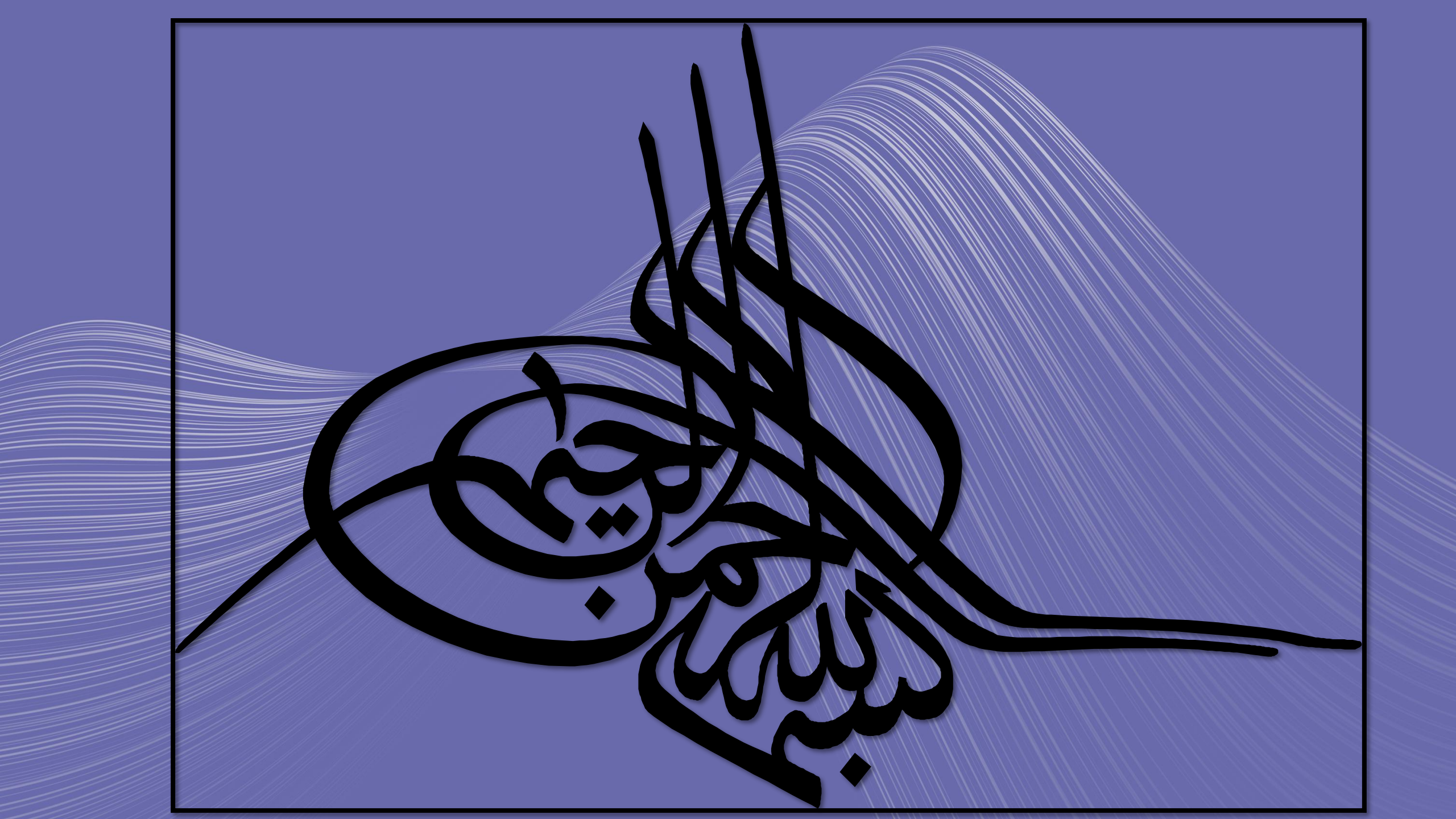
بسم الله الرحمن الرحيم

Prevention of the Emerging and Reemerging Aedes-Transmitted Arbovirus Infections in pregnancy

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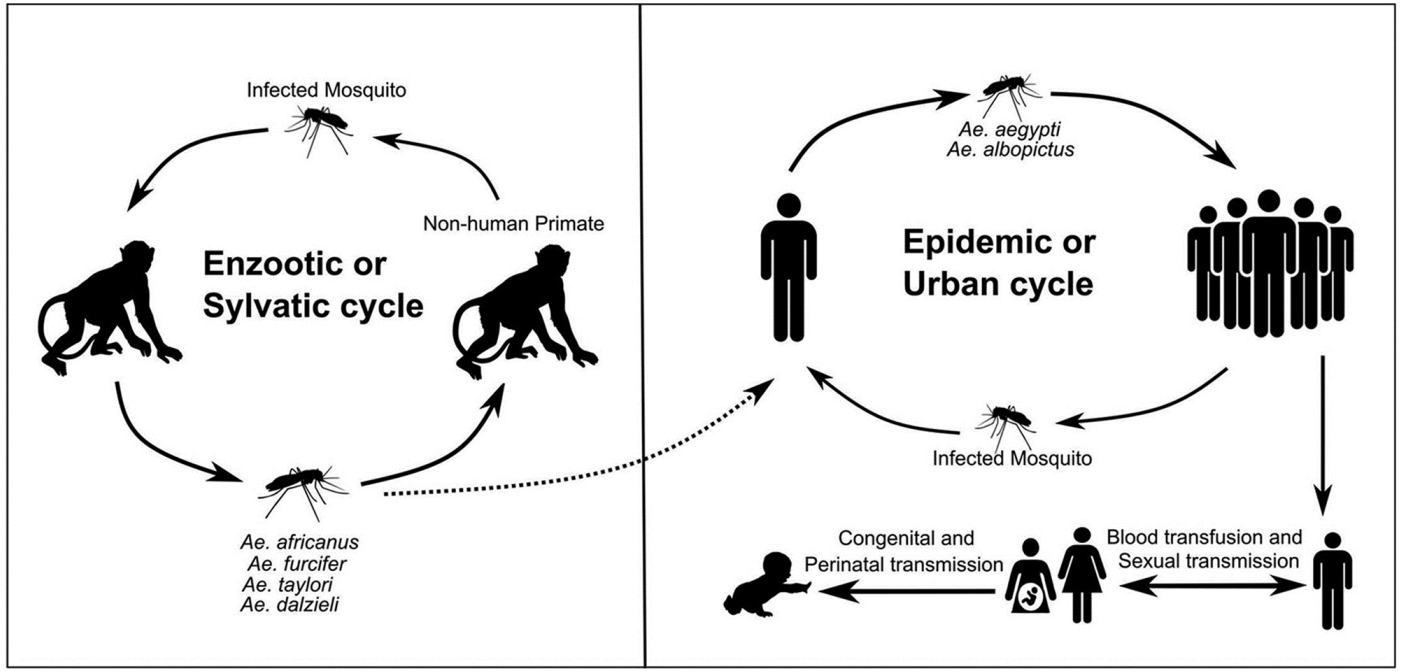
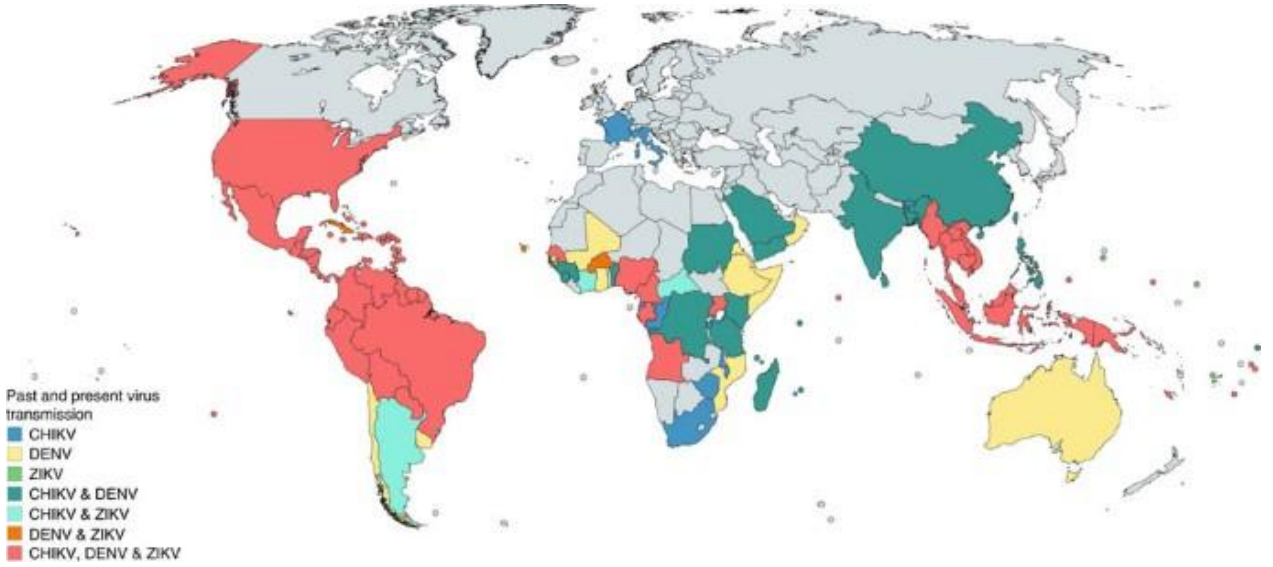
First recognized in **1950s**.
Flaviviridae (more than **70 viruses**)
Mosquito borne infection.
Leading **cause of serious disease and death** in children and increased incidence in adults.
Pregnant women are more and more susceptible.



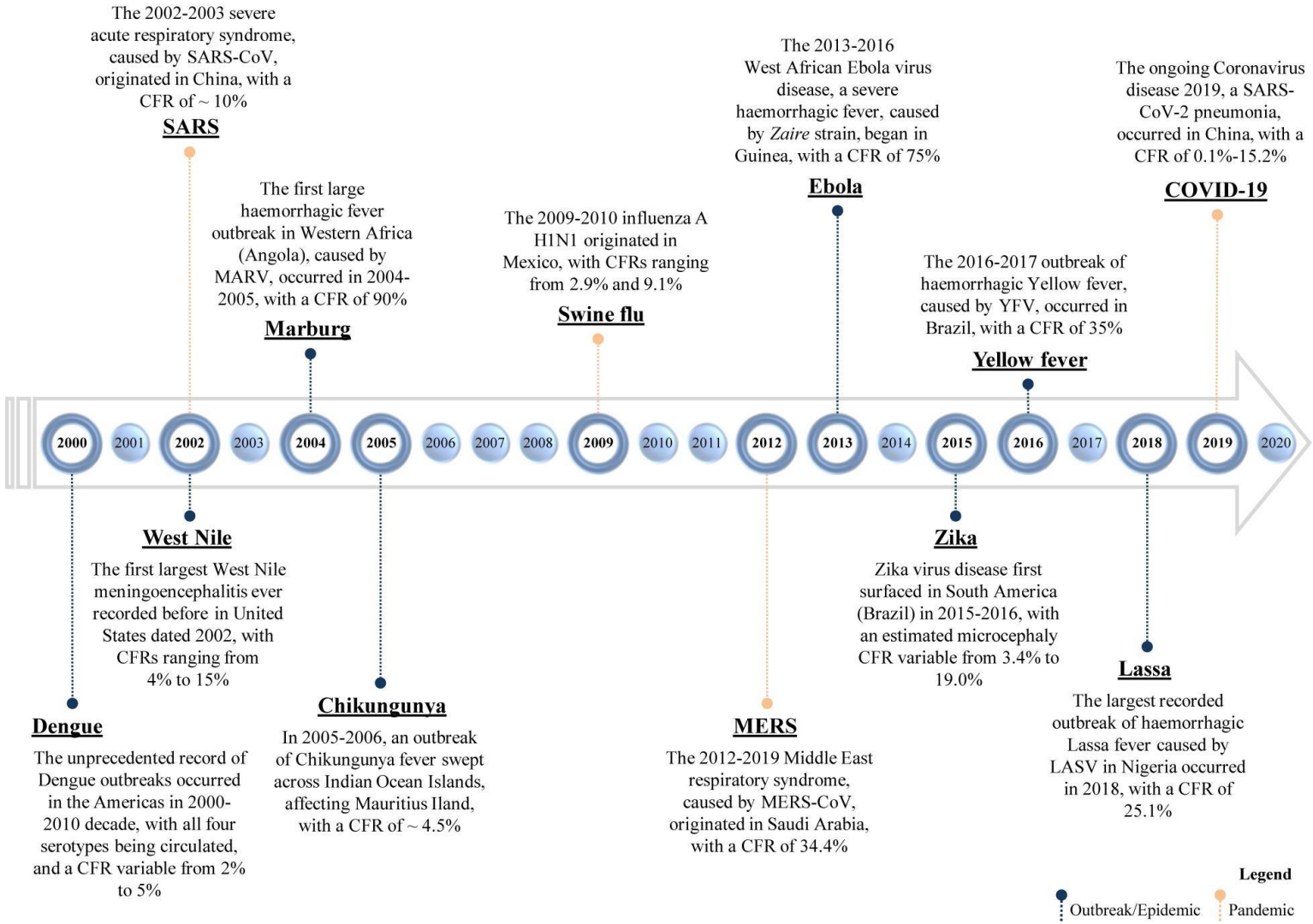
The Emerging and Reemerging Aedes-Transmitted Arbovirus Infections

The increasing geographical spread and disease incidence of arboviral infections are among the greatest public health concerns in the world. The region has observed an increasing trend in dengue incidence in the last decades, evolving from low to hyper endemicity. Yellow fever incidence has also intensified in this period, expanding from sylvatic-restricted activity to urban outbreaks.



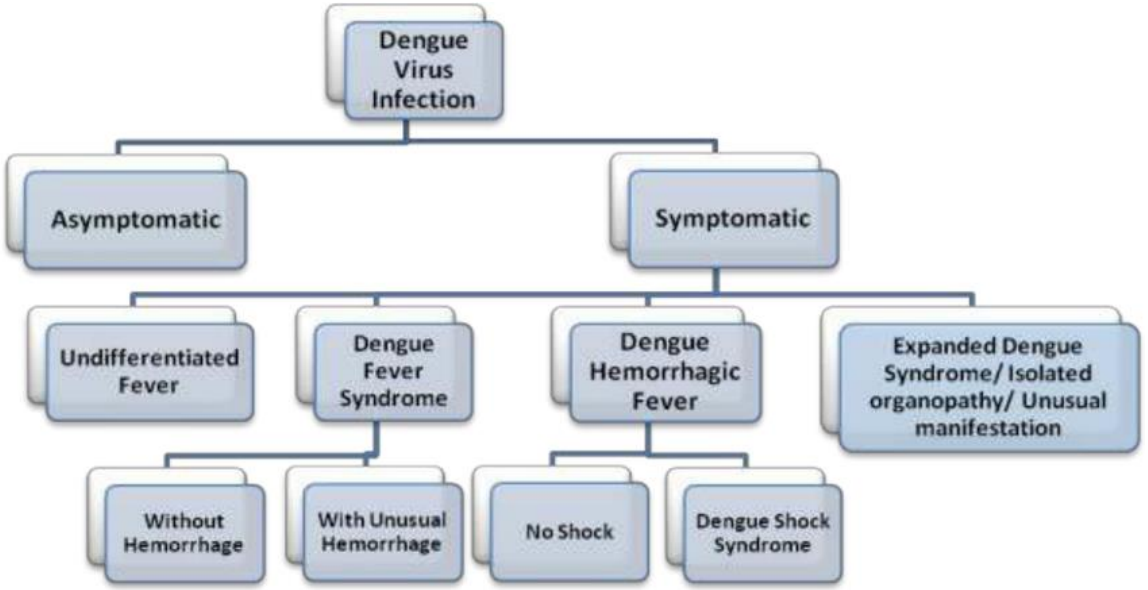
CDC map 2020

The important outbreaks of emerging viruses



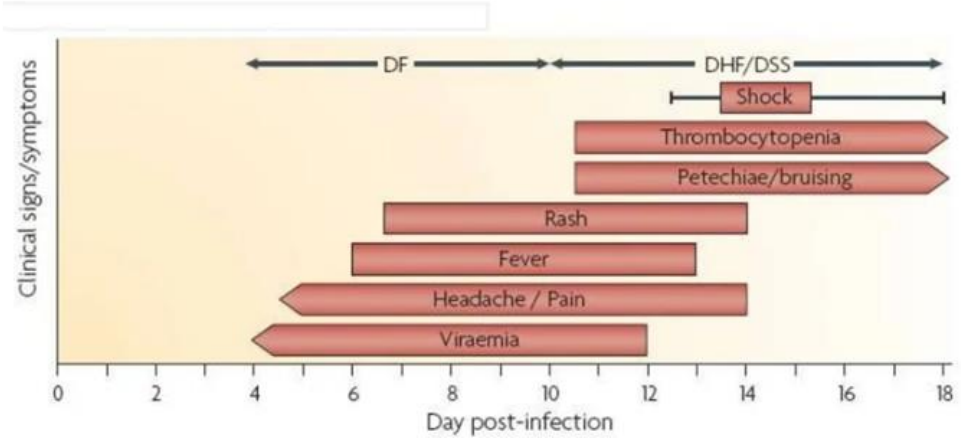
The Emerging and Reemerging Aedes-Transmitted Arbovirus Infections

- Dengue virus (**DENV**) and yellow fever virus (**YFV**) are two of the globally prevalent vector-borne **viruses**. Dengue infection is an **Aedes-borne disease** caused by flaviviruses and **is second** only to malaria as a cause of vector-borne **disease mortality and morbidity,** with epidemics recurring ap-proximately **every 3 to 5 years**. In 2010, 1.7 million dengue cases were reported to the Pan American Health Organization (PAHO).



The Emerging and Reemerging Aedes-Transmitted Arbovirus Infections

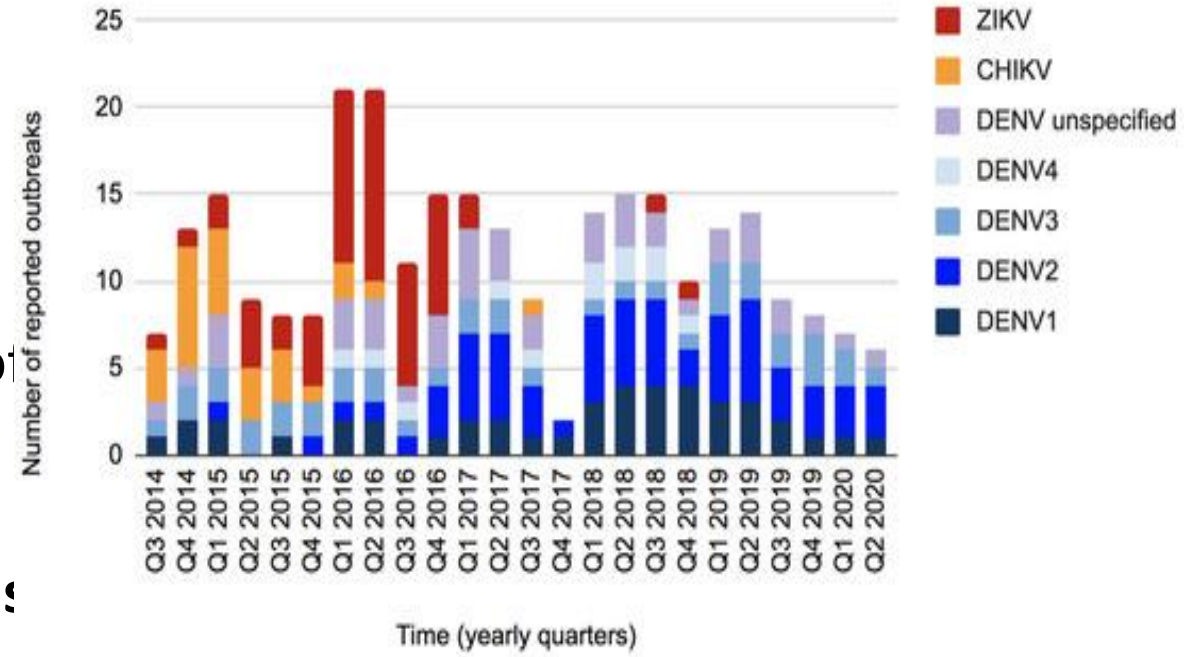
- Also, Dengue is an emerging tropical disease. It is one of the most serious disease among mosquito-borne diseases. Its burden globally is 465000 disability-adjusted life years. About 2.5- 3billion people (40% of the global population) live at risk of infection.
- Severe clinical forms of dengue occur in pregnant women and children. Therefore, they are considered to be a susceptible group globally.



The Emerging and Reemerging Aedes-Transmitted Arbovirus Infections

In addition to the re-emergence of dengue virus(DENV) and yellow fever virus(YFV), new arboviral pathogens once confined to specific regions of the world, such as CHIKV and ZIKV, recently resulted in pandemics associated with significant morbidity.

In 2005, **CHIKV** caused an outbreak on the island of **Comoros**, & spread pandemically at an un-precedented pace, reaching the Americas in 2013, rapidly resulting in more than **1.3 million infections** reported in more than**43 countries**. Incidence rates climbed as high as 137.1 infections per 1000 person-years among Nicaraguan children during the peak of the epidemic.

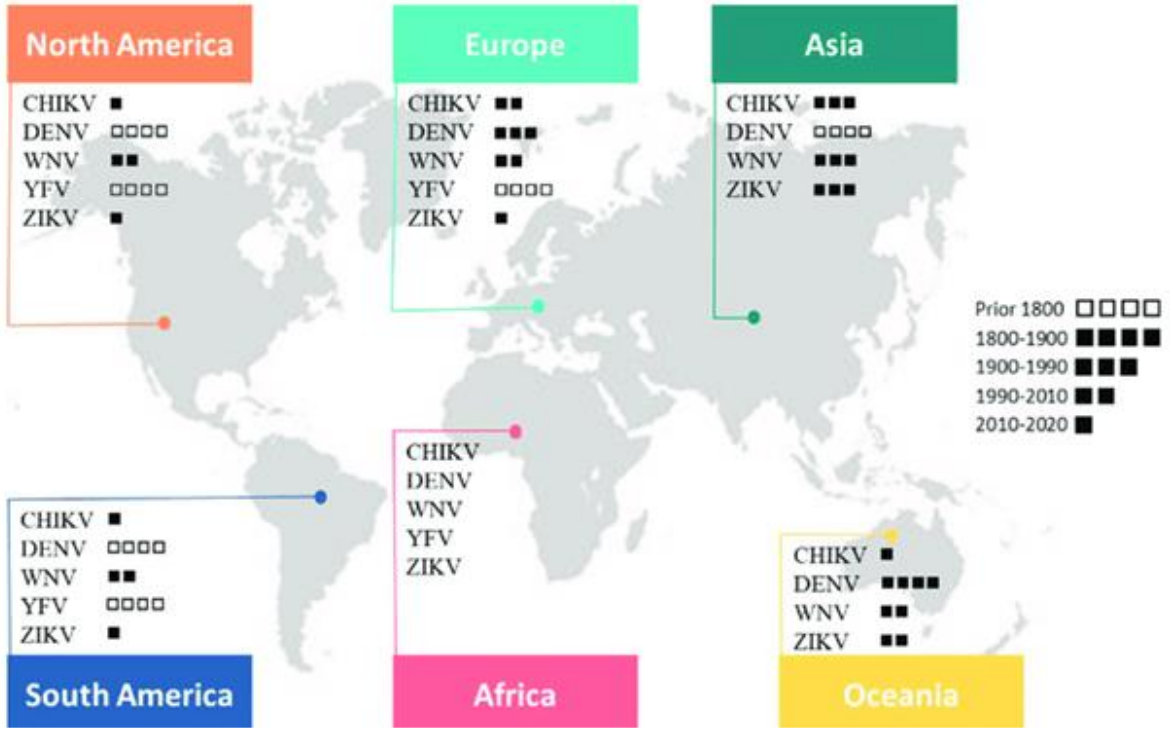


The Emerging and Reemerging Aedes-Transmitted Arbovirus Infections

ZIKV, like CHIKV, had not previously circulated within the Western Hemisphere, and resulted in an explosive outbreak in the Americas, with its identification first on Easter Island, **Chile, in 2014**, followed by northeast **Brazil in 2015**, and then spreading throughout the **Americas**. By late 2015, **Zika had become one of the greatest global health crises** in years and was associated with **devastating congenital abnormalities** including **microcephaly Guillain-Barré syndrome**, and other **neurologic disorders**, and with the ability to spread by **sexual contact**. By late2016, ZIKV transmission had **extended to 48 countries**.

The Emerging and Reemerging **Coinfections** in Aedes-Transmitted Arbovirus

Zika also emerged in the regions with an explosive out-break, carrying devastating **congenital abnormalities and neurologic disorders** and becoming one of the greatest **global health crises** in years. The inadequate arbovirus surveillance in the region and the **lack of serologic tests to differentiate among viruses poses substantial challenges.** The evidence for **vector control interventions remains weak**. Clinical management remains the mainstay of arboviral disease control.



Treatment

- **No specific treatment**
- Fluids
- Rest
- Antipyretics (avoid aspirin and NSAIDs
- Monitor blood pressure, hematocrit, Platelet count, level of awareness

The Emerging and Reemerging Aedes-Transmitted Arbovirus Infections

- Currently, only yellow fever **YF-VAX** and dengue vaccines[**Dengvaxia**: dengue tetravalent vaccine (live, attenuated)] are licensed in the Americas, with several candidate vaccines in clinical trials .The value of the vaccine is **limited by the fact that it may increase the risk of severe dengue in those who have not previously been infected**. In 2017, more than 733,000 children and more than 50,000 adult volunteers were vaccinated with **CYD-TDV**(a tetravalent, live attenuated, chimeric dengue vaccine in a yellow fever 17D backbone developed by Sanofi Pasteur) **regardless of serostatus**, which le**d to a controversy.**
- The ever-increasing geographical spread and rising disease incidence of arboviral infections are among the most significant public health concerns in the Americas.

The Emerging and Reemerging Aedes-Transmitted Arbovirus Infections

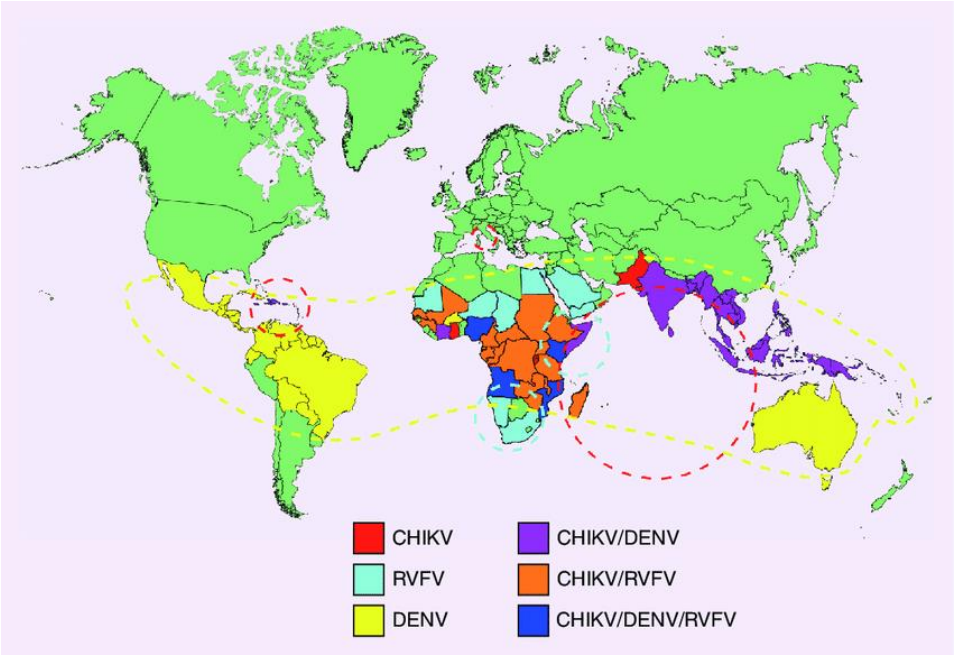
- The recent emergences of ZIKV and CHIKV in 2016 created an unprecedented situation: the cocirculation of 4 important human arboviruses transmitted by the same mosquito, primarily **Aedes aegypti,** in the same time and place. Intense and **prolonged rainy seasons and an increase of 2 degrees centigrade in average temperature probably also contributed to an** abundance of vectors.
- **De-forestation** has been associated with yellow fever and Zika outbreaks. **Migration of un-vaccinated populations** to endemic areas has also been a key factor in yellow fever occurrence in South America.

SURVEILLANCE Limitations of Existing Systems and Rationale

- Currently, **the inconsistent and inadequate surveillance** in the region along with **the lack of laboratory serologic testing that can consistently differentiate** between closely related flaviviruses poses substantial challenges to respond adequately to these diseases.
- several limitations, including problems intrinsic to **passive surveillance, lack of organizational structure and integration within existing systems, and in-adequate laboratory capacity.**
- No access or fewer access to **serologic and molecular diagnostic testing** for existing arboviral pathogens, on the other hand fewest laboratories have **sequencing and genotyping capability** for identifying **novel emerging** pathogens, genotypes, and out-breaks.
- **Data analysis, reporting, and data sharing systems also vary**.

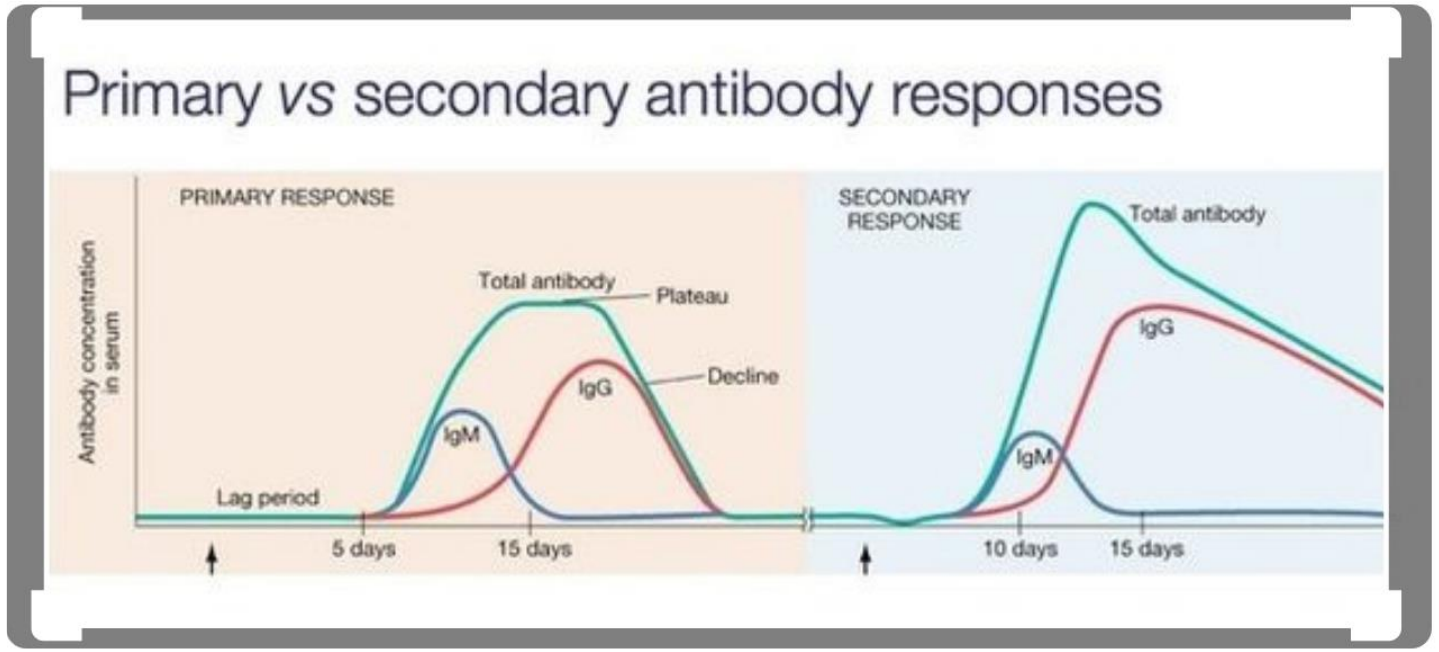
SURVEILLANCE& Limitations of Existing Systems and Rationale

- **Published data from *Turkey* shows that DENV or an antigenically-similar flavivirus was probably present in Iran neighboring region and sporadic human exposure might have occurred their.**
- **Dengue fever is a risk factor for adverse pregnancy outcomes, especially in the *third trimester*.**
- **Effective anti vector control measures and hope for an effective future vaccine could overcome this infection in this population.**



The body's natural response

- As we know, the **antibodies produced in response** to the all types of pathogen's antigen are an important part of the immune system. You can consider antibodies **as the soldiers** in your body's defense system. Each antibody, in our system **is trained to recognize** one **specific antigen**. We have thousands of different antibodies in our bodies. When the human body is exposed to an antigen **for the first time, it takes time for the immune system to respond and produce antibodies specific** to that antigen.



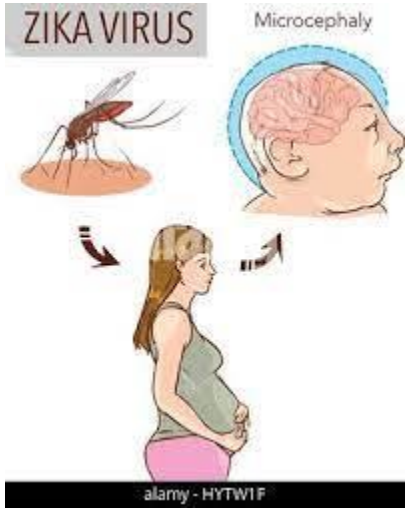
Seroprevalence of dengue infection in pregnant women and placental antibody transfer

- Dengue infection **in a mother results in transfer of antibodies to the newborn**. These antibodies **may protect the newborn** and infant against an infection of dengue with the **particular serotype**. However, it also **carries the risk of a dengue hemorrhagic infection following infection with a different serotype.**
- **Pregnant women and infants are vulnerable for developing severe dengue**. The seroprevalence assay of dengue infections among **pregnant women, their off springs** and its association with outcomes are important issue.
- Seroprevalence of dengue in prenatal women and in their off springs is lower than other areas endemic for dengue. Dengue infection (any time before pregnancy) may result **in preterm delivery and low birth weights.**

Confirmed Arbovirus vertical transmission and the hallmarks of their infections

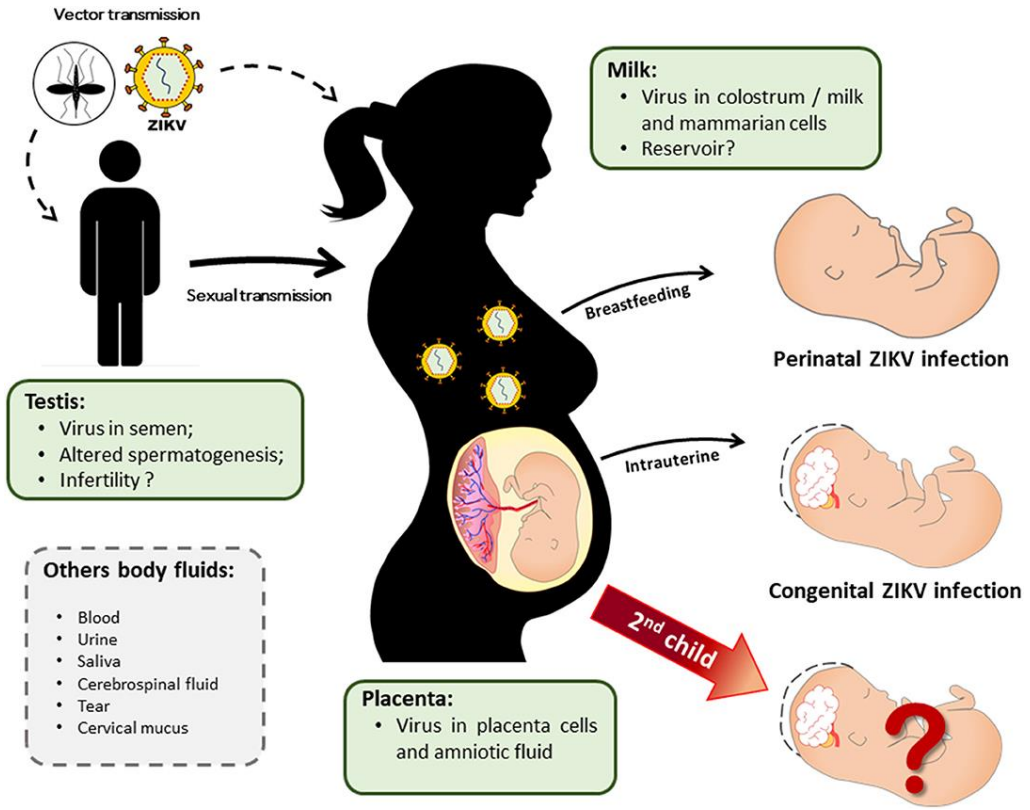
- **DENV & ZIKA & WNV & RVFV** along with **several emerging viruses [(Ebola virus (EBOV) and Eastern equine encephalitis virus (EEEV), SARS-CoV-2]** may have major impacts on the mother and fetus during pregnancy & transplacental transmission and vertical transmission were reported.

Zika virus	Arbovirus (*Aedes* species, sexual, blood borne)	Microcephaly; IUGR; hepatosplenomegaly; intrahepatic calcifications; ventriculomegaly; intracerebral calcifications; echogenic bowel; stillbirth/pregnancy loss
West Nile virus	Arbovirus (*Culex* species)	Chorioretinitis; meningitis/encephalitis; possible lissencephaly
Rift Valley fever virus	Arbovirus (*Aedes* species, *Culex* species, *Anopheles* and *Mansonia* species, contact with contaminated animal materials)	Stillbirth/pregnancy loss; preterm delivery



Seroprevalence of dengue infection in pregnant women

- **Clinical presentation of prenatal and postnatal dengue is similar to dengue infections in adult.**
- **Management of perinatal dengue deserves special attention.**
- **Mothers and newborn are prone to dengue shock syndrome and other bleeding manifestations.** It may be intensified by the wounds and trauma during childbirth.
- **The mortality and morbidity due to perinatal dengue can be significantly reduced** by improving **awareness** for early recognition.
- **This requires the strengthening of laboratories for early case detection**.

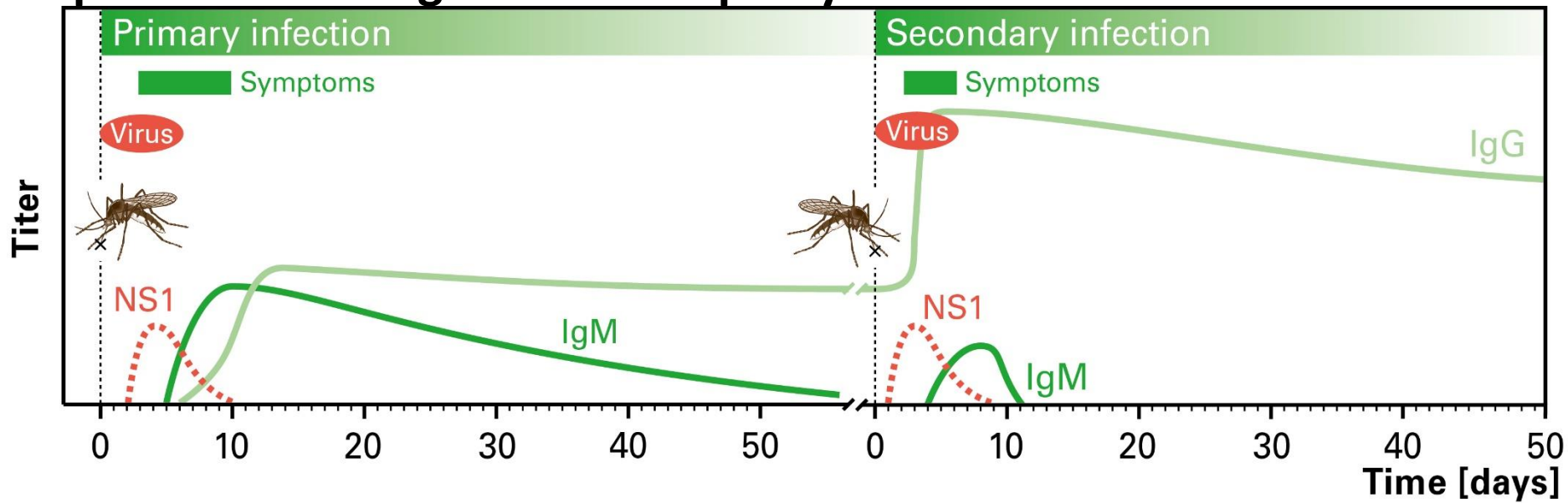


Seroprevalence of dengue infection in pregnant women and placental antibody transfer

- Evidence regarding symptomatic dengue and its effects on pregnancy is abundant, but few seroprevalence studies done in pregnant women.
- We need to determine the **serum prevalence of arbovirus infections in pregnant women** in **late pregnancy** and also, to find the **positive ratio of arbovirus IgG in cord blood for avoiding atypical neurological**, **gastrointestinal, cardiovascular, and respiratory manifestation** of arboviruses for **making the right decision to find a correlation between positive IgG of mother and offspring**.
- This requires **strengthening laboratories** for early detection of cases.
- There is sufficient evidence of dengue fever and other symptomatic Arboviruses **and their effects on pregnancy**, but few studies have been performed on the prevalence of serum in pregnant women and cord blood.

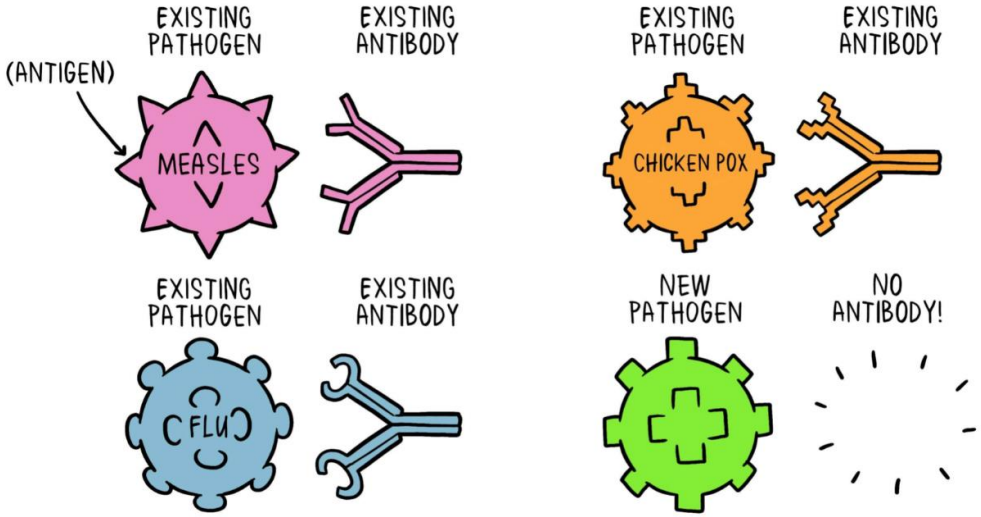
Seroprevalence of dengue infection

- **Newborn weight and gestational age at delivery were significantly lower for newborns born to mothers with IgG positivity for dengue.**
- An **earlier infection** (before pregnancy) with dengue can result in **preterm delivery and low birth weights.**
- The person is exposed to the any dangerous pathogen in the future, their immune system will be able to respond immediately, protecting against disease.
- **In secondary dengue infections, IgG titers rise to extremely high levels** (much higher than in primary infections**) from the day 7 of fever to the next two weeks** . **Anti-Dengue IgG antibodies persist for a long time even up to years**.



The body's natural response

- Once the **antigen-specific antibodies are produced, they work with the rest of the immune system to destroy the pathogen and stop the disease**.
- **Antibodies to one pathogen generally don't protect against another** pathogen **except when two pathogens are very similar** to each other.
- Once the body produces **antibodies in its primary response to an antigen**, it also **creates antibody-producing memory cells**, which remain alive even after the pathogen is defeated by the antibodies. If the body is exposed to the same pathogen more than once, the antibody response is much faster and more effective than the first time around because the memory cells are at the ready to pump out antibodies against that antigen.



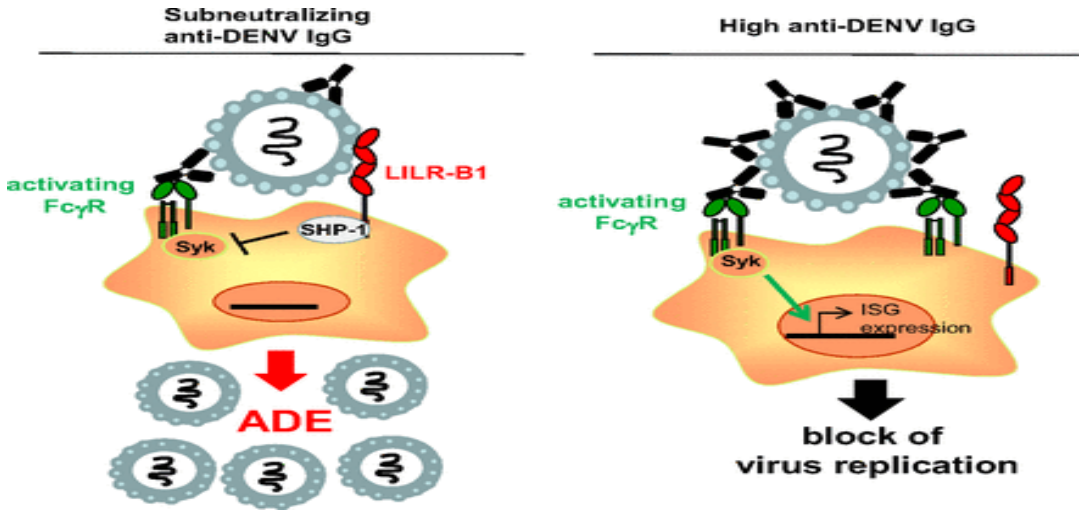
The immune system response to exposed person to the pathogen

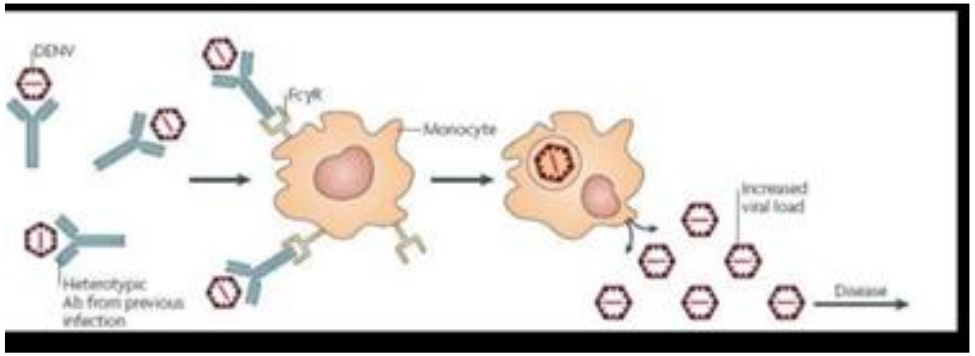
The body's natural response

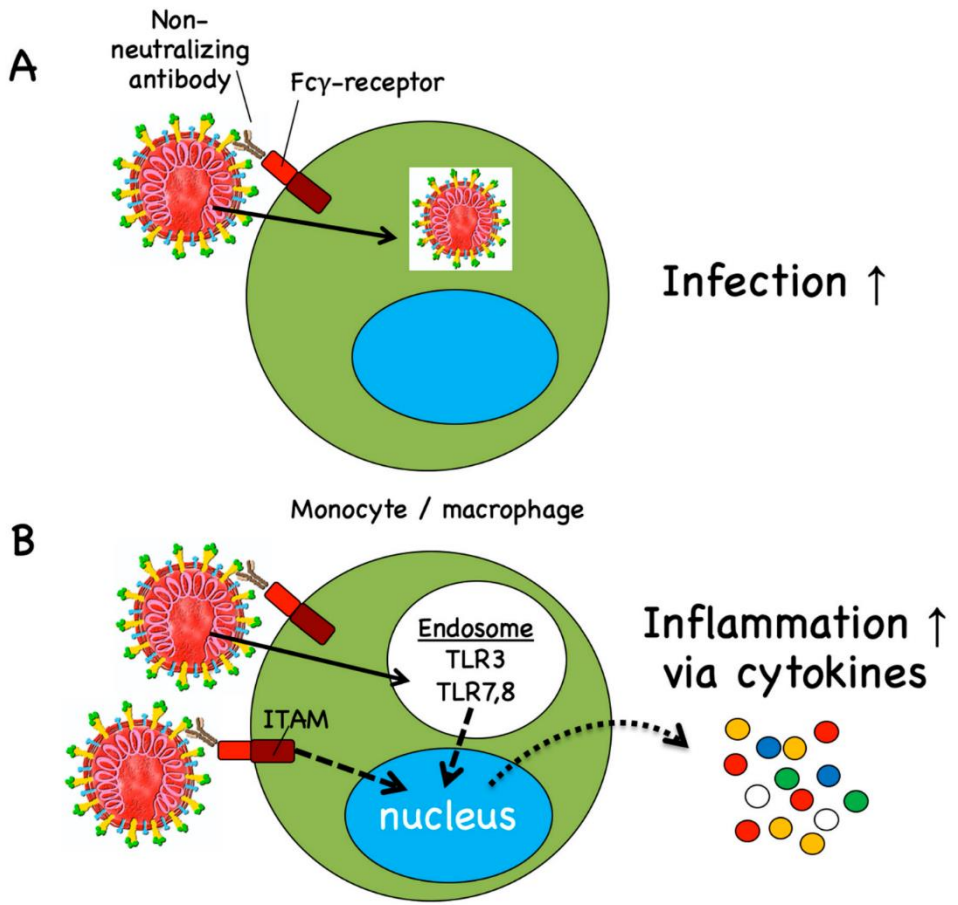
- In **secondary dengue infections, IgG titers rise to extremely high levels (much higher** than in primary infections) from the day 7 of fever to the next two weeks . Anti-Dengue IgG antibodies **persist for a long time even up to years**.
- **Antibody-dependent enhancement and viral infection: ADE pathways can occur when non-neutralizing antibodies or antibodies at sub-neutralizing levels** bind to viral antigens **without blocking or clearing infection ADE** has been documented to **occur** through two distinct mechanisms in viral infections:

1. **by enhanced antibody-mediated virus uptake into Fc gamma receptor IIa** (FcγRIIa)-expressing phagocytic cells leading to increased viral infection and replication (dengue).
2. **by excessive antibody Fc-mediated effector functions or immune complex formation** causing enhanced inflammation and immunopathology (RSV and measles).

Antibody-dependent outcomes and virus infection







Does dengue antibodies pass through breast milk?

As per expert advice, breastfeeding is safe if the mother is infected with dengue. Research suggests that this risk of transmission of dengue virus from mother to the baby through breast milk is very low. The benefits of breastfeeding during maternal infection are much higher than the chances of infection to the baby.

Can dengue affect infants?

DHF/DSS occurs in infants <1 year of age born to dengue-immune mothers and in children 1 year and older **who are immune to one serotype of DV and are experiencing infection with a second serotype.**

Currently Available Arbovirus Vaccines

Vaccines contain weakened or inactive parts of a particular organism (antigen). **Newer vaccines contain** the blueprint for producing antigens rather than the antigen itself. Regardless of whether the vaccine is **made up of the antigen itself or the blueprint , they** will **not cause** the **disease** in the person receiving the vaccine, but it will **prompt** their **immune system to respond.** According to the official list of licensed vaccines of FDA and WHO, there are **vaccines available against DENV, YFV, WNV (horses), tick-borne encephalitis virus (TBEV) and JEV. There are also vaccines in development for CHIKV, ZIKV, and WNV (human) .**

The yellow fever (YF) vaccine was the first vaccine developed for an arbovirus, more than 80 years ago. This vaccine has been key in the control of YF-induced hemorrhagic disease. However, irrespective of vaccine use, **YF still emerges and reemerges cyclically in many areas.** When this occurs in areas **without immunization programs, deaths in nonhuman primates (NHP) and humans are common.**

Currently Available Arbovirus Vaccines

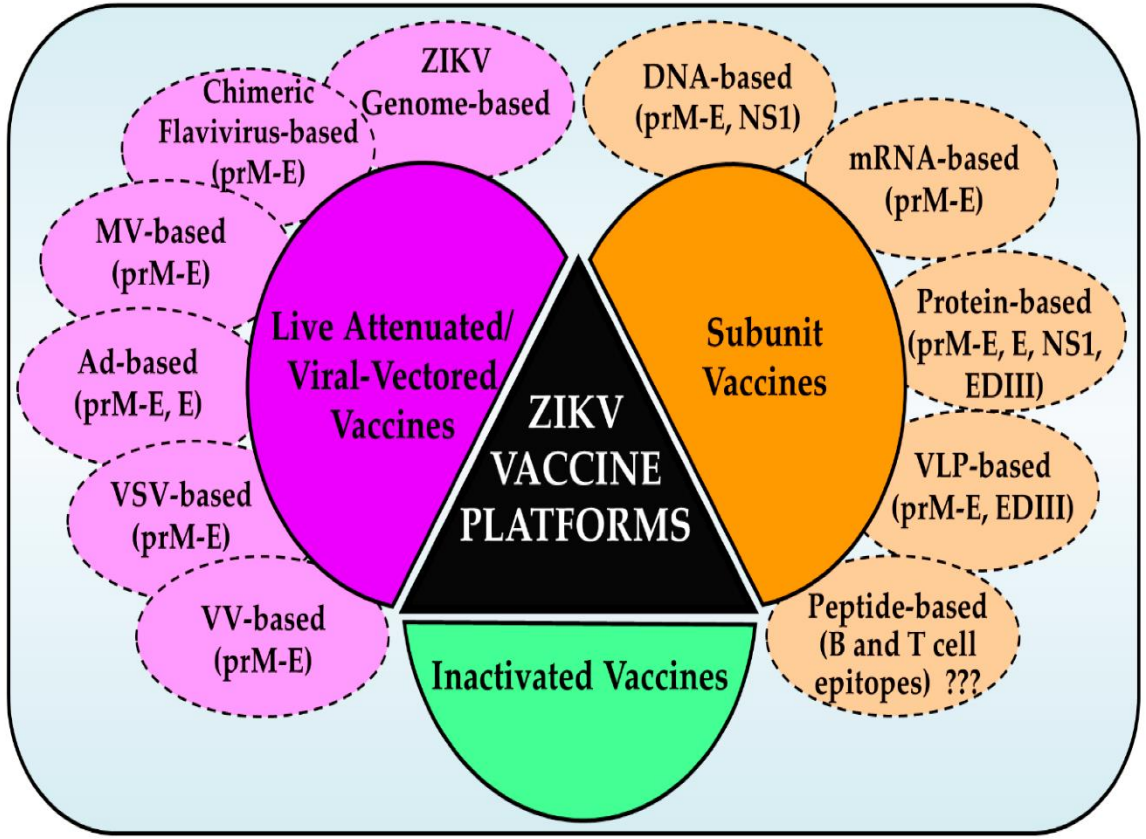
The vaccine for DENV was recently licensed (Dengvaxia, CYD-TDV,) for protection against **all four serotypes**, however efficacy between serotypes is highly variable: **DENV-1 (61.2%), DENV-2 (3.5%), DENV-3 (81.9%) and DENV-4 (90%).** This vaccine was recommended for individuals from **9–45 years** of age living in **endemic areas** with **previous laboratory-confirmed infection**. In 2017 Sanofi Pasteur indicated that their vaccine should be **only used in persons with prior exposure,** since **immunologically naive recipients were more at risk for hemorrhagic disease if infected after vaccination.** Because of the **restrictions and low efficacy for DENV-2**, use has been complicated serological screening should be performed to confirm previous exposure before vaccination.

The race for a vaccine

Some vaccines require multiple doses, for production of **long-lived antibodies** and development of **memory cells** and **trained** to **fight the specific disease-causing organism**, building up **memory of the pathogen.** so as to rapidly fight it if and when exposed in the future.

Even though the **world has advanced in vaccine technologies** recently .

Dengue virus (DENV) alone was estimated to **cause 96 million symptomatic cases/year, infections** such as Zika virus (ZIKV), West Nile virus (WNV) and Chikungunya virus (CHIKV) have **long term consequences** that contribute to this burden. There is **no specific treatment to these diseases**; and, few vaccines are available to prevent the establishment of the Disease.



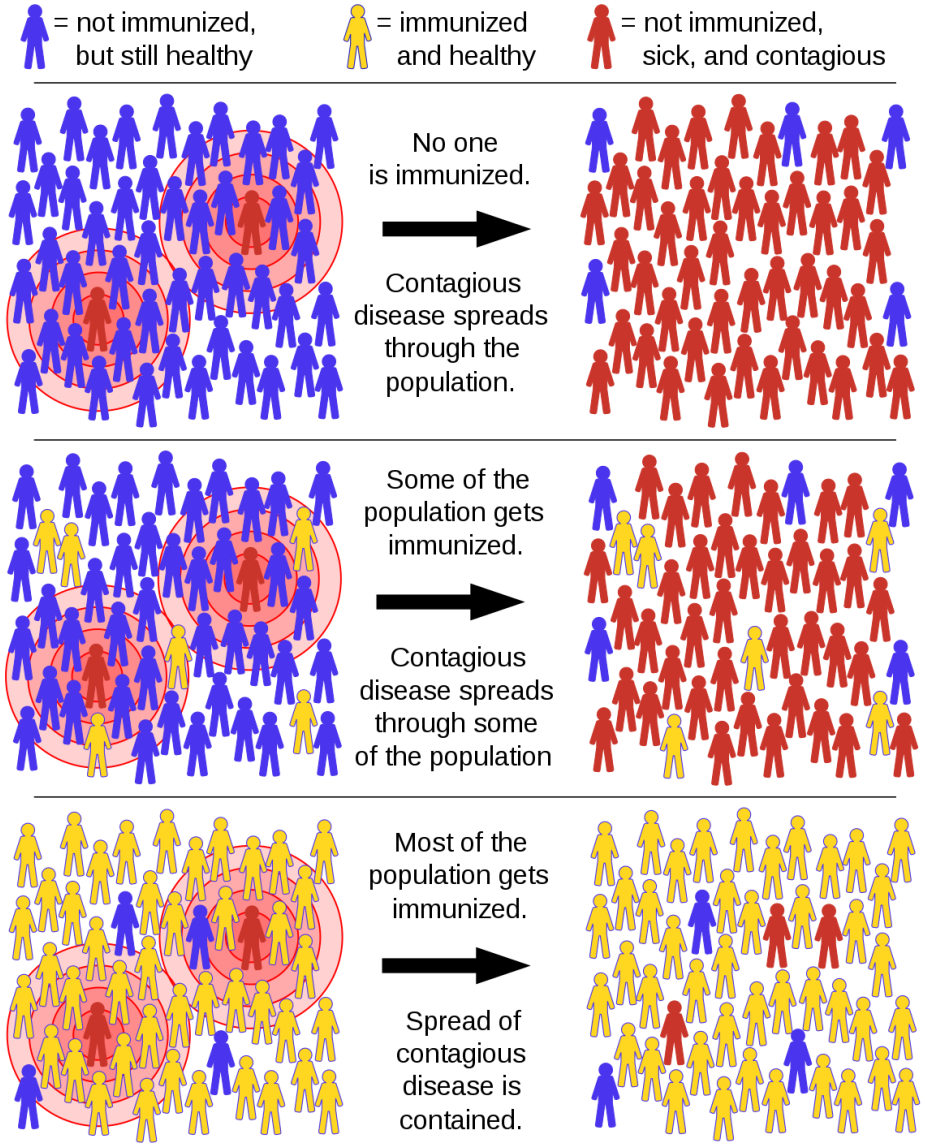
The race for a vaccine

Since Zika pandemic in 2015, a race to develop a safe and **effective vaccine was initiated ,**including **inactivated vaccines, whole virus vaccines, live virus vaccines, subunit vaccines, and messenger RNA (mRNA), DNA, protein- and vector-based preparations,** are in a variety of stages of testing including **preclinical, and stage 1 and 2 clinical trials There are also promising vaccine candidates against CHIKV** in clinical phases of development such as **virus-like particle (VLP) vaccines, live attenuated** CHIKV, **measles vector platforms, inactivated vaccines, subunit vaccines, chimeric vaccines, and nucleic acids.**

Arbovirus	Strategy	Titer of virus	Vaccine Available
CHIKV	Chimeric with cDNA clone &SP E1, E2 & C	10^{10}PFU/ml	No
EEEV & VEEV	Chimeric with cDNA clone &SP E1, E2 & C	$10^{6\text{-}8}$PFU/ml	No
DENV	Chimeric with cDNA clone &SP of viruses	Up to $10^{9.5}$PFU/ml	Yes
YFV	Chimeric with cDNA clone &SP of viruses	Up to $10^{9.5}$PFU/ml	Not everywhere , Yes in US
JEV	Chimeric with cDNA clone &SP of viruses	Up to $10^{9.5}$PFU/ml	Yes
WNV	Chimeric with cDNA clone &SP of viruses	Up to $10^{9.5}$PFU/ml	Not for human , Yes for horses

Herd immunity 1

When **someone is vaccinated, they are very likely to be protected against the targeted disease**. But **not everyone can be vaccinated**. People with underlying health conditions that **weaken their immune systems** (cancer or HIV) or who **have severe allergies** to some vaccine components may not be able to get vaccinated with certain vaccines. **These people can still be protected if they live in and amongst others who are vaccinated**. When **a lot of people in a community are** vaccinated the pathogen has a hard time circulating because most of the **people it encounters are immune**. So the more that others are vaccinated, **the less likely people who are unable to be protected by vaccines are at risk of even b**eing exposed to the harmful pathogens. This is called **herd immunity**.



Herd immunity 2

Herd immunity is especially important for those people who not **only can't be vaccinated but may be more susceptible to the diseases** we vaccinate against. **No single vaccine provides 100% protection**, and **herd immunity does not provide full protection to those who cannot safely be vaccinated**. But with herd immunity, these people will have substantial protection, thanks to those around them being vaccinated.

Vaccinating not only protects yourself, but also protects those in the community who are unable to be vaccinated. If you are able to, get vaccinated

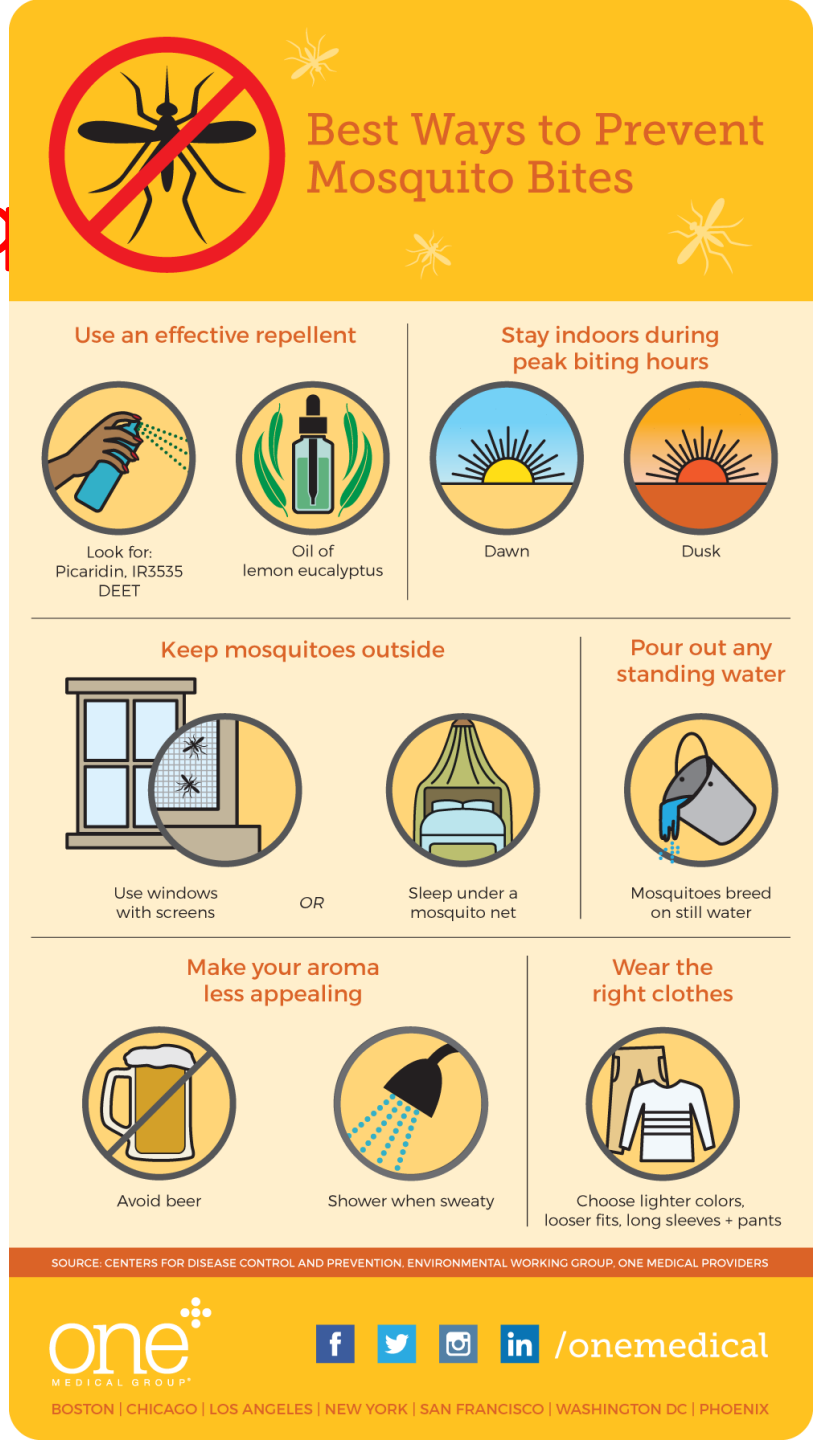
Critical protection to prevent mosq

The best protection from Arbovirus is mosquito control(Larval, Adult) **preventing mosquito bites indoors and outdoors**, especially from **sunrise to sunset** when mosquitos are most active. Such measures include:

Use mosquito repellent in accordanc e with the instructions indicated on the product label.

Personal protection.

Vaccine







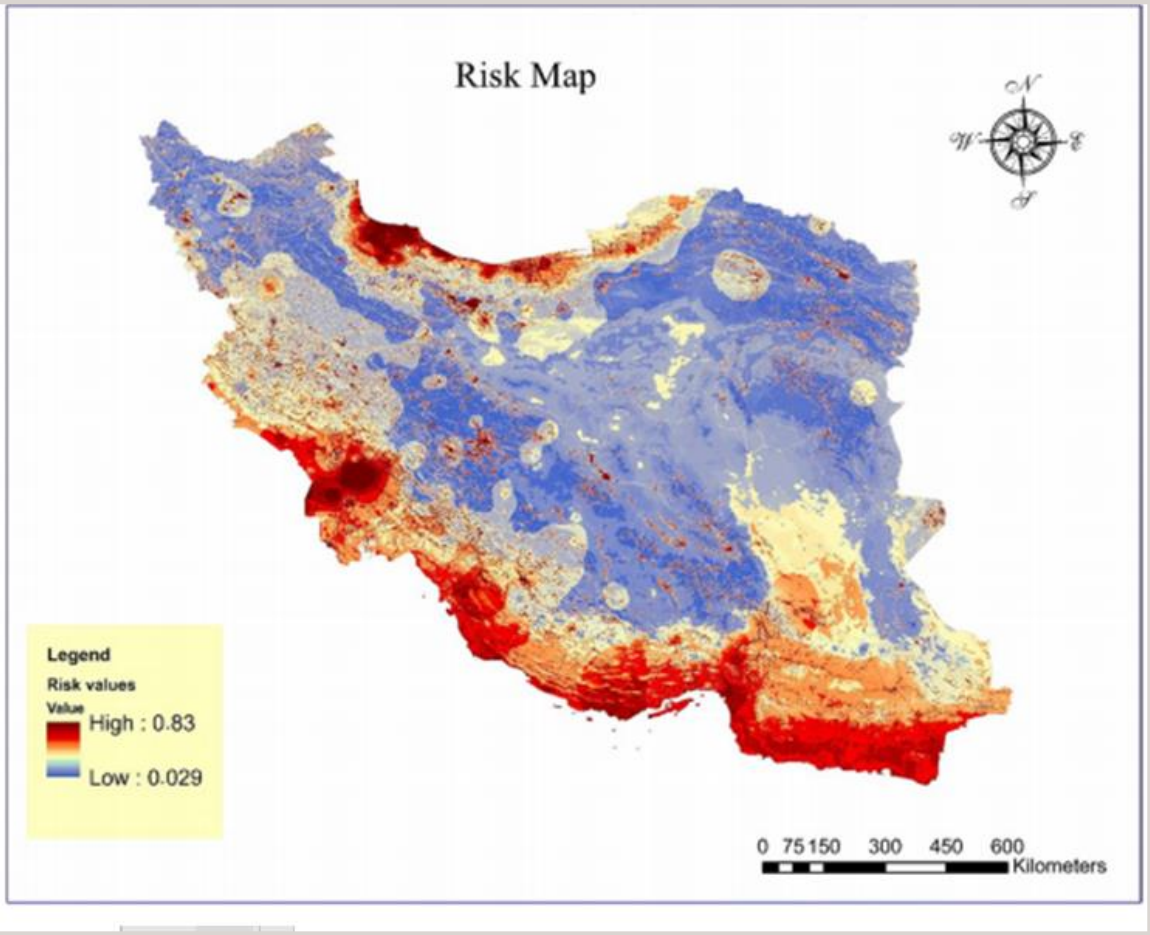






EVER DELVA

THE RISK MAP (IRAN)



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THANK
YOU


Q&A