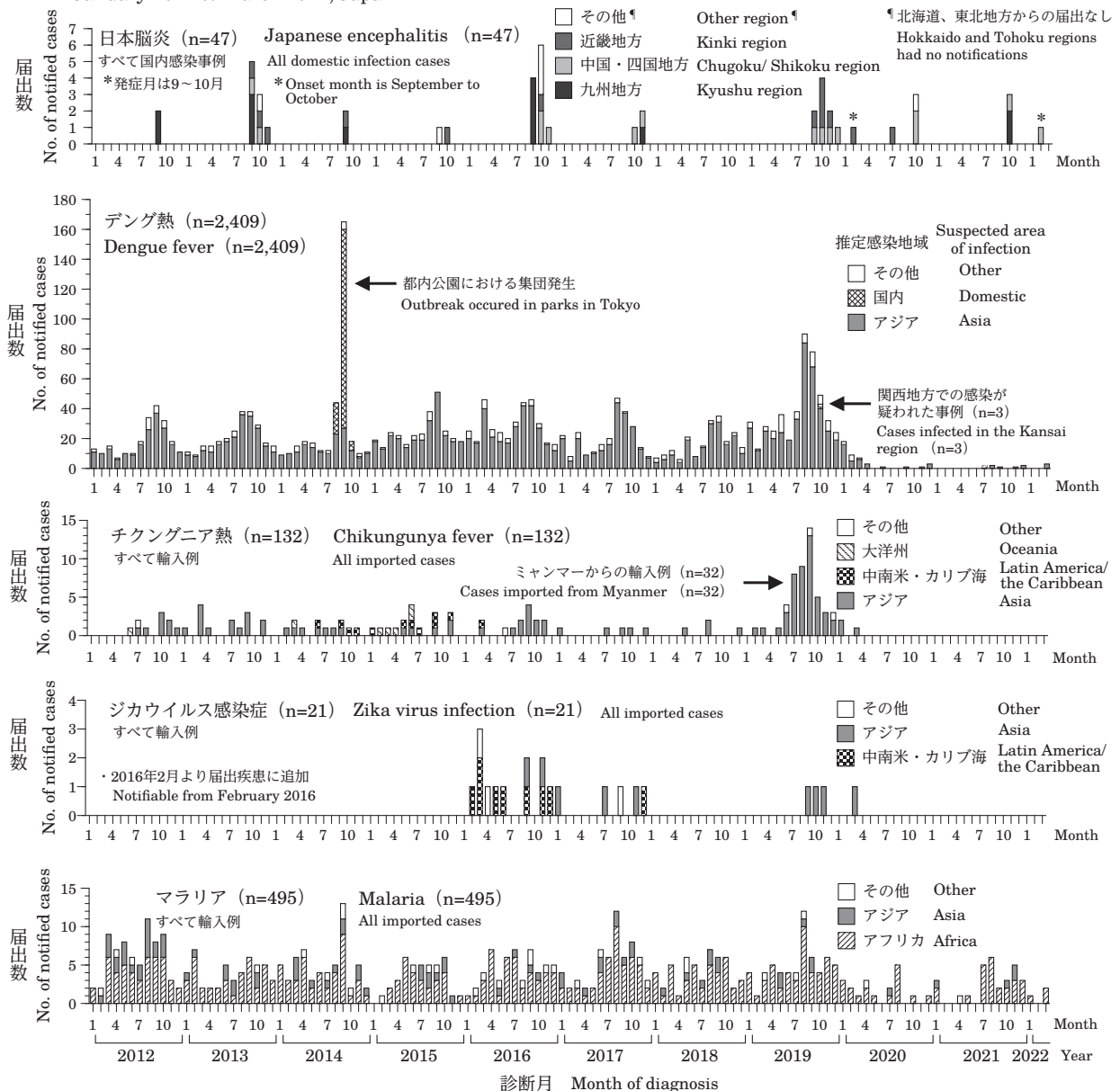
*Domestic infection of Japanese encephalitis are reported every year. On the other hand, for dengue fever, the majority of cases are imported infections, with notifications of cases where the infection was suspected to have been transmitted domestically from an imported case.

(感染症発生動向調査：2022年5月6日現在届出数)

(National Epidemiological Surveillance of Infectious Diseases: as at 6 May 2022)

図. 蚊媒介感染症の推定感染地域別診断月別の届出数, 2012年1月～2022年3月

Figure. Monthly number of notified mosquito-borne infection cases by area of suspected infection, January 2012 to March 2022, Japan



(感染症発生動向調査：2022年5月6日現在届出数)

(National Epidemiological Surveillance of Infectious Diseases: as at 6 May 2022)

(THE TOPIC OF THIS MONTH-Continued)

Table 3. Characteristics of mosquito-borne diseases

Disease	Japanese encephalitis	Dengue fever	Chikungunya fever	Zika virus infection	Malaria
Pathogen	Japanese encephalitis virus Family: <i>Flaviviridae</i> Genus: <i>Flavivirus</i>	Dengue virus Family: <i>Flaviviridae</i> Genus: <i>Flavivirus</i>	Chikungunya virus Family: <i>Togeviridae</i> Genus: <i>Alphavirus</i>	Zika virus Family: <i>Flaviviridae</i> Genus: <i>Flavivirus</i>	<i>Plasmodium</i> spp.
Vector mosquito	<i>Culex</i> spp. (<i>Culex tritaeniorhynchus</i>)	<i>Aedes</i> spp. (<i>Aedes aegypti</i> , <i>Aedes albopictus</i>)	<i>Aedes</i> spp. (<i>Aedes aegypti</i> , <i>Aedes albopictus</i>)	<i>Aedes</i> spp. (<i>Aedes aegypti</i> , <i>Aedes albopictus</i>)	<i>Anopheles</i> spp.
Life cycle	Pig → Mosquito → Pig Bird → Mosquito → Bird	Human → Mosquito → Human	Human → Mosquito → Human	Human → Mosquito → Human	Human → Mosquito → Human ^a Monkey → Mosquito → Human ^b
Geographic distribution	Asia, Micronesia, Australia	Tropical and subtropical regions (Southeast Asia, South Asia, Latin America, Caribbean, Africa, Australia, China, Taiwan)	Outbreaks have been confirmed in Africa, Asia, the Americas, and southwestern Indian Ocean islands, and Europe • Outbreaks were reported in the Caribbean at the end of 2013	Latin America, Africa, Southeast Asia, Oceania	Tropical and subtropical regions (Africa, Asia, Oceania, Latin America)
Incubation period	6-16 days	2-15 days (mostly 3-7 days)	3-12 days (mostly 3-7 days)	2-12 days (mostly 2-7 days)	8-30 days
Symptom	99-99.9% of infected persons are asymptomatic. - JE has a case-fatality rate of 20-30%. 45-70% of survivors have neurologic or psychiatric sequelae. - Initial symptoms are fever, headache, nausea, vomiting, and dizziness, followed by rapid neurological symptoms (impaired consciousness, easy agitation, photosensitivity, involuntary movements, tremors, paralysis). Seizures are more common in children. - Also some case reports of fever only.	50-80% of infected persons are asymptomatic. - Common presentation is the sudden onset of fever accompanied by headache (especially around the eyes), muscle and joint pain, appetite loss, abdominal pain, and constipation. - A rash frequently appears on the chest and trunk 3-4 days after onset, spreading to the extremities and face in some cases (dengue fever). - Dengue symptoms subside in about a week, and most patients recover without complications. - Bleeding, organ damage, or shock may occur in some patients (severe dengue).	75-80% of infected persons are asymptomatic. - Among symptomatic patients, fever and arthralgia almost always appear, with rash occurring in about 80%. - Arthralgia may be strong, and may last for several weeks to months. - Fatigue, headache, myalgia, lymphadenopathy, bleeding tendency, nausea, or vomiting may also occur. - Severe patients presenting with encephalopathy, fulminant hepatitis, or myocarditis have been reported.	- Approximately 80% of infected persons are asymptomatic. - Common presentations include maculopapular rash, fever, arthralgia/arthritis, and conjunctivitis (Zika virus infection). Symptoms are similar to dengue fever but milder. - Outbreaks in French Polynesia in 2013 and in Latin America since 2015 saw an increase in the number of Guillain-Barre syndrome cases, suggesting an association with Zika. - Infection in a pregnant woman may result in birth defects such as microcephaly in the newborn (congenital Zika virus infection).	- Initial symptoms include cycles of fever and chills. First infection without any immunity almost always results in fever. - Other symptoms such as fatigue, headache, myalgia, arthralgia, gastrointestinal symptoms and respiratory symptoms may occur; lack of disease-specific symptoms. <i>Plasmodium falciparum</i> infection has a tendency to become severe.
Diagnosis	- Measurement of antibodies in serum (IgM antibody detection by IgM capture ELISA, neutralizing antibody test, IgG ELISA, hemagglutination inhibition test) - Detection of viral genes (RT-PCR) - Virus isolation	- Detection of viral genes (RT-PCR) - Virus isolation - Detection of dengue virus nonstructural protein 1 (NS1) antigen - Measurement of antibodies in serum (IgM antibody detection by IgM capture ELISA, neutralizing antibody test)	- Detection of viral genes (RT-PCR) - Virus isolation - Measurement of antibodies in serum (IgM antibody detection by IgM capture ELISA, neutralizing antibody test)	- Detection of viral genes (RT-PCR) - Virus isolation - Measurement of antibodies in serum (IgM antibody detection by IgM capture ELISA, neutralizing antibody test)	- Morphological diagnosis (Direct microscopic examination of intracellular parasites on stained blood films) - Detection of protozoan-specific antigens (Rapid diagnostic tests) - Detection of protozoan genes (PCR, LAMP)
Treatment	- No specific treatment - Symptomatic treatment	- No specific treatment - Symptomatic treatment	- No specific treatment - Symptomatic treatment	- No specific treatment - Symptomatic treatment	- Administration of antimalarial drugs (Drugs used depend on the geographic area where infection was acquired and the type of malaria) <i>Plasmodium vivax</i> and <i>Plasmodium ovale</i> require acute treatment followed by primaquine administration (curative therapy)
Vaccine / Chemoprophylaxis	- Vaccine available - No prophylaxis	- No vaccine available in Japan - No prophylaxis	- No vaccine - No prophylaxis	- No vaccine - No prophylaxis	- No vaccine available in Japan - When traveling to endemic areas prophylactic administration of antimalarial drugs is recommended.
Classification under the Infectious Diseases Control Law in Japan	Notifiable disease, Category IV				

^a: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae*^b: *Plasmodium knowlesi*