Emerging Arboviruses

Laura D. Kramer
Wadsworth Center
New York State Dept Health
and
State University of New York at Albany
laura.Kramer@health.ny.gov

ASM Northeast regional meeting
20-21 October 2015

Atlantic Monthly, 1997
Why have we seen such a dramatic increase in epidemic activity and geographic spread of vector-borne diseases?

- Background and concepts
- Reasons for epidemic transmission and spread
- Emerging mosquito-borne viruses
  - *West Nile virus*
  - *Dengue virus*
  - *Chikungunya virus*
- Risk in US
Global Emergence of Epidemic Arboviral Diseases

**Arthropod-borne (arbo) viruses:**
- Almost exclusively RNA viruses
- >120 associated with human disease
- Most imppt families Flaviviridae, Togaviridae, or Bunyaviridae
- Significant global expansion in recent decades
Important factors in emergence and spread of arthropod-borne viruses
Estimated Number of People Living in Urban Areas

Source: UN
Urbanization
The Case of Dhaka, Bangladesh

Source: UN
Mosquitoes that have travelled the world...

...and spread many viruses to humans

- **Aedes aegypti**
  - DENV, YFV, CHIK, etc.

- **Culex pipiens**
  - WNV, SLEV, etc.

- **Aedes albopictus**
  - DENV, CHIK, etc.
Mean Annual Number of Airline Passengers by Decade, United States, 1954-2007

Source: RITA, DOT
Civil Aviation Traffic

Hufnagel et al, 2004 PNAS

There is nowhere on Earth one cannot reach
Speed of Global Travel in Relation to World Population Growth

Days to Circumnavigate the Globe

Year

1850 1900 1950 2000

World Population in billions

Murphy and Nathanson Sems Virol 5, 87, 1994
Why have we seen such a dramatic increase in epidemic activity and geographic spread of vector-borne diseases?

- Background and concepts
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- Emerging mosquito-borne viruses
  - *West Nile virus*
  - *Dengue virus*
  - *Chikungunya virus*
- Risk in US
West Nile virus- a case study for geographical expansion
West Nile virus (*Flavivirus; Flaviviridae*)

West Nile Virus Transmission Cycle

Mosquito vectors *Culex* species

Amplification hosts

Secondary Hosts

Epizootic
Host competence: the vertebrate host

**Blood titers**

- *Columba livia* (Pigeon): 0% mortality, $LD_{50}>10^5$
- *Passer domesticus* (Sparrow): 20% mortality, $LD_{50}>10^5$
- *Corvus brachyrhynchos* (Crow): 100% mortality, $LD_{50}<10^1$

**Spinal cord titers**

**Graphs**

- X-axis: Time post-inoculation (days)
- Y-axis: Avg Log 10 virus titer (PFU/ml or g)
- Graphs show the average log 10 virus titers for Pigeon, Sparrow, and Crow, with the LOD for blood and spinal cord.

**Legend**

- Blue: Pigeon
- Pink: Sparrow
- Black: Crow
- Dotted: LOD blood
- Dashed: LOD CNS
West Nile virus strain displacement

Year of isolation

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E - V159A

Percent transmission

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Cx. pipiens

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Cx. tarsalis

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Cx. quinquefasciatus

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Snappin et al., 2007, *J Virol*
Ebel et al., 2004, *AJTMH*; Moudy et al., 2007, *AJTMH*
Transmission accelerates with increasing temperature, $tT^4$ (fitted model)*

* Integrating viral genotype, time, temperature

ENVIRONMENTAL FACTORS

Importance of socioeconomic conditions and land use

Pools at foreclosed homes raise West Nile threat in Dallas County
By THEODORE KIM / The Dallas Morning News
May 22, 2009
tkim@dallasnews.com
Dengue
Dengue

- **Worldwide Impact**
  - Currently > 2.5B at risk
  - 50-100M cases DEN fever per year
  - 250,000 – 500,000 cases of DHF

- **Virus Classification**
  - *Flaviviridae, Flavivirus*
  - Single-stranded, + sense, RNA genome
  - Enveloped virus

Mature dengue virus viewed through cryo-electron microscopy
Dengue Virus

- 4 genetically distinct serotypes
  - Lifetime homologous (within serotype) immunity
  - Short-term heterologous (between serotype) cross-protection
- Significant variation within serotypes (strains)

Figure. Partial phylogeny of flaviviruses
Dengue disease

- **Dengue fever** (breakbone fever)
  - Fever, retro-orbital headache, muscle and joint pain, nausea/vomiting, rash

- **DHF/DSS** (~ 0.5-10%)-often associated with secondary infection with heterologous serotype
  - Fever
  - Hemorrhagic manifestations
  - Leaky capillaries
  - Low platelet count
  - DSS = DHF + signs of circulatory failure

- **2009 WHO classification:**
  - Den without warning
  - Den with warning
  - Severe DEN
Transmission Cycle

Rural cycle: Ae. albopictus
Ae. polynesiensis

Ae. aegypti

Amplification Cycles

Sylvan Cycle

Ae. africanus
Ae. luteocephalus
Ae. furcifer-taylori
DHF in the Americas (1980 – 2007)

* Data: PAHO (Nov. 30, 2007)
Chikungunya
(Togaviridae: Alphavirus)

In Swahili, “chikungunya” : “that which contorts or bends “up”

Disease:
- High fever (103-104 F)
- Rash
- Severe incapacitating arthritis/arthralgia
  - Generalized
  - Usually acute
- Rarely fatal

A.M. Powers and C.H. Logue, 2007 J Gen Virol,
G. Pialoux et al., 2007, Lancet Infect Dis
Chikungunya Virus and Disease

- First isolated in Tanzania 1952
- Family - Togaviridae, Genus – Alphavirus
  - Single-stranded + RNA virus, enveloped
- Symptoms
  - Typical: Sudden onset of fever with severe joint pain (often hands/feet), headache, nausea, vomiting, rash, muscle pain
  - Joint pain can persist for weeks or months
  - Prior to recent outbreaks, no fatal cases
- Similar symptoms and range as dengue – misdiagnosed?
CHIKV Transmission Cycle
forested areas in West & Central Africa

eg. Forest redtail monkey

Forest Aedes spp.

Ae africanus
Ae luteocephalus
Ae furcifer-taylori

Modified from Gould EA and Higgs S 2009 Trans Royal Soc Trop Med Hyg
CHIKV Transmission Cycle

urban areas Asia, Indian Ocean islands, Europe, Caribbean

Aedes aegypti & Ae. albopictus
Chikungunya outbreak 2004-2007


266,000 cases (IR 34%)
Chikungunya Virus Outbreak

878 imported cases to France

Pialoux et. al 2007 Lancet Inf Dis, 7:319-327
Chikungunya outbreak 2004-2007

>1.4 million cases

Chikungunya outbreak 2004-2007

New emergence in 2007: ~270 cases

The Perfect Microbial Storm: Chikungunya

- A Virus from Africa (an alphavirus – Chikungunya)
- A mosquito from Asia (Aedes albopictus: tiger mosquito)
- A tourist from India (1.25 million human cases in 2006)
- A report of 270 people infected with Chikungunya in Ravenna, Italy
Factors involved in re-emergence of Chikungunya virus

- **Biologic and genetic**
  - Non-immune population
  - Adaptation of virus to new mosquito: *Ae. albopictus*

- **Ecologic conditions**
  - Standing water due to droughts
  - Hot European summer
  - Mosquito abundance

- **Social, economic, political**
  - International travel
  - Previous introduction of *Ae. albopictus* into Reunion Island & Italy
  - Delayed identification and control of initial outbreaks

- **Physical environment**
  - Stored water/artificial breeding sites

Modified from Chretien JP, Linthicum KJ. Lancet. 2007
6 December 2013

St. Martin,
French West Indies, Caribbean
Distribution of CHIKV in the Americas – 18 months
Asian CHIKV genotype circulating in Caribbean
The 2nd perfect microbial storm: Chikungunya

- A virus from Africa (an alphavirus – Chikungunya)
- A mosquito from Africa (Aedes aegypti)
- (A shipment from the Philippines)
- A completely naïve population
- Outbreak total: 1,722,188, cases
  (PAHO 18 Sept 2015)
Outline

- Background and concepts
- Reasons for epidemic transmission and spread
- Emerging mosquito-borne viruses
  - West Nile virus
  - Dengue virus
  - Chikungunya virus
- Risk in US

Atlantic Monthly, 1997
Dengue - Risk in U.S.?

- Imported cases
  - 380 laboratory confirmed cases of dengue in 2013
  - Became notifiable in 2010
- *Ae. aegypti* & *Ae. albopictus* occur here (spreading)

- Local transmission
  - Hawaii: 2001 (122)
  - Florida: 2009-10 (28)
  - New York: Suffolk County 2013 (1)
CHIKV: Future Outlook for the Americas

• Large CHIKV outbreaks in tropical America will continue for several years
  – Millions of cases likely
  – Tens of thousands of travel-associated cases into US

• CHIKV outbreak potential in contiguous US:
  – *Aedes aegypti* present:
    • Sporadic autochthonous cases continue
    • Small focal outbreaks possible
    • US-Mexico border could be a problem area
  – Only *Aedes albopictus* present:
    • *Aedes albopictus* in Americas are competent vectors
Distribution of *Ae. albopictus* in US, year 2000

http://www.cdc.gov/ncidod/dvbid/Arbor/albopic_97_sm.htm
Climate Change and Range Expansion of the Asian Tiger Mosquito (Aedes albopictus) in Northeastern USA: Implications for Public Health Practitioners

Ilia Rochlin¹, Dominick V. Ninivaggi¹, Michael L. Hutchinson², Ary Farajollahi³,⁴

¹ Suffolk County Vector Control, Yaphank, New York, United States of America, ² Division of Vector Management, Pennsylvania Department of Environmental Protection, Harrisburg, Pennsylvania, United States of America, ³ Mercer County Mosquito Control, West Trenton, New Jersey, United States of America, ⁴ Center for Vector Biology, Rutgers University, New Brunswick, New Jersey, United States of America
Approximate distribution of *Aedes aegypti* in the United States*

*This map was developed using currently available information. *Aedes aegypti* mosquito populations (a known vector of chikungunya) may be detected in areas not shaded on this map, and may not be consistently found in all shaded areas. The shaded areas are NOT locations of chikungunya transmission.*
Exotic Pathogens That Have Recently Been Introduced to the US

- Dengue Fever
- West Nile Fever
- Yellow Fever
- Mayaro Fever
- Chikungunya
- Ross River
- SARS
- Influenza
- Lassa Fever
- Monkeypox
- CJD/BSE
- HIV/AIDS
- Cholera
- E. coli O157
- Malaria
- Leishmaniasis
- Chagas Disease
- Cyclospora
Exotic **Mosquito Species** Recently Introduced and Established in the US

- *Aedes (Stegomyia) albopictus*
- *Ochlerotatus (Aedes Finlaya) togoi*
- *Ochlerotatus (Aedes Finlaya) japonicus*
- *Aedes bahamensis*
- *Culex biscayensis*
Live Animal Importation into the USA

- 47,000 mammals
  28 species of rodents
- 379,000 birds
- 2 million reptiles
  & poisonous snakes
- 49 million amphibians
- 223 million fish

U.S. Fish & Wildlife Service Data (2002)
Factors that **Decrease** the Risk of Epidemic Transmission the United States

- **Living Conditions**
  - Housing construction
  - Window and door screens
  - Reliable piped clean water systems
  - Air conditioning

- **Human Behavior**
  - Social practices
  - Television

- **Human Population Density**
Environmental Parameters Limit DENV (CHIKV) Transmission in the Contiguous States
Example: 2005 Outbreak on the US-Mexico Border

- 8 times more infections in Matamoros
  - 4% infected in Brownsville
  - 32% in Matamoros
- Substantial *Aedes aegypti* infestations in both locations
- Different environmental conditions
  - 85% homes air conditioned in Brownsville; 29% in Matamoros
  - Lot size 3 times greater in Brownsville
- No air conditioning increased dengue risk 7 fold
- Smaller lot size increased dengue risk 15 fold
Dengue, West Nile virus, Chikungunya, Zika, Powassan, Heartland, … WHAT’S NEXT?
One World – One Health

Questions?