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Review

Zika virus, vectors, reservoirs, amplifying hosts, and their potential to spread worldwide: what we know and what we should investigate urgently

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SUMMARY

Objectives: The widespread epidemic of Zika virus infection in South and Central America and the Caribbean in 2015, along with the increased incidence of microcephaly in fetuses born to mothers infected with Zika virus and the potential for worldwide spread, indicate the need to review the current literature regarding vectors, reservoirs, and amplification hosts.
Vectors: The virus has been isolated in Africa in mosquitoes of the genera *Aedes*, *Anopheles*, and *Mansonia*, and in Southeast Asia and the Pacific area in mosquitoes of the genus *Aedes*. *Aedes albopictus* has invaded several countries in Central Africa and all Mediterranean countries, and continues to spread throughout Central and Northern Europe. The wide distribution of the virus in animal hosts and vectors favors the emergence of recombinants.
Animal hosts: The virus has been isolated in monkeys, and antibodies have been detected in domestic sheep, goats, horses, cows, ducks, rodents, bats, orangutans, and carabaos.
Conclusions: It is a public health imperative to define the domestic and wild animal reservoirs, amplification hosts, and vector capacity of the genera *Aedes*, *Anopheles*, and *Mansonia*. These variables will define the geographic distribution of Zika virus along with the indicated timing and scale of the environmental public health interventions worldwide.

1. Introduction

A widespread epidemic of Zika virus (ZIKV) infection was reported in 2015 in Central and South America and the Caribbean. This epidemic was associated with an increased incidence of microcephaly in fetuses born to mothers infected with ZIKV, with Brazil being the country most affected by both epidemics.[1–4] This rare, devastating, and untreatable complication of the fetus was declared a public health emergency of international concern (PHEIC).[1–4] The neurotropism of the virus was recognized early,[5] and this has been evident in the recent rise in microcephaly incidence in Brazil .[3,4,6] The virus has been found in the amniotic fluid of two pregnant women with fetuses suffering a reduction in the circumference of the head.[6] The virus has also been found in the central nervous system (CNS) of fetuses,[3,4] with negative tests excluding other congenital infections.[6]

Thirty-two countries and territories of the Americas are affected by ZIKV, in addition to Rio de Janeiro, Brazil, where the Olympics and Paralympics are due to be held in August 2016; this poses a threat to international travelers and the local host-country residents .[2] Local transmission has not been observed in Europe yet, and there is a global alert for travelers returning from endemic countries with symptoms consistent with ZIKV infection.

The immediate public health measures feasible at present, in the absence of a vaccine, are interventions relevant to the vector and a better understanding of the wide and unknown range of possible amplification hosts. Two main concerns prompted this exhaustive review of the literature: the historical paradigm of the introduction of yellow fever virus from Africa to the Americas, where it adapted to local sylvatic vectors and primates,[7] and the fact that we do not yet know which could be the competent vectors or amplifying hosts of ZIKV in temperate climate regions, thus hampering any future surveillance and intervention control programs. The range of vectors and animals in which the virus has been detected worldwide was reviewed in order to assess the likelihood of an established circulation of the virus in novel areas.

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2. Epidemiology

ZIKV is an emerging vector-borne pathogen that was first isolated in 1947 in a sentinel rhesus macaque monkey and again in 1948 from a pooled specimen of *Aedes africanus* mosquitoes from the Zika Forest in Uganda.[5] During the years 1947 through 2007, only serological data, entomological data, and the diagnosis of 14 human cases with viral isolation or serology were reported from Asia and Africa.[8–13] It has been speculated that among those human cases, a few may have represented an unrecognized outbreak. One unrecognized outbreak took place in 1977–1978 in Indonesia.[14,15] The first outbreak outside of Africa and Asia occurred in 2007, on Yap Island in the Federated States of Micronesia, with 49 confirmed cases and 73% of residents aged ≥3 years infected according to IgM seropositivity.[16,17] There are limitations to the seroprevalence studies resulting from the cross-reactive nature of ZIKV with dengue and other flaviviruses. However, IgM antibodies against dengue virus persist for up to 12 weeks, and the specimens for the IgM measurement were collected during a 12-week period from April 1 through July 31, 2007. During this time, the specimens had been collected within 10 days from symptom onset. They tested positive only for ZIKV RNA and not for dengue or other flavivirus RNA.[17]

From 2007 through 2013, no new instances of human seropositivity or disease were reported. In 2013, the virus reemerged in French Polynesia, and from 2013 through 2014, it disseminated to the Cook Islands, New Caledonia, Easter Island, and throughout the Pacific.[18] French Polynesia reported 396 epidemiologically confirmed cases and 29 000 suspected cases.[19] The virus has been isolated or has had its nucleic acid extracted by PCR and then sequenced from samples collected in Southeast Asia (e.g., Thailand, Indonesia, Cambodia[20–22]). All strains collected in Asia and the Pacific belong to the Asian lineage and are closely related, indicating that the virus was present in the area for several years but remained undetected, as the clinical manifestations resemble those of other known endemic arboviruses such as dengue virus and chikungunya virus.[20] However, the possibility that the virus has spread to the Pacific and Southeast Asia successively, causing a wave of clinical disease and subsequent detection of the virus, cannot be excluded.[20]

In March 2015, Brazil notified the World Health Organization of an illness compatible with but not suspected to be a ZIKV infection. Soon after, in May 2015, it documented the first confirmed ZIKV transmission in mainland South America, along with the assumption that the virus had been introduced to the country via the Va'a World Sprint Championship canoe race held in Rio de Janeiro in August 2014.[23] Four Pacific countries participated (French Polynesia, New Caledonia, the Cook Islands, and Easter Island). The virus was subsequently transferred from the major cities across the country via the infected Brazilian participants and spectators who returned to their home towns.[24] The strain found in Brazil was phylogenetically closer to the strain in the French Polynesia outbreak of 2013–2014, with both belonging to the Asian lineage. It is estimated that 440 000 to 1.3 million cases had been reported as of December 2015.[23]

3. Virus

ZIKV is an approximately 11-kb single-stranded, positive-sense ribonucleic acid (RNA) virus of the *Flaviviridae* family. It is related to dengue, West Nile, and Yellow fever viruses and is a member of the Spondweni serocomplex, whose transmission cycle consists mainly of vectors from the *Aedes* genus mosquitoes (*A. furcifer*, *A. taylori*, *A. luteocephalus*, and *A. africanus*) and monkeys.[25,26] Phylogenetic analyses have revealed three lineages: two African lineages, i.e., the MR 766 cluster and the Nigerian cluster, and one Asian lineage (Table 1).[16,27,28]

Table 1
Lineages of Zika virus

1. African lineages (two clusters)	2. Asian lineage
a. MR 766 cluster	One Asian genotype
b. Nigerian cluster	

All lineages share a common origin in Uganda early in the 20th century, from where it dispersed west to West Africa via two introductions and east to Southeast Asia and then to the Pacific as follows: (1) a relative of the MR 766 prototype strain was introduced from Uganda to Côte d'Ivoire in 1940 and from there to Senegal in 1985 resulting in the MR 766 lineage; (2) a relative of the Nigerian strain was introduced from Uganda to the Central African Republic and Nigeria around 1935, and from Nigeria to Senegal and Côte d'Ivoire around 1960, forming the Nigerian lineage; and (3) a ZIKV cluster was probably spread from Uganda to Malaysia in 1945, making its way to Micronesia sometime around 1960, where it formed the Asian lineage.[25] However, it is unknown whether to attribute this migration only to human and vector movements, or also to birds carrying the virus along migratory routes.

Regarding the African lineages, the phylogenetic analysis of ZIKV strains collected from 1968 through 2002 in Senegal, Côte d'Ivoire, Burkina Faso, and the Central African Republic indicated that there are more recombinants than in other flaviviruses; however, they all clustered in the two African lineages, the MR 766 cluster and the Nigerian cluster.

4. Transmission

Transmission has been demonstrated to occur mostly via infected female mosquito vectors of the *Aedes* genus (*Culicidae* family). Transmission is mainly urban and sylvatic, with humans serving as primary amplification hosts in areas where there are no non-human primates.[17] The latter constitute the amplification host in a sylvatic cycle.[17] Mosquitoes, as hematophagus arthropods, acquire the virus via a blood meal, and they host it throughout their life-span without being affected. They transmit it to the next amplification host, i.e., their target during the next blood meal.[29] Other routes of transmission are sexual intercourse,[30–33] perinatal transmission from mother to fetus,[34] and blood transfusion.[35] Breast feeding has not been reported as a mode of transmission.

5. Clinical manifestations

The majority of infections are subclinical, estimated to reach 81% of infected individuals. The clinical manifestations mimic those of other arboviral infections, e.g., dengue and the chikungunya endemic in tropical areas (West Africa, Southeast Asia, Pacific area, South America).[2,17,22,36] A macular or papular rash (90%), fever (65%), arthritis or arthralgia (65%), non-purulent conjunctivitis (55%), myalgia (48%), headache (45%), and retro-orbital pain (39%) have been the most commonly reported symptoms,[20] followed by anorexia, vomiting, diarrhea, stomach aches, dizziness, leg pain, lymphadenopathy, and hypotension. No deaths, hospitalizations, or hemorrhagic manifestations have been documented.[17,20] In the Indonesian outbreak among humans in 1977–1978, no rash was reported.[14] In Eastern Nigeria, two patients presented jaundice.[37]

There was early evidence of neurotropism of the virus,[5] which spares all body tissue except for nervous tissue.[38] Intracerebral inoculation of infected human blood in suckling albino Swiss mice was followed by proliferation of the virus in their nervous tissue.[8] ZIKV infection has been associated with Guillain–Barré syndrome (GBS) in Martinique and French Polynesia.[39,40] During the ZIKV outbreak in French Polynesia in 2013–2014, the incidence of GBS

increased 20-fold,[39] and a case–control study of a large series of patients confirmed the link between ZIKV infection and GBS. Further, the same study did not find any evidence that past or concurrent dengue infection was a causative or predisposing factor for GBS.[41] Additionally, microcephaly and various ophthalmological findings and neurological symptoms have been observed in fetuses and infants born to infected mothers.[1–4] The autopsy findings in the CNS of fetuses were a very small brain, complete absence of the cerebral gyri, severe dilation of both cerebral lateral ventricles, dystrophic calcifications throughout the cerebral cortex, and hypoplasia of the brain stem and spinal cord. Particles consistent with ZIKV were detected on electron microscopy of brain tissue, but not in other tissues.[3,4]

6. Diagnosis

It is challenging to diagnose pregnant women or symptomatic individuals living in or returning from areas endemic for flaviviruses. Flaviviruses trigger the production of cross-reactive antibodies in humans, and they cause dengue, Japanese encephalitis, Saint Louis encephalitis, West Nile fever, yellow fever, and Zika infection, diseases that share some similar symptoms.[42–44] The emphasis for diagnostics should be on molecular testing, such as reverse-transcription PCR (RT-PCR), during the first 7 days after symptom onset. After the 7th day, viremia decreases gradually; consequently, a negative RT-PCR does not exclude flavivirus infection, and serological testing should be performed.[20] IgM antibodies persist for about 2 to 12 weeks and can be detected by ELISA. If this assay is positive, neutralizing antibody detection assays, e.g., plaque reduction neutralization tests (PRNT), may enable us to identify the virus causing infection.[43,44]

Confirmation of the diagnosis of ZIKV infection relies on the detection of ZIKV RNA (RNA extraction) in blood through RT-PCR or pan-flavivirus PCR amplification, followed by sequencing, or virus isolation. Alternatively, a confirmatory diagnosis may be achieved with the co-detection of anti-ZIKV IgM antibodies (ELISA) and a ZIKV $PRNT_{90}$ (or $PRNT_{80}$) titer of at least 20, and if West Nile virus or dengue virus needs to be ruled out, a ratio of ZIKV to either dengue virus or West Nile virus PRNT titers of $\geq$4. In contrast, a probable case of ZIKV infection tests negative by RT-PCR but positive for IgM antibody (ELISA), and has a ZIKV PRNT titer of at least 20, and a ratio of ZIKV to dengue virus or to West Nile virus PRNT titers of $<$4.[17,20,43,45]

The detection of the virus in pooled specimens of mosquitoes is performed with quantitative real-time PCR.[46]

7. Vectors

The vectors of ZIKV in Africa are distinct from those in South America, Southeast Asia, and the Pacific area. Outside Africa, *Aedes aegypti* is the principal vector, while *Aedes albopictus* is also becoming established as a competent vector (Table 2).

In Africa, ZIKV was first isolated from *Aedes africanus* mosquitoes collected in Zika Forest, Bwamba county, Uganda, in 1948,[5]

Table 2
Mosquitoes in which Zika virus has been detected

Year of sampling	Location	Mosquito genus and species	Study/assay	Ref.
Africa				
1948	Zika Forest, Uganda	*Aedes africanus*	Mosquito catches in Zika Forest and first isolation of ZIKV from *Aedes africanus* pooled specimens	5,38
1958	Zika Forest, Uganda	*Aedes africanus*	Virus isolation	47
1964	Zika Forest, Uganda	*Aedes africanus*	Virus isolation	10
1969	Uganda, Bwamba county, Zika Forest	*Aedes africanus*, *Aedes apicorgenteus*	Virus isolation from pooled specimens of mosquitoes trapped in Zika Forest	12
1976–1980	Central African Republic	*Aedes africanus*, *Aedes opok*	Retrospective entomological study with RT-PCR and sequencing	48
1968–2002	West Africa: Côte d'Ivoire, Senegal, Burkina Faso, Central Africa Republic	*Aedes dalzieli*, *Aedes africanus*, *Aedes aegypti*, *Aedes furcifer*, *Aedes grahamii*, *Aedes luteocephalus*, *Aedes vittatus*, *Aedes opock*	Retrospective study; phylogenetic analysis, reverse transcription PCR, nucleotide sequencing; numerous recombination events were detected	25
1962–2008	Senegal	*Aedes aegypti*, *Aedes dalzieli*, *Aedes fowleri*, *Aedes furcifer* (known as *Aedes taylori*), *Aedes luteocephalus*, *Aedes vittatus*, *Aedes neoafricanus*, *Aedes metallicus*, *Aedes minutus*, *Anopheles africanus, Anopheles coustani, coustani*, *Anopheles gambiae* s.l., *Mansonia uniformis* (the higher number of ZIKV isolation events was detected in *Aedes furcifer* (known as *Aedes taylori*), *Aedes luteocephalus*, and *Aedes dalzieli*)	Virus isolation in the mosquito cell line AP61 (*Aedes pseudoscutellaris*) Identification of isolates by immunofluorescence with virus-specific immune ascitic fluid; this was confirmed by complement fixation or neutralization tests	49
2011	Southeastern Senegal	*Aedes africanus*, *Aedes hirsutus*, *Aedes metallicus*, *Aedes unilineatus*, and *Culex perfuscus* had the highest infection rates compared to *Aedes (Diceronyia) furcifer*, *Aedes (Fredwardsius) vittatus*, *Aedes taylori*, *Aedes luteocephalus*, *Aedes dalzieli*, *Aedes aegypti*, *Mansonia uniformis*, and *Anopheles coustani*, with the lower infection rates	Virus isolation, RT-PCR	50
2007	Gabon	*Aedes albopictus*	Retrospective sero-epidemiological and entomological study in 2014; RT-PCR and sequencing of pooled specimens	36
Asia				
1969	Malaysia	*Aedes aegypti*	Virus isolation	11
NA; experiment in 2012	Singapore	(Local in Singapore) *Aedes aegypti*	Inoculation of Ugandan ZIKV in (local in Singapore) *Aedes aegypti* and subsequent mosquito-borne transmission of the virus	54
NA; experiment in 2014	Yap Island, Federated States of Micronesia; human outbreak in 2007	Field collected *Aedes henselli* and *Culex quinquefasciatus* tested negative for ZIKV; *Aedes henselli* laboratory infection	Experiment; laboratory infection of *Aedes henselli*	55

ZIKV, Zika virus; NA, not applicable.

1958,[47] and 1964.[10] In 1969, ZIKV was isolated from *A. africanus* and *Aedes apicoergenteus* collected in Zika Forest, Uganda.[12] In 2014, a retrospective study investigated *A. africanus* and *Aedes opok* collected in the Central African Republic, West Africa, from 1976 through 1980. The phylogenetic analysis of this research revealed that the detected ZIKV strains clustered together in the African lineages of ZIKV.[48] Viral isolates from the years 1968 to 2002 in West Africa revealed that ZIKV detected in *Aedes dalzieli*, *A. africanus*, *A. aegypti*, and *A. furcifer* exhibited many recombination events, which could be attributed principally to the zoophilic mosquito *A. dalzieli*, which takes blood meals from distinct animal species harboring different ZIKV strains at the same time.[25] Another retrospective study in Senegal, West Africa, investigated samples collected from 1962 through 2008 and detected the ZIKV in *Aedes aegypti*, *Aedes dalzieli*, *Aedes furcifer* (known as *A. taylori*), *Anopheles africanus, Anopheles coustani* , *Anopheles gambiae* s.l., and *Mansonia uniformis*.[49] In 2011, in southeastern Senegal, ZIKV was isolated from *M. uniformis*, *Culex perfuscus*, and *Anopheles coustani*, but without adequate clarification of their vector competency.[50]

However, in 2007, the first human infection with ZIKV was recognized in Gabon, Central Africa, as a result of the presence of *A. albopictus*, a species that has invaded the urban areas of the country.[36] Until then, the ZIKV epidemic had gone unrecognized as a result of the co-existence with dengue and chikungunya viruses.[36] *A. albopictus* has invaded Cameroon in Central Africa and Mozambique in Southeast Africa, gradually replacing the indigenous *A. aegypti*,[51] and depicts a dynamic expansion in temperate climates across the globe.[52]

In the Pacific, vectors of ZIKV are mosquitoes of the genus *Aedes*, principally the prevalent *A. aegypti*, followed by the invading *A. albopictus*,[53] which are known to transmit chikungunya virus, dengue virus, and ZIKV.[42] They are considered to be competent vectors of the ZIKV Asian lineage, and their prevalence increased from 2011 to 2014.[42] ZIKV was isolated from *A. aegypti* in Malaysia in 1969.[11] In Indonesia in 1978, a human epidemic of ZIKV was presumably propagated by *A. aegypti* during the rainy season, but no study has been conducted to establish the presence of the virus in mosquitoes.[14] In Singapore, the experimental inoculation of

Table 3
Animals in which Zika virus was detected

Year of sampling	Location	Animal	Assay virus/antibody	Number of animals tested	Positive animals (%)	Ref.
1947	Zika Forest, Uganda	Rhesus monkeys	Intracerebral inoculation into mice and subsequent virus isolation	One rhesus diagnosed with the virus; two others underwent successful experimental inoculation		5, 38
1967–1968 1962 and 1964	Senegal 1967–1968 Ethiopia 1962 and 1964	Wild mammals, monkeys	Antibody detection with HI	Not reported	Wild mammals 2.4%, monkeys 25%	61
1969	Uganda, Kisubi, Bwamba county, Zika Forest	Bwamba county monkeys[a]	Antibody detection with HI test	Kisubi red-tail 21 Bwamba red-tail 52 Bwamba others 16	4/21 23/52 7/16	12
1978	Lombok, Indonesia; human outbreak in 1977	Ducks, goats, cows, horses, bats, rats, carabaos (water buffalo)	HI antibodies (HIA) and detection of antibodies (DA)	HIA: 15 horses 41 cows 13 carabaos 35 goats 78 chickens 52 ducks 71 bats 25 rats 17 wild birds DA: 6 horses, 8 cows, 1 carabao, 9 goats, 1 chicken, 2 ducks, 1 bat	HIA: 3/15 (20%) 4/41 (10%) 1/13 (8%) 7/35 (20%) 0/78 (0) 2/52 (4%) 6/71 (8%) 0/25 (0) 0/17 (0) DA: All tested negative	15
1982	Gabon	Monkeys	Antibody detection with HI/complement fixation test			13
1983	Pakistan	Rodents, domestic sheep and goats (at slaughter), humans	Antibody detection	157 rodents 45 cows 33 buffaloes 46 sheep 48 goats	6/157(3.8%) 0 0 1(2.57%) 1(2.083%)	9
1996–1997	Malaysia, Borneo	Wild orangutans, semi-captive orangutans	Antibodies	40 wild orangutans, 31 semi-captive orangutans	5/40 (13%) wild, 1/31 (3%) semi-captive	62
1968–2002	West Africa: Côte d'Ivoire and Senegal, Burkina Faso, Central Africa Republic; retrospective study of viral isolates	Monkeys	RT-PCR, nucleotide sequencing, recombination detection	NA		25
1962–2008	Senegal; retrospective study of viral isolates	Monkey (*Erythrocebus patas*), *Chlorocebus aethiops* (also named grivet and African green monkey)	Virus isolation in the mosquito cell line AP61 (*Aedes pseudoscutellaris*); identification of isolates by immunofluorescence with virus-specific immune ascitic fluid and confirmed by complement fixation or neutralization tests	NA		49

HI, hemagglutination inhibition; NA, not applicable.
[a] Red-tail monkey, black mangabey, and lowland colobus were positive for Zika virus.

local *A. aegypti* with the Uganda strain of ZIKV was followed by transmission of the virus.[54]

However, on Yap Island, in the Federated States of Micronesia, the most prevalent among the 12 mosquito species belonging to four genera collected was *Aedes henselli*, and pooled specimens tested negative for ZIKV in two studies; consequently, there is uncertainty about the vector.[17,55] The laboratory inoculation of ZIKV into this mosquito was conducted on Yap Island, with 80% being colonized (when a high inoculum was provided), among which 23% developed infection.[55] Similarly, in French Polynesia, where an extended epidemic occurred in October 2013, the prevalence of *A. henselli* is higher than any other species, supposedly rendering it a vector for ZIKV; however, no study has been conducted to detect the virus in pooled specimens,[24] and at the peak of the epidemic, the entomological study pointed at *A. aegypti* and *Aedes polynesiensis*.[19]

In Brazil, transmission has been attributed to *A. aegypti* and *A. albopictus*. *A. aegypti* can be found in rural and urban areas transmitting chikungunya virus and four dengue serotypes, but *A. albopictus* is prevalent in the country.[2,31] Human travel among several commercial urban areas allows for the rapid movement of vectors (in cars, trucks, planes) along with the infected humans.

A. albopictus has colonized almost every Mediterranean country and continues to spread through Central and Northern Europe. *Aedes japonicus* has spread widely in Central Europe, *Aedes atropalpus* in Northern Italy and the Netherlands, *Aedes koreicus* on the Swiss–Italian border, Belgium,[56] and Germany, and *A. aegypti* has established itself on Madeira and around the Black Sea coast (Russia, Abkhazia, Georgia).[29]

Similar to all arboviruses, ZIKV vectors are influenced by animal population density. Thus, ZIKV could reveal a surprising vector, reservoir, and amplifying host range should it be introduced into novel tropical or temperate natural ecosystems, including Europe.[25,57] Additionally, vectors such as *A. aegypti* and *A. dalzieli*, which feed on several animal species and humans, enhance the transmission rate, as well as concurrent infections and the recombination and reassortment of the genetic material of ZIKV strains.[24,57]

As *A. aegypti* and *A. albopictus* thrive in stagnant water collections like those in peri-domestic water supplies used in the absence of piped water provision, proliferation may be encouraged by human population growth or the migratory waves from areas of civil upheaval and the possible subsequent formation of uncontrolled slums. Therefore, consistent public awareness about the significance of eliminating any peri-domestic stagnant water is of critical public health importance.[56,58–60]

8. Animal hosts

The virus reservoir was not identified in a 1947 study in Zika Forest, Uganda, where ZIKV was first isolated from rhesus monkeys.[5] The monkeys displayed mild or absent clinical presentations, while 5 days after experimental infection, they developed neutralizing antibodies.[38] Additionally, anti-ZIKV antibodies were detected in wild mammals in Senegal in 1967–1968.[61] In 1969, in Zika Forest, ZIKV was isolated from samples taken from monkeys.[12] In Lombok, Indonesia, in 1978, anti-ZIKV antibodies were detected in ducks, goats, cows, horses, bats, and carabaos (water buffalo), but not in chickens, rats, or wild birds, indicating the widespread circulation of the virus in domestic animals.[15] The question of whether birds transfer the virus over long distances remains unanswered.[15]

In 1982 in Gabon, antibodies against the virus were again detected in monkeys.[13] In 1983, antibodies against ZIKV were detected in Pakistan among rodents, domestic sheep, and goats, as well as in human sera.[9] Samples collected in 1996–1997 from wild and semi-captive orangutans in Borneo, Malaysia, tested positive for anti-ZIKV antibodies.[62] Samples collected from monkeys in West Africa from 1968 through 2002 were examined and the virus detected with RT-PCR,[25] and samples collected between 1962 and 2008 from monkeys in West Africa tested positive for specific ZIKV antigens with serology assays (Table 3).[49]

The antibody detection assays run the risk of cross-reaction with other flaviviruses co-circulating with the ZIKV, thus challenging the safe interpretation of published data. Furthermore, early laboratory methods for the detection of antibodies were of uncertain specificity and sensitivity, and antigen and molecular assays had not been developed.

9. Conclusions

There are few entomological and vector capacity studies and limited literature regarding the investigation of the prevalence of the virus in wild and domestic animals in temperate and tropical climates. This is probably because the virus has caused mild or no clinical symptoms in humans and animals until recently.

The dissemination of ZIKV throughout the Pacific and South America after the French Polynesia outbreak of ZIKV in 2013 is not in doubt. There is no information about the possibility of transovarian transmission of the virus in mosquitoes. The virus has been identified in the genera *Aedes*, *Anopheles*, and *Mansonia* only in Africa, and there has been no such pooled specimen examination of these genera in Asia, the Pacific, or the Americas. In the Pacific and Southeast Asia, however, experimental inoculation of *A. aegypti* and *A. henselli* was successful.

A. albopictus has expanded worldwide and can adapt to distinct ecosystems and trigger arboviral outbreaks. *A. aegypti*, which is prevalent in densely populated areas of South America, is recognized as difficult to eradicate and control.[31]

There are concerns about the vast majority of asymptomatic while contagious infections, the recent neurological complications and sequelae in adults and fetuses/newborns,[25] and the potential genetic evolution of this RNA virus, which pose a threat for subsequent novel neurological and other manifestations. This is a vector-borne infection that can be transmitted via sexual intercourse.

In summary, there is insufficient information regarding the animal reservoirs and amplification hosts, including domestic animals, and the vectors of ZIKV, as well as the vector capacity of the genus *Aedes* and genus *Anopheles*. This represents a public health emergency, and it is essential that we improve our understanding of these factors because they will define the transmission dynamics and geographic distribution of ZIKV, as well as indicate the timing and scale of environmental public health interventions.

Ethical approval: Approval was not required.

Conflict of interest: None declared.

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