

## V. Disease Pathogenesis



---

---

---

---

---

---

---

---

## Risk Factors Reported for DHF

- Virus strain
- Pre-existing anti-dengue antibody
  - previous infection
  - maternal antibodies in infants
- Host genetics
- Age



---

---

---

---

---

---

---

---

## Risk Factors for DHF (continued)

- Higher risk in secondary infections
- Higher risk in locations with two or more serotypes circulating simultaneously at high levels (hyperendemic transmission)



---

---

---

---

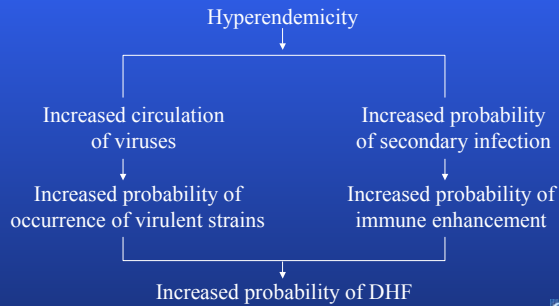
---

---

---

---

## Increased Probability of DHF



Gubler & Trent, 1994



---

---

---

---

---

---

---

---

## Hypothesis on Pathogenesis of DHF (Part 1)

- Persons who have experienced a dengue infection develop serum antibodies that can neutralize the dengue virus of that same (homologous) serotype



---

---

---

---

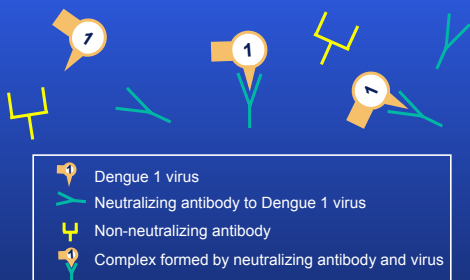
---

---

---

---

## Homologous Antibodies Form Non-infectious Complexes



---

---

---

---

---

---

---

---

## Hypothesis on Pathogenesis of DHF (Part 2)

- In a subsequent infection, the pre-existing **heterologous** antibodies form complexes with the new infecting virus serotype, but do not neutralize the new virus



---

---

---

---

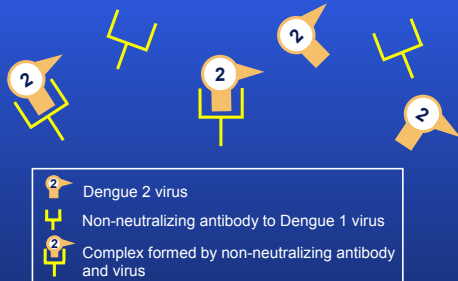
---

---

---

---

## Heterologous Antibodies Form Infectious Complexes



---

---

---

---

---

---

---

---

## Hypothesis on Pathogenesis of DHF (Part 3)

- **Antibody-dependent enhancement** is the process in which certain strains of dengue virus, complexed with non-neutralizing antibodies, can enter a greater proportion of cells of the mononuclear lineage, thus increasing virus production



---

---

---

---

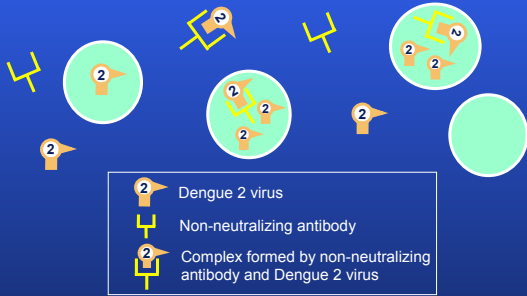
---

---

---

---

## Heterologous Complexes Enter More Monocytes, Where Virus Replicates



---

---

---

---

---

---

---

---

---

---

## Hypothesis on Pathogenesis of DHF (Part 4)

- Infected monocytes release vasoactive mediators, resulting in increased vascular permeability and hemorrhagic manifestations that characterize DHF and DSS



---

---

---

---

---

---

---

---

---

---

## Viral Risk Factors for DHF Pathogenesis

- Virus strain (genotype)
  - Epidemic potential: viremia level, infectivity
- Virus serotype
  - DHF risk is greatest for DEN-2, followed by DEN-3, DEN-4 and DEN-1



---

---

---

---

---

---

---

---

---

---