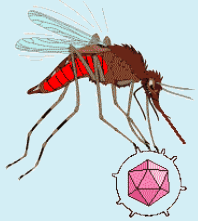


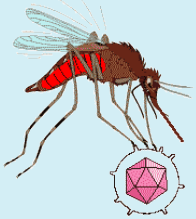
Dengue virology and diagnosis

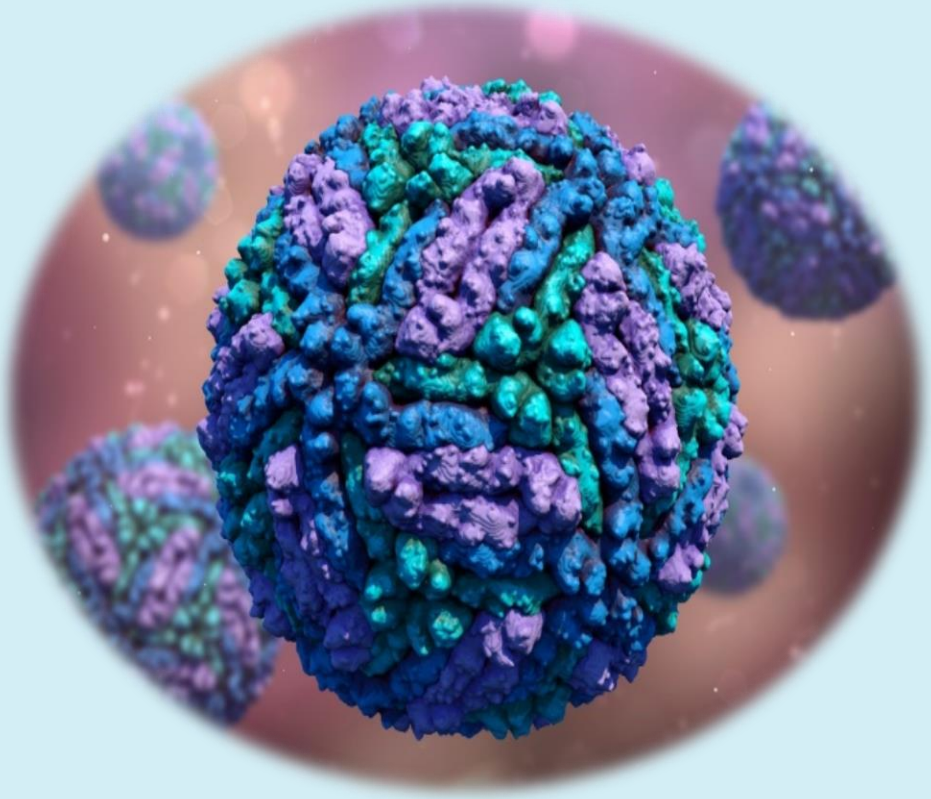
Dr. Behzad Khansarinejad

Associate professor of Medical Virology

Arak University of Medical Sciences

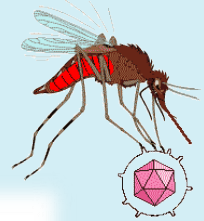
- Family Flaviviridae
- Genus Flavivirus.

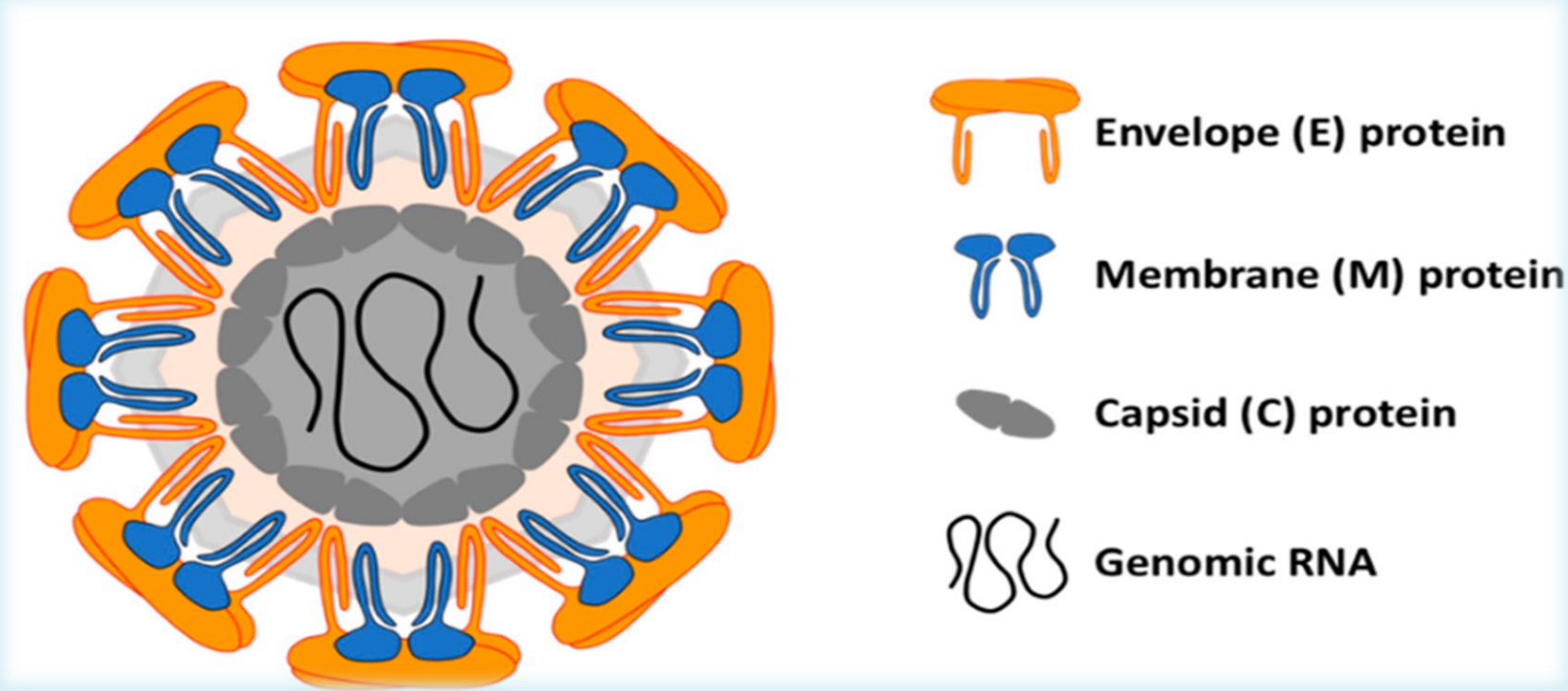




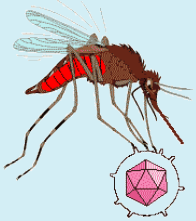
Virus	Serocomplex	Clade	Cluster
West Nile	Japanese encephalitis	XIV	Mosquito-borne
Kunjin			
Japanese encephalitis			
Murray Valley encephalitis			
St Louis encephalitis		XI	
Dengue-1	Dengue	IX	
Dengue-3			
Dengue-2			
Dengue-4			
Yellow fever	None	VII	
Central European encephalitis	Tick-borne encephalitis	IV	Tick-borne
Far Eastern encephalitis			
Powassan			
Dakar bat	None	III	No vector

Nature Reviews | Microbiology

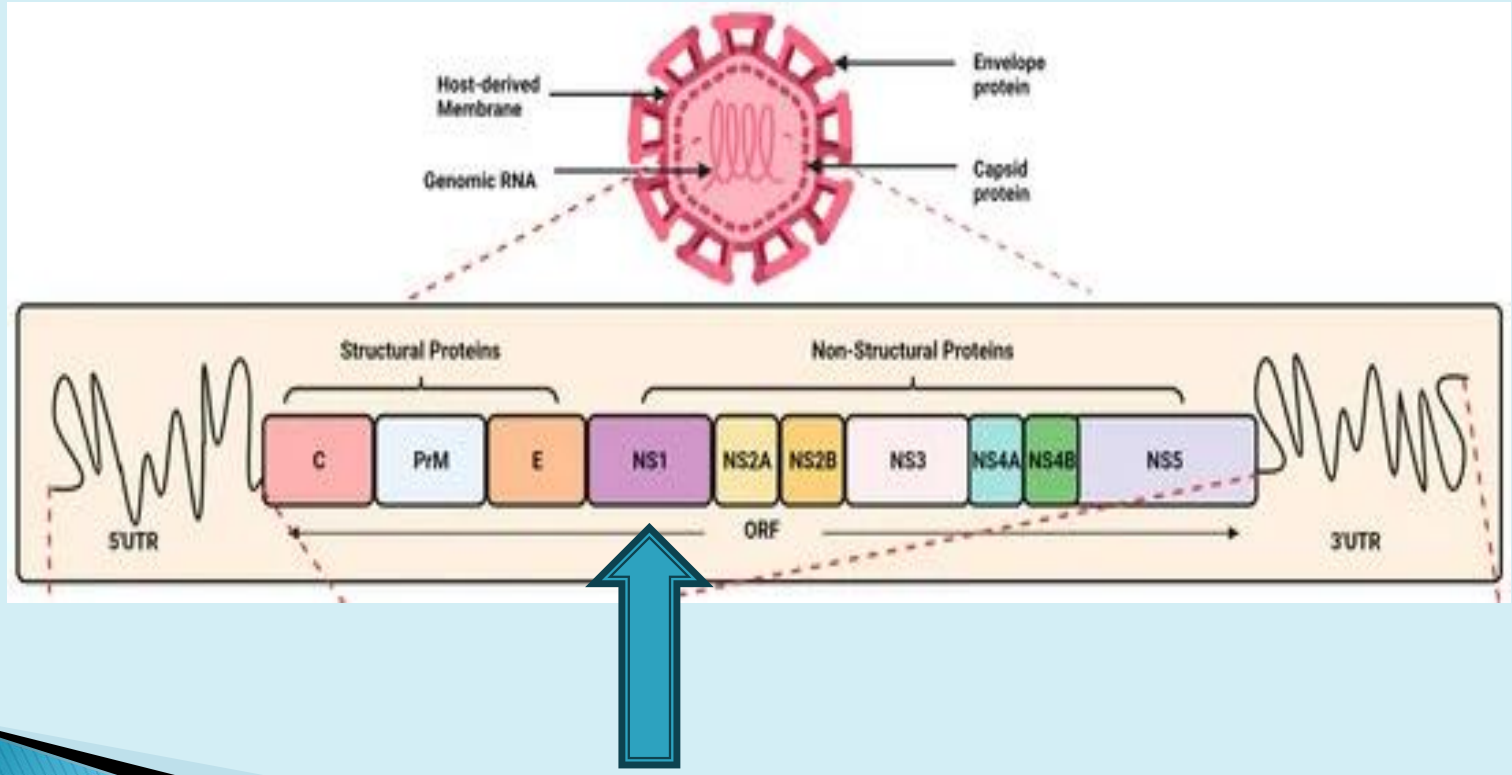


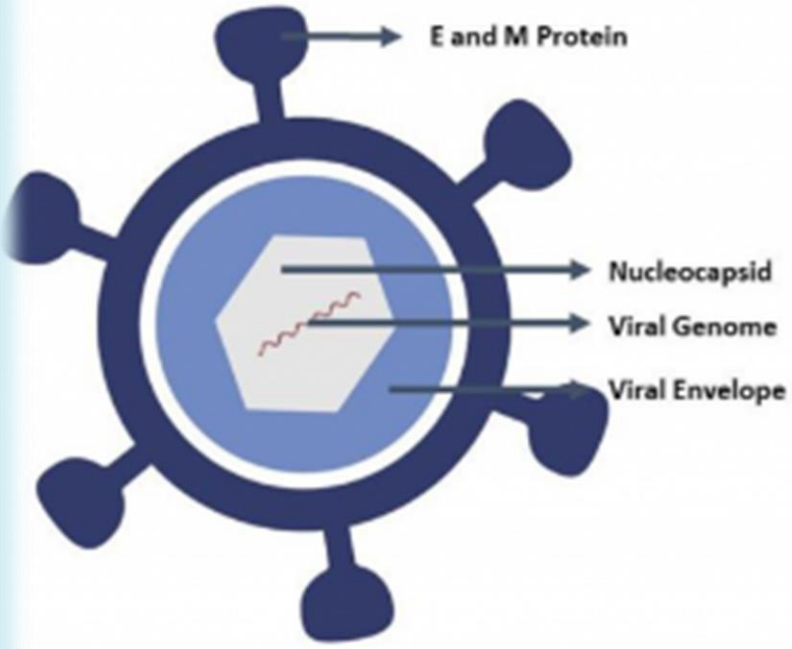

Envelope (E) protein
Membrane (M) protein
Capsid (C) protein
Genomic RNA

Genomic Properties

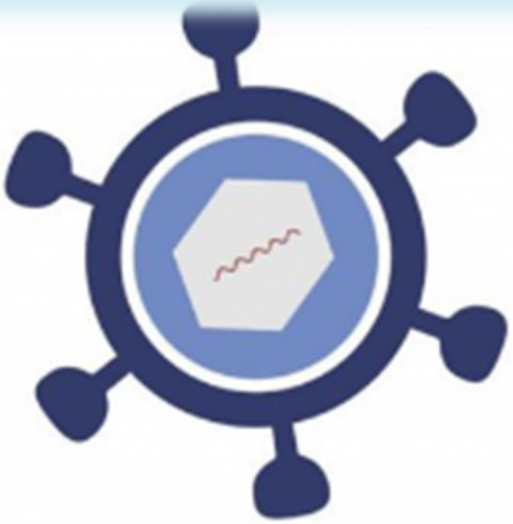


The Dengue genome is ~11 kb in length which is translated single complete polyprotein, with RNA helicase and RNA-dependent RNA polymerase (RdRp).

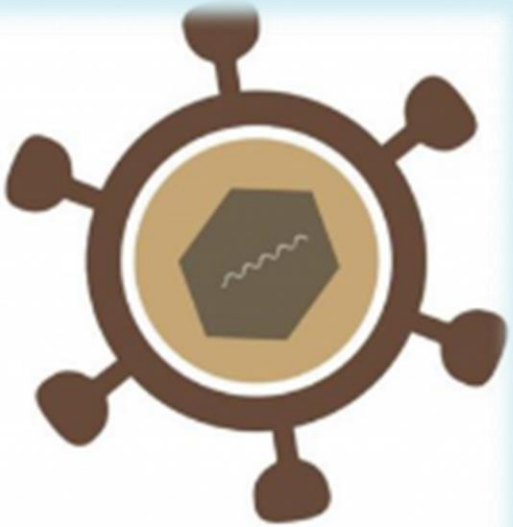




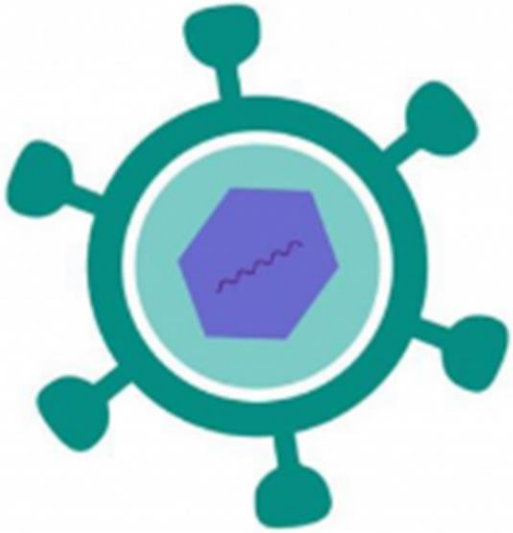
DENV



DENV Serotype 1

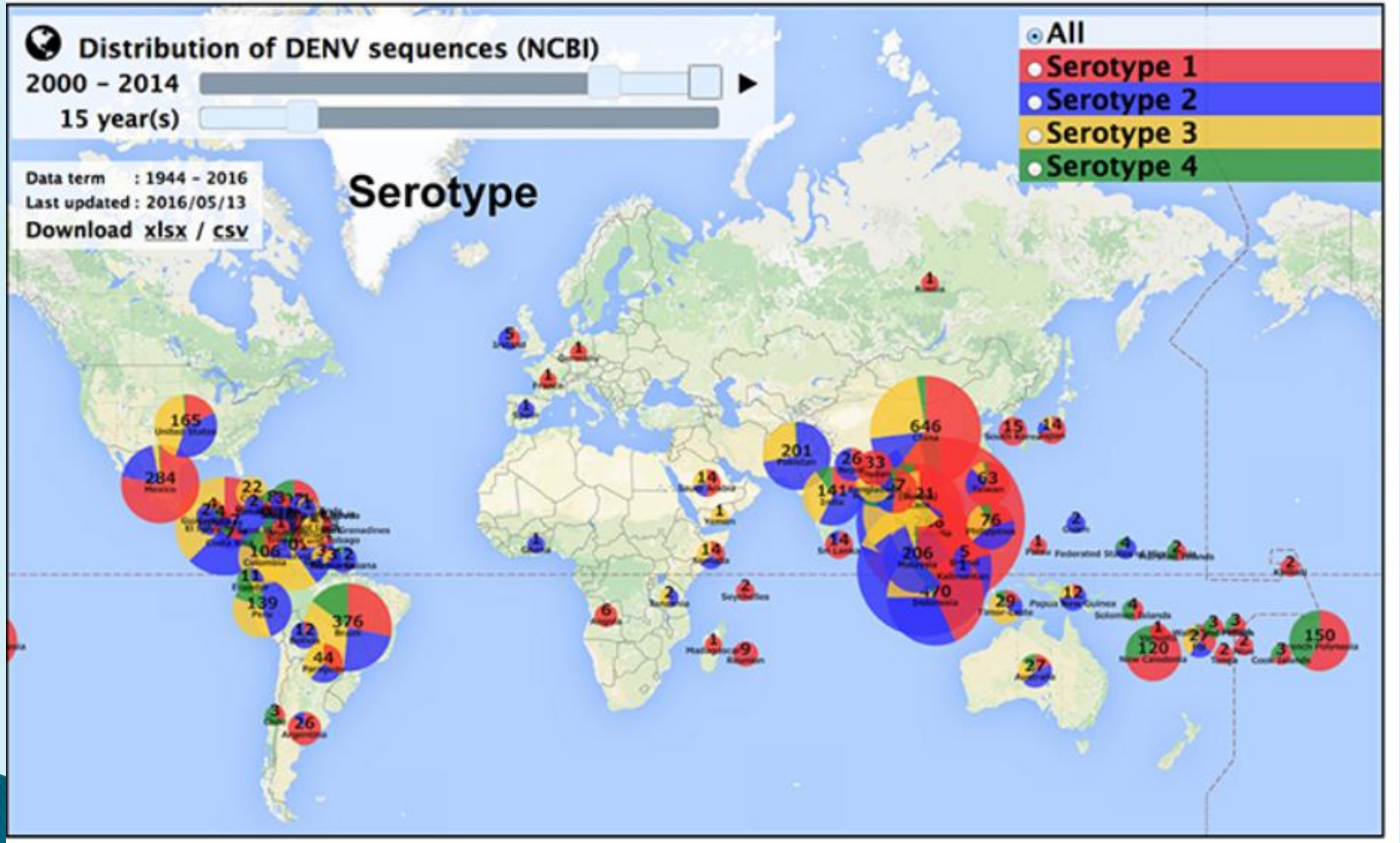


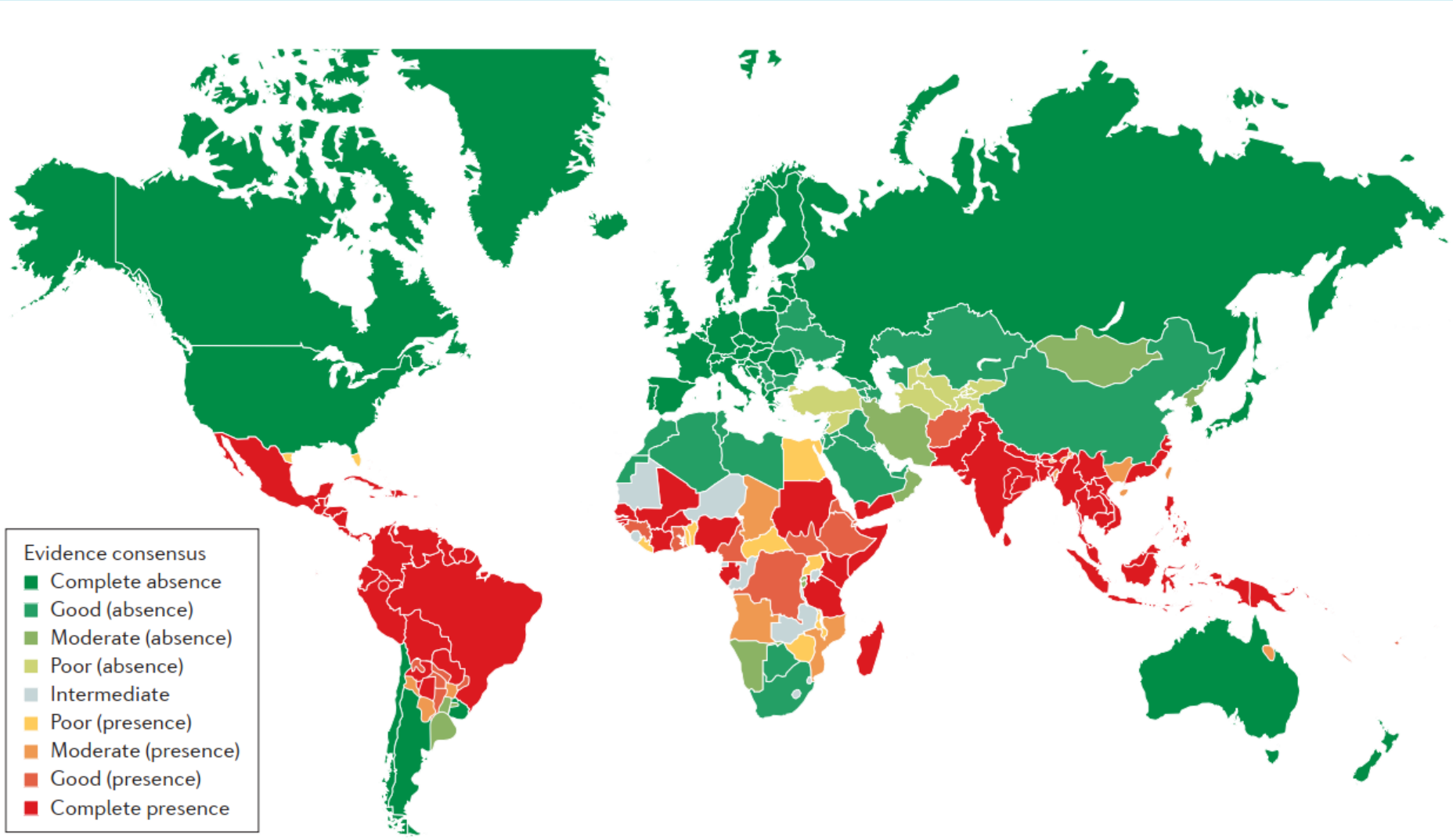
DENV Serotype 2

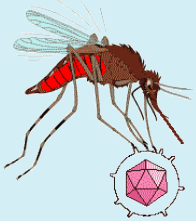


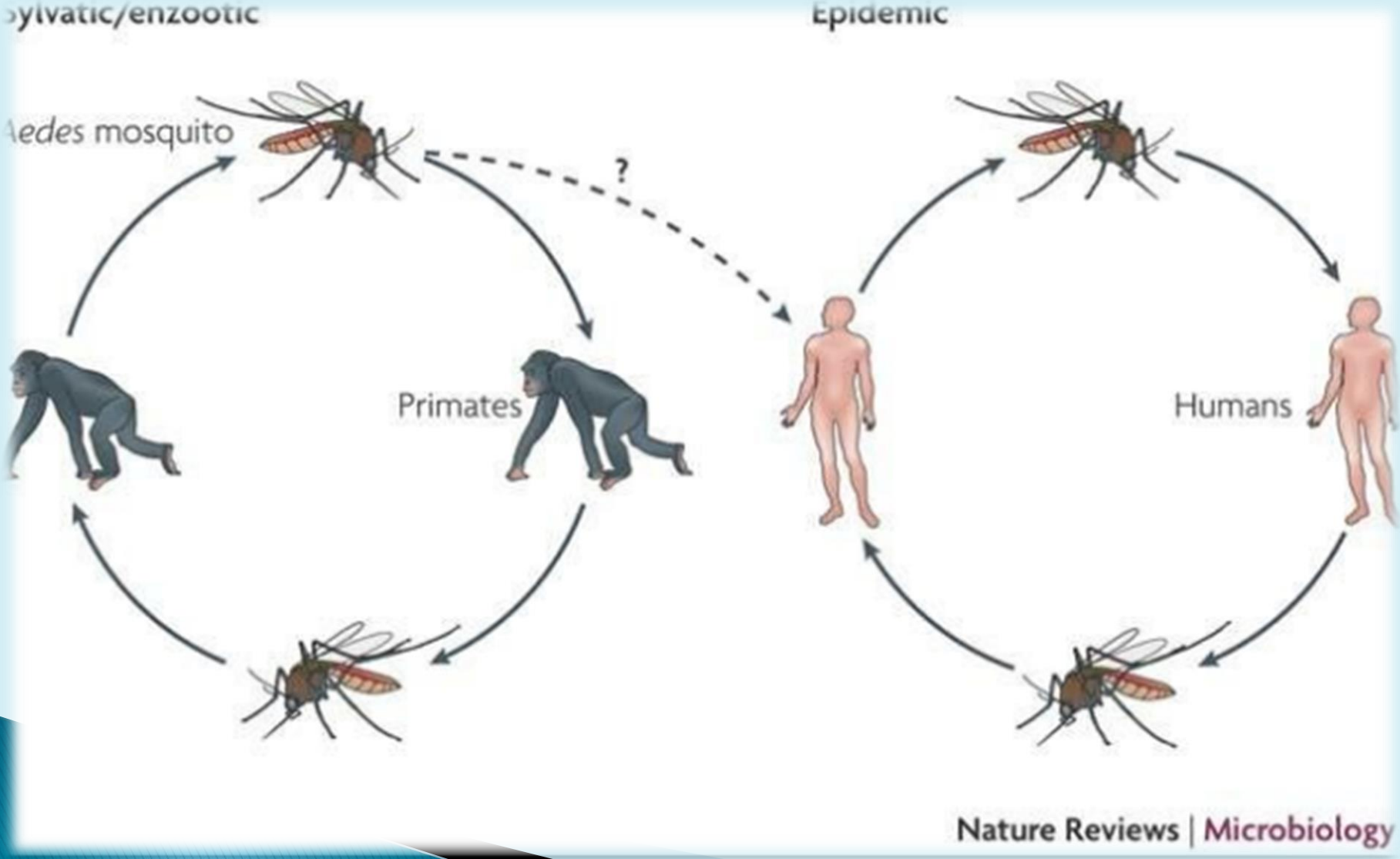
DENV Serotype 3

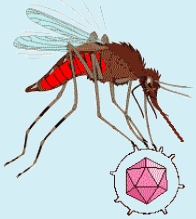
DENV Serotype 4

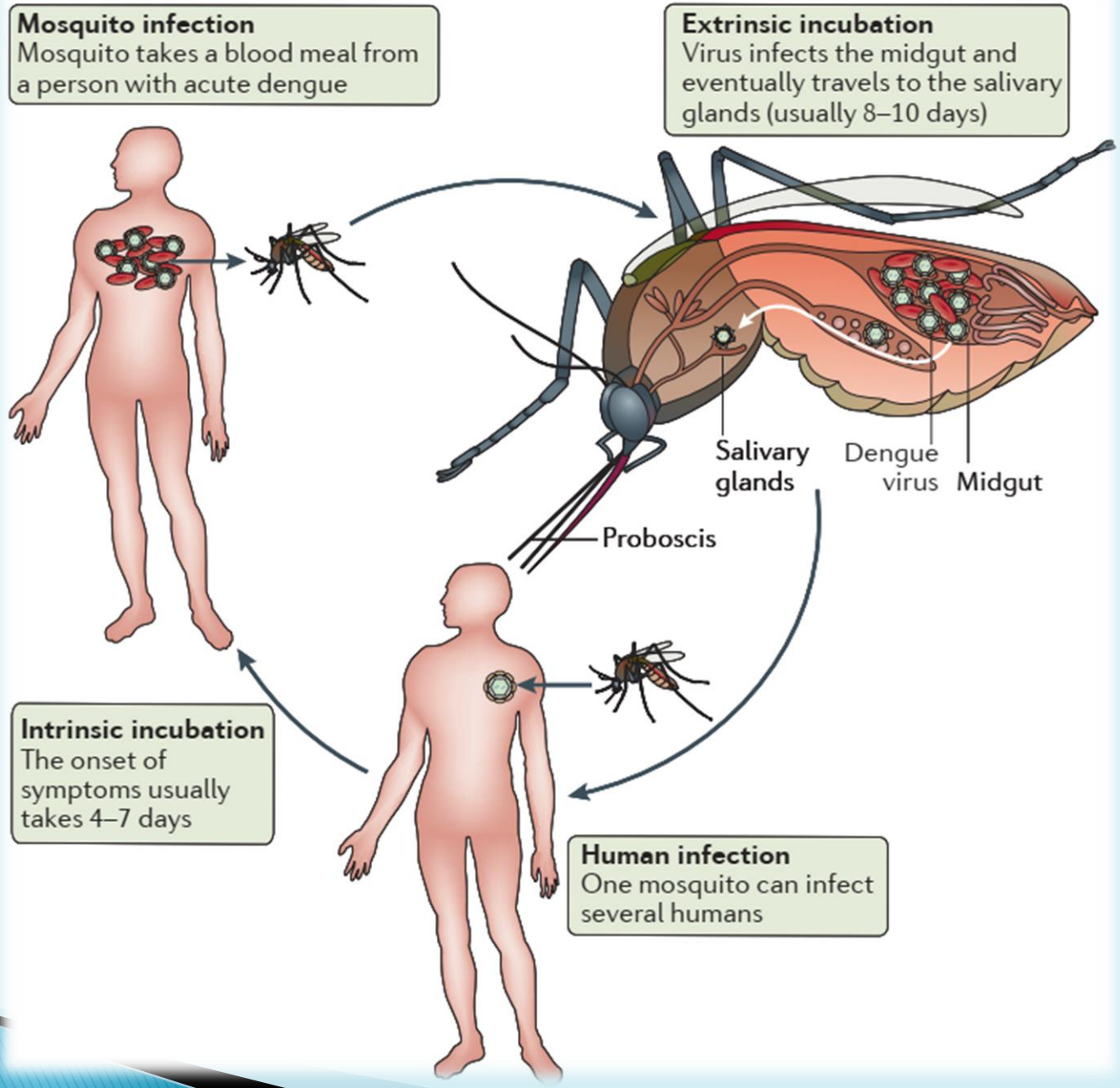

Distribution of DENV sequences (NCBI)
2000 – 2014
15 year(s)
Data term : 1944 – 2016
Last updated : 2016/05/13
Download xlsx / csv
Serotype
All
Serotype 1
Serotype 2
Serotype 3
Serotype 4


Evidence consensus
Complete absence
Good (absence)
Moderate (absence)
Poor (absence)
Intermediate
Poor (presence)
Moderate (presence)
Good (presence)
Complete presence



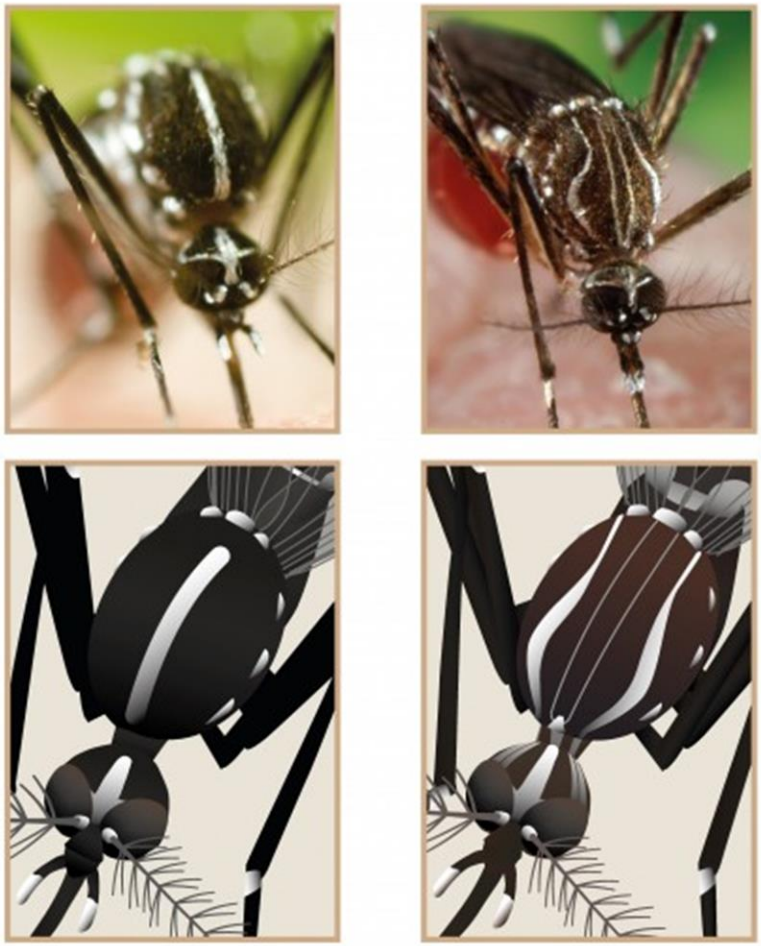

ylvatic/enzootic
Epidemic
Aedes mosquito
?
Primates
Humans
Nature Reviews | Microbiology



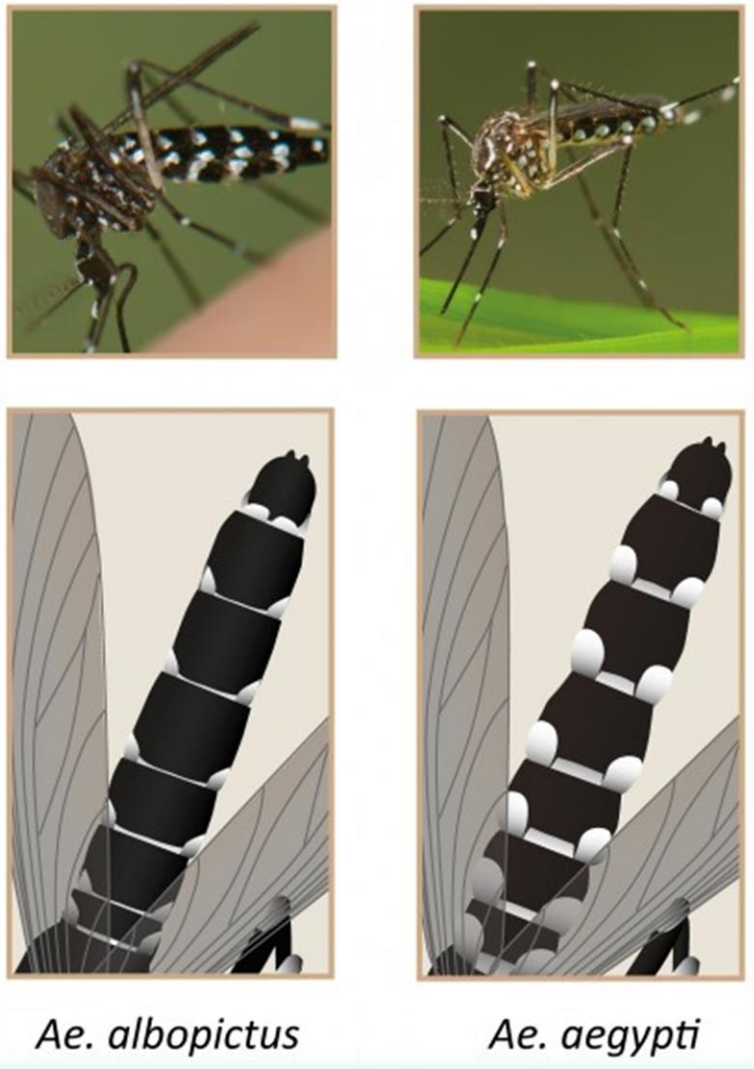

Mosquito infection
Mosquito takes a blood meal from a person with acute dengue
Extrinsic incubation
Virus infects the midgut and eventually travels to the salivary glands (usually 8–10 days)
Salivary glands
Dengue virus
Midgut
Proboscis
Intrinsic incubation
The onset of symptoms usually takes 4–7 days
Human infection
One mosquito can infect several humans


Adults
Life cycle of
Aedes aegypti
Pupae
Larvae

morphological difference between Ae. aegypti and Ae. albopictus



Ae. albopictus *Ae. aegypti*

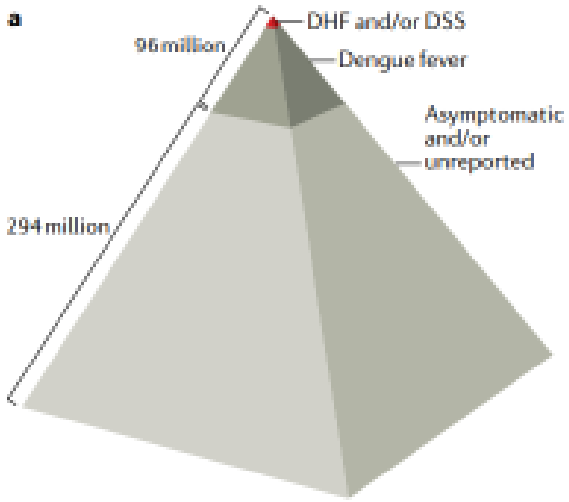


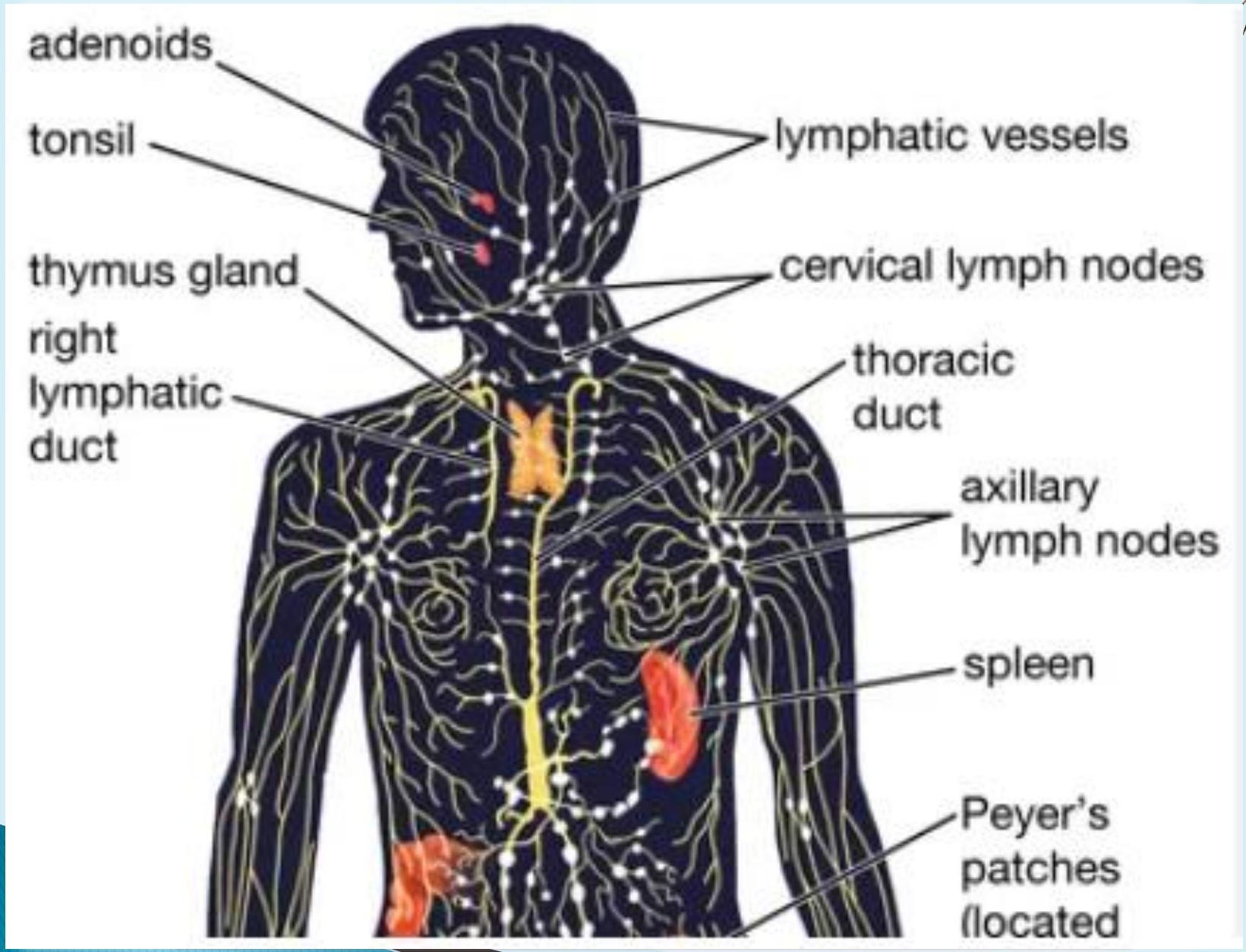
Ae. albopictus *Ae. aegypti*

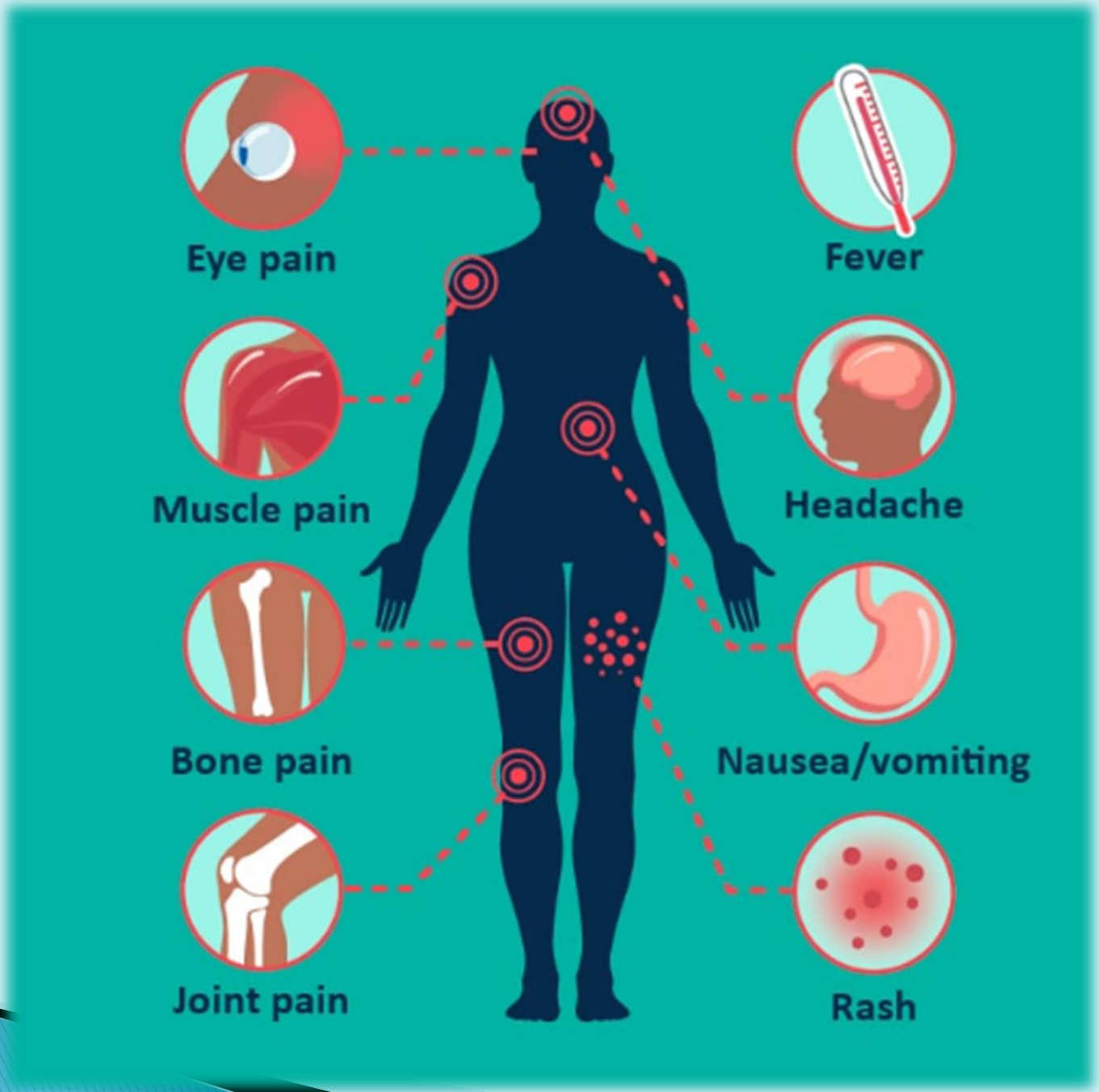
Global burden of disease

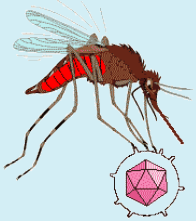
- Recent best estimates of dengue disease burden suggest that over half of the world's population (3.6 billion people) live in areas that place them at risk of DENV infection,

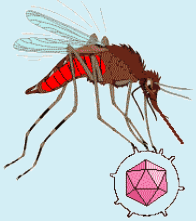
1. **390 million overall DENV infections,**
2. **96 million symptomatic infections10,**
3. **2 million cases of severe disease and**
4. **21,000 deaths per year**




adenoids
tonsil
thymus gland
right lymphatic duct
lymphatic vessels
cervical lymph nodes
thoracic duct
axillary lymph nodes
spleen
Peyer's patches (located


Eye pain
Fever
Muscle pain
Headache
Bone pain
Nausea/vomiting
Joint pain
Rash



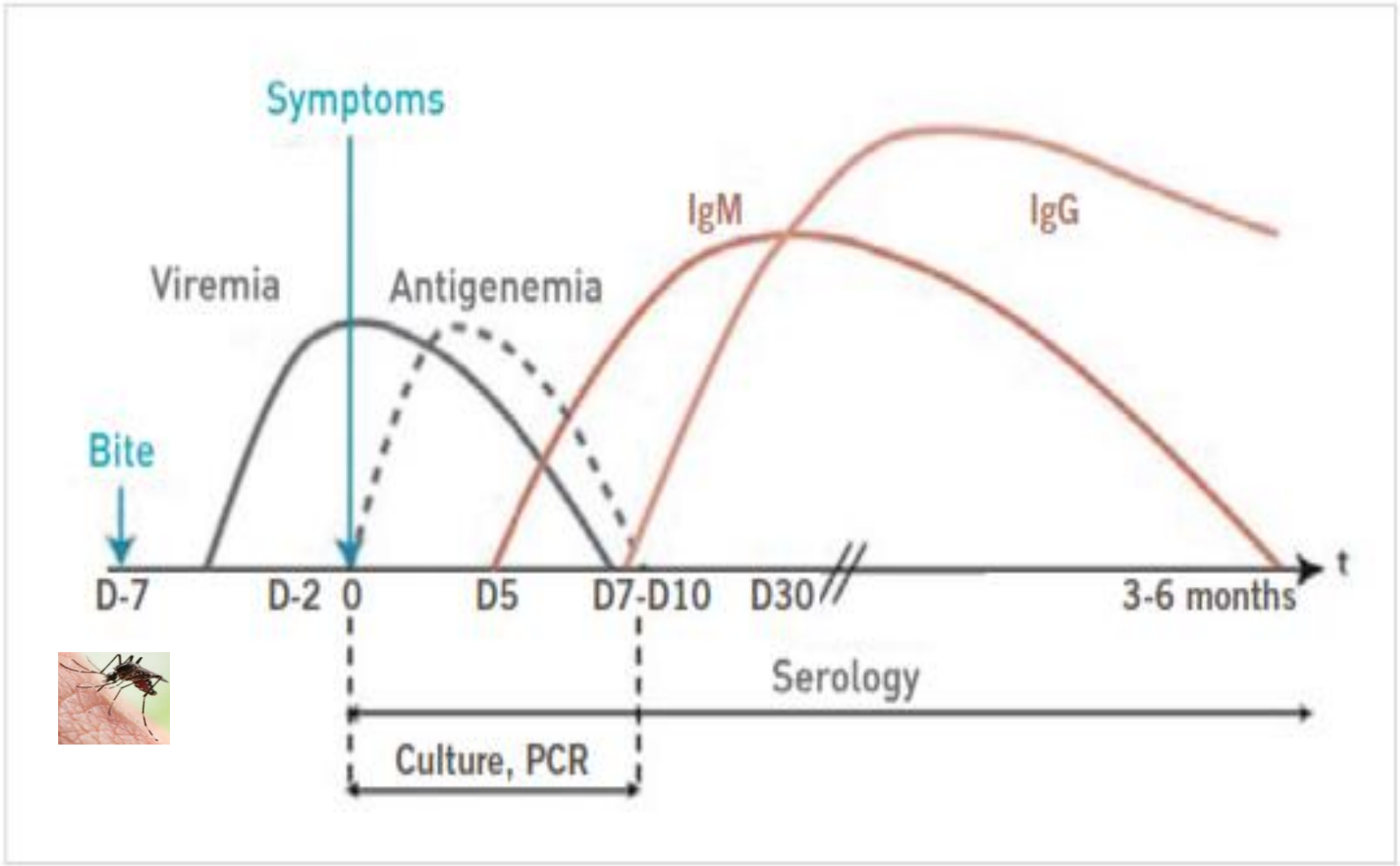


Diagnosis

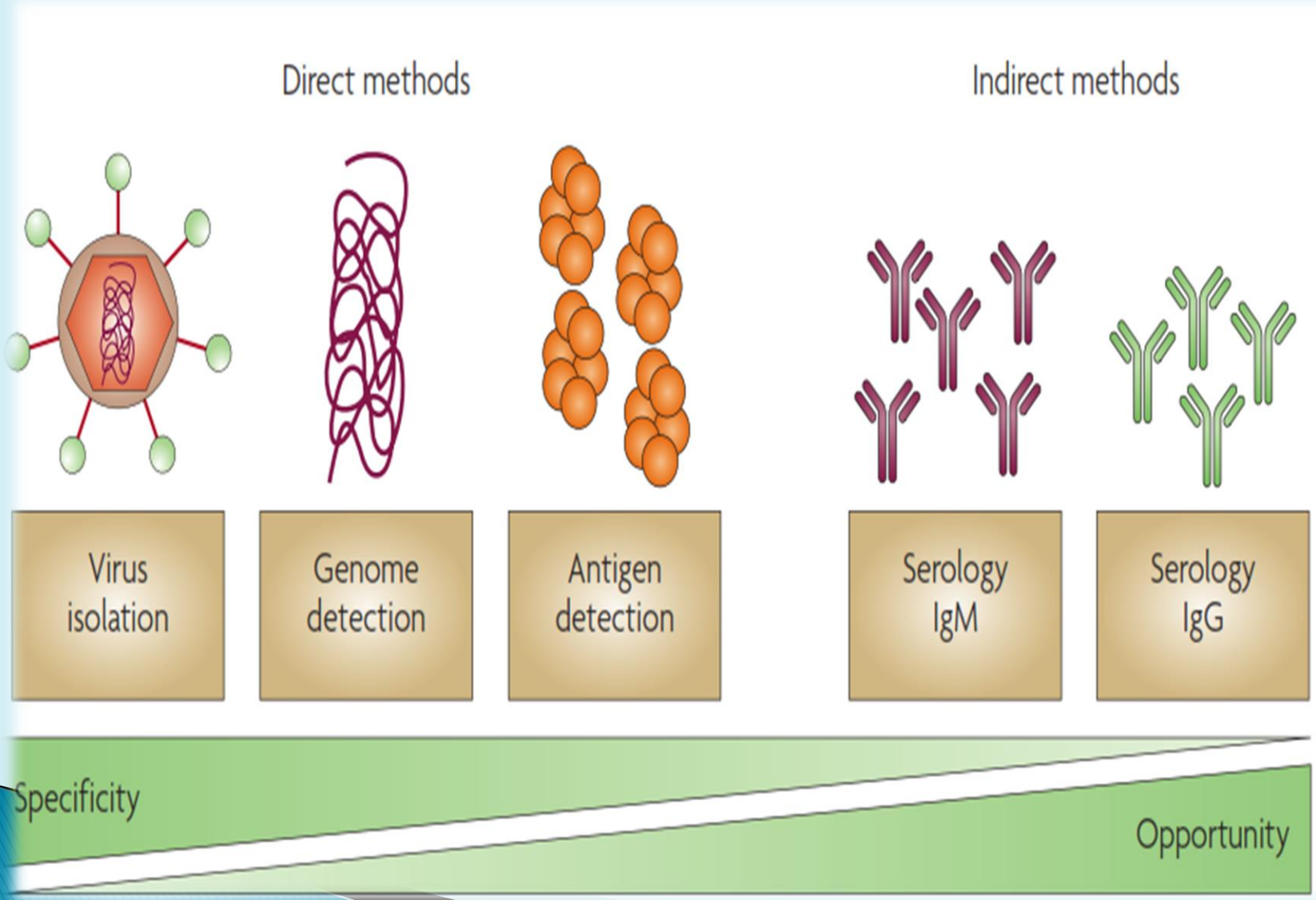
Importance of Comprehensive Assessment

- Accurate diagnosis relies on integrating laboratory findings with:
  - **Patient history: especially travel to endemic areas**
  - **Clinical symptoms** (e.g. fever, headache, arthralgia, myalgia, rash, nausea, ….)
  - **Routine clinical laboratory**.

Dengue Virus infection Kinetics



Diagnostic methods



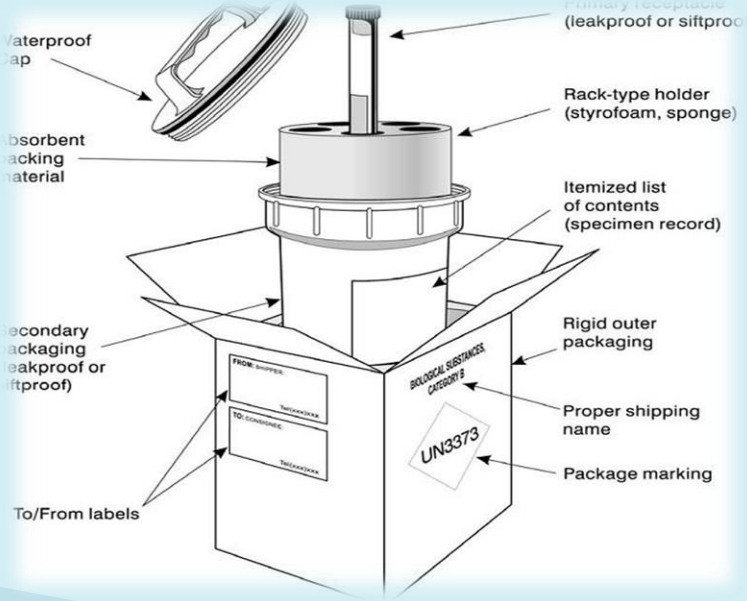
Sampling strategy

Sample Type: **Serum**

Two sets of samples are required for each DENV suspected case:

1: **Acute phase sample** (<7 days after onset of symptoms)**:**
Real Time PCR& شELISA(IgM + IgG)

2: **Convalescent phase sample** (2 weeks after acute sample):
ELISA (IgM + IgG)



Single Specimen

	Laboratory tests				Interpretation
	NS1	Real time RT-PCR #	IgM	IgG	
Single specimen	+	+	+	+	DENV Infection
	+	+	+	-	DENV Infection
	+	+	-	+	DENV Infection
	+	+	-	-	DENV Infection
	+	-	-	-	DENV Infection
	+	unknown	unknown	unknown	DENV Infection
	unknown	+	unknown	unknown	DENV Infection
	-	+	-	-	DENV Infection
	+	-	+	+	DENV Infection
	+	-	+	-	DENV Infection
	+	-	-	+	DENV Infection
	-	+	+	+	DENV Infection
	-	+	+	-	DENV Infection
	-	+	-	+	DENV Infection
	-	-	+	+	Presumptive DENV Infection*
	-	-	+	-	Presumptive DENV Infection*
	-	-	-	+	Presumptive DENV Infection*
					Negative***

Paired Specimen

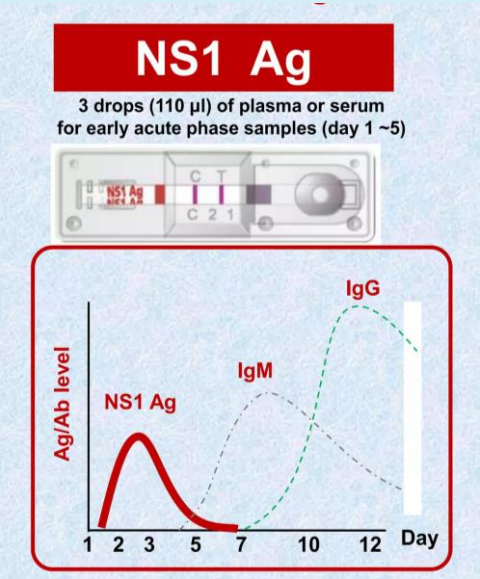
	Laboratory tests				Interpretation
	NS1	Real time RT-PCR #	IgM	IgG	
Paired specimen	-	-	-	-	DENV Infection
	-	-	+	-	
	-	-	-	-	DENV Infection
	-	-	+	+	
	-	-	-	-	DENV Infection
	-	-	-	+	
	-	-	+	-	DENV Infection
	-	-	+	+	
	-	-	+	+	DENV Infection
	-	-	+	-	
	-	-	+	+	DENV infection
	-	-	+	++**	
	-	-	+	+	Presumptive Past DENV or other falaviviruses Infection
	-	-	+	+	
	-	-	+	+	Presumptive Past DENV or other falaviviruses Infection
	-	-	-	+	
	-	-	-	-	Negative
	-	-	-	-	
	-	-	+	+	Inconclusive
	-	-	-/+	-	
	-	-	+	+	Negative****
	-	-	-	-	

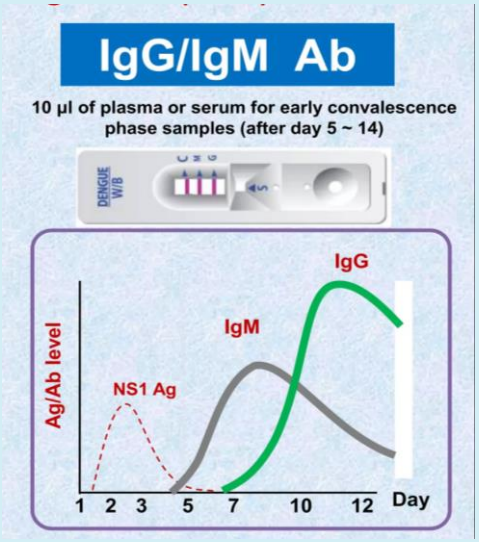
Rapid Diagnosis Assay

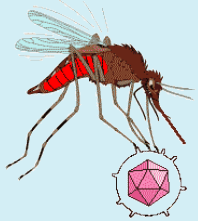
•Performance

- Sensitivity :
•92.4% (Dengue NS1 Ag),
•94.2% (Dengue IgG/IgM)

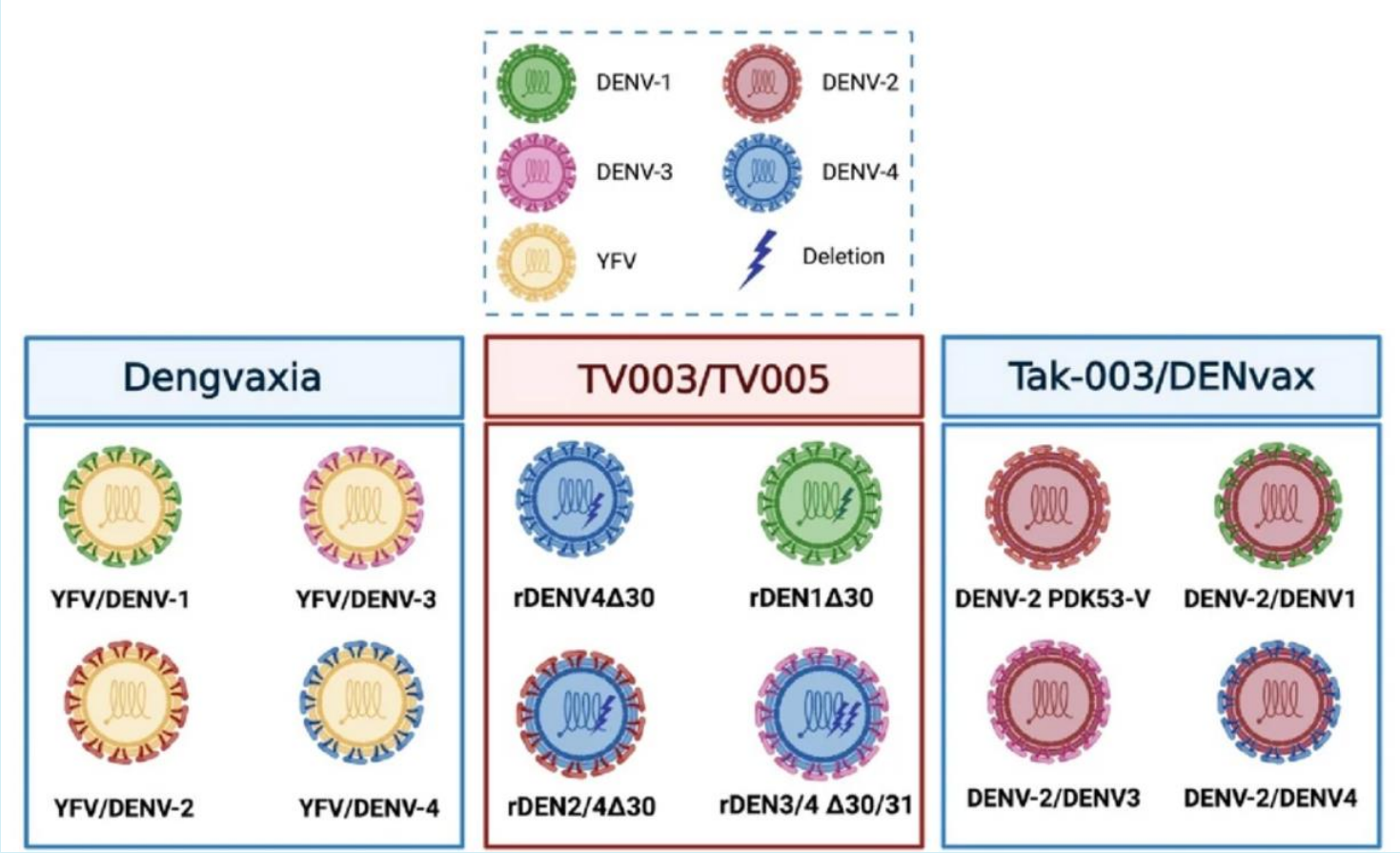
- Specificity :
•98.4%(Dengue NS1 Ag),
•96.4% (Dengue IgG/IgM)

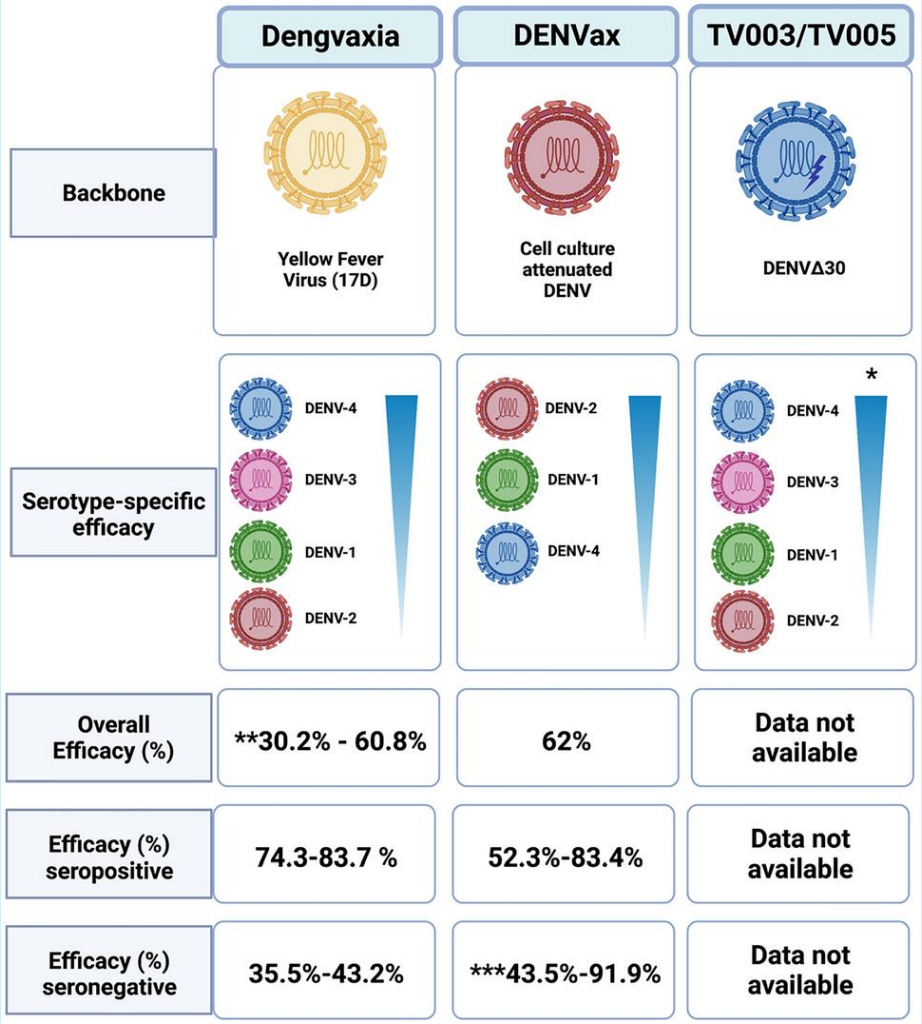






Immunization


DENV-1
DENV-2
DENV-3
DENV-4
YFV
Deletion
Dengvaxia
YFV/DENV-1
YFV/DENV-3
YFV/DENV-2
YFV/DENV-4
TV003/TV005
rDENV4Δ30
rDEN1Δ30
rDEN2/4Δ30
rDEN3/4 Δ30/31
Tak-003/DENvax
DENV-2 PDK53-V
DENV-2/DENV1
DENV-2/DENV3
DENV-2/DENV4


Dengvaxia
DENVax
TV003/TV005
Backbone
Yellow Fever Virus (17D)
Cell culture attenuated DENV
DENVΔ30
Serotype-specific efficacy
DENV-4
DENV-3
DENV-1
DENV-2
DENV-2
DENV-1
DENV-4
*
DENV-4
DENV-3
DENV-1
DENV-2
Overall Efficacy (%)
**30.2% - 60.8%
62%
Data not available
Efficacy (%) seropositive
74.3-83.7 %
52.3%-83.4%
Data not available
Efficacy (%) seronegative
35.5%-43.2%
***43.5%-91.9%
Data not available

Thanks for your attention

JMZ