

## Emergence of Zika Virus

Didier Musso\* and Tu-Xuan Nhan

Unit of Emerging Infectious Diseases, Institut Louis Malardé, PO Box 30, 98713 Papeete, Tahiti, French Polynesia

\*Corresponding author: Didier Musso, Unit of Emerging Infectious Diseases, Institut Louis Malardé, PO Box 30, 98713 Papeete, Tahiti, French Polynesia, Tel: 689-40-416-470; E-mail: [dmusso@ilm.pf](mailto:dmusso@ilm.pf)

Received date: August 22, 2015; Accepted date: September 29, 2015; Published date: October 06, 2015

Copyright: © 2015 Musso D, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### Abstract

Zika virus was first described in the 1940s. During more than all of a century, less than 20 human infections have been reported. Emergence of Zika virus started with a first outbreak in the Pacific area in 2007 (Federated States of Micronesia), a second large outbreak occurred in the Pacific in 2013/2014 (French Polynesia) and subsequently the virus spread in other Pacific Islands. Zika virus emerged in the Americas (Brazil) in 2015. Emergence of Zika virus in the Pacific was associated with the description of severe neurological complications.

**Keywords:** Zika virus; ZIKV; Arbovirus; Pacific; Emergence; French Polynesia

### Introduction

During the last decades, a number of arthropod-borne viruses (arboviruses) emerged or reemerged as west Nile virus (WNV), dengue virus (DENV) or chikungunya virus (CHIKV) [1]. If Zika virus (ZIKV) has been described in the 1940s [2], it was involved in only 14 human infections [3] until its unexpected emergence in the Pacific in 2007 in which it was responsible for a first large outbreak [4]. ZIKV caused a second large outbreak in French Polynesia before spreading in the Pacific (2013-2015) [5-7]. ZIKV is now emerging in South America (2015) [8,9].

### History and Epidemiology of ZIKV

ZIKV was isolated in Uganda in 1947 from rhesus monkeys and from the mosquito *Aedes africanus* in 1948 [2]. The first human ZIKV infection was reported in 1954 in Nigeria [10]. ZIKV antibodies were detected in serosurvey studies conducted in all parts of Africa [11-15], India [16] and Asia [17]. ZIKV antibodies were also detected from animal species, especially non-human primates [18]. ZIKV was isolated from several mosquitoes species in Africa and Asia including arboreal mosquitoes as *Aedes africanus* (2) or mosquitoes with a large tropical and subtropical distribution as *Aedes aegypti* [19] and *Aedes albopictus* [20].

### Classification of ZIKV

ZIKV is classified in the *Flavivirus* genus of the *Flaviviridae* family [21]. It is a single-strand RNA virus with 10,794 kb of length [22]. Two ZIKV lineages have been described, African and Asian, with the African lineage spitted in East and West African clusters [3,23], some authors described three different lineages (West African, East African and Asian) [24]. The Asian lineage is expanding [23], this lineage emerged in the Pacific [5] and in South America [8,9].

### Emergence of ZIKV

The first ZIKV outbreak occurred in the remote island of Yap (7,500 inhabitants), Federated States of Micronesia, in 2007 [4]. Forty nine human infections were firmly confirmed, the estimate of infected patients was 73% of the population, hospitalization and fatal cases were not reported. It was the first detection of Zika fever out of Africa and Asia.

The second and largest ZIKV outbreak occurred in French Polynesia in 2013/2014 [5], the number of consultations for Zika fever was estimated at 28,000 (11% of the population) [6]. Subsequently, ZIKV spread in the Pacific: New Caledonia, Cook Islands, Eastern Island, Vanuatu, Solomon, Fiji [6-7,25-27]; ZIKV is still circulating in the Pacific in 2015.

ZIKV emerged in North East Brazil in 2015 [8,9] and is spreading in this country. The closest strain to the strain that emerged in Brazil is the one that circulated in French Polynesia suggesting that ZIKV was introduced in Brazil from the Pacific area [28]. ZIKV is emerging in South America in the same context of co-circulation of arboviruses than in the Pacific area [29]. Countries in which ZIKV has been isolated or antibodies against ZIKV have been detected are reported in the Figure 1.

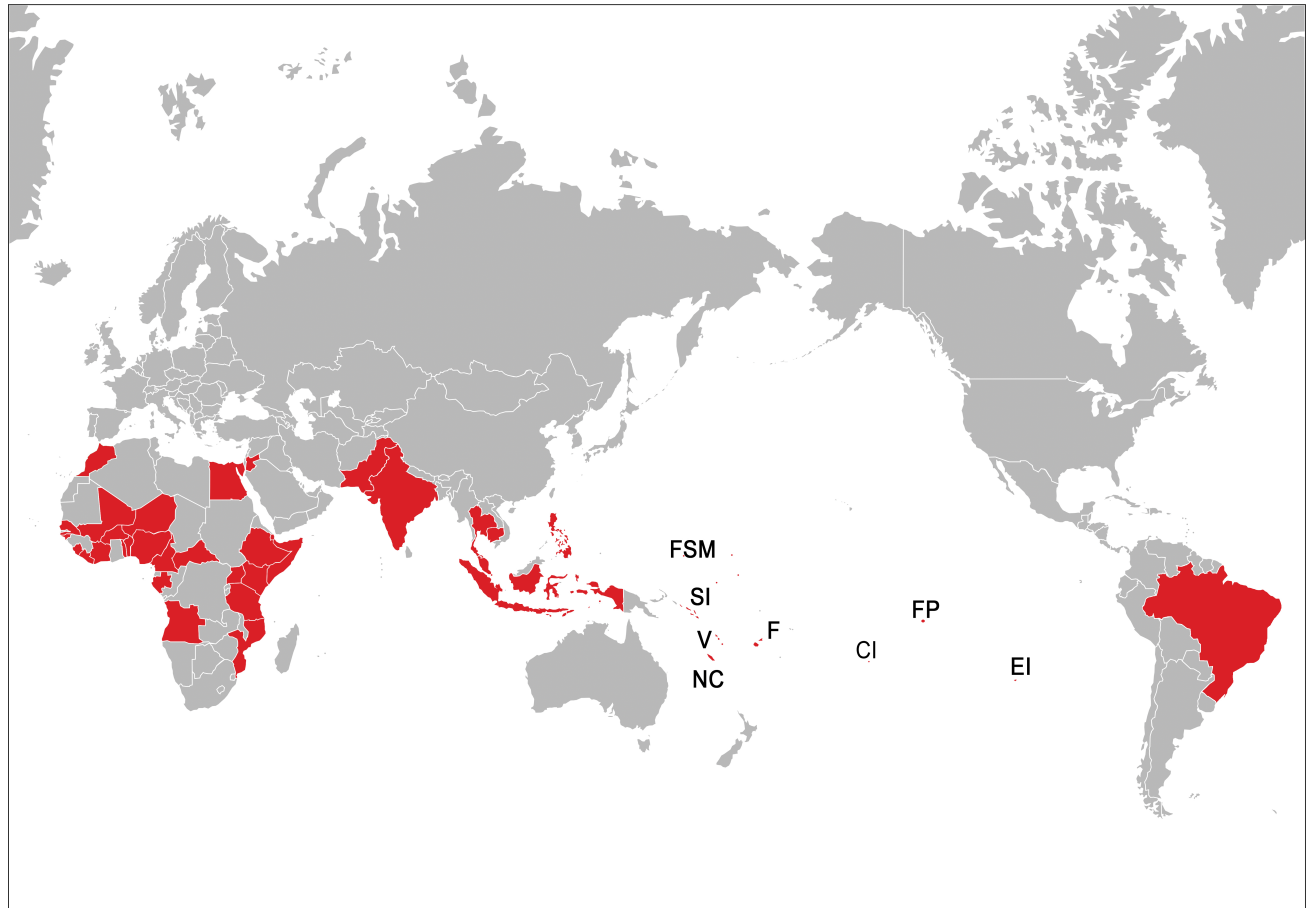
Imported cases of ZIKV infections from travelers returning from endemic areas have been reported in Europe [30,31], Americas [32] and Asia [33]. If the risk of ZIKV dissemination is low in countries as Norway [30] in which there is no known potential vectors for ZIKV, the risk is high in countries as Italy in which competent vectors for arboviruses are present [31].

### Zika Fever

### Transmission

ZIKV is transmitted by the bite of infected female mosquitoes. ZIKV adapted to an enzootic cycle involving arboreal mosquitoes in Africa to a new urban cycle including humans as reservoirs and urban mosquitoes as vectors [7].

Perinatal [34] and laboratory contamination [35] transmission have been reported. Sexual [36] and transfusion transmitted infections have been suspected [37].



**Figure 1:** Countries in which ZIKV has been isolated or antibodies against ZIKV have been detected. FSM: Federated States of Micronesia; SI: Solomon Islands; V: Vanuatu; F: Fiji; CI: Cook Islands; NC: New Caledonia; FP: French Polynesia; EI: Eastern Island.

### Clinical presentation

In the majority of cases, Zika fever is a self-limited disease. The most frequent reported symptoms (over 60% during the French Polynesia outbreak) are mild fever, fatigue, cutaneous rash, arthralgia-myalgia and conjunctivitis [38,39]. Other reported symptoms are headache, malaise, dizziness, oedema of the extremities, retro orbital pain, anorexia, photophobia, gastro intestinal disorders, sore throat, cough, aphthous ulcers, back pain, sweating and lymphadenopathies. None of these symptoms are specific and Zika fever can be misdiagnosed with other bacterial and viral infections, especially with other arboviruses in endemic areas.

During the French Polynesia outbreak, severe neurological complications of Zika fever were described; the incidence of Guillain-Barré syndrome was 20-fold higher than usually observed [39-41].

There is no specific treatment and no vaccine against Zika fever. Acetylsalicylic acid and non-steroidal anti-inflammatory drugs are not recommended due to the increased risk of hemorrhagic syndrome described with other arboviruses as DENV [38]. Symptomatic

treatment is based on acetaminophen and antihistaminic for pruritic rash.

### Laboratory diagnosis

If mild leucopenia and mild thrombocytopenia have been described during Zika fever, standard laboratory results are not informative for Zika fever diagnosis.

Serological diagnosis is limited due to cross-reactions within the *Flavivirus* genus [24], especially with dengue, then caution should be observed if diagnosis relies only on serological results, even when using neutralization test [42] which is the more specific method for *Flavivirus* serology.

ZIKV can be isolated from cell culture [36] but the protocol is reserved to specialized laboratories. Zika fever diagnosis relies in routine on the detection of ZIKV RNA by molecular tools. Detection of ZIKV RNA is possible on blood and saliva collected at the acute phase of the disease [24,43]. The use of saliva sample is of particular interest when blood samples are difficult to collect [43]. Detection of ZIKV RNA after the first week after symptoms onset can be performed

in urines [44]. Molecular diagnosis of Zika fever is reserved to reference laboratory because there is no commercial test available.

## Prevention

Prevention measures for Zika fever are the same as for other arboviruses: mosquito bite prevention and vector control. Disease surveillance is corner stone of response to emerging disease threats. Risk assessment and outbreak preparedness are imperative. Surveillance indicates where and when a disease has appeared and gives clues about how the emerging infection may spread in nature.

## Conclusion

Due to similar clinical presentation with other arbovirolosis and to the lack of laboratory capacities in most of the potential endemic areas, the incidence and prevalence of Zika infections are probably underestimated. The future of ZIKV is unpredictable [7], but as ZIKV can be transmitted by mosquitoes as *A. aegypti* and *A. albopictus*, the potential of emergence is very large and includes the entire tropical and subtropical world. It should be kept in mind that, if in most of the case ZIKV is responsible of a mild disease, severe neurological complication have been reported. The present and future ZIKV threats must be mitigated by priority actions such as improving integrated disease surveillance and response, while strengthening the prevention and control programmes for arboviruses in general. Laboratory capacities to confirm ZIKV infections should be strengthened in areas where competent mosquito vectors for ZIKV are established.

## References

- Gubler DJ (2002) The global emergence/resurgence of arboviral diseases as public health problems. Arch Med Res 33: 330-342.
- Dick GW, Kitchen SF, Haddow AJ (1952) Zika virus. I. Isolations and serological specificity. Trans R Soc Trop Med Hyg 46: 509-520.
- Faye O, Freire CC, Iamarino A, Faye O, de Oliveira JV, et al. (2014) Molecular evolution of Zika virus during its emergence in the 20(th) century. PLoS Negl Trop Dis 8: e2636.
- Duffy MR, Chen TH, Hancock WT, Powers AM, Kool JL, et al. (2009) Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med 360: 2536-2543.
- Cao-Lormeau VM, Roche C, Teissier A, Robin E, Berry AL, et al. (2014) Zika virus, French polynesia, South pacific, 2013. Emerg Infect Dis 20: 1085-1086.
- Musso D, Nilles EJ, Cao-Lormeau VM (2014) Rapid spread of emerging Zika virus in the Pacific area. Clin Microbiol Infect 20: O595-596.
- Musso D, Cao-Lormeau VM, Gubler DJ (2015) Zika virus: following the path of dengue and chikungunya? Lancet 386: 243-244.
- Campos GS, Bandeira AC, Sardi SI (2015) Zika Virus Outbreak, Bahia, Brazil. Emerg Infect Dis 21: 1885-1886.
- Zanluca C, de Melo VC, Mosimann AL, Dos Santos GI, Dos Santos CN, et al. (2015) First report of autochthonous transmission of Zika virus in Brazil. Mem Inst Oswaldo Cruz 110: 569-572.
- Macnamara FN (1954) Zika virus: a report on three cases of human infection during an epidemic of jaundice in Nigeria. Trans R Soc Trop Med Hyg 48: 139-145.
- Smithburn KC, Taylor RM, Rizk F, Kader A (1954) Immunity to certain arthropod-borne viruses among indigenous residents of Egypt. Am J Trop Med Hyg 3: 9-18.
- Kokernot RH, Smithburn KC, Gandara AF, McIntosh BM, Heymann CS (1960) [Neutralization tests with sera from individuals residing in Mozambique against specific viruses isolated in Africa, transmitted by arthropods]. An Inst Med Trop (Lisb) 17: 201-230.
- Chippaux-Hyppolite C, Chippaux A, Hannoun C (1965) Enquête immunologique sur l'indidence des arbovirus chez l'homme en République Centrafricaine. Immunologic investigation on the frequency of arbovirus in man in the Central African Republic. Preliminary note. Bull Soc Pathol Exot Filiales 58: 812-820.
- Henderson BE, Metselaar D, Cahill K, Timms GL, Tukei PM, et al. (1968) Yellow fever immunity surveys in northern Uganda and Kenya and eastern Somalia, 1966-67. Bull World Health Organ 38: 229-237.
- Salaün JJ, Brottes H (1967) [Arbovirus in Cameroon: serologic investigation]. Bull World Health Organ 37: 343-361.
- Smithburn KC, Kerr JA, Gatne PB (1954) Neutralizing antibodies against certain viruses in the sera of residents of India. J Immunol 72: 248-257.
- Hammon WM, Schrack WD Jr, Sather GE (1958) Serological survey for a arthropod-borne virus infections in the Philippines. Am J Trop Med Hyg 7: 323-328.
- Kirya BG, Okia NO (1977) A yellow fever epizootic in Zika Forest, Uganda, during 1972: Part 2: Monkey serology. Trans R Soc Trop Med Hyg 71: 300-303.
- Marchette NJ, Garcia R, Rudnick A (1969) Isolation of Zika virus from Aedes aegypti mosquitoes in Malaysia. Am J Trop Med Hyg 18: 411-415.
- Grard G, Caron M, Mombo IM, Nkoghe D, Mboui Ondo S, et al. (2014) Zika virus in Gabon (Central Africa)--2007: a new threat from Aedes albopictus? PLoS Negl Trop Dis 8: e2681.
- Gubler DJ, Kuno G, Markoff L (2007) Flaviviruses. Fields Virology. (5th edn.) Lippincott Williams and Wilkins Publishers, Philadelphia, USA.
- Kuno G, Chang GJ (2007) Full-length sequencing and genomic characterization of Bagaza, Kedougou, and Zika viruses. Arch Virol 152: 687-696.
- Haddow AD, Schuh AJ, Yasuda CY, Kasper MR, Heang V, et al. (2012) Genetic characterization of Zika virus strains: geographic expansion of the Asian lineage. PLoS Negl Trop Dis 6: e1477.
- Lanciotti RS, Kosoy OL, Laven JJ, Velez JO, Lambert AJ, et al. (2008) Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. Emerg Infect Dis 14: 1232-1239.
- European Centre for Disease Prevention and Control (2015) Rapid Risk Assessment: Zika virus infection outbreak, Brazil and the Pacific region.
- SIBC (2015) Health authorities declare outbreak of new virus in Solomons. Sibconline.
- Secretariat of the Pacific Community (2015) Epidemic and emerging disease alerts in the Pacific region.
- Musso D (2015) Zika Virus Transmission from French Polynesia to Brazil. Emerg Infect Dis 21: 1887.
- Cao-Lormeau VM, Musso D (2014) Emerging arboviruses in the Pacific. Lancet 384: 1571-1572.
- Wæhre T, Maagaard A, Tappe D, Cadar D, Schmidt-Chanasit J (2014) Zika virus infection after travel to Tahiti, December 2013. Emerg Infect Dis 20: 1412-1414.
- Zammarchi L, Stella G, Mantella A, Bartolozzi D, Tappe D, et al. (2015) Zika virus infections imported to Italy: clinical, immunological and virological findings, and public health implications. J Clin Virol 63: 32-35.
- Brust KB, Prince WS, Fader RC (2014) Trouble in paradise. IDCases 1: 95-96.
- Kutsuna S, Kato Y, Takasaki T, Moi M, Kotaki A, et al. (2014) Two cases of Zika fever imported from French Polynesia to Japan, December 2013 to January 2014 [corrected]. Euro Surveill 19.
- Besnard M, Lastier S, Teissier A, Cao-Lormeau V, Musso D (2014) Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. Euro Surveill 19.
- Filipe AR, Martins CM, Rocha H (1973) Laboratory infection with Zika virus after vaccination against yellow fever. Arch Gesamte Virusforsch 43: 315-319.
- Musso D, Roche C, Robin E, Nhan T, Teissier A, et al. (2015) Potential sexual transmission of Zika virus. Emerg Infect Dis 21: 359-361.
- Musso D, Nhan T, Robin E, Roche C, Bierlaire D, et al. (2014) Potential for Zika virus transmission through blood transfusion demonstrated

- 
- during an outbreak in French Polynesia, November 2013 to February 2014. Euro Surveill 19.
38. Bel M (2007) Zika virus Information for clinician and other health professionals. Yap State Department of Health Services.
39. Mallet HP, Vial AL, Musso D (2015) Bilan de l'épidémie à virus Zika en Polynésie française, 2013-2014. Zika virus outbreak in French Polynesia, 2013-2014. Bulletin d'information sanitaire, épidémiologique et statistique 13: 1-5.
40. Oehler E, Watrin L, Larre P, Leparc-Goffart I, Lastere S, et al. (2014) Zika virus infection complicated by Guillain-Barre syndrome-case report, French Polynesia, December 2013. Euro Surveill 19.
41. Ios S, Mallet HP, Leparc Goffart I, Gauthier V, Cardoso T, et al. (2014) Current Zika virus epidemiology and recent epidemics. Med Mal Infect 44: 302-307.
42. Kuno G (2003) Serodiagnosis of flaviviral infections and vaccinations in humans. Adv Virus Res 61: 3-65.
43. Musso D, Roche C, Nhan TX, Robin E, Teissier A, et al. (2015) Detection of Zika virus in saliva. J Clin Virol 68: 53-55.
44. Gourinat AC, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M (2015) Detection of Zika virus in urine. Emerg Infect Dis 21: 84-86.