MEDICAL AND VETERINARY ENTOMOLOGY

CULICIDAE (Mosquitoes)

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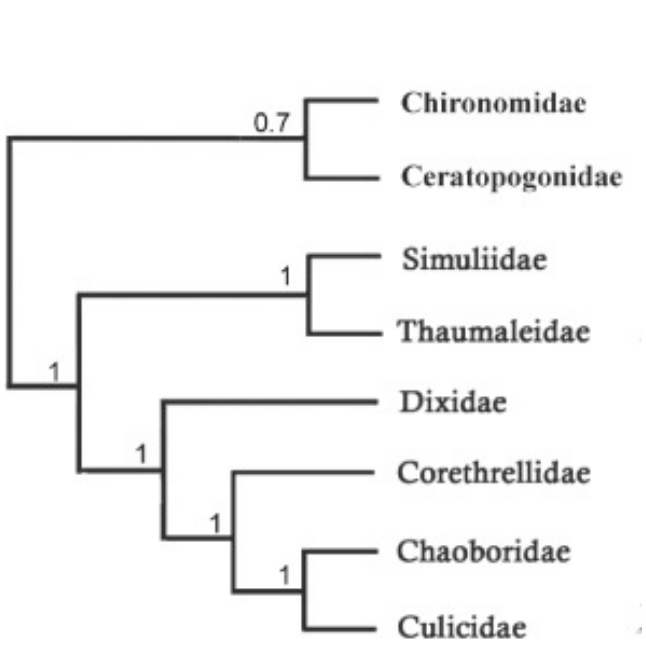
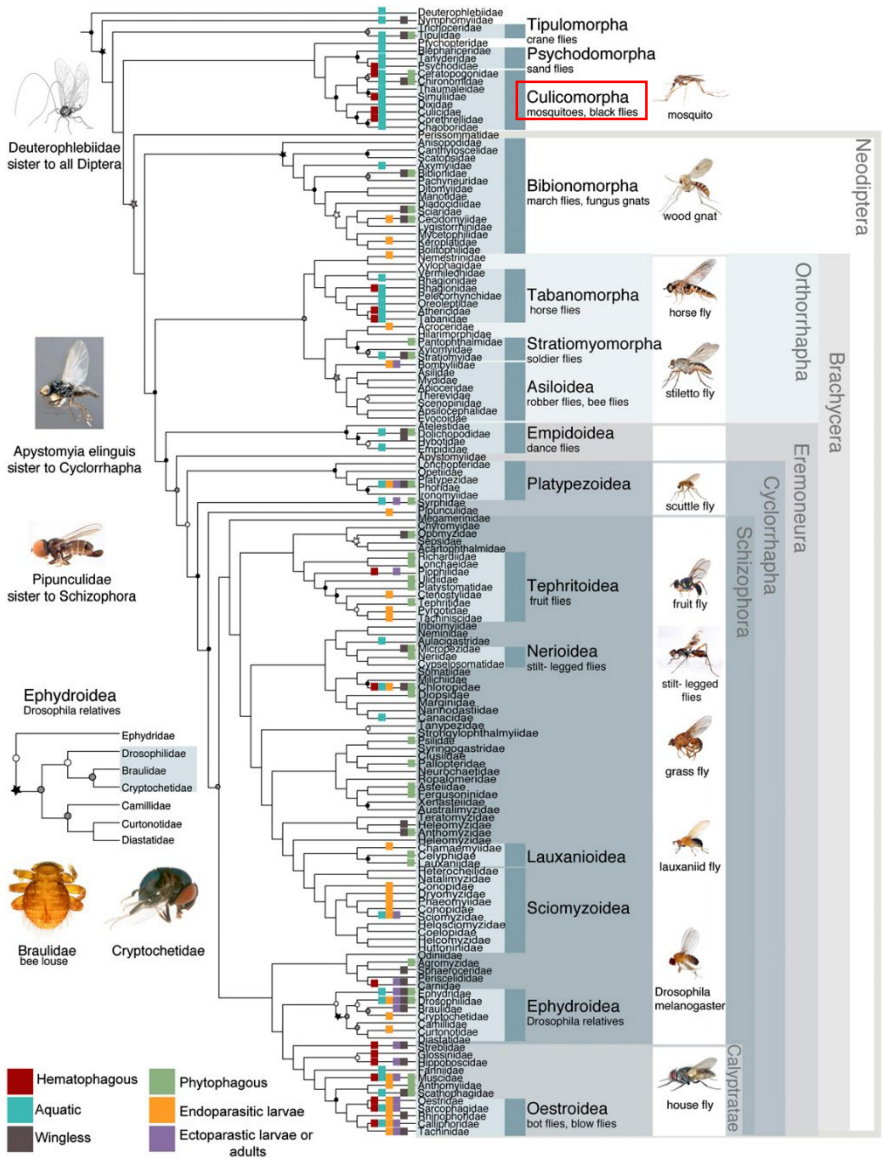
Medically significant Arthropoda - Diptera





Woodbridge & Walker 2019

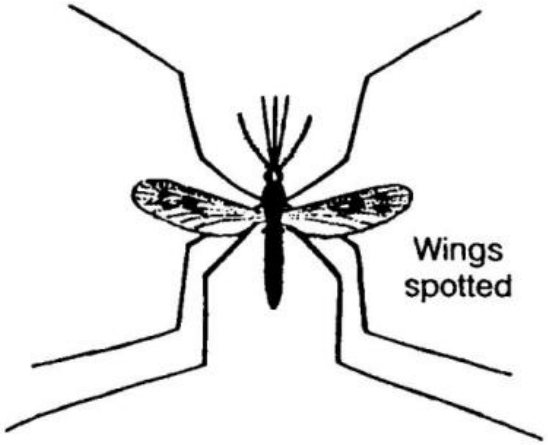
Medically significant Arthropoda - Culicidae

- **Anophelinae: 3 genera, *Anopheles* among the most important medicinal species**
- **→ vectors of malaria and several arboviruses and filarial nematods**
- **Culicinae: Most species, 37 genera, many of great medical importance, genera *Aedes* and *Culex***
- **→ vectors of arboviruses (more than 100 viruses that affect humans) and hosts of filarial nematods**

Anopheles sp.

Culex sp.

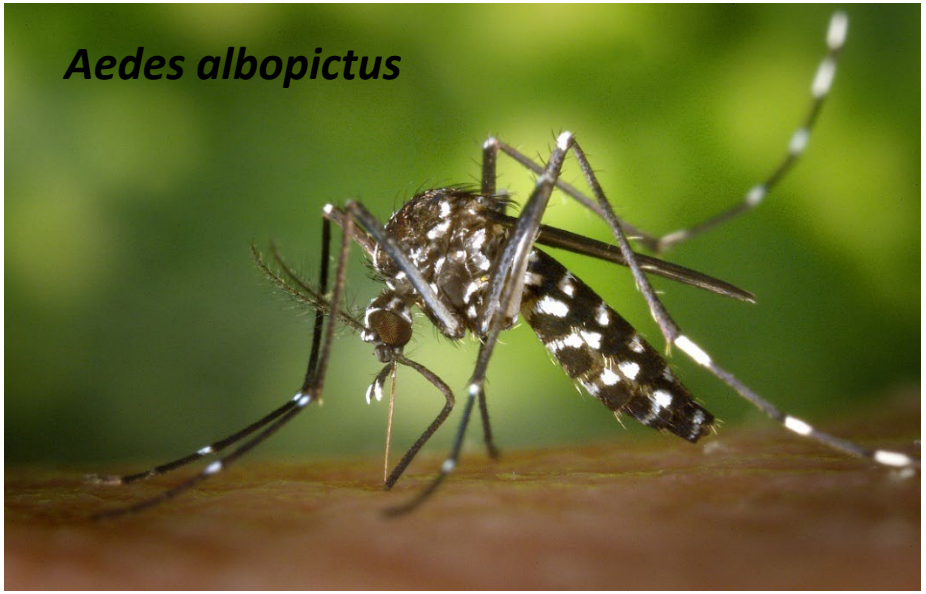
Medically significant Arthropoda - Culicidae



Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

- 37 genera,~3000 species
- More irritating species of mosquitoes than species of the subfamily Anophelinae
- Vectors of pathogens, mostly arboviruses and filarial forms
- Large variations in the period of activity in different species, some diurnal, some nocturnal
- The most important vectors in the genera *Aedes* and *Culex*



Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

- **Arbovirus vectors – about 100 viruses that can infect humans**
- **4 genera of viruses in 3 families of viruses: Togaviridae - genus *Alphavirus*; Flaviviridae – genus *Flavivirus*; Bunyaviridae – genera *Orthobunyavirus* and *Phlebovirus***

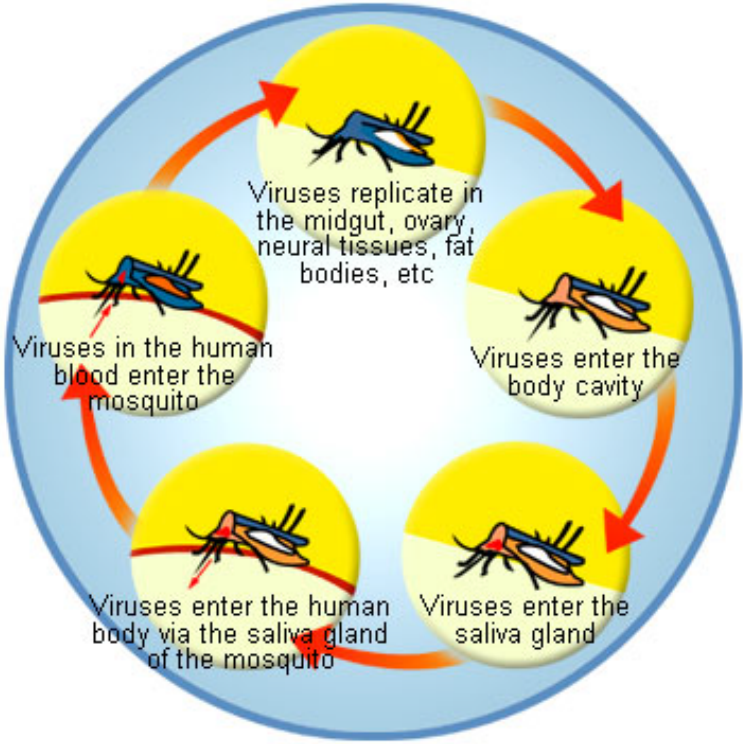


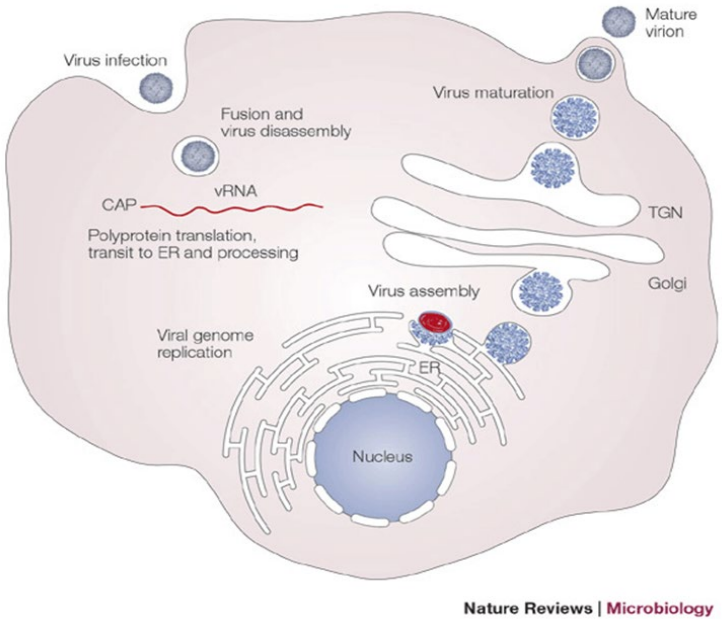
TABLE 15.2 Geographic Distribution of Selected Mosquito-Borne Viruses of Importance to Humans or Domestic Animals

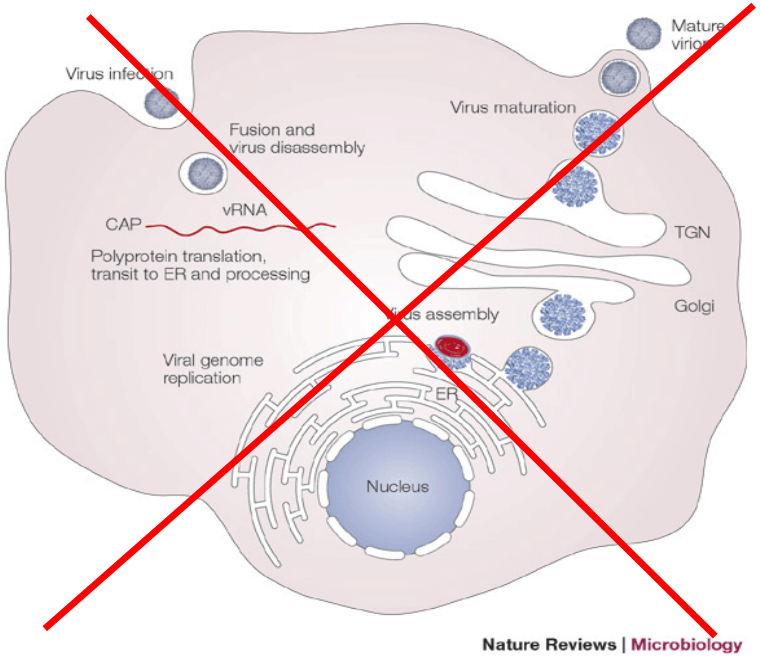
Family (Genus)	Virus Species and Serotypes	Distribution
Togaviridae (*Alphavirus*)	Eastern equine encephalomyelitis	Americas
	Venezuelan equine encephalomyelitis	South and Central America, Mexico, United States (Florida)
	Western equine encephalomyelitis	North America, Mexico, South America (eastern)
	Chikungunya	Africa, Asia, incl. Philippines, South, Central, and North America
	O'nyong nyong	Africa
	Ross River	Australia, New Guinea, Fiji, American Samoa
	Semliki Forest	Africa, Asia, incl. Philippines
	Mayaro	South America (northern), Trinidad
Flaviviridae (*Flavivirus*)	Dengue (4 serotypes)	Tropics, especially southern Asia and Caribbean
	Yellow fever	Africa, Central and South America
	St. Louis encephalitis	Americas
	Murray Valley encephalitis	Australia, New Guinea
	Japanese encephalitis	Asia (eastern), incl. Philippines
	West Nile	Africa, Europe, Israel, Asia; South, Central, and North America
	Ilheus	Central and South America
	Rocio	Brazil
	Wesselsbron	Africa, Asia (southern)
	Zika	Africa, Asia, South Pacific, South and Central America, Caribbean, southern North America
Bunyaviridae (*Orthobunyavirus*)	Bunyamwera	Africa
	Germiston	Africa
	Ilesha	Africa
	Wyeomyia	Central America
	Itaqui	South America
	Marituba	South America
	Murutucu	South America
	Oriboca	South America
	Madrid	Central America
	Nepuyo	Central and South America
	California encephalitis	United States (western)
	Jamestown Canyon	North America
	La Crosse encephalitis	United States (eastern)
	Inkoo	Finland
	Tahyna	Europe
	Guaroa	South America
Bunyaviridae (*Phlebovirus*)	Rift Valley fever	Africa (northern, eastern)

Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

- **VIRAL INFECTIONS**
- **In mosquitoes, infection of cells with the virus is usually without cytopathology and amplification usually lasts about 10 days**
- **In vertebrate hosts, infected cells lyse after releasing large amounts of virions**
- **The duration of viremia (the presence of the virus in the blood) depends on the type of virus**





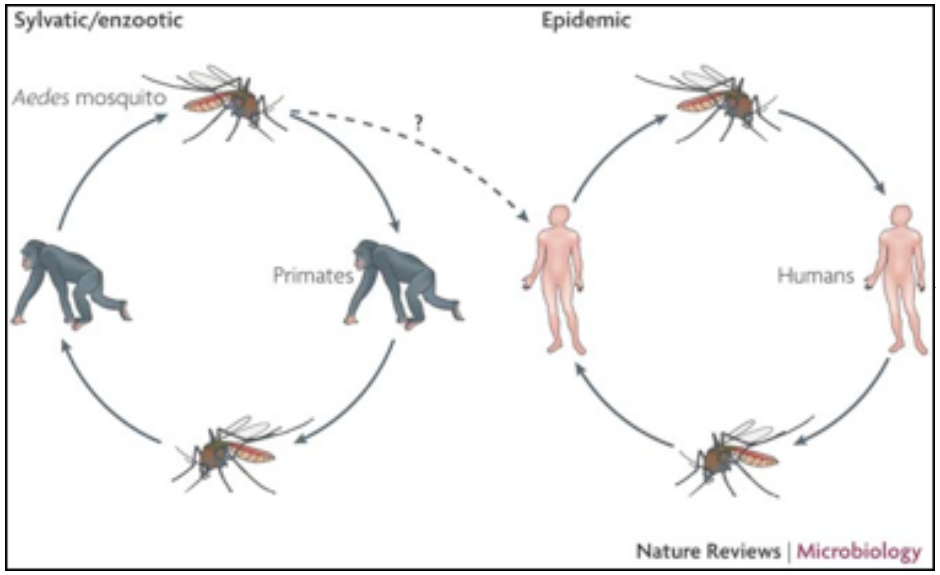
Woodbridge & Walker 2019

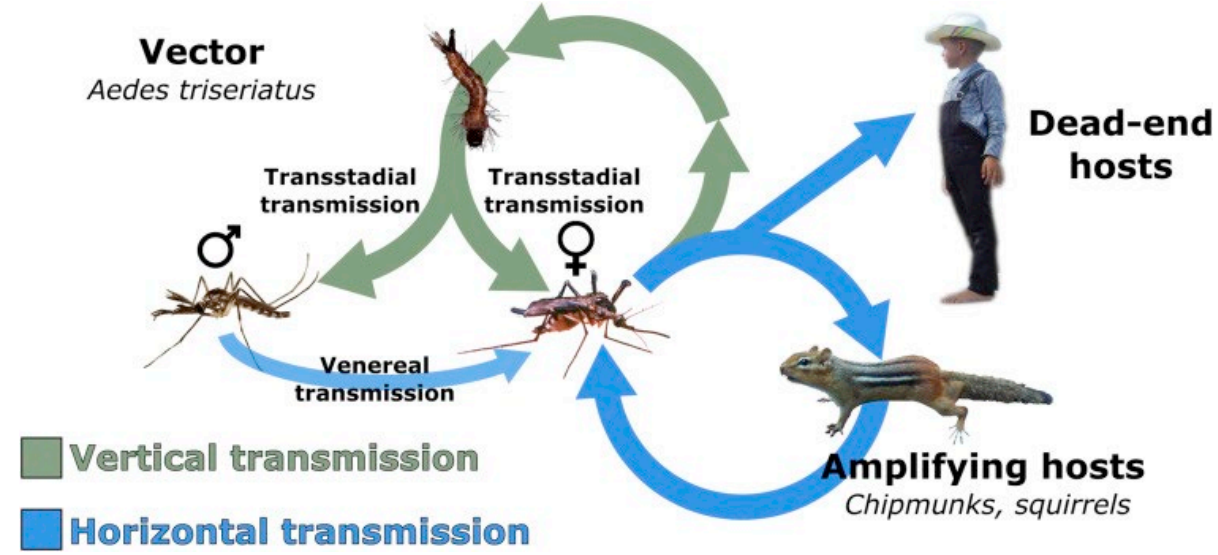
Medically significant Arthropoda - Culicinae

- **VIRAL INFECTIONS AND TRANSMISSION**
- **Horizontal transmission:** transmission of viruses between vectors and hosts
- **Vertical transmission:** transmission of virus to other individuals, life stages or generations within a vector population
- **Transstadic**
- **Transgenerational**

(most often Transovarian)

- **Venerable**

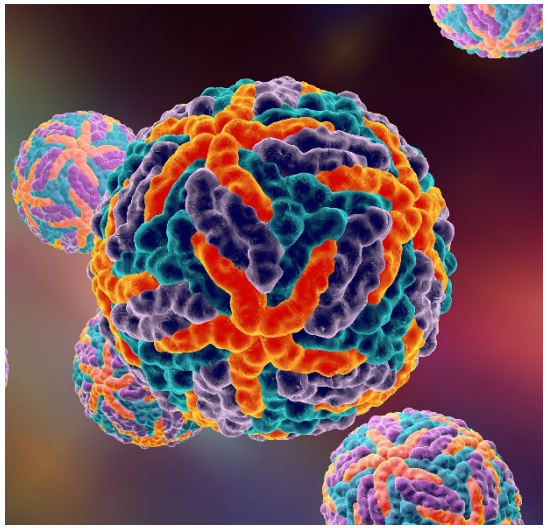


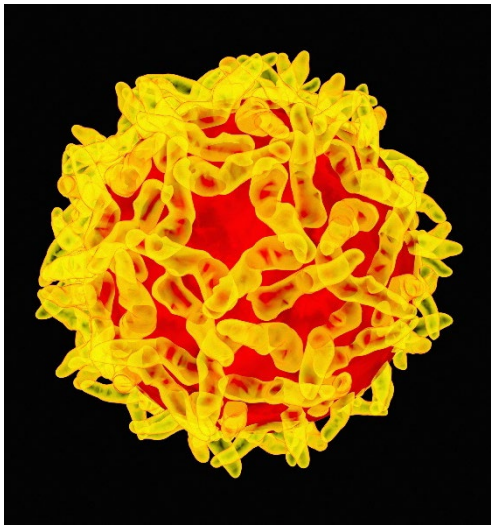


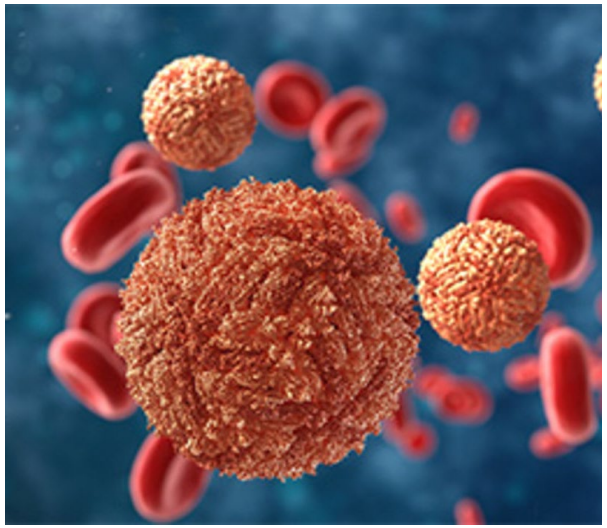
Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

- **ARBOVIRUS SYMPTOMS**
- **Most cause only fever and muscle aches, but some can progress to acute illnesses, hemorrhagic fevers (eg. Dengue and Yellow Fever) and Encephalitis (eg. West Nile Virus, Eastern Equine Encephalitis, La Crosse, etc….)**
- **Some, like the Zika virus, can interfere with the fetal development of the child**
- **Viruses (especially RNA viruses) mutate very quickly and that's why sometimes they just "come" and "go"**

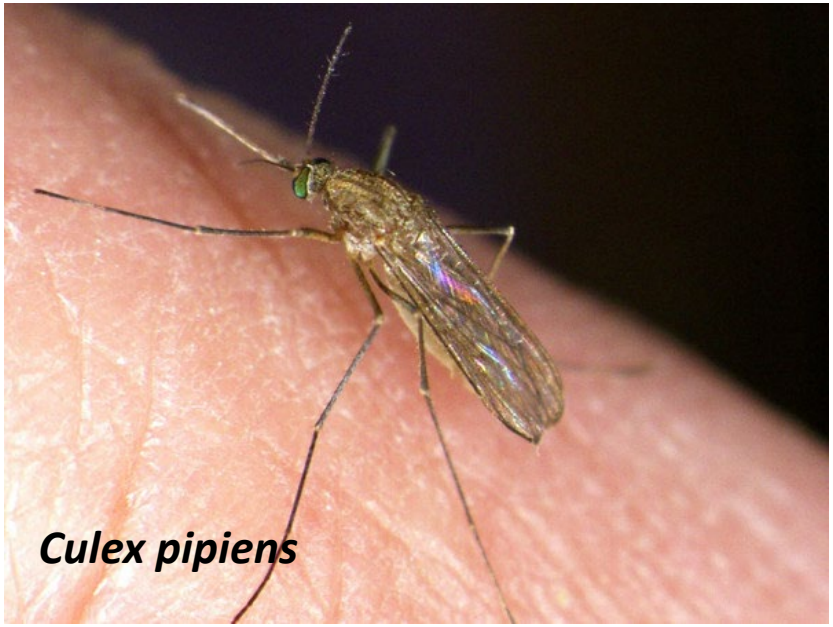






Medically significant Arthropoda - Culicinae

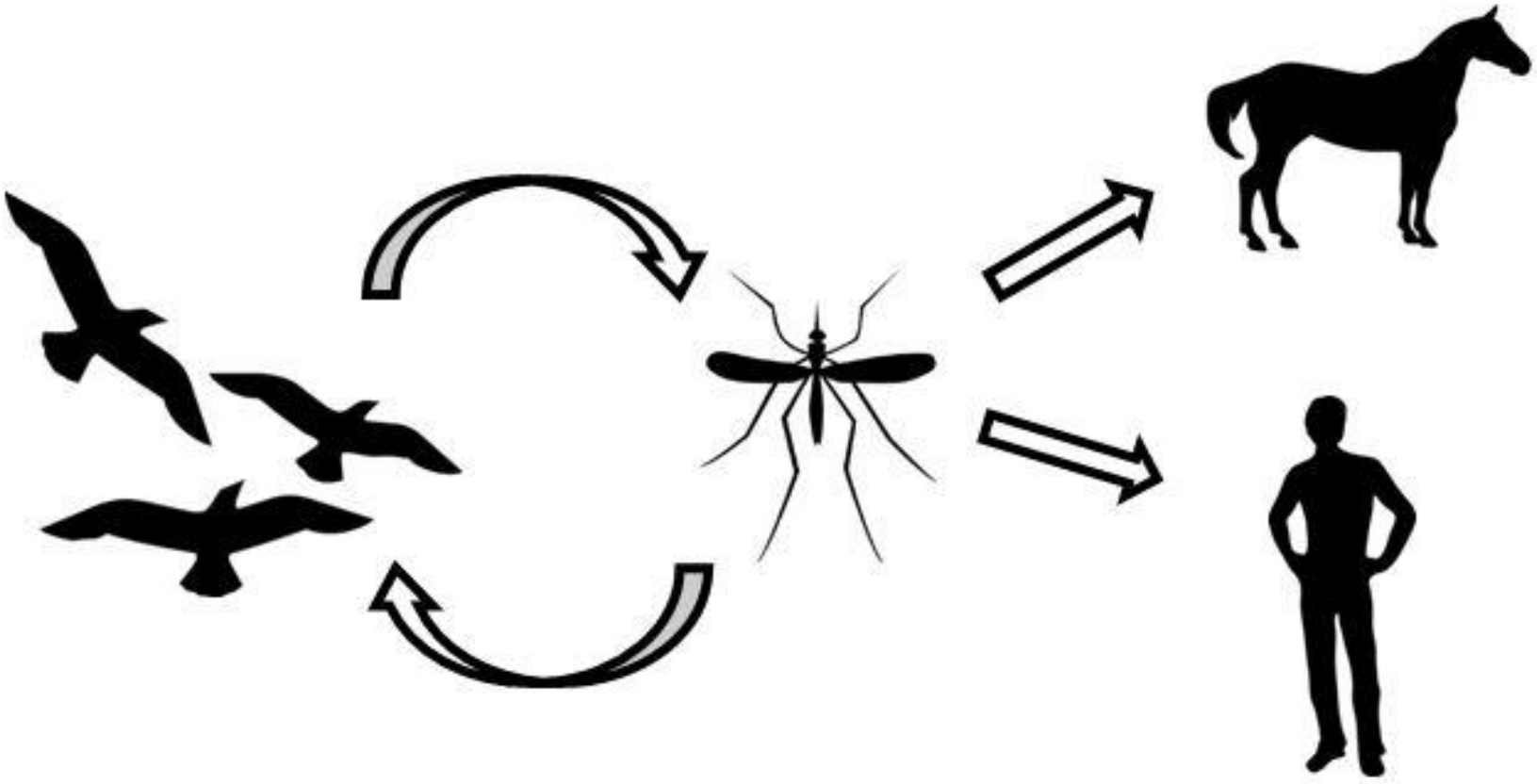
- **WEST NILE VIRUS**
  - **It is caused by West Nile Flavivirus**
  - **Zoonosis with birds (> 150 species) as a virus reservoir**
  - **It is transmitted by numerous species of Culicinae (and several species of Anophelinae) with the species *Culex pipiens* as the most common vector of the disease**



Culex pipiens

Medically significant Arthropoda - Culicinae

- **WEST NILE VIRUS**
  - **Amplifying hosts are numerous birds (can be lethal to some of them)**
  - **Vertical transmission to offspring through female mosquitoes has been confirmed**



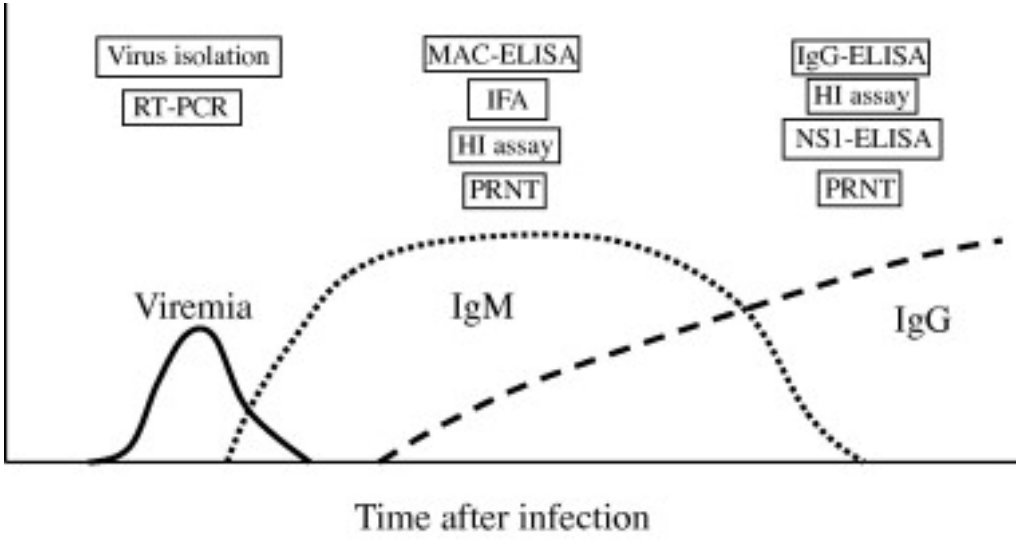
Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

- **WEST NILE VIRUS – SYMPTOMS**
- **Most people are asymptomatic**
  - **5-20% will develop West Nile Fever – flu-like symptoms lasting 3 to 6 days (headache, fever, chills, exhaustion,…)**
  - **Less than 1% of infected people will develop a form of neuro-invasive disease (WNND) - Encephalitis, muscle weakness, neck stiffness, paralysis, meningitis, and numerous other neurological problems**
  - **According to data from the European Center for Disease Prevention and Control, in 2018 (until August 30), a total of 710 cases of infection with the West Nile virus were recorded in Europe (at most 327 cases in Italy, 213 in Serbia, 147 cases in Greece, 117 in Romania, 96 in Hungary, etc.)**
  - **In Croatia, the disease first appeared in 2012.**
  - **A total of 26 confirmed cases with one deceased person were reported in Croatia in 2018 (until the beginning of September), and 39 cases were confirmed in 2023 alone. Based on the available data, all newly infected persons are infected in the northwestern and eastern parts of the Republic of Croatia**

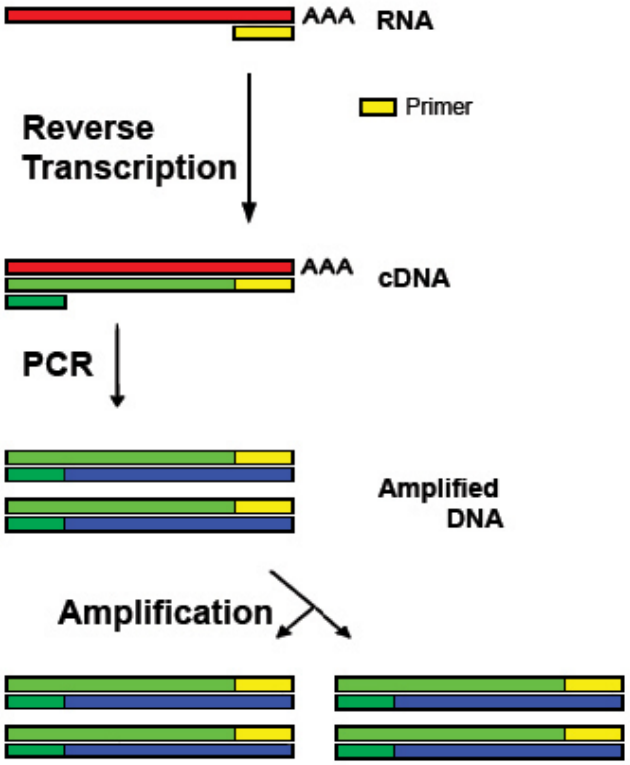
Medically significant Arthropoda - Culicinae

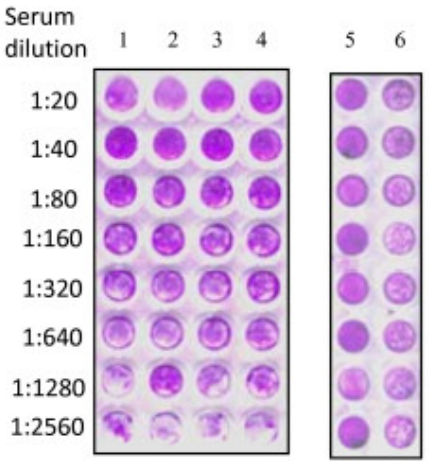
- **WEST NILE VIRUS – DIAGNOSIS**
- **The clinical picture is similar to all other flaviviruses – laboratory confirmation of the virus is required**
- **Incubation lasts 2-12 days after infection and viremia lasts about 2 weeks (up to 40 days in some)**
- **Detection of WNV-specific IgM antibodies in serum or cerebrospinal fluid is possible within 3-8 days from the onset of symptoms (and within 90 days), WNV-specific IgG antibodies are also detected a little later (and even years later), but IgM antibodies are also produced with other flavoviruses – false positive results**

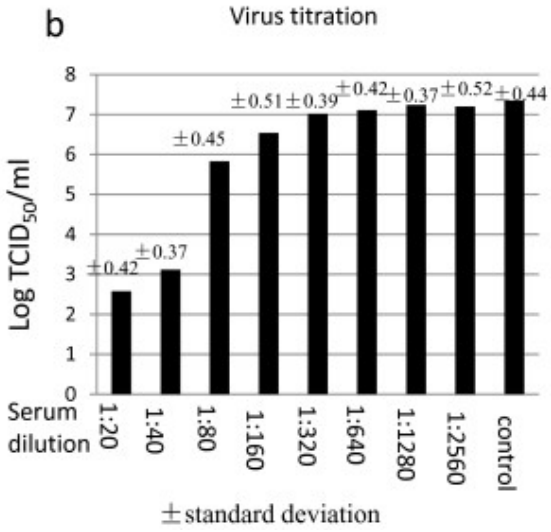


Medically significant Arthropoda - Culicinae

- **WEST NILE VIRUS – DIAGNOSIS**
- **Other tests: PCR for viral RNA ("Real time" Reverse Transcriptase RT-PCR) in acute samples or Plaque Reduction Neutralization Test (TNSP) in convalescent samples (in people who have recovered from the disease)**
- **There is no medicine, hospitalization, ventilator in severe cases, drugs against fever and pain, ... - long recovery even in mild cases**



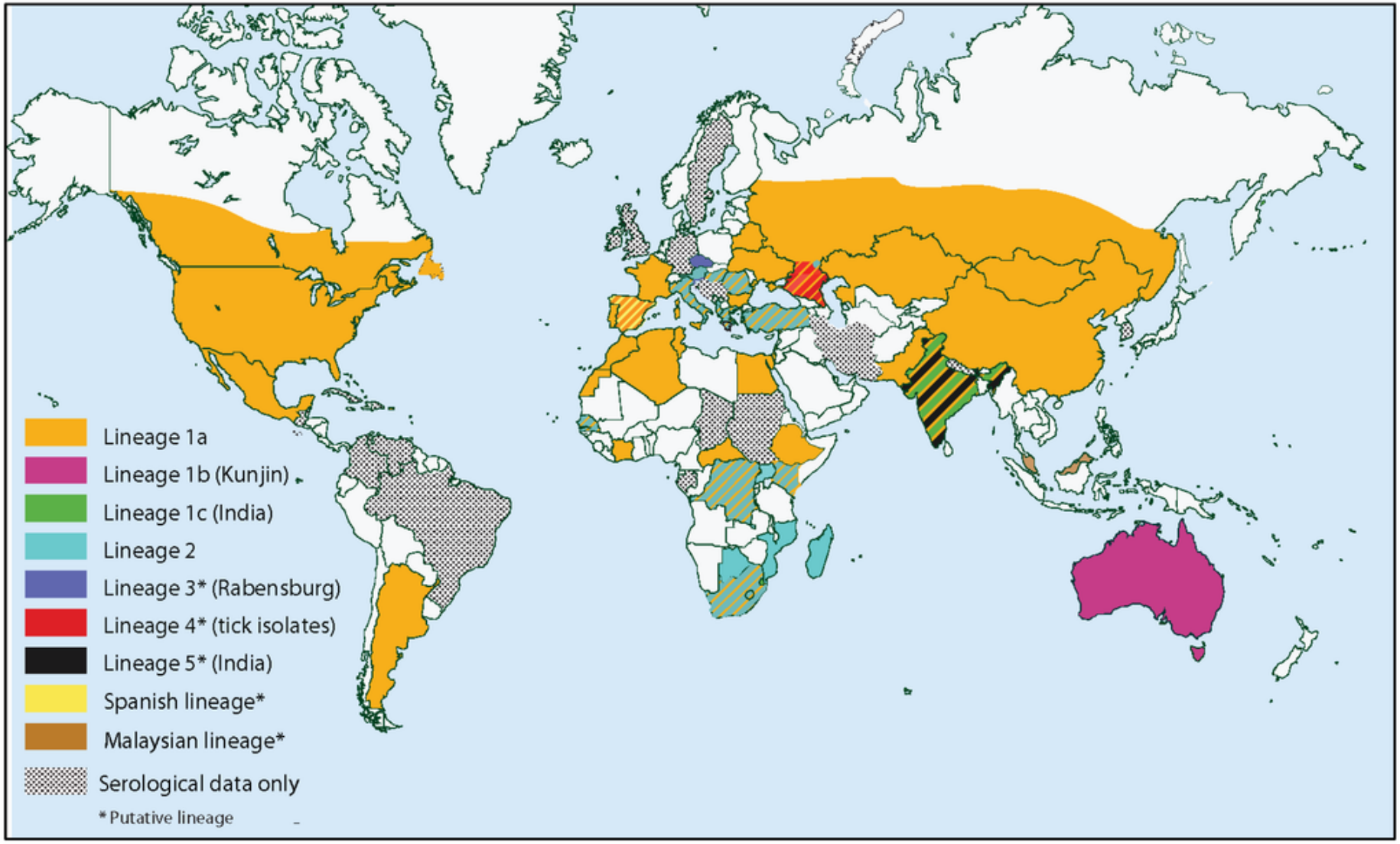




Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

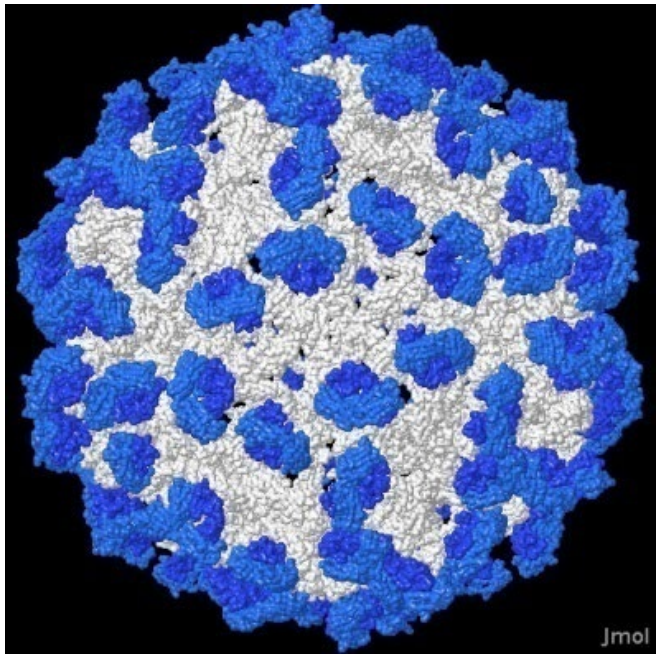
- **WEST NILE VIRUS**



Ciota & Kramer 2013; Woodbridge & Walker 2019

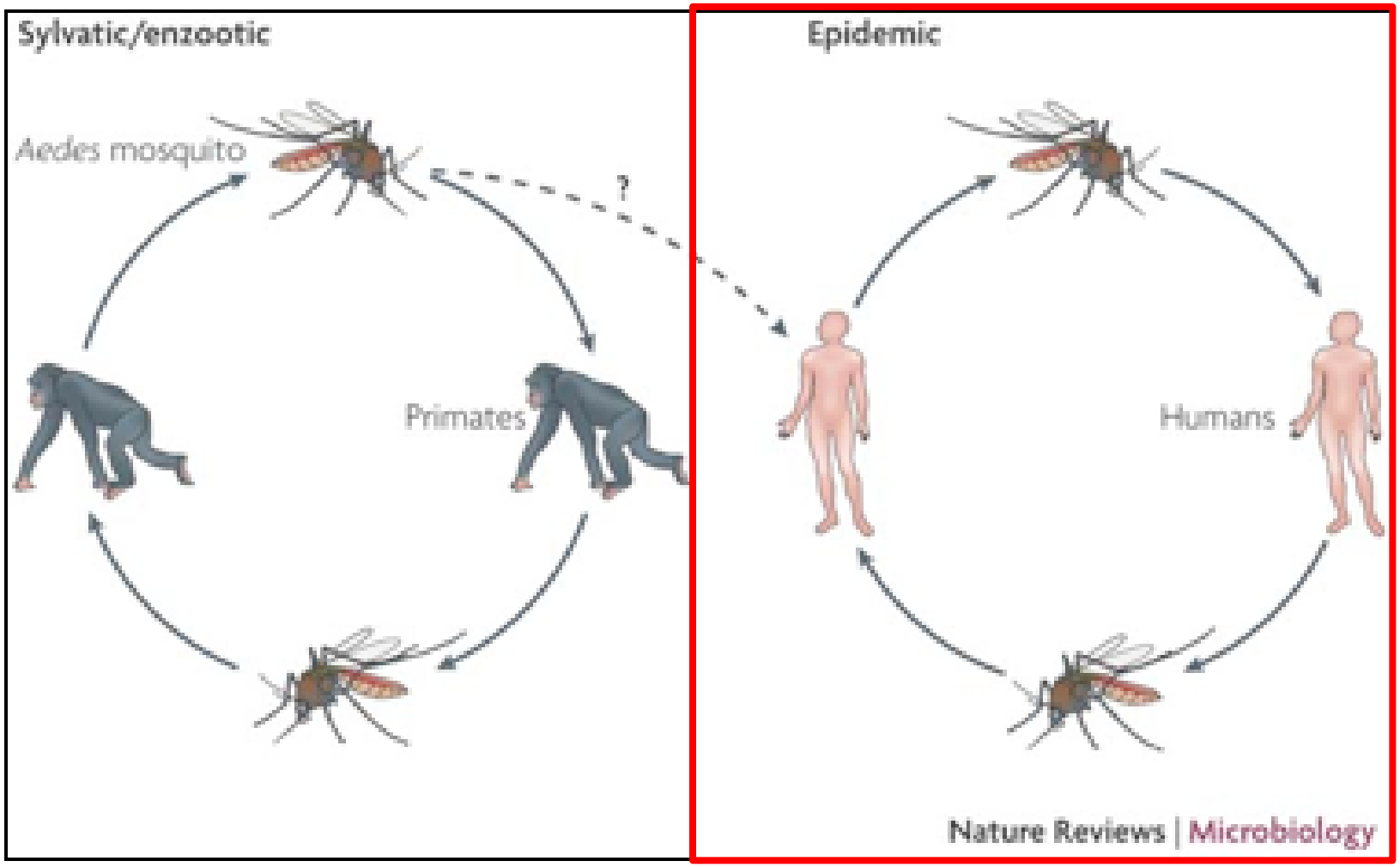
Medically significant Arthropoda - Culicinae

- **DENGE FEVER**
- **4 serotypes of Dengue Flavovirus (DENV 1, DENV 2, DENV 3 and DENV 4)**
- **Humans are the main hosts where the virus multiplies, but the number of new infections in other primates has increased**
- **It is transmitted by different species of the subfamily Culicinae, but the most important vector is the species *Aedes aegypti*, but also *Aedes albopictus***



Medically significant Arthropoda - Culicinae

- **DENGE FEVER**



RARELY **USUALLY**

Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

- **DENGE FEVER**

  - **Incubation of the virus is 5-8 days after a mosquito bite**
  - **About 50% of people are asymptomatic or have only a mild fever**
  - **Others have an extreme fever that starts suddenly, severe headaches, rashes, muscle and joint pain**
  - **Viremia lasts for a short time (2-7 days), but in the case of secondary infections, it can be prolonged**
  - **In English, another name for Dengue is "breakbone fever" because of the severe pain**
  - **It usually lasts about 1 week and after that the person fully recovers**
  - **In some people, the disease passes into the hemorrhagic phase - most often in children under 15 years of age or with secondary infections (also in some with serotype DENV-1 and DENV-2 infection)**

Medically significant Arthropoda - Culicinae

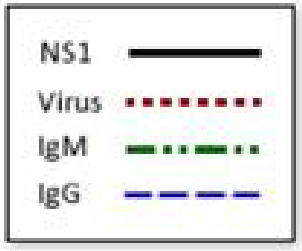
- **DENGE FEVER – SYMPTOMS**
  - **DENGE HAEMORRHAGIC FEVER (DHF)**
  - **The first stage of complications – Plasma comes out of the blood vessels, bleeding from the nose, gums and under the skin (purple blisters). It usually lasts 24-48 hours, after which recovery follows, especially if it is treated with fluid and plasma intake**
  - **The virus mainly infects dendritic cells, monocytes and lymphocytes, but also hepatocytes and endothelial cells**
  - **DHF is associated with increased vascular endothelial permeability rather than cell damage**

Medically significant Arthropoda - Culicinae

- **DENGE FEVER – SYMPTOMS**
- **DENGE SHOCK SYNDROME (DSS)**
- **All symptoms of DHF + abdominal pain, hypotension (low blood pressure) and eventually collapse of the circulatory system**
- **Very often it ends in death, unless fluids are replaced intravenously, often in children who have received dengue antibodies through their mother???**
- **DHF and DSS are significantly more common in people who have been exposed to one dengue virus serotype and then within 5 years are exposed to another dengue virus serotype**
- **Mortality just under 1%**
- **There is no treatment, only intravenous fluids can prevent death**

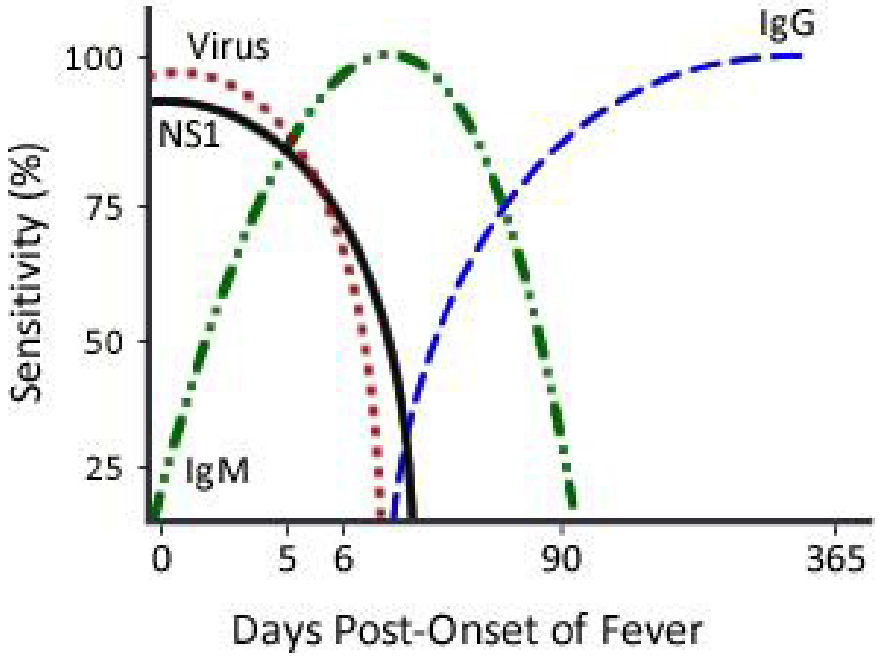
Medically significant Arthropoda - Culicinae

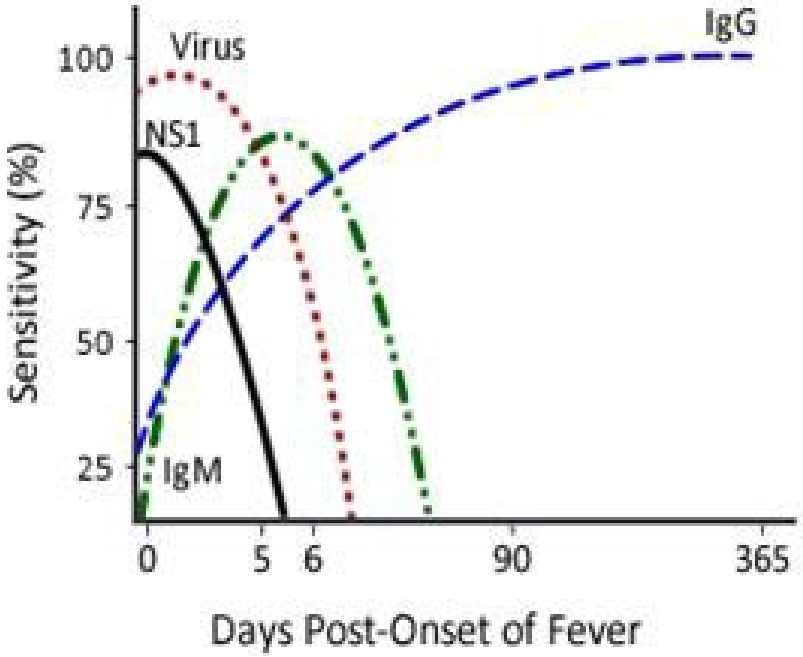
- **DENGE FEVER – IMMUNE RESPONSE**



DENV-reactive IgG
DENV-reactive IgM
Dengue viral protein, NS1

Secondary infection

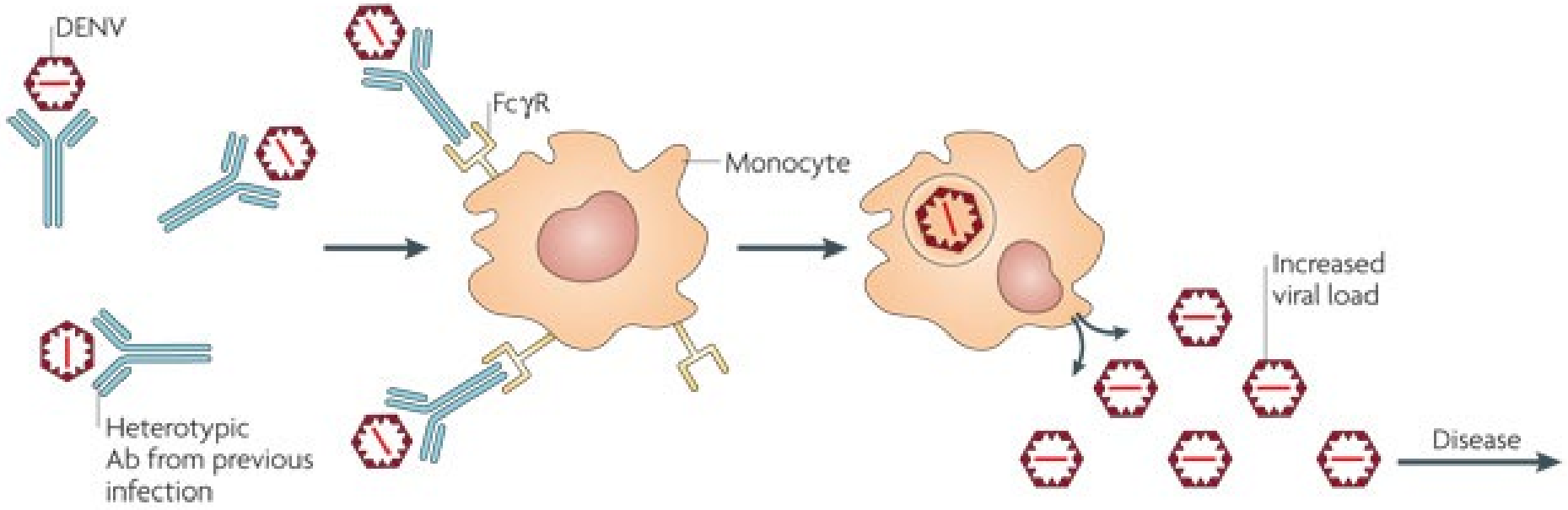




SOURCE: https://www.cdc.gov/dengue/clinicallab/laboratory.html

Medically significant Arthropoda - Culicinae

- **DENGE FEVER – IMMUNE RESPONSE**



Model of antibody-dependent enhancement of dengue infection
Antibody (Ab)-dependent enhancement of infection occurs when preexisting antibodies present in the body from a primary (first) dengue virus (DENV) infection bind to an infecting DENV particle during a subsequent infection with a different dengue serotype. The antibodies from the primary infection cannot neutralize the virus. Instead, the Ab–virus complex attaches to receptors called Fcγ receptors (FcγR) on circulating monocytes. The antibodies help the virus infect monocytes more efficiently. The outcome is an increase in the overall replication of the virus and a higher risk of severe dengue.

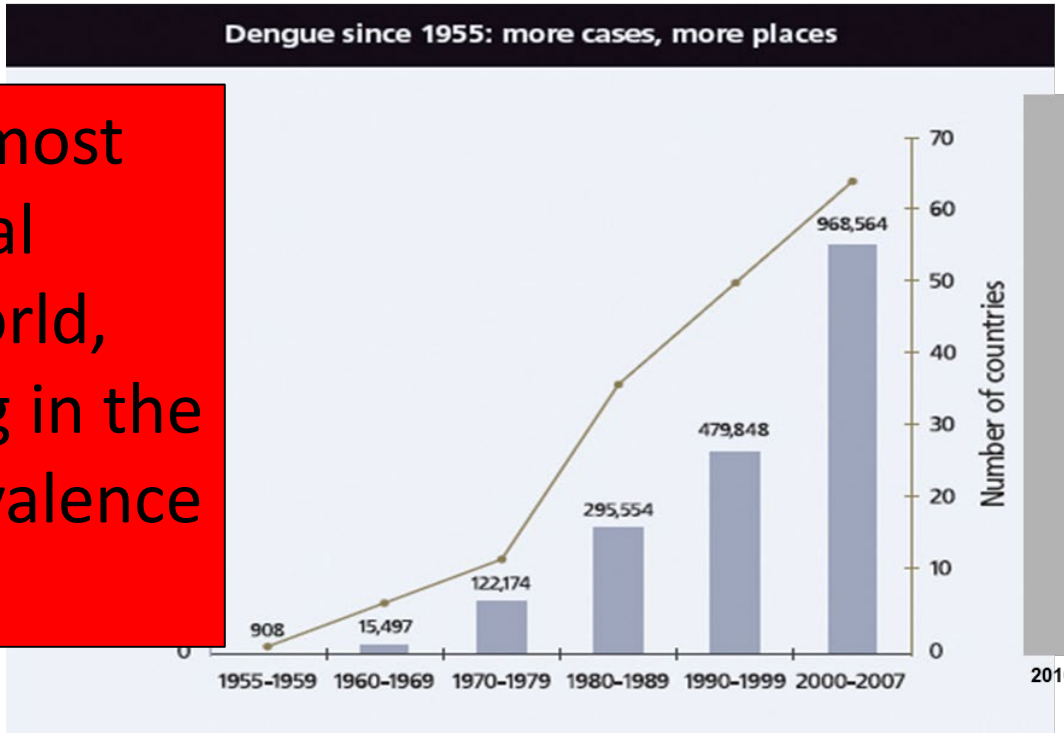
Medically significant Arthropoda - Culicinae

- **DENGE FEVER – DIAGNOSIS**
- **Clinical diagnosis is easier than with WNV, especially in areas where the disease is common**
- **Given that it can still be confused with some other diseases, laboratory diagnosis is necessary**
- **Acute phase (first 5 days of symptoms) Real-time RT PCR – enables serotype detection often in combination with IgM and IgG tests**
- **Late acute/early convalescent (early recovery) – IgM detection (ELISA (Enzyme-linked immunosorbent assay) or TNSP (Plaque Reduction Neutralization Test))**
- **Late convalescent or testing for previous infections - IgG detection (ELISA or TNSP)**

Medically significant Arthropoda - Culicinae

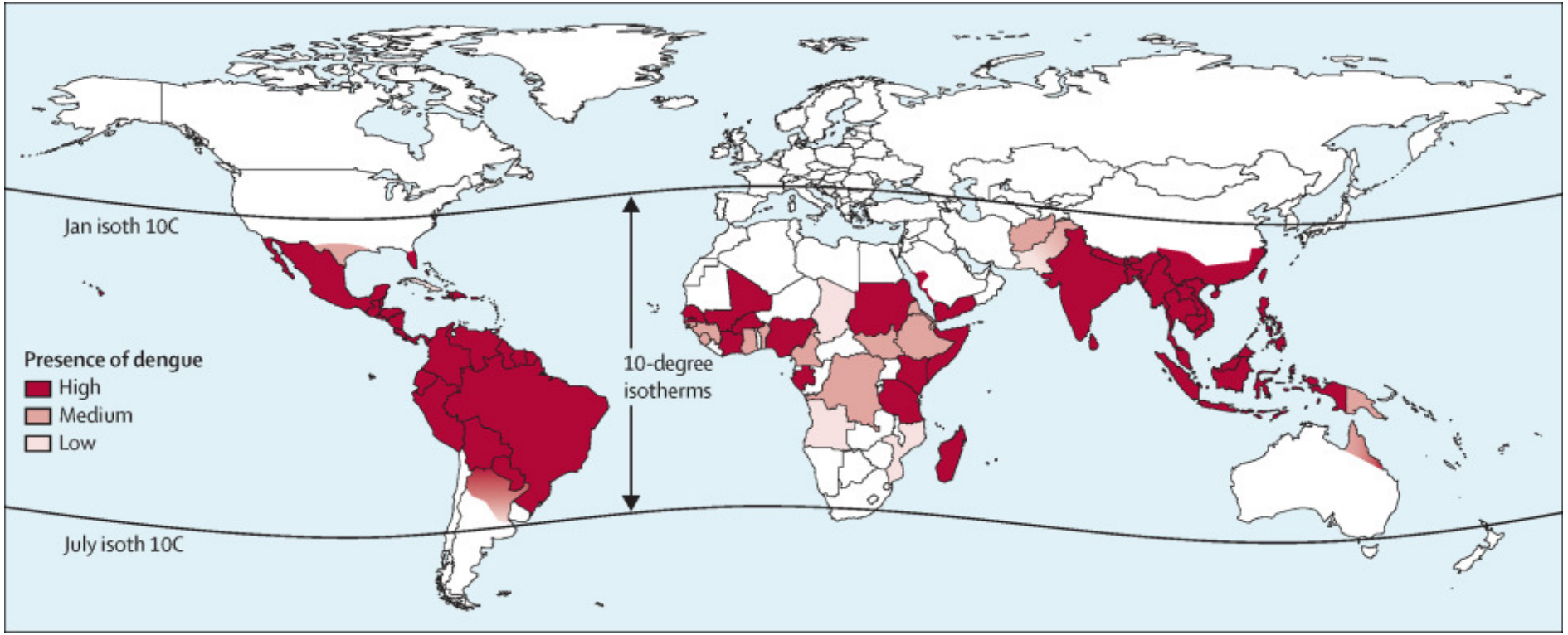
- **DENGE FEVER – IN THE WORLD**
  - **It is estimated that more than 400 million people are infected annually**
  - **Very fast progression and number of cases – 1.6 million cases in 2010, 2.3 million in 2013, 3.2 million in 2015,….**

→Currently the most common arboviral disease in the world, rapidly increasing in the number and prevalence of cases



Medically significant Arthropoda - Culicinae

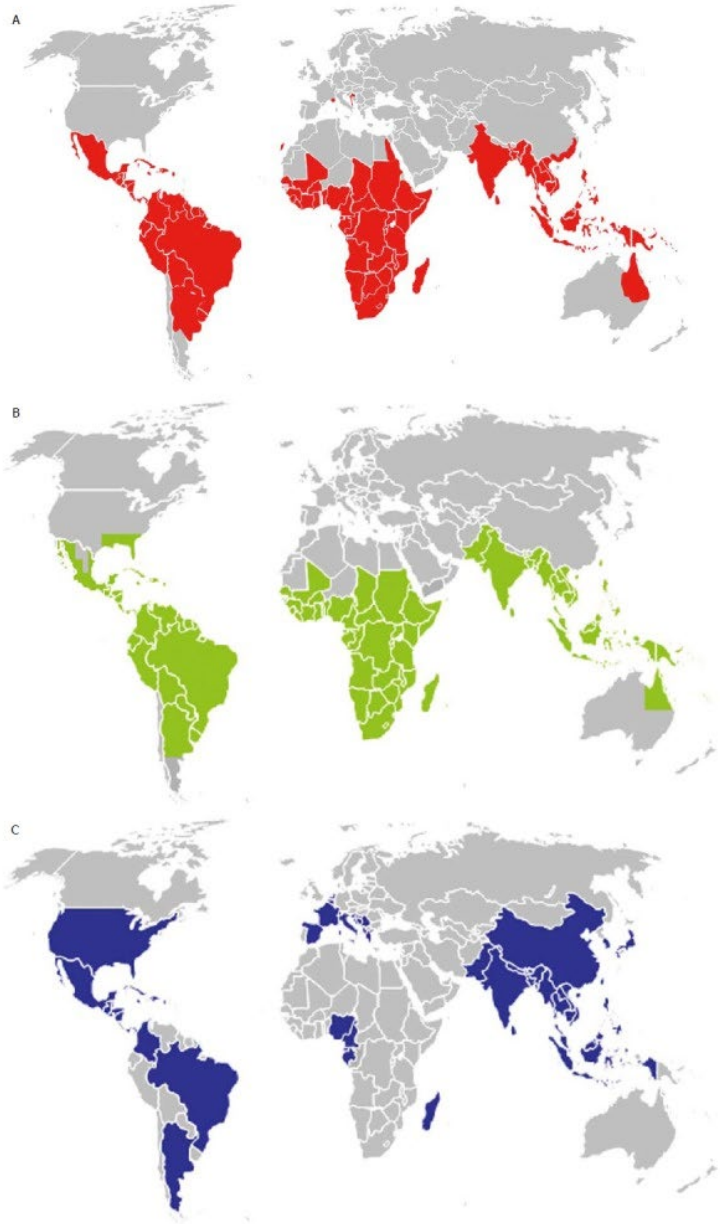
- **DENGE FEVER – IN THE WORLD**
  - **Imported dengue fever has been recorded in Croatia on several occasions, and the first autochthonous (infected here) disease was described in 2010 on the Pelješac Peninsula in Podobuč by a guest from Germany. After that, two more cases were recorded from Pelješac among the local population**



Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

- **DENGE FEVER – IN THE WORLD**



- **Distribution of dengue cases worldwide (A) and expansion of the two main vectors, *Aedes aegypti* (B) and *Aedes albopictus* (C)**

Pozetto et al. 2015; Woodbridge & Walker 2019

Medically significant Arthropoda - Culicinae

- **DENGE FEVER – IN THE WORLD**
  - **Since the 1940s, more and more epidemics**
  - **The latest outbreaks are becoming more frequent and appear to be significantly more virulent**
  - **Infections through blood transfusion are possible, but rarely reported**
  - **In America, the Dengue virus has replaced the yellow fever virus in urban areas**
  - **Transovarial virus transmission confirmed in *Aedes aegypti***
  - **First Dengue vaccine (CYD-TDV, Dengvaxia) approved commercially from 2021**
  - **Making the vaccine was very challenging, why?**
  - **CYD-TDV is only recommended for people aged 9-45 and is effective against serotypes 3 and 4, but it should only be used in people who have already had dengue or in populations where dengue is extremely common, it should not be used in children**
  - **New vaccines are currently being developed**

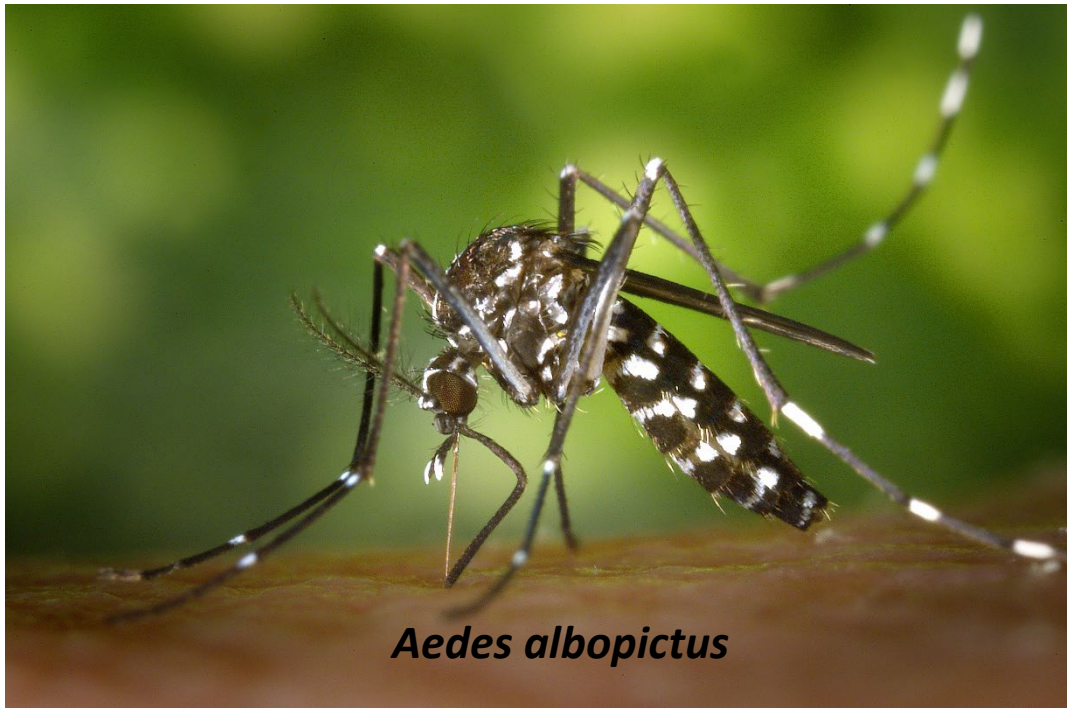
Medically significant Arthropoda - Culicinae

- **DENGE FEVER – IN THE WORLD**

Dengue fever has arrived in Europe Paris, Italy!!!!!

Medically significant Arthropoda - Culicinae

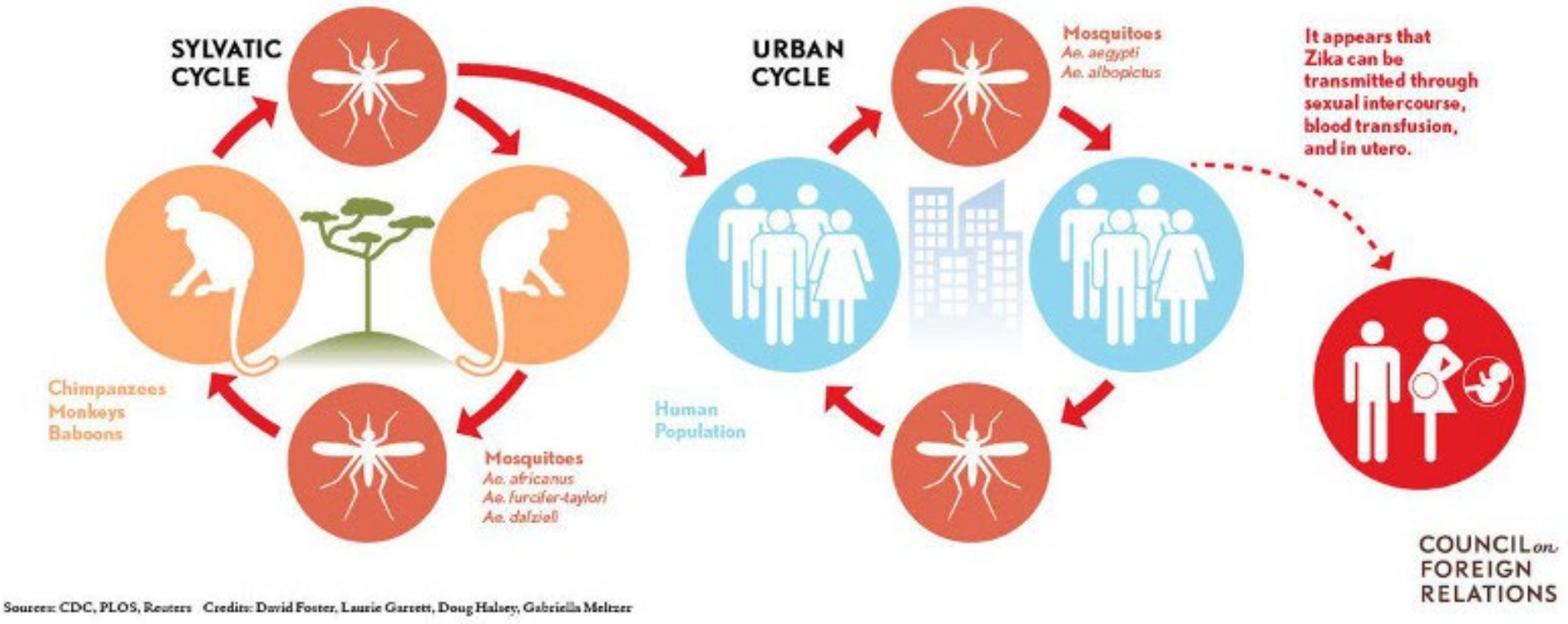
- **ZIKA**
- **It is caused by the Zika Flavivirus**
- **Primates (including) humans are the main hosts and reservoirs of the virus, and antibodies have been detected in other mammals as well**
- **It is transmitted by various mosquitoes of the Culicinae subfamily, but the most common vectors are *Aedes aegypti* and *Aedes albopictus***



Aedes albopictus

Medically significant Arthropoda - Culicinae

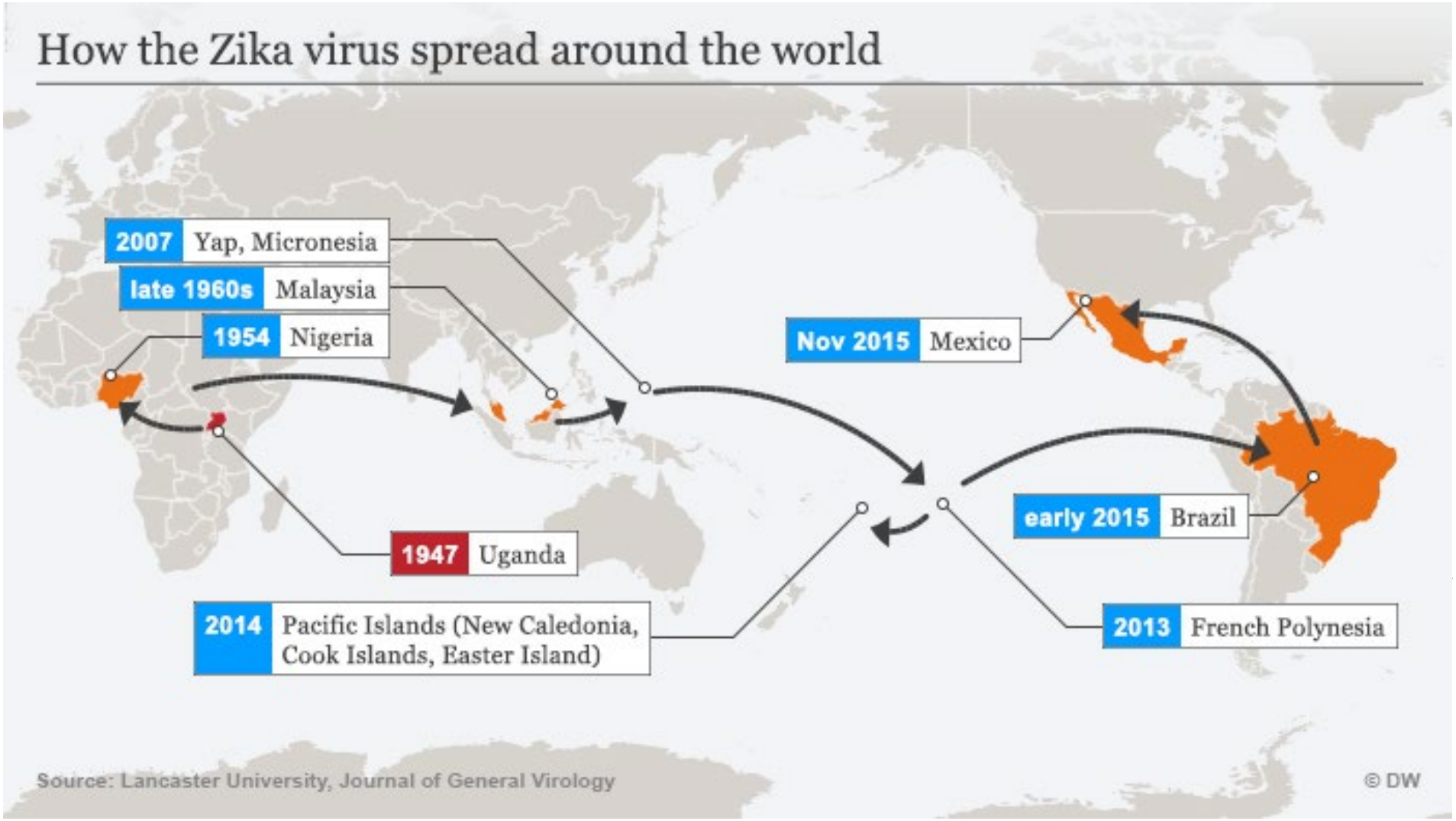
- **ZIKA**



WARNING! Knowledge about the Zika virus and the disease is constantly updated and changing, so this may not all be correct and will change with time and new knowledge

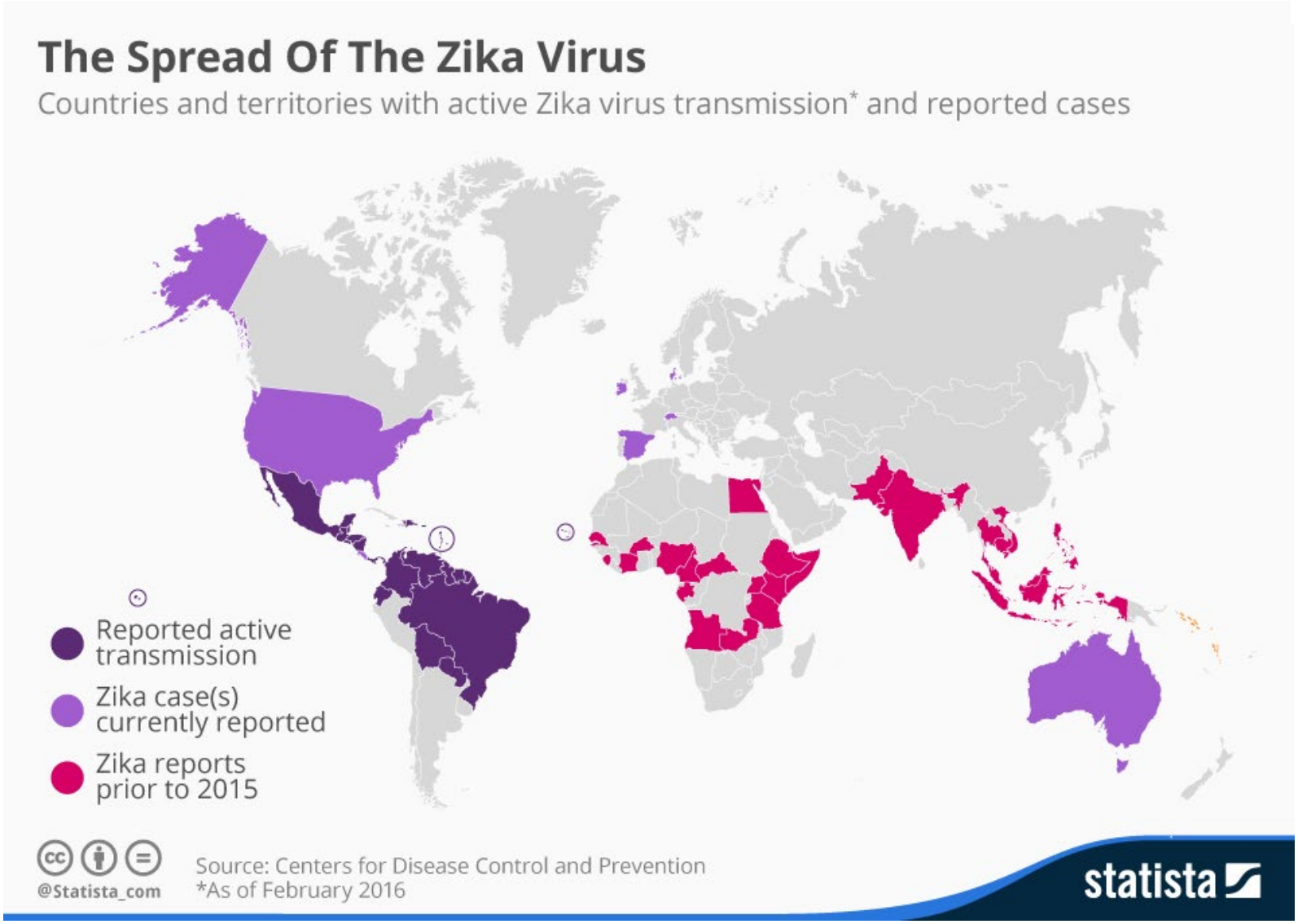
Medically significant Arthropoda - Culicinae

- **ZIKA**



Medically significant Arthropoda - Culicinae

- **ZIKA**



Medically significant Arthropoda - Culicinae

- **ZIKA**
  - **Incubation 3-12 days after injection**
  - **60-80% of people will be asymptomatic or have mild flu symptoms (fever, rash, conjunctivitis, joint pain, headache, etc.) for up to a week**

Medically significant Arthropoda - Culicinae

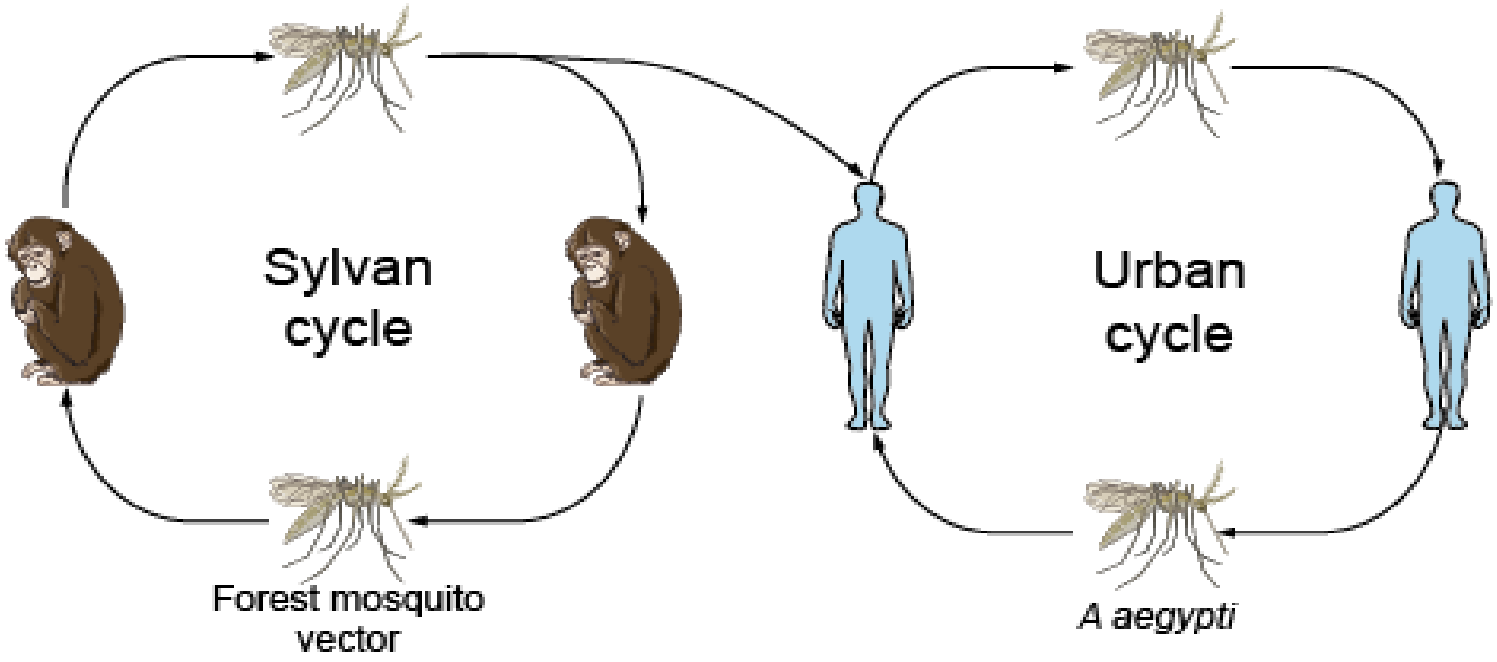
- **ZIKA**
  - **Viremia is about 10 days in plasma, but longer in whole blood (about 22 days) and prolonged during pregnancy (up to 100 days), in amniotic fluid (where the concentration is very high) and in sperm (up to 69 days)**
  - **Complications - abortions, stillborn children, microcephaly and numerous other neurological disorders and malformations of newborns (CONGENITAL ZIKA SYNDROME), activation of Guillain-Barre syndrome (immune system attacks the peripheral nervous system),....**

Medically significant Arthropoda - Culicinae

- **ZIKA – DIAGNOSIS**
  - **Clinical diagnosis + travel history**
  - **Recommendations for laboratory testing (RT-PCR, serology (IgM) or TNSP) depending on country and patient**
  - **Pregnant women should be especially careful and tested because of potential implications**

Medically significant Arthropoda - Culicinae

- **YELLOW FEVER**
- **It is caused by the yellow fever virus, which is also a Flavivirus - the first discovered arbovirus associated with human disease and transmitted by mosquitoes - isolated in 1927 in Ghana**
- **It is transmitted by various mosquitoes of the genus *Aedes*, but the only vector in humans is *Aedes aegypti***



Medically significant Arthropoda - Culicinae

- **YELLOW FEVER – SYMPTOMS**
- **Hemorrhagic disease with mortality from 5% to 75%**
- **Post-sting incubation of 3 to 6 days, followed by sudden onset of fever (> 40˚C), headache, nausea and pain**
- **Viremia lasts only 3 days, but the virus causes necrosis of liver parenchyma cells, which leads to an increased amount of bilirubin in the blood and jaundice, which is why it is called yellow fever**
- **Hemorrhage manifests itself as bleeding gums, slight bruising on the skin and peeling of the stomach lining, which leads to vomiting of black blood ("black vomit")**
- **Delirium and coma occur before death**

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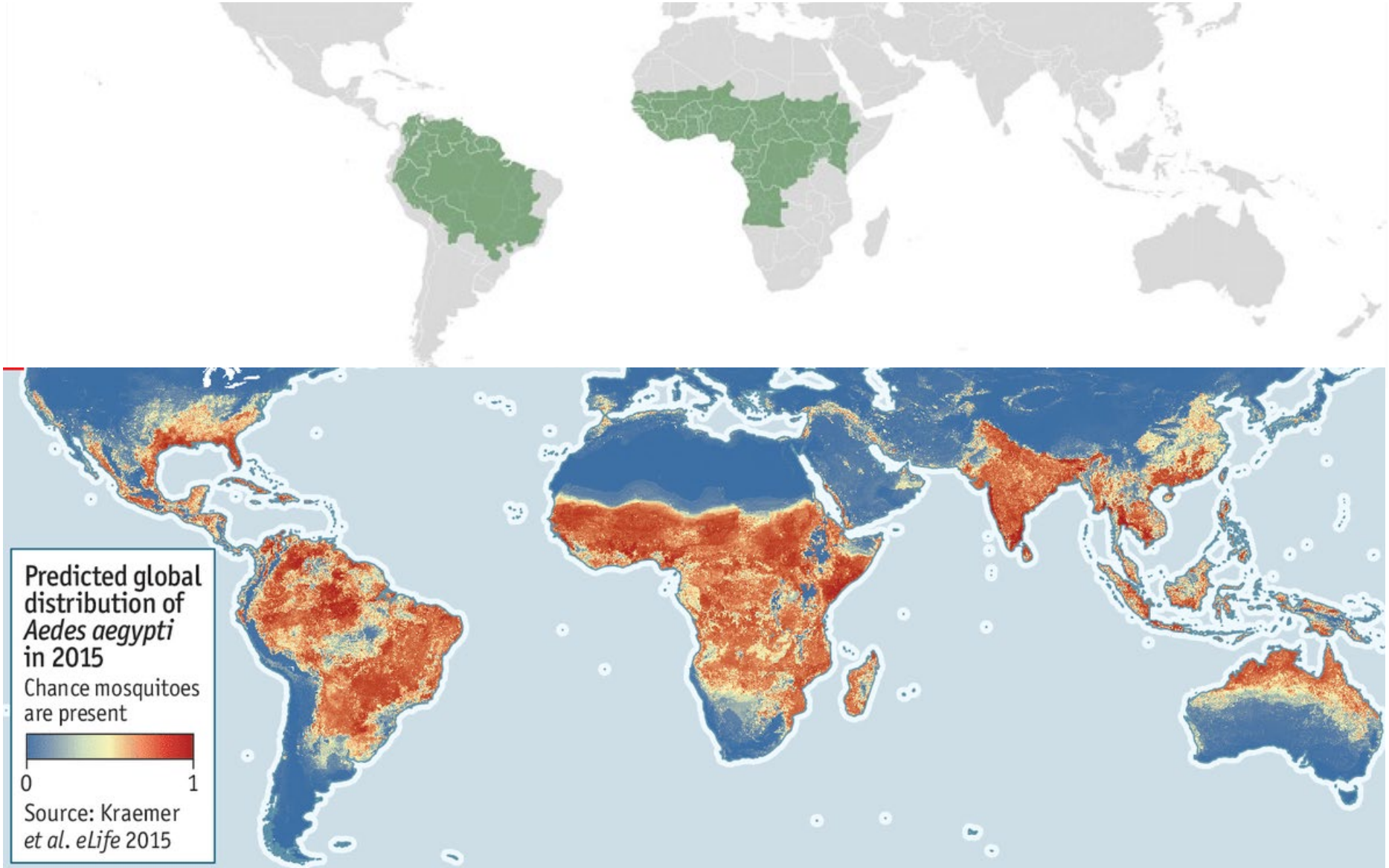
Medically significant Arthropoda - Culicinae

- **YELLOW FEVER**



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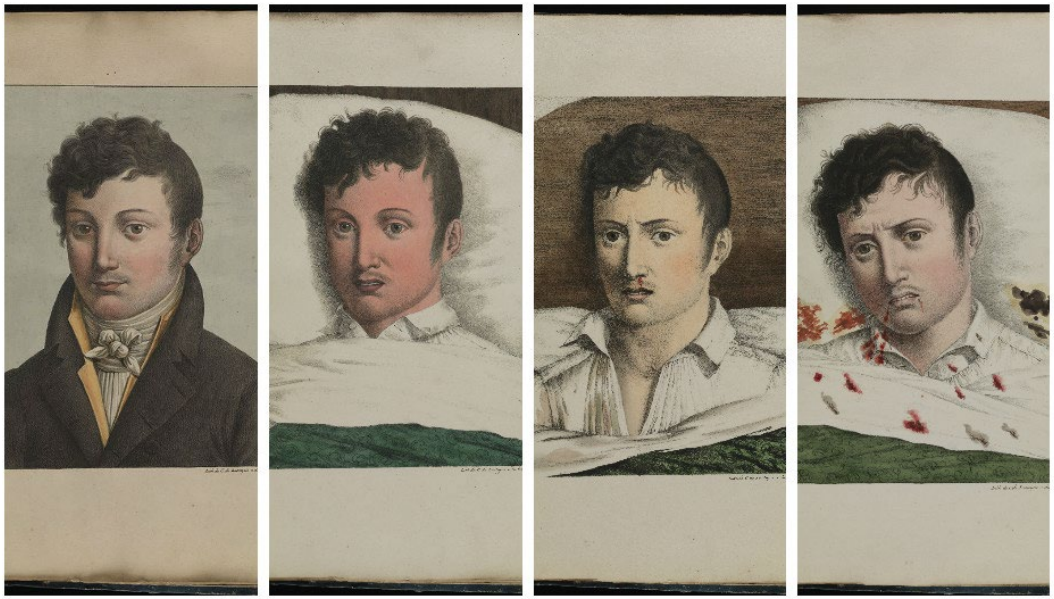
Medically significant Arthropoda - Culicinae

- **YELLOW FEVER**
- **In past centuries, yellow fever had a devastating effect on temperate and subtropical areas, especially in North America**
- **Today, it is still one of the major causes of death in the villages of tropical Africa, with occasional epidemics around the world - in 2016, an epidemic in Angola and the Democratic Republic of Congo, and in 2017 in Brazil**
- **The virus, together with the vector, was transferred from Africa to the Americas 400 years ago due to the slave trade**



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Medically significant Arthropoda - Culicinae

- **YELLOW FEVER**
- **From 1600 to 1900, yellow fever ravaged the New World and caused numerous deaths, especially in port cities**
- **New Orleans had regular epidemics from 1796 to 1905, which was also the last epidemic in N America**
- **Unlike Old World monkeys, some New World monkeys can have very high mortality in the sylvatic cycle (e.g. howlers), while others do not die from infection but are only viremic (e.g. capuchins)**

Medically significant Arthropoda - Culicinae

- **YELLOW FEVER**
- **Carlos Finlay, a Cuban doctor, proved in an experiment in 1900 that *Aedes aegypti* transmits the virus**
- **Systematic vector control and destruction of breeding sites and successful elimination of urban yellow fever began**
- **After the isolation of the virus, a vaccine was made, which proved extremely effective and Max Theiler received the Nobel Prize for it**
- **MANDATORY VACCINATION WHEN GOING TO SOUTH AMERICA and AFRICA**

Medically significant Arthropoda - Culicinae

- And many, many viral diseases of humans and animals,…….
- Encephalitis (Japanese Encephalitis, Murray Valley Encephalitis, St. Louis Encephalitis, La Crosse Encephalitis, Eastern Equine Encephalitis, Western Equine Encephalitis, Venezuelan Equine Encephalitis, ……..), Chikungunya Virus, Rift Valley Fever, …..
- Filarian nematods in animals (Dilofilaria – heartworm, subcutaneous worm,...)