WHO Collaborating Centre for Arbovirus and Hemorrhagic Fever Reference and Research

Meeting of Collaborating Centres and Dengue National Reference laboratories for the Americas, June 10-12, 2008, Panama

Harvey Artsob, PhD
Director, Zoonotic Diseases and Special Pathogens Program
National Microbiology Laboratory, Public Health Agency of Canada,
WHO Collaborating Centre for Arboviruses and Hemorrhagic Fever Reference and Research 1995-2008


Arbovirus diagnostic/reference services, field studies, molecular diagnostics


Major program expansion, level 3 and 4 laboratories, clean and high containment insectories.
Development of viral hemorrhagic fever and emergency response programs. Involvement in international outbreak responses.
WHO Collaborating Centre - Redesignation Pending

The WHO Collaborating Centre is currently being redesignated as a WHO Collaborating Centre for Emerging and Zoonotic Diseases Detection, Diagnosis, Reference and Research.

Institute Director – Dr Frank Plummer

Head of Collaborating Centre – Dr Harvey Artsob

The Collaborating Centre is housed within the Division of Zoonotic Diseases and Special Pathogens which currently has 31 indeterminate staff including 9 professionals. In addition there are 7 casuals, 5 post docs, 12 students and 2 visiting scientists (June 1, 2008).
National Microbiology Laboratory

- Opened in June, 1998
- Initially part of Health Canada but currently is within the Public Health Agency of Canada
National Microbiology Laboratory

Housed within the Canadian Science Centre for Human and Animal Health. One Facility, Two Labs:

The Public Health Agency of Canada’s National Microbiology Laboratory (NML)

The Canadian Food Inspection Agency’s National Centre for Foreign Animal Disease (NCFAD)
National Microbiology Laboratory (NML)

Scientific Director General, Dr. Frank Plummer

The National Microbiology Laboratory consists of four programs supported by a Division of Core Services, which includes DNA sequencing, Animal Resources and a Central Laboratory for Decontamination and Wash-up Services.

The four programs are as follows:

- **Bacteriology and Enterics** - focussing on bacterial diseases such as tuberculosis and meningitis, along with food and water-borne pathogens such as *E. Coli* and *salmonella*, and infections affecting the human nervous and/or motor system.
- **Host Genetics and Prion Disease** - dealing with transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease.
- **Viral Diagnostics** - addressing a range of viral diseases including hepatitis and other blood-borne diseases, respiratory viruses and viral exanthemata, such as measles.
- **Zoonotic Diseases and Special Pathogens** - dealing with viral, bacterial and rickettsial zoonoses (diseases transmitted to humans from other species) such as West Nile virus, along with Biosafety Level 4 agents such as Ebola.

WHO Collaborating Centre
Program Mandates

Public Health

Biodefense

Canadian Science Centre for Human and Animal Health
WHO-LED COLLABORATIVE STUDY IN COTE D'IVOIRE TO IDENTIFY NATURAL HOST RESERVOIR OF EBOLA VIRUS 1996-1997

Initial field endeavour - setting the stage for international activities
Outbreak Investigation
- gaining experience & international reputation -

SARS, China

Ebola, Congo

Nipah, Bangladesh

CCHF, Iran
Outbreak Investigation
- gaining experience & international reputation -

- Expertise: diagnostic field support using mobile lab unit
- Experience:
  - Ebola HF, Mbomo, DRC
  - Nipah encephalitis, Faridpur, Bangladesh
  - Crimean-Congo HF, Zahedan, Iran
  - SARS, Hong Kong & Guangzhou, China
  - Marburg HF, Uige, Angola
  - Rift Valley Fever, Kenya
  - Ebola HF, Luebo, DRC
Mobile lab response – deployed to international outbreaks
Bilateral collaborations – Paraguay

Collaborations were undertaken to study the dynamics of hantavirus transmission by rodents in the Chaco region of Paraguay (2003)

Project status - completed
Bilateral consultation and capacity building at PAHO’s request

Bolivian hemorrhagic fever activities, Bolivia, October, 2004
Collaborations have been initiated with Bolivian colleagues concerning training and diagnostics for arenaviruses including improved front line diagnostics for Bolivian hemorrhagic fever.

Project status - ongoing
Bilateral collaborations – Cuba (1)

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West Nile Virus Infection in Humans and Horses, Cuba

Maritza Pupo,* Maria Guadalupe Guzmán,* Roberto Fernández,* Alina Llop,* Félix Orlando Dickinson,* Daniel Pérez,* Raúl Cruz,† Tayri González,† Gonzalo Estévez,† Hiram González,‡ Paulino Santos,§ Gustavo Kouri,* Maya Andonova,¶ Robbin Lindsay,¶ Harvey Artsob,¶ and Michael Drebot¶

A surveillance system to detect West Nile virus (WNV) was established in Cuba in 2002. WNV infection was confirmed by serologic assays in 4 asymptomatic horses and 3 humans with encephalitis in 2003 and 2004. These results are the first reported evidence of WNV activity in Cuba.

Collaborative studies have resulted in the first demonstration of West Nile Virus activity in Cuba based on serological studies of horses and the demonstration of human symptomatic infections due to West Nile virus.
Bilateral collaborations – Cuba (2)

West Nile virus field (mosquito & bird) studies (March, 2008)
Project status - ongoing
Bilateral collaborations – Argentina

Development of a VSV pseudotype platform that incorporates hantaviral genes to allow for improved hantavirus typing.
Project status – initial stages of development
Arboviruses: locally contracted and travel-associated
## Mosquito transmitted arboviruses isolated in Canada

<table>
<thead>
<tr>
<th>Virus</th>
<th>Antigenic group</th>
<th>Disease in humans/animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern equine encephalitis</td>
<td>alphavirus</td>
<td>+ humans, + animals</td>
</tr>
<tr>
<td>Western equine encephalitis</td>
<td>Alphavirus</td>
<td>+ humans, + animals</td>
</tr>
<tr>
<td>St Louis encephalitis</td>
<td>flavivirus</td>
<td>+ humans, - animals</td>
</tr>
<tr>
<td>West Nile</td>
<td>flavivirus</td>
<td>+ humans, + animals</td>
</tr>
<tr>
<td>California encephalitis</td>
<td>California</td>
<td>+ humans, + animals</td>
</tr>
<tr>
<td>Snowshoe hare</td>
<td>California</td>
<td>+ humans, + animals</td>
</tr>
<tr>
<td>Jamestown Canyon</td>
<td>California</td>
<td>+ humans, + animals</td>
</tr>
<tr>
<td>Trivittatus</td>
<td>California</td>
<td>+ humans, - animals</td>
</tr>
<tr>
<td>Cache Valley</td>
<td>Bunyamwera</td>
<td>- humans, - animals</td>
</tr>
<tr>
<td>Northway</td>
<td>Bunyamwera</td>
<td>+ humans, + animals</td>
</tr>
<tr>
<td>Turlock</td>
<td>Turlock</td>
<td>- humans, - animals</td>
</tr>
<tr>
<td>Flanders</td>
<td>Rhabdovirus</td>
<td>- humans, - animals</td>
</tr>
</tbody>
</table>
Mosquito-transmitted arboviruses of medical importance isolated in Canada

CAL = snowshoe hare (SSH) &/or Jamestown Canyon (JC) viruses

Aedes/Ochlerotatus
Culex spp
Culiseta melanura
Yearly WNV Case Numbers

Human Cases

Year | Cases
--- | ---
2001 | >400
2002 | 25
2003 | 1481
2004 | 224
2005 | 151
2006 | 25
2007 | 2353

US: 3510
**Simplified WNV Testing Algorithm**

**Acute Sample (Suspect Cases)**

\[ \downarrow \]

IgM ELISA +

(IgG ELISA, Avidity Testing if IgG Positive)

**Convalescent Sample**

\[ \downarrow \]

Confirmatory Serology*

(Eg. Plaque Reduction Neutralization Test-PRNT)

(Demonstration of Seroconversion, HI, IgG ELISA)

*Confirmation of first 5 cases in jurisdiction or province

Additional probables will not require PRNTs to be designated cases
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</tr>
</thead>
<tbody>
<tr>
<td>Powassan</td>
<td>flavivirus</td>
<td>+ humans, - animals</td>
</tr>
<tr>
<td>Colorado tick fever</td>
<td>Colorado tick fever</td>
<td>+ humans, - animals</td>
</tr>
<tr>
<td>Silverwater</td>
<td>Kaisodi</td>
<td>- humans, - animals</td>
</tr>
<tr>
<td>Bauline</td>
<td>Kemerovo</td>
<td>- humans, - animals</td>
</tr>
<tr>
<td>Great Island</td>
<td>Kemerovo</td>
<td>- Humans, - animals</td>
</tr>
<tr>
<td>Avalon</td>
<td>Sakhalin</td>
<td>? humans, - animals</td>
</tr>
</tbody>
</table>
Tick-transmitted arboviruses of medical importance isolated in Canada
Human arbovirus infections with histories of recent travel outside Canada

**Diagnostic testing algorithm:**

1. Hemagglutination inhibition serology is routinely undertaken using alphavirus (eastern equine encephalitis, western equine encephalitis, Chikungunya, Sindbis) and flavivirus (dengue, St Louis encephalitis, Powassan) antigens

2. IgM and IgG ELISA’s and neutralization tests are undertaken for dengue virus on selected serum samples

3. Referral testing is undertaken at CDC Fort Collins for selected arbovirus infections such as Venezuelan equine encephalitis and Mayaro.
Human arboviral disease documented in Canadians with histories of travel

The majority of arbovirus infections documented are flavivirus infections, likely due to dengue virus.
IMPORTED CANADIAN FLAVIVIRUS INFECTIONS,
PRIMARILY DENGUE - 1974-2003

Dengue in the Americas, 1980-1999
- 6 month secondment to WHO by Dr Artsob to set up lab network.
- Participation in WHO/PDVI sponsored study to evaluate commercial diagnostic kits.
- Hosted diagnostics network meeting in Winnipeg.
Non dengue human arboviral disease documented in Canadians with histories of travel

<table>
<thead>
<tr>
<th>Virus</th>
<th>Travel history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ross River</td>
<td>Australia, Fiji</td>
</tr>
<tr>
<td>Chikungunya/O’Nyong-Nyong</td>
<td>Uganda</td>
</tr>
<tr>
<td>Eastern equine encephalitis</td>
<td>United States (New Jersey)</td>
</tr>
<tr>
<td>Western equine encephalitis</td>
<td>United States (Oregon)</td>
</tr>
<tr>
<td>Tick-borne encephalitis</td>
<td>Austria</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>Manchuria</td>
</tr>
<tr>
<td>Powassan</td>
<td>New York state</td>
</tr>
<tr>
<td>St Louis encephalitis</td>
<td>Ohio</td>
</tr>
<tr>
<td>West Nile</td>
<td>United States (Louisiana, Colorado, etc)</td>
</tr>
<tr>
<td>Colorado tick fever</td>
<td>Colorado</td>
</tr>
<tr>
<td>Rift Valley fever</td>
<td>Kenya</td>
</tr>
</tbody>
</table>
Importation of Chikungunya Virus from Indian Ocean: Canadian Cases During Ongoing Outbreak 2005-2007

Total Chikungunya Exposures / Cases* = 35 Canadians (7 provinces)

2005-1 case (Quebec)
2006-20 cases (BC-1, AB-1, SK-1, MB-2, Ontario-11, PQ-4)
2007-12 cases (AB-2, MB-2, Ontario-6, PQ-3, NS-1)

Travel History Included: Reunion Island, Mauritius, India, Madagascar, Sri Lanka, Cote d’Ivoire

Clinical symptoms/disease: fever, myalgia, arthralgia & rash