Alphaviruses

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Alphaviruses

Togaviridae
+ ssRNA monopartite genome (~11.5kb)
Infest diverse range of organisms
  – Most transmitted by arthropod vectors
Two groups of pathogenic alphaviruses
  – Encephalitic
  – Arthralgic
No available vaccines or therapeutics


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Alphavirus genus

Different human disease outcomes

1. **Arthralgic disease**
   Inc. RRV, CHIKV, MAYV

2. **Encephalitic disease**
   Inc. VEEV, WEEV, EEEV
Recent disease burden

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Prototypes

Chikungunya (Arthralgic)  |  Venezuelan equine encephalitis virus (Encephalitic)

Chikungunya is transmitted through the bite of the Aedes Aegypti and the Aedes Albopictus mosquitoes. The second is only found in Israel.

**Symptoms**
- fever
- headaches
- flulike symptoms
- nausea

**Prevention**
- do not store water in open containers so that they do not become breeding sites for mosquitoes
- cover tanks or containers for water for domestic use
- do not accumulate trash, dispose of trash in your yard
- cut your grass regularly to destroy potential breeding or resting sites
- use mesh or screens on your windows and doors
- use repellent or long sleeves to avoid getting bitten

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Chikungunya virus

3-7 (2-12) day incubation period
3-25% are asymptomatic (Queyriaux et al., Lancet, 2008; Retuya et al., Microbiol Infect Dis, 1998; Sissoko et al., PLoS ONE, 2008)

Fever
Joint pain
  - Up to 64% of patients report pain lasting >1 year post-infection (Staples et al., Emerging Infections, 2009)
  - 12% reported symptoms 3-5 years later (Staples et al., Emerging Infections, 2009)

Muscle pain
Headache
Nausea
Fatigue
Maculopapular rash

Source: Expert Rev Vaccines © 2012 Expert Reviews Ltd
Chikungunya virus outbreaks
CHIKV Vaccines and antivirals

One licensed vaccine VLA1553 – recently approved by the FDA as *IXCHIQ

No available therapeutic other than anti-inflammatories.
Venezuelan equine encephalitis virus

Humans
- Disease spectrum
- Symptoms appear 2-5 days after infection
- Fever
- Malaise
- Chills
- Headache
- Myalgia
- Neurologic disease
  - More likely in children
  - Convulsions, somnolence, confusion, photophobia
  - 4-14%
- Mortality: <1%
  - Associated with diffuse congestion, edema, and hemorrhage in the brain, GI tract, and lungs

Enzootic

Epizootic

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VEEV outbreaks

After discovery in 1938, outbreaks occurred approximately once/decade
- Since the mid-90’s, incidence has dramatically increased

Major outbreaks
- 1960’s: Colombia
  • 200,000 human cases
  • 100,000 equine deaths
- 1995: Venezuela and Colombia
  • 75-100,000 human cases
VEEV Vaccines and antivirals

Live-attenuated vaccine, IND
Serial passage of TrD strain in guinea pig heart tissue (Berge et al. Am J Hyg. 1961;73:209-218)
Two mutations cause the attenuation (Kinney et al. J Virol 1993;67:1269-1277)
  – Position 3 in 5’UTR
  – Position 120 of E2

Humans
  – Limited protection against all VEEV subtypes
  – Short-lived immunity
    • Must boost with C-84 (Pittman et al. Vaccine 1996;212:102-110)

Horses
  – C-84 used in USA
  – TC-83 used in more at-risk regions
  – TC-83 can cause febrile illness, leukopenia, and low-titer viremia (Fine et al. Vaccine 2007:1868-1876)
Summary

Alphaviruses are a diverse group with two distinct pathologies

Prototype from each pathology

Vaccine for CHIKV – live attenuated
  Potential to drive new vaccines forward for other species.