



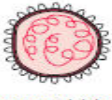











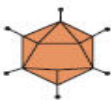




Infectious diseases

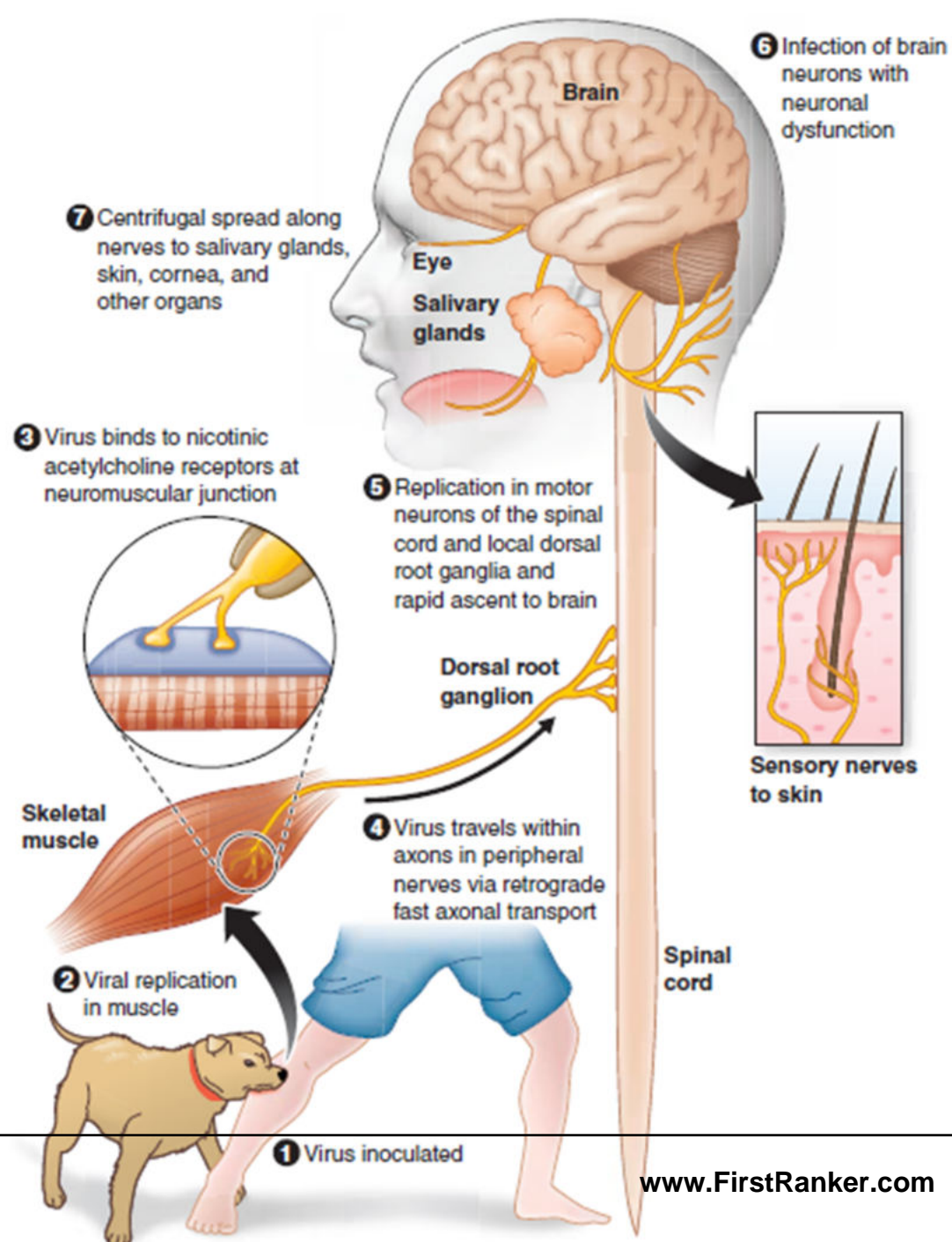
	4/5 th Semester Classes on Infectious Diseases, 8-9AM, Tuesdays (LT-1)
	Topics
1	Approach to Infectious Diseases and their prevention
2	Antibiotic stewardship practices
3	Community-Acquired Infections
4	Health Care–Associated Infections
5	Gram-Positive Bacteria (part-1)
6	Gram-Positive Bacteria (part-2)
7	Gram-Negative Bacteria (part-1)
8	Gram-Negative Bacteria (part-2)
9	Spirochetal Diseases
10	Diseases Caused by Atypical/Miscellaneous Bacterial Infections
11	Revision-cum-exam on bacteria (Must to know type)
12	Infections Due to DNA Viruses
13	Infections Due to RNA Viruses (part 1)
14	Infections Due to RNA Viruses (part 2)
15	HIV/AIDS – part 1
16	HIV/AIDS – part 2
17	Fungal Infections
18	Parasitic Infections (part 1)
19	Parasitic Infections (part 2)
20	Revision-cum-exam on Virus, Fungal, and Parasite (Must to know type)

Positive-strand RNA viruses	
	Picornaviridae
Genome size (kb)	7.2–8.4
Envelope	No
Capsid symmetry	Icosahedral
	Caliciviridae
Genome size (kb)	8
Envelope	No
Capsid symmetry	Icosahedral
	Togaviridae
Genome size (kb)	12
Envelope	Yes
Capsid symmetry	Icosahedral
	Flaviviridae
Genome size (kb)	10
Envelope	Yes
Capsid symmetry	Icosahedral
	Coronaviridae
Genome size (kb)	16–21
Envelope	Yes
Capsid symmetry	Helical
Negative-strand RNA viruses	
	Rhabdoviridae
Genome size (kb)	13–16
Envelope	Yes
Capsid symmetry	Helical
	Filoviridae
Genome size (kb)	13
Envelope	Yes
Capsid symmetry	Helical
	Paramyxoviridae
Genome size (kb)	16–20
Envelope	Yes
Capsid symmetry	Helical
Segmented negative-strand RNA viruses	
	Orthomyxoviridae
Genome size (kb)	14
Envelope	Yes
Capsid symmetry	Helical
	Bunyaviridae
Genome size (kb)	13–21
Envelope	Yes
Capsid symmetry	Helical
	Arenaviridae
Genome size (kb)	10–14
Envelope	Yes
Capsid symmetry	Helical
Segmented double-strand RNA viruses	
	Reoviridae
Genome size (kb)	16–27
Envelope	No
Capsid symmetry	Icosahedral
Retroviruses	
	Retroviridae
Genome size (kb)	3–9
Envelope	Yes
Capsid symmetry	Icosahedral
DNA viruses	
	Parvoviridae
Genome size (kb)	5
Envelope	No
Capsid symmetry	Icosahedral
	Papillomaviridae
Genome size (kb)	5–9
Envelope	No
Capsid symmetry	Icosahedral
	Hepadnaviridae
Genome size (kb)	3*
Envelope	Yes
Capsid symmetry	Icosahedral
	Adenoviridae
Genome size (kb)	36–38
Envelope	No
Capsid symmetry	Icosahedral
	Herpesviridae
Genome size (kb)	100–250
Envelope	Yes
Capsid symmetry	Icosahedral
	Poxviridae
Genome size (kb)	240
Envelope	Yes
Capsid symmetry	Complex

Family	Common virus
Picornaviridae	Polio Entero
Caliciviridae	Noro
Reoviridae	Rota
Orthomyxviridae	Influenza
Paramyxoviridae	Measle Mumps Parainfluenza
Coronaviridae	SARS MARS
Togaviridae	Rubella Chikungunya
Flaviviridae	Dengue West nile
Filoviridae	Ebola
Rhabdoviridae	Rabies
Bunyaviridae	Hanta Nairo (CCHF)
Retroviridae	HIV

RABIES

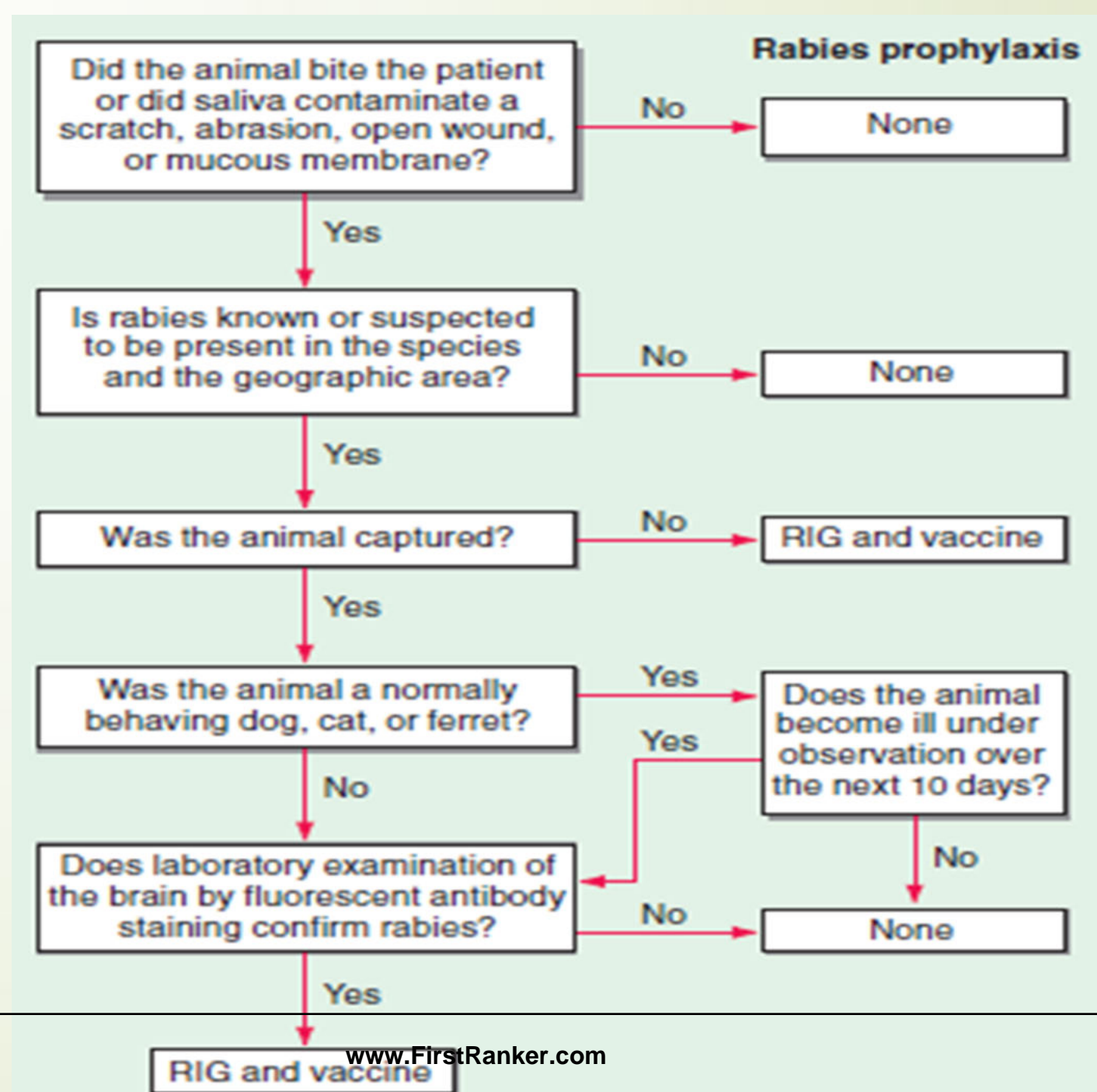
- Zoonotic infection that occurs in a variety of mammals throughout the world except in Antarctica and on some islands
- **Canine rabies** continues to be a threat to humans; others – **bat/raccoon** rabies
- **IP:** 20–90 days but in rare cases is as short as a few days or >1 year
- usually transmitted to humans **by the bite**; rarely aerosol, transplantation, human-human possibly
- **Neuronal dysfunction—rather than neuronal death—is** responsible; microglial nodules called *Babes nodules & Negri bodies* (eosinophilic cytoplasmic inclusions)
- Disease usually presents as **atypical encephalitis** with relative preservation of consciousness
- **Prodromal** – nonspecific, sometimes earliest specific neurologic symptoms that include paresthesias, pain, or pruritus near the site of the exposure
- **Acute neurologic** – encephalitic (**furious**) in 80% and **paralytic** in 20%.
- **Comatose** -



- Autonomic dysfunction is common and may result in hypersalivation, gooseflesh, cardiac arrhythmia, and priapism
- Episodes of **hyperexcitability are typically followed** by periods of complete lucidity that become shorter as the disease progresses
- Early brainstem involvement (**hydrophobia, aerophobia**)
- In paralytic type, commonly **misdiagnosed as Guillain-Barre syndrome**



- **Diagnosis should be considered** in patients presenting with acute atypical encephalitis or acute flaccid paralysis, including those in whom Guillain-Barre syndrome is suspected
- Diagnostically useful specimens include serum, CSF, fresh saliva, **skin biopsy samples from the neck**, and brain tissue
- Presence of rabies virus-specific antibodies in the CSF suggests rabies encephalitis, **regardless of immunization status**
- **Other methods:** RT-PCR, Direct fluorescent antibody
- **DD:** Anti-N-methyl-d-aspartate receptor (anti-NMDA) encephalitis, Postinfectious (immune-mediated) encephalomyelitis, psychiatric disorder (**Rabies hysteria**)
- There is **no established treatment** for rabies
- There are **seven** well-documented cases of survival from rabies
- **Postexposure Prophylaxis (PEP)** –
 - Healthy **dogs, cats, or ferrets** may be confined and observed **for 10 days**
 - If an animal escapes after an exposure, it must be considered rabid, and PEP must be initiated
 - Includes local wound care and both active and passive immunization
 - If anatomically feasible, the **entire dose of RIG (20 IU/kg) should be infiltrated at the site** of the bite
- Vaccines; Four 1-mL doses of rabies vaccine should be given IM in the deltoid area (**NOT gluteal**) – **0, 3, 7, and 14**



Zoonotic viruses: Arthropod-Borne and Rodent-Borne Virus Infections

- *Extrinsic incubation*, typically lasts 1–3 weeks in mosquitoes; Arboviruses infect their vectors after ingestion of a blood meal from vertebrate; some arthropods by saliva-activated transmission, Rarely *transovarial transmission*
- *Intrinsic incubation*, as per type of infections
- Seven families: Arenaviridae, **Bunyaviridae**, **Flaviviridae**, Orthomyxoviridae, Reoviridae, **Rhabdoviridae**, and Togaviridae
- Arena and hanta viruses are *rodent borne viruses*
- **Diagnosis**; recognized history of mosquito bite or **tick bite (more diagnostic)** or rodent exposure; serology; PCR;

Hantavirus infections differ from other viral infections in that severe acute disease is immunopathologic;

SYNDROMES - grouped into one of five broad categories

TABLE 233-3 CLINICAL SYNDROMES CAUSED BY ZOO NOTIC ARTHROPOD-BORNE OR RODENT-BORNE VIRUSES	
Syndrome	Virus*
Arthritis and rash (A/R)	Bunyaviridae: Gan Gan and (Trubanaman) viruses
	Flaviviridae: Kokobera and Zika viruses
	Togaviridae: Barmah Forest, chikungunya, Mayaro, o'nyong-nyong, Ross River, Semliki Forest, and Sindbis viruses
Encephalitis (E)	Arenaviridae: lymphocytic choriomeningitis and (Whitewater Arroyo) viruses
	Bunyaviridae: Bhanja, California encephalitis, Chios, Inkoo, Jamestown Canyon, La Crosse, Lumbo, Rift Valley fever, snowshoe hare, Tahyna, and Toscana viruses
	Flaviviridae: Japanese encephalitis, Murray Valley encephalitis, Powassan, Rocio, St. Louis encephalitis, tick-borne encephalitis, (Usutu), and West Nile viruses
	Orthomyxoviridae: Dhori and Thogoto viruses
	Reoviridae: Banna, Colorado tick fever, Eyach, Kemerovo, Orungo, and Salmon River viruses
	Rhabdoviridae: Chandipura virus
	Togaviridae: eastern equine encephalitis, Everglades, Mucambo, Tonate, Venezuelan equine encephalitis, and western equine encephalitis viruses
Fever and myalgia (F/M)	Arenaviridae: Lassa and lymphocytic choriomeningitis viruses
	Bunyaviridae: Alenquer, Apeú, Bangui, Batal, Bhanja, Bunyamwera, Bwamba, Cache Valley, California encephalitis, Candiru, Caraparú, Catu, Chagres, Choclo, Dugbe, Escharate, Fort Sherman, Germiston, Guama, Guaroa, Heartland, Ilesha, Inkoo, Iquitos, Itaqui, Jamestown Canyon, La Crosse, Lumbo, Madrid, Maldonado, Marituba, Morumbi, Nairobi sheep disease, Nepuyo, Ngari, Nyando, Oriboca, Oropouche, Ossa, Pongola, Punta Toro, Restan, Rift Valley fever, sandfly fever Cyprus, sandfly fever Naples, sandfly fever Sicilian, sandfly fever Turkey, Serra Norte, "severe fever with thrombocytopenia syndrome," Shokwe, snowshoe hare, Tacaluma, Tahyna, Tataguine, Thogoto, Toscana, Uukuniemi, Wyeomyia, Xingu, and Zungarococha viruses
	Flaviviridae: dengue 1–4, tick-borne encephalitis, and Zika viruses
	Orthomyxoviridae: Dhori and Quarantil viruses
	Reoviridae: Colorado tick fever, Eyach, Kemerovo, Leborombo, Orungo, Salmon River, and Tribeč viruses
	Rhabdoviridae: Chandipura, Isfahan, Pirý, vesicular stomatitis Indiana, and vesicular stomatitis New Jersey viruses
	Togaviridae: Everglades, Mucambo, Tonate, Una, and Venezuelan equine encephalitis viruses
Pulmonary disease (P)	Bunyaviridae: Anajatuba, Andes, Araucária, Bayou, Bermejo, Black Creek Canal, Blue River, Castelo dos Sonhos, El Moro Canyon, Juquitiba, Laguna Negra, Lechiguana, Maciel, Monongahela, Muleshoe, New York, Orán, Paranoá, Pergamino, (Puumala), Río Mamoré, Sin Nombre, (Tula), and Tunari viruses
Viral hemorrhagic fever (VHF)	Arenaviridae: Chapare, Guanarito, Junín, Lassa, Lujo, (lymphocytic choriomeningitis), Machupo, and Sabiá viruses
	Bunyaviridae: Amur/Soochong, Crimean-Congo hemorrhagic fever, Dobrava-Belgrade, Gou, Hantaan, (Ilesha), Kurkino, Muju, Ngari, Puumala, Rift Valley fever, Saaremaa, Seoul, "severe fever with thrombocytopenia syndrome," Sochi, and Tula viruses
	Flaviviridae: dengue 1–4, Kyasanur Forest disease, Omsk hemorrhagic fever, (tick-borne encephalitis), and yellow fever viruses

ARTHRITIS AND RASH

- **D/D** - hepatitis B, parvovirus B19 infection, and rubella, and occasionally due to adenoviruses, enteroviruses, herpesviruses, and mumps virus
- **Chikungunya:**
 - *Aedes albopictus* was identified as the major vector with IP – **2-10 DAYS**
 - **Abrupt onset** of Fever (often severe) with a **saddleback pattern** and severe arthralgia accompanied by chills and constitutional symptoms and signs, such as abdominal pain, anorexia, conjunctival injection, headache, nausea, and photophobia
 - Migratory polyarthritis mainly affects **the small joints** of the ankles, feet, hands, and wrists; rarely large joints
 - **Rashes often coincides with defervescence**; Children also often develop a bullous rather than a maculopapular/petechial rash
 - Maternal-fetal transmission has been reported
 - petechiae are occasionally seen and epistaxis is not rare, but **chikungunya virus should not be considered a VHF agent**
 - Mildly decreased platelet counts may be seen
 - Nonsteroidal anti-inflammatory drugs and sometimes **chloroquine for refractory arthritis**

ENCEPHALITIS

- Seasonal diseases, commonly occurring in the **warmer months**
- **Japanese encephalitis** is the most important viral encephalitis in Asia
- The virus is particularly common in areas of **irrigated rice fields** (attract the natural avian vertebrate hosts and provide abundant breeding sites for mosquitoes such as *Culex tritaeniorhynchus*)
- Additional **amplification host** by pigs and horses
 - Unspecific febrile presentation (nausea, vomiting, diarrhea, cough)
 - aseptic meningitis,
 - meningoencephalitis,
 - acute flaccid paralysis,
 - severe encephalitis

- Common findings in JE are cerebellar signs, cranial nerve palsies, and cognitive and speech impairments
- Diagnosis by CSF/serum PCR study along with clinical features
- Symptomatic treatment only
- Usually **two intramuscular doses of the vaccine** are given 28 days apart

Chandipura virus seems to be an emerging in India

- It is transmitted among **hedgehogs** by mosquitoes and sandflies
- It is characterized by high lethality in children

West Nile virus is the primary cause of arboviral encephalitis in the United States

- Few cases are reported from India

FEVER AND MYALGIA

- Typically begins with the **abrupt onset** of fever, chills, intense myalgia, and malaise; “influenza-like” symptoms
- The most clinically important flaviviruses that cause this syndrome are **dengue viruses** 1–4

Hantavirus syndrome: It was in 1966 that **Thottapalayam virus**, the first indigenous hantavirus species was isolated.

The Old World hantaviruses cause haemorrhagic fever with renal syndrome (**HFRS**) in **Asia** and Europe while the New World hantaviruses cause hantavirus cardiopulmonary syndrome (HCPS) in the America.

Dengue

Agent- Dengue Virus

- Single stranded RNA Virus
- Family: Flaviviridae
- Genus: Flavivirus
- 4 serotypes: DENV-1, DENV-2, DENV-3 and DENV-4



Vector- Mosquito

- *Aedes aegypti*, *Aedes albopictus*
- Day feeders, Recurrent biter, Anthropophilic¹
- Fresh water mosquitoes
- White bands or scale patterns on its legs and thorax



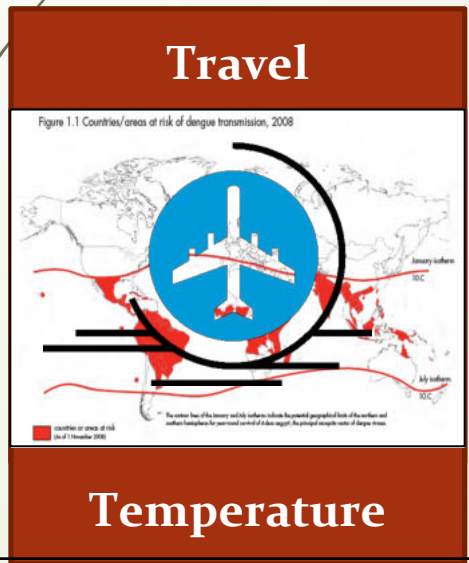
DENV- Dengue virus

Gubler Djet al. New York: CAB International; 1997. p. 1–22.

Dengue- An emerging disease



Mosquito



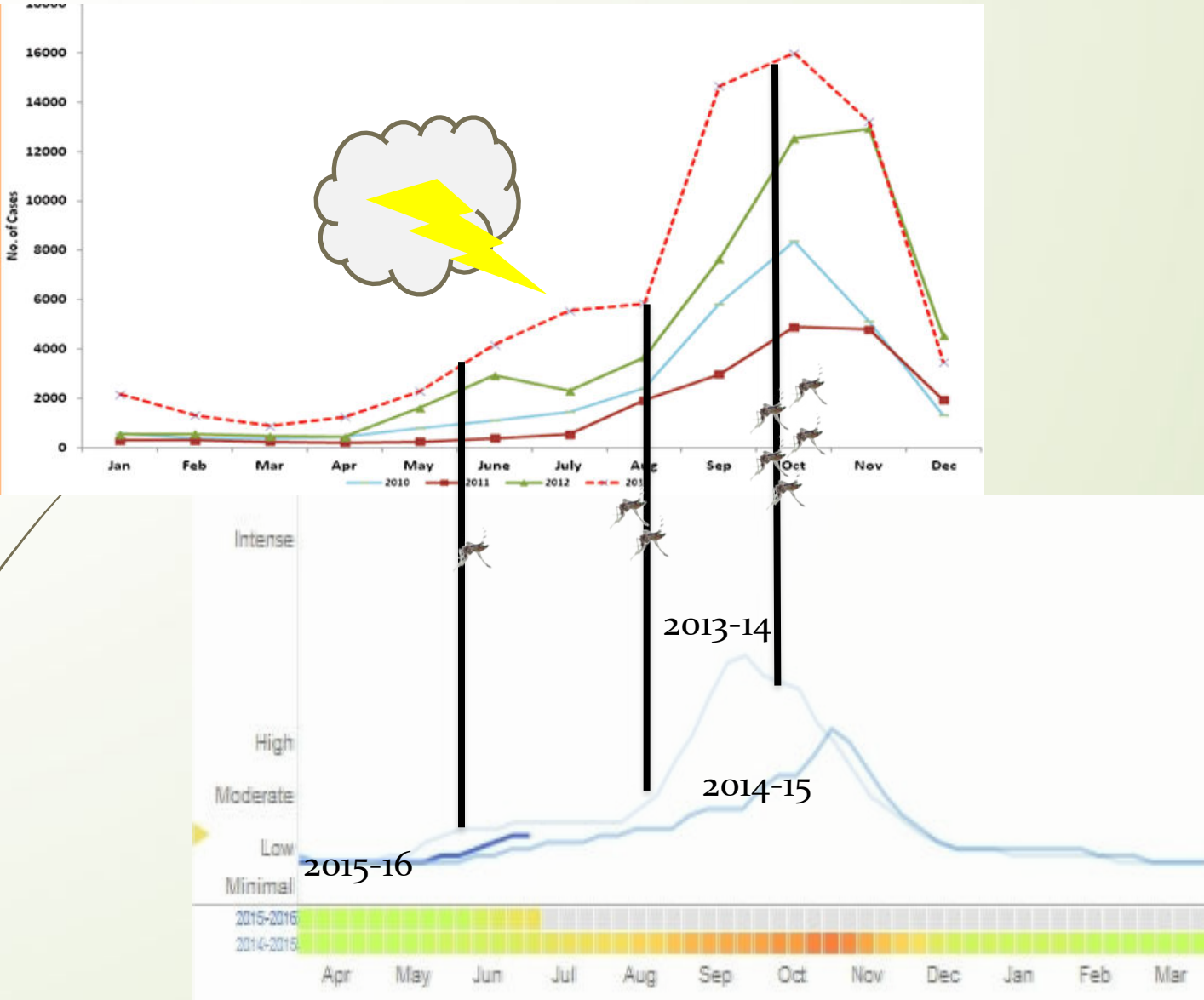
Travel

Temperature



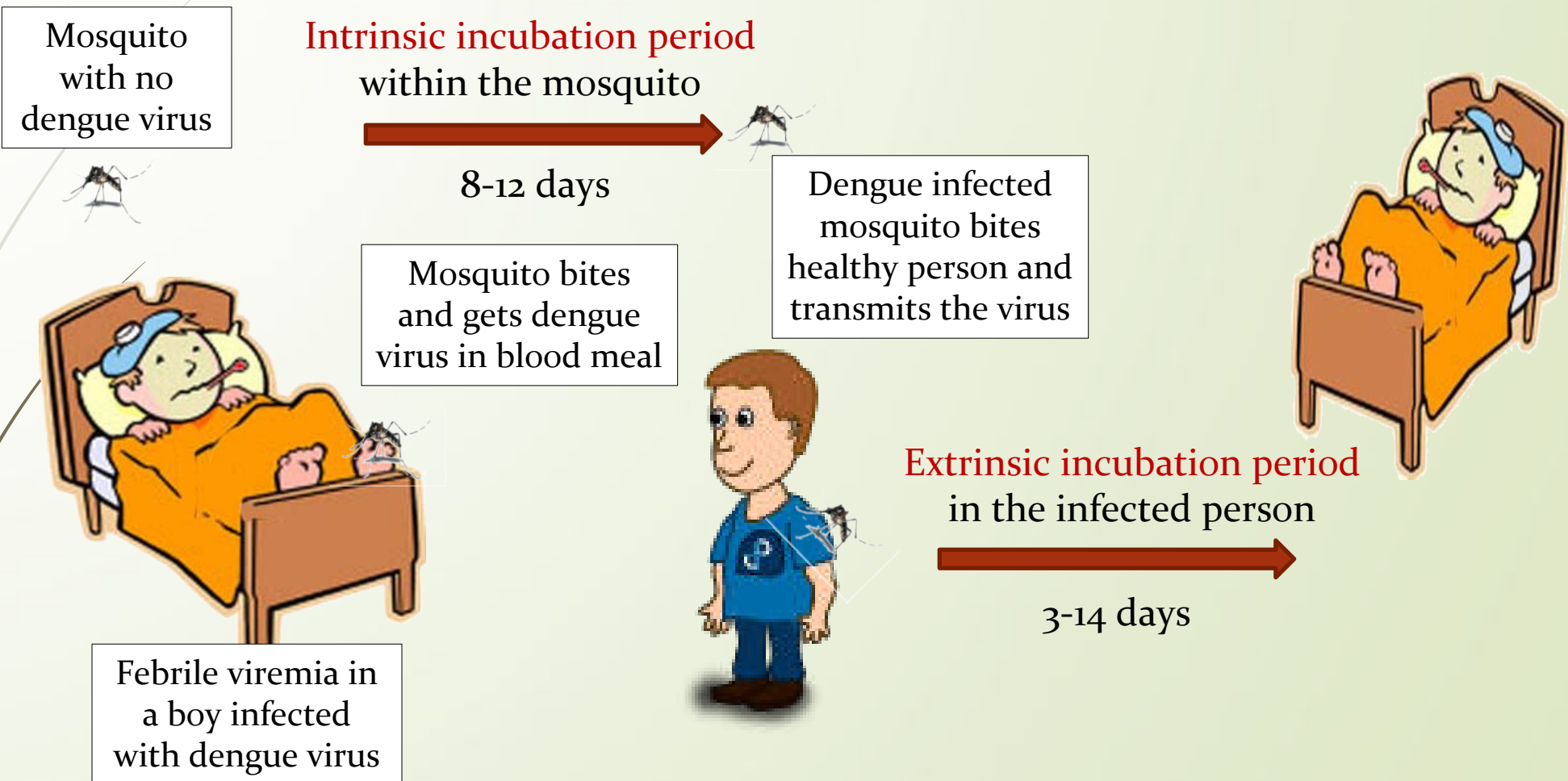
Organization

Dengue- Seasonal Trends

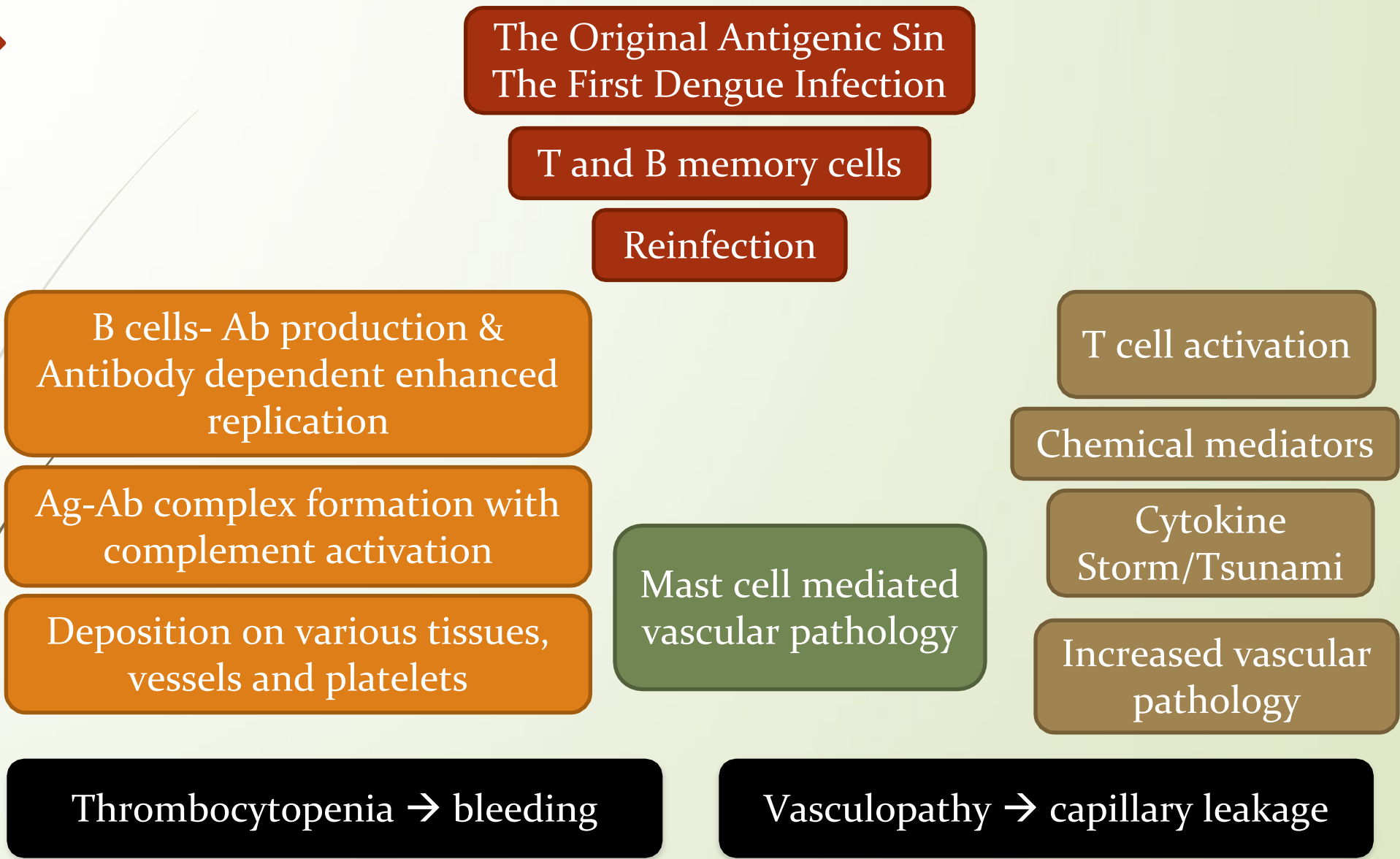


Source: Dengue Trends, https://www.google.org/denguetrends/intl/en_us/

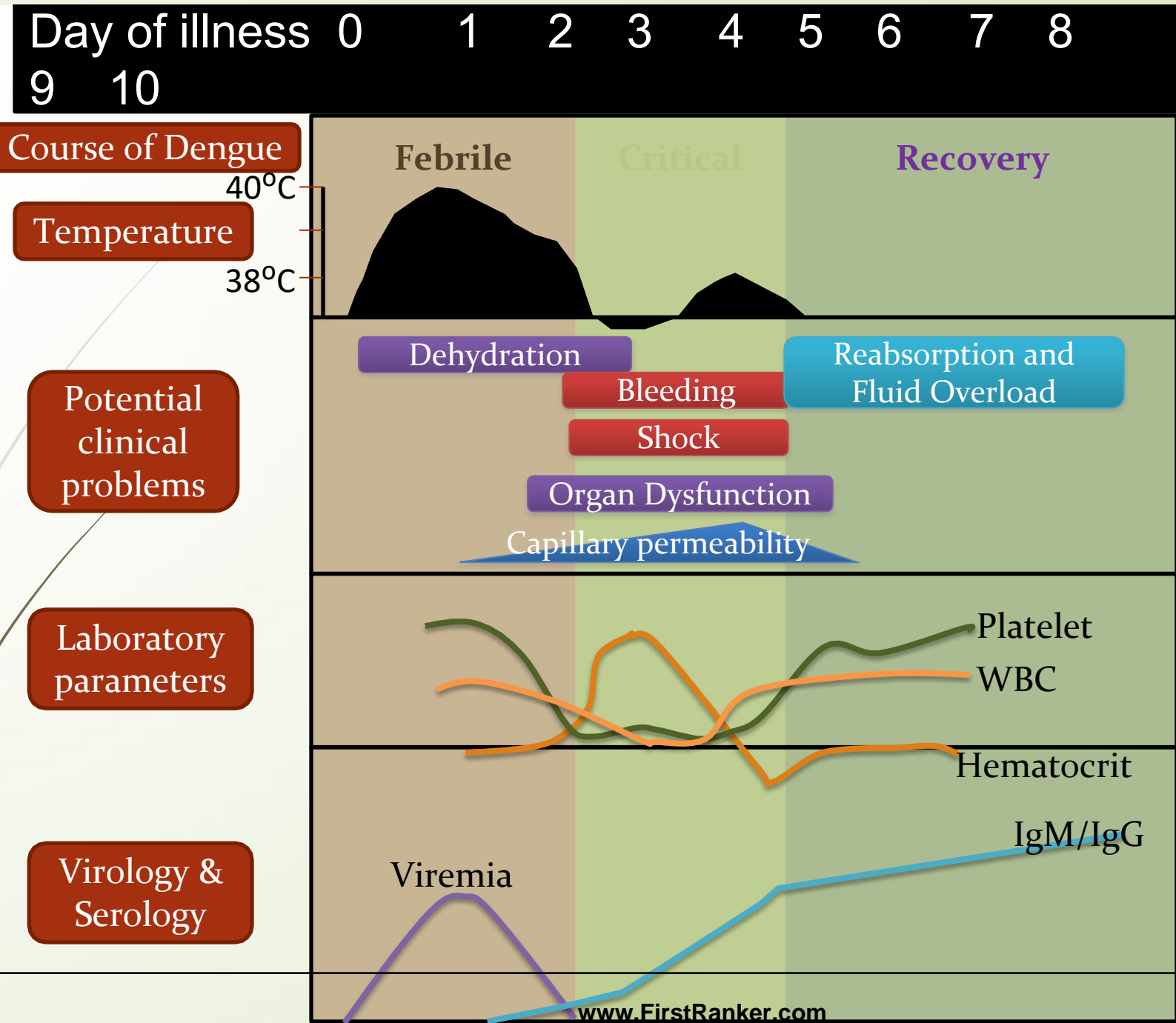
Man-Mosquito-Man Cycle



Immune-pathogenesis



Ref: Mongkolsapaya J et al. 2003. Nat Med 9: 921–927
Mathew A et al. 2008. Immunol Rev 225: 300–313

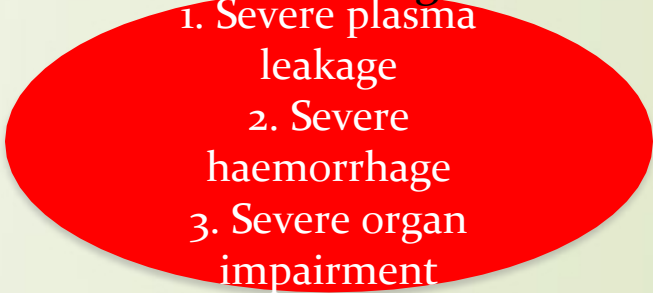


Dengue Case classification (2009)

Dengue +/- warning symptoms



Severe Dengue



Criteria for Dengue +/- warning symptoms

Probable dengue
live in /travel to dengue endemic area.
Fever and 2 of the following criteria:
• Nausea, vomiting
• Rash
• Aches and pains
• Tourniquet test positive
• Leukopenia
• Any warning sign

Laboratory-confirmed dengue
(important when no sign of plasma leakage)

Warning signs*
• Abdominal pain or tenderness
• Persistent vomiting
• Clinical fluid accumulation
• Mucosal bleed
• Lethargy, restlessness
• Liver enlargement >2 cm
• Laboratory: increase in HCT concurrent with rapid decrease in platelet count

*(requiring strict observation and medical intervention)

Criteria for Severe Dengue

Severe plasma leakage leading to:
• Shock (DSS)
• Fluid accumulation with respiratory distress

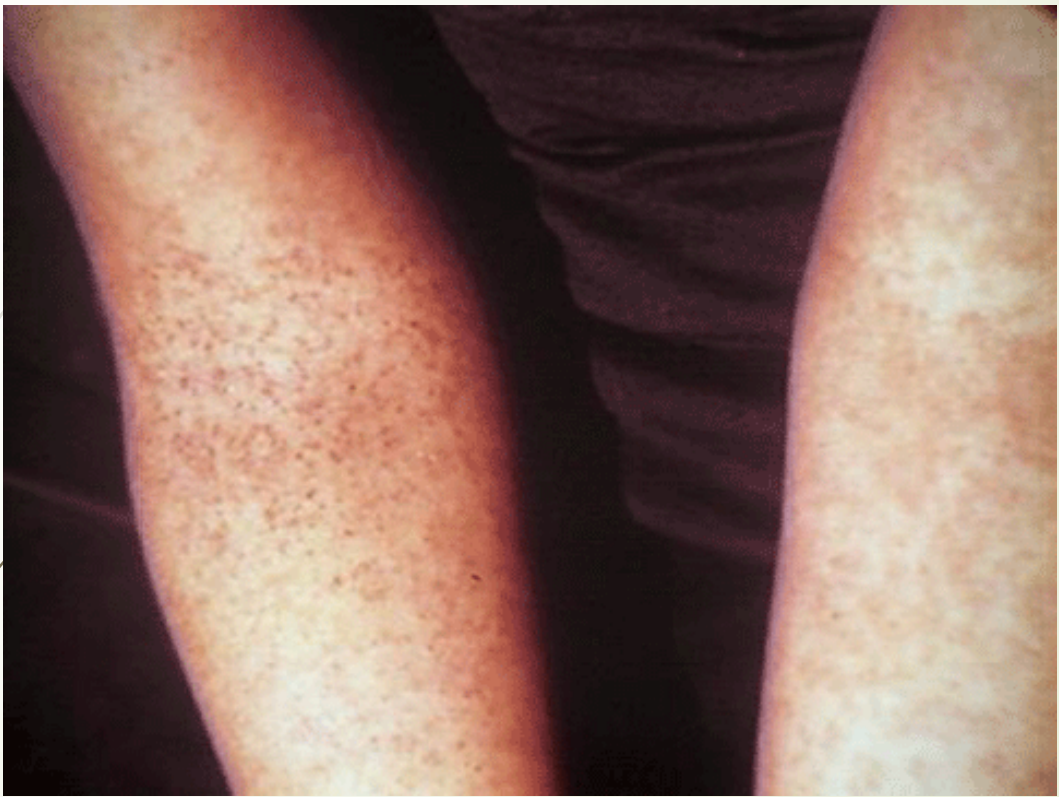
Severe bleeding as evaluated by clinician

Severe organ involvement
• Liver: AST or ALT ≥ 1000
• CNS: Impaired consciousness
• Heart and other organs

DSS-Dengue shock syndrome

Ref: WHO-TDR Guidelines for diagnosis, management, prevention and control of dengue 2009

Clinical Features



Tourniquet test

- Midpoint between SBP and DBP
- 5 minutes

SBP- systolic blood pressure
DBP- diastolic blood pressure

- +ve when 10 or more petechia per 1 square inch area over forearm
- Definite positive test with 20 petechiae or more

Confirming a case of Dengue

Isolation of Virus	Up to 6 days of onset of illness	Have to process the sample without delay. Definite test Takes 7-10 days
PCR	Up to 6 days of onset of illness	RT-PCR, one step nested RT-PCR, NASBA, real time RT-PCR
ELISA and Dot blot for EM and NS1 Ag	Up to 6 days of onset of illness	
MAC ELISA	From day5 till day 60	
IgG ELISA		Represents past infection
Hemagglutination Inhibition Test		Not commonly used
Neutralisation test		Not commonly used
Rapid diagnostic tests		For anti dengue IgM, IgG, NS1.high false positive

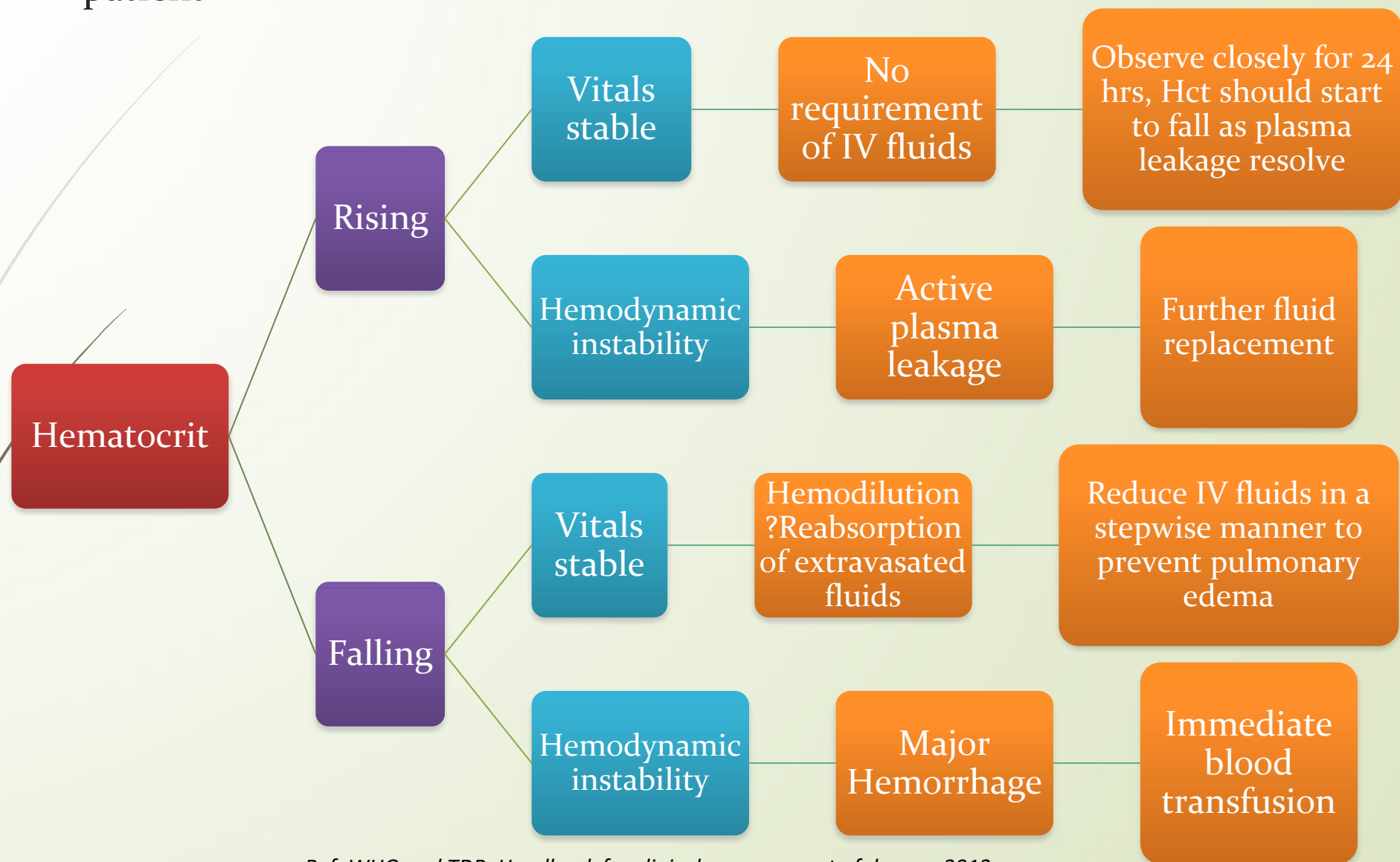
PCR- polymerase chain reaction, ELISA- Enzyme linked immunosorbent assay, NASBA-

Management of Dengue

Group A- Sent Home (all of the following)	Group B (any of the following)	Group C (any of the following)
<ul style="list-style-type: none">•Getting adequate volumes of oral fluids•Passing urine at least once every six hours•No warning signs•Stable hematocrit•Hemodynamically stable	<ul style="list-style-type: none">•Has warning signs•Has coexisting conditions- diabetes mellitus, renal failure, pregnant, infant or elderly•Has social circumstances: Living alone or living far away without reliable methods of transport	<ul style="list-style-type: none">•Severe plasma leakage leading to dengue shock and/or fluid accumulation with respiratory distress•Severe haemorrhages•Severe organ impairment (hepatic damage, renal impairment, cardiomyopathy, encephalopathy or encephalitis)
<ol style="list-style-type: none">1.Oral fluids- ORS, fruit juices2.Paracetamol3.Anticipatory guidance to caregivers4.Follow up daily5.Serial hemograms6.Identify Warning signs early	<ol style="list-style-type: none">1.Inpatient care2.Monitor Hct and hemodynamic stability3.Use IV fluids judiciously4.Correct acidosis and electrolyte disturbances	<ol style="list-style-type: none">1.Emergency treatment with intensive care facility and blood transfusion2.Fluid resuscitation

Use of Hematocrit

Hematocrit should be interpreted alongside clinical condition of the patient



Ref: WHO and TDR, Handbook for clinical management of dengue 2012.

IV Fluids

- When to start?
 - In critical phase for 24-48 hrs
 - In presence of features of shock
 - In febrile phase if oral fluids are insufficient
- What fluids to be used?
 - Isotonic solutions like Ringer lactate and Normal saline
 - Colloids used to restore blood pressure immediately
- Which IV fluids to be avoided?
 - Hypotonic saline, FFP, Dextrose solution, albumin solutions
- How much fluids to give and how fast?
 - Compensated shock: 5 to 10 ml/kg over one hour
 - Hypotensive shock: 10 to 20 ml/kg over 15-30 minutes
 - Maintenance fluids according to Holliday- Segar formula
 - 4ml/kg/hour for first 10 kg body weight
 - 2ml/kg/hour for next 10 kg body weight
 - 1ml/kg/hour for onward each kg body weight

Discharge criteria

- All of the following conditions must be present:
- **Clinical**
 - No fever for 48 hours
 - Improvement in clinical status (general well-being, appetite, haemodynamic status, urine output)
 - No respiratory distress
- **Laboratory**
 - Increasing trend of platelet count
 - Stable haematocrit without intravenous fluids

Fever patient with history, symptoms and signs of Dengue

Natural course of Dengue fever- Temperature, Potential clinical problems, Lab parameters, Virology/ Serology

Criteria for Dengue: Confirm the case, ?Warning signs and coexisting conditions

Classify into Groups A, B, C for management

Management according to protocol

IV fluids <48hrs
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Dengue Vaccine

- Most promising candidate is **CYD-TDV vaccine/Dengvaxia**
- Approval by WHO in Dec 2015
- Each engineered to express surface envelope and membrane proteins of 4 serotypes of dengue virus
- Administered as 3 doses (0/1/6 months)
- Striking benefit of reduction in hospitalizations among children > 9 years of age
- Short term safety profile encouraging
- Recently withdrawn from Philippines after 14 children death

Cure for Dengue?

Therapeutic Uses of Papaya

- The chymopapain and papain extracts of the leaves are useful in the treatment of digestive disorders
- The extracts from fruits and seeds have bactericidal properties
- The fruit juice and leaf extract have been demonstrated to have anticancer, antioxidative, anti-inflammatory, anti-bacterial, nephroprotective, hepatoprotective, hypoglycemic and hypolipidemic effects
- Anti-sickling effect in sickle cell disease



Papaya extract is used against A. and T. thermophilus
by Bhat? Journal of medicinal 2014

Papaya
leaves are
very
effective in
treatment of
dengue fever



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