Overview of emerging and detection of arboviral disease in South Africa.

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Arbovirus infections endemic to South Africa

Rift Valley fever (Phlebovirus)  West Nile fever (Flavivirus)

Chikungunya fever (Alphavirus)  Sindbis fever (Alphavirus)

Wesselbron disease (Flavivirus)

(Courtesy: Dr Monica Birkhead, NICD)
Imported arboviral infectious diseases to South Africa

Dengue (Flavivirus)

Chikungunya (Alphavirus)

Yellow fever (Flavivirus)

No human yellow fever cases have ever been recorded in South Africa

(Courtesy: Dr Monica Birkhead, NICD)
Diagnosis of arboviral disease

Integrated approach for diagnosis

- Arbovirus infections are most often mild, febrile illness not unlike enterovirus, influenza and herpes infection
- Encephalitis, Haemorrhagic fever, polyarthritis

Case histories: travel and exposure histories, dates

Travel, exposure to arthropods (mosquitoes, ticks, biting flies, midges, tabanids, ...)

Clinical manifestation, pathology testing

Diagnostic testing

Flavivirus crossreaction
Laboratory Investigations

Routine blood screens / scans not very informative
Specialized laboratory testing only provided in selected reference laboratories

Specimens
• Blood, serum for acute and sero-converted cases
• CSF for acute neurological cases
• Liver, CSF, brain for post mortem cases

Arbovirus case
Confirmed
• Case found positive for acute infection by polymerase chain reaction (PCR)
• Fourfold IgG titre increase of long-lived antibodies (IgG) between convalescent specimens (10-14 d apart) by Enzyme-linked immunosorbant assay (ELISA)

Highly suggestive
• Case found positive for short-lived antibodies (IgM) (90% recent infection)

Persistence of arbovirus virus-specific IgM responses
• Flaviviruses: variable up to 3 years
• Alphaviruses: variable up to 2.5 years
• Rift Valley virus (Bunyavirus): 4-6 weeks
Laboratory Investigations

Routine blood screens / scans not very informative
Specialized laboratory testing only provided in selected reference laboratories

HAI Haemagglutination Inhibition assay

Chantel le Roux performing ELISA (24-48h)

Haemagglutination +ve

Haemagglutination -ve

N 2 4 8 16 32 64 128 256 512 1024 2048

PCR Polymerase chain reaction

Virus isolation

Virus Neutralizing Antibody Assays

Indirect immunofluorescence tests
Proliferation of mosquitoes near water

Rift Valley fever virus mosquitoes

Flood water - *Aedes*

Culex
Amplification of virus in animals via \textit{Culex} mosquitoes.

Infection of animals via feeding mosquitoes.

Risk of infection for people increases.
Rift Valley Fever Virus at risk populations and clinical manifestation

**Animals**
- Sudden onset of abortion storms
- Mortality in young animals
- Haemorrhages

**Humans**
- Fever, often accompanied by headaches, muscle pains and nausea
- Light sensitivity, watery eyes, early signs of retinal detachment, which could lead to partial blindness
- Haemorrhagic fever, encephalitis and necrotic hepatitis
Endemic West Nile, Sindbis and chikungunya

West Nile Sindbis

Widespread in South Africa

Culex mosquitoes

Horse ill with West Nile virus

severe arthritis

chikungunya

North-Eastern South Africa

Aedes mosquitoes

rash
Sylvatic environment and vectors of Dengue and chikungunya virus

Tree hole breeding spot

Aedes furcifer

SYLVATIC (JUNGLE) CYCLE

Tropical forest

Senegal-green monkeys
Urban environment and vectors of Dengue and chikungunya virus

Aedes (stegomyia) Aegypti

Monsoon season

Tyres breeding spot

Aedes (stegomyia) Albopictus

Urban Cycle

man

arthropod

arthropod

man
Rift Valley Fever Virus


Occurs in periodic outbreaks with long intervals of 7-15 years.
RVF Outbreaks followed period of above normal rainfall
Large pan in the Northern Cape

EASTERN FREE STATE: SMALL PANS FLOODED, LARGE PANS PARTIALLY FLOODED
APRIL 2010
RVF epidemic 2010-2011: human cases

Maps created by V. Msimang
In 2010 all deaths were among 244 persons infected with lineage H virus, while no deaths were recorded in areas where lineage C virus was active, only 22 cases were diagnosed (NICD, unpub. Data, Grobbelaar, A.A., et al., Molecular epidemiology of Rift Valley fever virus. Emerg Infect Dis, 2011. 17(12): p. 2270-6.)
1. Information sessions

2. Data collection

3. Blood sampling

Kruger National park survey of Arboviral exposure
Arbovirus results considerations

<table>
<thead>
<tr>
<th>TOTAL N=200</th>
<th>Past exposure Long-term antibodies</th>
<th>Recent exposure Short-term antibodies</th>
<th>Symptoms</th>
<th>RICK</th>
<th>Q F</th>
</tr>
</thead>
<tbody>
<tr>
<td>SINDBIS VIRUS</td>
<td>8</td>
<td>5</td>
<td>Fever headache tiredness</td>
<td>X</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sore eyes</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Unknown</td>
<td>Y</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tick bite fever malaria</td>
<td>Y</td>
<td>X</td>
</tr>
<tr>
<td>CHIKUNGUNYA VIRUS</td>
<td>1</td>
<td>0</td>
<td>Rash</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>WEST NILE VIRUS</td>
<td>11</td>
<td>2**</td>
<td>Fever sore joints, sore eyes neck stiffness blurred vision</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Unknown</td>
<td>X</td>
<td>Y</td>
</tr>
<tr>
<td>RIFT VALLEY FEVER</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>21</td>
<td>7</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

* High titre ≥ 1:320

- Males between 27-62 years old
- 2 southern, 5 central region
- 5 general workers, 1 rangers, 1 scientist

- Serological cross reaction
- Persistence of virus-specific IgM responses:
  - Alphas: variable up to 2.5 years
  - Flavis: variable up to 3 years
  - RVF (Bunyavirus): 4-6 weeks
Rift Valley Fever Virus IEP Project

- Climate
- Mosquitoes
- Wild antelope
- Game farms
- Free-ranging
- Domestic ruminants
- People

Testing for RVF virus and antibodies
Rift Valley Fever Virus IEP Project
Pilot farmers surveillance 10-17 May 2015
### Arboviral infectious outbreaks in South Africa

<table>
<thead>
<tr>
<th>Year/s</th>
<th>Area</th>
<th>Animal cases*</th>
<th>Human cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RVF</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1950-51, 1952-53, 1955-59</td>
<td>Western FS, sthn Gauteng, NW, Limpopo; Zimbabwe; Namibia</td>
<td>600 000+</td>
<td>numerous</td>
</tr>
<tr>
<td>1968-69</td>
<td>Southeastern Zimbabwe; KZN coastal plain, Mozambique</td>
<td>widespread, large numbers</td>
<td>unknown</td>
</tr>
<tr>
<td>1969-71**, 1973-76, 1978**</td>
<td>RSA; Namibia; Zimbabwe; Zambia</td>
<td>140 000+**; widespread, catastrophic</td>
<td>Numerous, some deaths</td>
</tr>
<tr>
<td>1981</td>
<td>Mtubatuba</td>
<td>Localised, many cattle</td>
<td>unknown</td>
</tr>
<tr>
<td>1990-91, 1999</td>
<td>Madagascar; KNP</td>
<td>Extensive; localised***</td>
<td>Some, 1 death; suspected***</td>
</tr>
<tr>
<td><strong>CHIK</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1962; 1956, 1964</td>
<td>Southeastern Zimbabwe; Phalaborwa, Ndumo</td>
<td>Widespread, large nos.; localised, small nos.</td>
<td>38+; some</td>
</tr>
<tr>
<td>1975-76</td>
<td>Mica/Phalaborwa region</td>
<td>Localised, 76+</td>
<td>57+</td>
</tr>
<tr>
<td><strong>SIN/WN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1962-63</td>
<td>Sthn Gauteng, nthn Free State</td>
<td>widespread</td>
<td>14/2+5?</td>
</tr>
<tr>
<td><strong>WN/SIN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1974</td>
<td>Karoo</td>
<td>widespread</td>
<td>18 000+/4000+****</td>
</tr>
<tr>
<td><strong>SIN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1983-84</td>
<td>Witwatersrand/Pretoria/Bela Bela</td>
<td>widespread</td>
<td>100s</td>
</tr>
<tr>
<td><strong>DEN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1926/1927</td>
<td>Coastal KZN (Stanger to Durban)</td>
<td>unknown</td>
<td>40 000+</td>
</tr>
</tbody>
</table>

Data compiled by Alan Kemp
Sindbis and West Nile virus prevalence

Severe West Nile CNS case

West Nile clinical manifestation

Fatal case 2014

- A 38-year-old man from Nelspuit, Mpumalanga presented late July 2014 with fever and neurological disturbances.
- Rabies was considered as a potential diagnosis for this patient given the exposure history and his encephalitic presentation.
- Ultimately a history of travel to Escourt, KwaZulu Natal came to light were the patient had contact with horses.
- Based on the history and the clinical presentation of encephalitis, arboviral disease was suggested as a diagnosis.
- Blood specimens collected over the course of the patient’s illness were tested for anti-West Nile fever antibodies and
- Seroconversion was indicated in testing of the serial specimens. RT-PCR analysis on the earliest collected blood and
- Cerebrospinal fluid specimens were however negative for West Nile.
- The patient progressively deteriorated and required intubation and ventilation. The patient died about three weeks after onset of illness.
Dengue is on the rise globally

Source: WHO. Emergencies preparedness, response Pandemic and Epidemic Diseases Dengue/dengue haemorrhagic fever
South Africa is connected to the world.....

- DENV-endemic countries interconnectivity with South Africa
- Important airport in Africa
- Recent research estimates the burden of dengue infection in Africa to be similar to that of the America’s


Epidemics in Africa

Testing and confirmation of imported dengue cases in South Africa increases

Fig. 1 Increasing trend of testing for Dengue and confirmation of DENV-cases by CEZD-NICD arbovirus laboratory

Number DENV-confirmed cases
Number tested cases
Detection rate (%)
Linear (Detection rate (%))
**Returning travellers from Angola to SA; total estimated cases linked to Angola outbreak confirmed in NICD n=19**

2013: Viraemia confirmed by PCR after return to SA in travellers n=5 (out of 13 tested)

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### DENV-cases in returned to non-endemic SA travellers per DENV-endemic country of travel

<table>
<thead>
<tr>
<th>Country</th>
<th>2014</th>
<th>2013</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>28</td>
<td>34</td>
<td>19</td>
</tr>
<tr>
<td><strong>Returning travellers from Asia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>6</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>India</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Philippines</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Malaysia</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Indonesia</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Vietnam</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Singapore</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Returning travellers from West Central Africa</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cameroon</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Mali</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Burkina Faso (/Ethiopia)</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Angola</td>
<td>4</td>
<td>14*</td>
<td>-</td>
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<tr>
<td><strong>Returning travellers from East Africa</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tanzania</td>
<td>4</td>
<td>-</td>
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</tr>
<tr>
<td>Kenya</td>
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</tr>
<tr>
<td>Africa</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Returning travellers from South America</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>-</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Bolivia</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td><strong>Unknown/no travel</strong></td>
<td>6</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

*Returning travellers from Angola to SA; total estimated cases linked to Angola outbreak confirmed in NICD n=19

2013: Viraemia confirmed by PCR after return to SA in travellers n=5 (out of 13 tested)
CCHF virus transmission

**Tick life and enzootic cycle**

*Hyalomma rufipes marginatum* = 2 hosts-tick cycle
(larva molts to nymph while attached to first host (bird or small mammal))

**Transmission to humans**

Example of 3 hosts-tick cycle

*Hyalomma rufipes marginatum*
Human exposure routes in South Africa

60 to 75% tick-related
Differential diagnosis: What is Malaria

Serious, sometimes fatal disease caused by a parasite spread by mosquitoes

Anopheles

Parasite in blood as seen under microscope

Plasmodium Falciparum

Malaria test for ill patient
Acknowledgements

• NICD-Centre for Emerging and Zoonotic Diseases, Arbovirus reference laboratory personnel
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