Emerging Mosquito Viruses of Concern to Travelling Canadians

Dengue, Chik, JE virus and other agents

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Arboviruses: important human and animal pathogens (West Nile, Dengue, JE, etc.)

Arthropod vectors

Virus amplification

Amplifying hosts or reservoirs

Arbovirus (Arthropod-borne virus): Ecological term used to define viruses that require a blood sucking arthropod for transmission between hosts.
West Nile virus in North America 1999-2011
>30,000 cases of febrile and neurological disease
>1 million infections!

West Nile Virus – Establishment of an imported virus!

~4500 West Nile virus cases in Canada
Significant portion are neurological!

West Nile virus cases in now identified in Argentina
Arbo Human Infection / Disease “Iceberg”

- **Asymptomatic**: ~80-90%
- **Fever, rash, etc.**: ~10-20%
- **Severe disease**: <1%, ~10% fatal (<0.1% of total infections)
- **Neurological Hemorrhagic**
Dengue viruses can cause dengue fever and/or dengue hemorrhagic fever and/or Dengue hemorrhagic shock (plasma leakage, increase in capillary permeability).

However, most infections are mild or asymptomatic.

Four serotypes (Den 1-4, flaviviruses) of the virus (all can cause disease).

Over two billion people are at risk for infection (Americas, Africa, Asia).

50 – 100 million people infected per year!

Major mosquito vector is *Aedes aegypti*.

Virus is re-emerging in many parts of the world.
>50 million dengue cases a year!
(DF, DHF, DSS)

> 700,000 cases in Brazil, several hundred deaths

Millions of cases in Asia, 2 billion at risk
Re-Emergence of Dengue Virus Disease (Southeast Asia)
Re-population of *Aedes aegypti* in the Americas

700,000 cases in Brazil in 2007
Amplification of Dengue Virus Occurs During Mosquito – Man Infect Cycle (urban). No Non-Human Animal Reservoir Required Unlike WNV.
1. Mosquitoes transmit dengue virus to human dendritic cells

2. Dengue targets areas with high WBC counts (liver, spleen, lymph nodes, bone marrow, and glands)

3. Dengue enters WBCs & lymphatic tissue

4. Dengue enters blood circulation
Risk Factors for DHF:

1. Pre-existing anti-dengue antibody (secondary infection)
2. Virus Strain
3. Host Genetics (race is a factor)
4. Age (children in southeast asia)

Gubler & Trent, 1994
IMPORTED CANADIAN FLAVIVIRUS INFECTIONS, PRIMARILY DENGUE - 1974-2003

Dengue in the Americas, 1980-1999
Imported Dengue Infections in Canada
(1974-2009)*

Dengue Diagnostics:
Seropositives identified at NML

Since 2004 Ont, Que labs conduct their own testing with yearly positives=
Ontario ~ 140 a year
Quebec ~ 20 a year
Since ~2005 total imported cases > 300 a year!
Treatment - mainly supportive-fluid replacement

There are various VACCINE candidates

- ChimeriVax-Dengue
  - Tetravalent
  - Uses yellow fever vaccine as base
  - 92% of monkeys passed “virulent virus challenge”

-- Clinical trials underway
Non dengue human arboviral disease documented in Canadians with histories of travel

Virus
- Ross River (alphavirus)
- Chikungunya (alphavirus)
- Eastern equine encephalitis
- Western equine encephalitis
- Tick-borne encephalitis
- Japanese encephalitis (flavivirus)
- Powassan
- St Louis encephalitis
- West Nile
- Colorado tick fever
- Rift Valley fever (bunyavirus)

Travel history
- Australia, Fiji
- Uganda, Indian Ocean
- United States (New Jersey)
- United States (Oregon)
- Austria
- Manchuria
- New York state
- Ohio
- United States (Louisiana, Colorado, etc)
- Colorado
- Kenya
Chikungunya Virus: Endemic Throughout Africa and Asia
New Strain emerges in late 2004 from Africa

Non-structural proteins
Structural proteins

Single Mutation in E protein → Epidemic

500,000 cases Indian Ocean Islands (Reunion, Madagascar, Mauritius, Java, etc.)
> 1 Million Cases in India, 300 cases in Italy
Symptoms/disease: fever, arthralgia & rash
Dengue and Chikungunya viruses may co-circulate and can cause similar diseases.
Chik may be causing chronic polyarthritis in previously infected patients.

**TOTAL PROBABLE- CONFIRMED CANADIAN CHIKUNGUNYA CASES BY YEAR**

(60 Cases 2005 – 2010)

- 2005: 20 cases
- 2006: 20 cases
- 2007: 14 cases
- 2008: 6 cases
- 2009: 7 cases
- 2010: 20+ cases

Evidence of persistent infection:
- IgM lingers, antigen & RNA
- Monocytic cells of Reunion patients for years
- Inflammatory
- Prolonged debilitating arthritis in Canadian cases?

Could Chik establish in the Americas?

Treatment- anti-inflammatory drugs

Vaccines being developed
Arbovirus Viremia and Antibody Response - Diagnostic Considerations

For Dengue & Chik viremia can reach 100 million viral particles /ml
LABORATORY DIAGNOSIS OF DENGUE and CHIKUNGUNYA

METHODS:

1. PCR & Antigen Detection

2. Antibody Detection (Eg. IgM ELISA)

3. Viral Isolation
Heavy rainfall in South East Australia – Increased mosquito abundance - **Ross River, Murray Valley** encephalitis virus outbreaks in horses, people in 2011!
Why are Ross River virus, etc. outbreaks of concern to Canadians?

Ross River Virus Disease Reemergence, Fiji, 2003–2004

Philipp Klapsing,*† J. Dick MacLean,* Sarah Glaze,‡ Karen L. McClean,‡ Michael A. Drebot,§ Robert S. Lanciotti,¶ and Grant L. Campbell¶

We report 2 clinically characteristic and serologically positive cases of Ross River virus infection in Canadian tourists who visited Fiji in late 2003 and early 2004. This report suggests that Ross River virus is once again circulating in Fiji, where it apparently disappeared after causing an epidemic in 1979 to 1980.

Canadians travelling to Australia get infected by viruses circulating in this Country, expect more imported cases in 2011 due to ongoing outbreaks.
Importation of Ross River Virus from Fiji:
Sentinel Travellers Indicate Viral Reemergence 2003-04

Ross River Virus: arbo alphavirus endemic in Australia, NG
Not Documented in Fiji Since 1979
Canadian Tourists --- polyarthritis
RRV + serology, exposure in late 03, early 2004
Japanese Encephalitis

- Flaviviridae
  - *Flavivirus*
- The name is derived from the Latin ‘flavus’
  - Flavus means “yellow”
    - Refers to yellow fever virus
- Enveloped
- Single stranded RNA virus
Geographic Distribution

- Endemic in temperate and tropical regions of Asia
- Reduced prevalence in Japan
- Has not occurred in U.S. or Canada
Morbidity/Mortality

• Swine
  – High mortality in piglets
  – Death rare in adult pigs

• Equine
  – Morbidity: 2%, during an outbreak
  – Mortality: 5%

• Humans
  – Mortality: 5-40% (if progresses to encephalitis)
  – Serious neurologic sequelae: 45-70%

Canada
Transmission

- Vector-borne disease
- Enzootic cycle
  - Mosquitoes: *Culex* species
    - *Culex tritaeniorhynchus*
  - Reservoir/Amplifying hosts
    - Pigs, bats
    - Ardeid (wading) birds
    - Possibly reptiles and amphibians
  - Incidental hosts
    - Horses, humans, others
Clinical Signs

- 35,000-50,000 cases annually
- Less than 1 case/year in U.S. or Canada (?)
  - Military, travelers
- Incubation period: 6 to 8 days
- Most asymptomatic or mild signs
- Children and Elderly
  - At highest risk for severe disease
    - Elderly: High case fatality rate (30%)
Clinical Signs: Severe

- Acute encephalitis
  - Headache, high fever, stiff neck, stupor
- Severe encephalitis
  - Paralysis, seizures, convulsions, coma, and death
- Neuropsychiatric sequelae
  - 45-70% of survivors
- In utero infection possible
  - Abortion of fetus
Diagnosis and Treatment

• Clinical

• Laboratory Tests
  – Tentative diagnosis
    • Antibody titer: HI, IFA, CF, ELISA
    • JE-specific IgM in serum or CSF
  – Definitive diagnosis
    • Virus isolation / PCR: CSF sample, brain

• No specific treatment
  – Supportive care
Prevention

• Vector control
  – Eliminate mosquito breeding areas
  – Adult and larvae control

• Vaccination
  – Equine and swine
  – Humans

• Personal protective measures
  – Avoid prime mosquito hours
  – Use of repellants containing DEET
Vaccination

• Live attenuated vaccine
  – Used in equine and swine
  – Successful for reducing incidence

• Inactivated vaccines (JE-VAX & IXIARO)
  • Used for humans
  • Japan, Korea, Taiwan, India, Thailand
  • Used for endemic or epidemic areas
  – Recommended for travelers
    • Visiting endemic areas for > 30 days
Rift Valley Fever: Transmission dynamics

Vector succession - *Aedes* spp., followed by *Culex* spp., then *Anopheles* spp.
Rift Valley Spread

- Late 1980s
- Late 1970s
- 2000
- Origin
- 1990s
- 1950s

Canada
### Rift Valley Fever – Burden of human illness

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<tr>
<th>Years</th>
<th>Countries</th>
<th>Estimated No. of cases</th>
<th>No. of cases reported</th>
<th>No. of deaths</th>
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<tr>
<td>2003</td>
<td>Egypt</td>
<td>300</td>
<td>148</td>
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</tr>
</tbody>
</table>

**Kenya Outbreak 2006-2007**! Hundreds of cases

**NB**: Small numbers of sporadic cases every year in Africa
Countries with endemic disease and substantial outbreaks of RVF: Gambia, Senegal, Mauritania, Namibia, South Africa, Mozambique, Zimbabwe, Zambia, Kenya, Sudan, Egypt, Madagascar, Saudi Arabia, Yemen

Countries known to have some cases, periodic isolation of virus, or serologic evidence of RVF: Botswana, Angola, Democratic Republic of the Congo, Congo, Gabon, Cameroon, Nigeria, Central African Republic, Chad, Niger, Burkina Faso, Mali, Guinea, Tanzania, Malawi, Uganda, Ethiopia, Somalia
RVFV infection in humans

• 98% of the cases are asymptomatic

• Illness characterized by a fever of sudden onset, myalgia, arthralgia & headaches

• Some patients develop stiffness of the neck, photophobia, anorexia, nausea/vomiting, in early stages RVF can be confused with meningitis

Kenya 2006-2007 Outbreak – 76% bleeding

• These symptoms typically last 4 to 7 days, after which antibodies (IgM & IgG) can be detected and usually virus disappears from the blood
• Avoid direct contact with body fluids of sick or dead animals (or use appropriate personal protection, gloves, respirator, face shield)
• High risk activities include animal contact when: assisting with births (fetus & placenta), slaughtering animals, burying carcasses or fetuses
• Wash hands thoroughly with disinfectant or soap immediately after contact with any animal body fluid
• All animal products (blood, meat and milk) should be well cooked prior to consumption (no raw milk)
• Persons with fever >48 h should seek prompt medical attention (high risk of confusion with malaria?)
Questions ?