ZIKA: is South Africa at risk?

Lucille Blumberg
National Institute for Communicable Diseases
South Africa
18th April 1947; 
Rhesus macaque (no 766) with fever 
‘Filtrable transmissable agent’

For nearly 7 decades Zika virus would remain a virological curiosity……..

‘The absence of the recognition of a disease in humans caused by Zika virus does not necessarily mean that the disease is either rare or unimportant’ Alexander Haddow

Trans Roy Soc Trop Med Hyg 1952 Haddow, Dick
an outbreak of illness characterized by fever, rash, conjunctivitis and arthralgia. Distinct from dengue

2013 Zika outbreak in French Polynesia - GBS
Lancet 2016

PHEIC, 1 FEB 2016
the cluster of microcephaly cases following on Zika outbreak constitute an extraordinary event
WHO DG Chan;

NEJM 2016
How Was Zika Introduced into Brazil? Three Theories

• Infected participants in 2014 World Cup in Brazil
• Va’a canoe event in Rio de Janeiro in August 2014 included participants from French Polynesia
• Confederation Cup soccer tournament June 2013
  – Phylogenetic analyses suggest single introduction of Zika virus May-Dec 2013

• Faria NR et al Science 2016
Circulation of the Zika virus - Asian lineage
Asian Viral Lineage- Americas outbreak


Figure: Phylogenetic relations between the envelope gene sequences of Suriname ZIKV and other ZIKV

…….and Africa (again)?
Flaviviridae: Zika, yellow fever, dengue
Alphaviridae: Chikungunya
• Two sub-species of *Aedes aegypti* exist:
  
  – In South America, *A. aegypti* is adapted to human, urban environments, and feeds on humans
  
  – In Africa, *Aedes aegypti* is preferentially an animal feeder
Countries ranked in order of increasing risk of Zika virus epidemic based on a composite index of risk derived from the hazards, vulnerabilities and lacking of coping capacities.

- Population density, urban population in slums
- Presence of *Aedes* – *aegypti/albopictus*
- Evidence of exposure to chikungunya, dengue
- Strength of health systems
WHO MEDIA RELEASE  19/5/2016

WHO confirms Zika virus strain imported from the Americas to Cabo Verde

BRAZZAVILLE / 20 May 2016 - Sequencing of the virus in Cabo Verde by Institut Pasteur, Dakar confirms that the Zika virus currently circulating in Cabo Verde is the same as the one circulating in the Americas - the Asian type- and was most likely imported from Brazil. This is the first time that the Zika strain responsible for the outbreaks linked to neurological disorders and microcephaly has been detected in Africa.

“The findings are of concern because it is further proof that the outbreak is spreading beyond South America and is on the doorstep of Africa. This information will help African countries to re-evaluate their level of risk and adapt and increase their levels of preparedness,”
Risk of introduction of Zika into South Africa? SAMJ March 2016

Communicable Diseases Communiqué
FEBRUARY 2016, Vol. 15(2)

Zoonotic and Vector-borne Diseases

a. Zika virus — a South African perspective

A 46-year-old industrial mechanic, resident in Cali, Colombia, arrived in Johannesburg on Wednesday 10 February. He became ill on Monday 15 February with anorexia, fever, and a fine, punctate-like rash on his hands, thorax and neck. He had no joint or muscle pain, or conjunctivitis. He visited a private general practitioner who advised Zika virus testing. His illness was short-lived, and he felt better within 3 days. His blood specimen was positive by PCR for Zika virus at a private laboratory in Johannesburg. A second PCR test on the same specimen was conducted by the NICD, and confirmed the positive result. This is the first case of Zika virus infection imported into South Africa.

Clinical diagnosis of ZIKV disease is complicated due to the non-specific clinical presentation and similarity with other arboviral infections especially dengue fever and chikungunya. About 80% of human infections are asymptomatic. Symptoms of ZIKV infection include fever (<38.5 °C), maculopapular rash, arthralgia (specifically involving the small joints of the hands and feet) and conjunctivitis. Laboratory diagnosis of acute ZIKV infection can be achieved through virus isolation in mice or tissue culture, and molecular testing by PCR.
Prevention and monitoring in South Africa

- Management of imported goods eg plants
- Disinsection of aircraft and cargo
- Entomological surveillance around ports
- Vector competence for Zika
- Active case surveillance – returning tourists
- Guillane Barre case testing
- Congenital abnormalities surveillance – microcephaly
150 health professionals call for Olympics in Rio to be postponed due to Zika

A group of 150 doctors, scientists and bioethicists have written a letter to the World Health Organization calling for the Rio Olympics to be postponed or moved because of concerns of the spread of the Zika virus.

The letter cites concerns about further spread of the virus and developing information about it calling for the Games to be delayed or moved. The letter writers questioned whether the WHO is rejecting alternatives of when and where the Games should be held because of a conflict of interest with the International Olympic Committee.

What is the experience from previous mass gathering events? Lessons for Zika virus and the Olympics 2016

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j) Special Infectious Agents Unit, King Faisal Medical Research Center and Medical Laboratory Technology Department, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, Saudi Arabia
k) World Health Organization, Geneva, Switzerland
l) Ministry of Health, College of Medicine, Aljouf University, Riyadh, Kingdom of Saudi Arabia
m) Institute of Clinical Medicine, University of Aarhus, Aarhus, Denmark
n) Department of Infectious Diseases, The Royal Hospital, Muscat, Sultanate of Oman

Summary

All previous experiences from different mass gathering show that vaccine preventable diseases is the most important infectious like influenza, hepatitis A, polio and meningitis. Three mass gathering held in Africa during the Ebola outbreak accepted participants from West Africa and was able to handle the theoretical risk without any incident. Therefore we believe that the Olympic games in Rio de Janeiro should not be cancelled. The number of visitors to the games is a time fraction ([1/4] of other visitors to Zika).
Two platelet transfusion recipients acquired the Zika virus from their transfusions. Both patients were transfused with leukoreduced platelets from one presymptomatic Zika-infected donor. Both recipients were negative for the virus pre-transfusion, but samples collected from both recipients after transfusion were positive for Zika virus’ NEJM Aug 2016

During the previous French Polynesian Zika virus outbreak, 2.8% of blood donors tested positive for Zika

USA tests all blood donations for Zika FDA Aug 2016
Congenital Zika Syndrome

- Microcephaly, arthrogryphosis
- Intracerebral calcification, cerebral atrophy, ventriculomegaly, macular atrophy

Proof of teratogenicity of Zika virus in pregnancy - early pregnancy

Evidence of CNS damage with infection in late pregnancy

NEJM Feb 2016; MMWR Jan 2016; UOG 2016
NEJM 2016; CID 2016
ZIKA: Clinical Signs & Symptoms

• Up to 80% of infections are asymptomatic
• Symptoms start 2-12 (14) days after mosquito bite: Sudden onset
  • Mild/moderate fever
  • Maculopapular skin rash (pruritic)
  • Arthralgia (small joints of hands and feet)
  • Conjunctivitis (non-purulent)
• Mild illness → clinical resolution in 1 week
• Rarely GBS

NEJM 2009; 2016
<table>
<thead>
<tr>
<th></th>
<th>ZIKA</th>
<th>CHIKUNGUNYA</th>
<th>DENGUE</th>
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<tr>
<td><strong>Fever</strong></td>
<td>Mild fever</td>
<td><strong>High fever</strong></td>
<td>High fever</td>
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<td><strong>Headache</strong></td>
<td>+</td>
<td>++</td>
<td>Intense headaches</td>
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<td><strong>Eye symptoms</strong></td>
<td><strong>Conjunctivitis.</strong></td>
<td>Conjunctivitis</td>
<td>Retro-orbital pain</td>
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<td></td>
<td>Retro-orbital pain</td>
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<td>Nausea</td>
<td>Nausea and vomiting</td>
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<td>++</td>
<td>No</td>
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<td>No</td>
<td>Uncommon</td>
<td><strong>Yes</strong></td>
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<td><strong>Joint pains</strong></td>
<td>++ (small joints of</td>
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<td>hand and feet)</td>
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<td>and back), Arthritis</td>
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<td><strong>Muscle pains</strong></td>
<td>+</td>
<td>++</td>
<td>+++ “Breakbone fever”</td>
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<td>+++ <strong>EARLY</strong></td>
<td>++</td>
<td>++</td>
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<td><strong>Thrombocytopenia</strong></td>
<td>-</td>
<td>-</td>
<td>+++</td>
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<td><strong>Complications</strong></td>
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<td>Post infection joint</td>
<td>Haemorrhagic fever</td>
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<td></td>
<td>? Guillain-Barre</td>
<td>pain (months to years)</td>
<td>and shock that can be</td>
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<td></td>
<td></td>
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<td>fatal, ?GBS</td>
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</tbody>
</table>

Halstead, et al. Yap DOH. Brazilian Health Ministry. CDC.WHO.
Clinical differential diagnosis

- Tropical/travel-related infections
  - Dengue
  - Chikungunya
  - Leptospirosis
  - Malaria
  - Rickettsia (Tick bite fever)

- Variety of bacterial and viral infections
  - Group A streptococcus
  - Rubella, measles, and parvovirus, enterovirus, adenovirus
Zika Lab Diagnosis

- PCR of blood (urine, saliva, CSF) in first 7 d post-symptom onset = current gold standard
- **Serology**: cross reactions with other flaviviruses
Prevention in travellers

• Pregnant women should avoid travel to Zika-risk areas

• Mosquito bite prevention
First U.S. Zika virus transmission reported, attributed to sex

AUSTRALIA, TEXAS | BY JON HERSKOVITZ

The first known case of Zika virus transmission in the United States was reported in Texas on Tuesday by local health officials, who said it likely was contracted through sex and not a mosquito bite, a day after the World Health Organization declared an international public health emergency.

The virus, linked to severe birth defects in thousands of babies in Brazil, is spreading rapidly in the Americas, and WHO officials on Tuesday expressed concern that it could hit Africa and Asia as well. Zika had been thought to be spread by the bite of mosquitoes of the Aedes genus, so sexual contact as a mode of transmission would be a potentially alarming development.

The U.S. Centers for Disease Control and Prevention confirmed it was the first U.S. Zika case in someone who had not traveled abroad in the current outbreak, said CDC Director Dr. Tom Frieden on Twitter.
Sexual Transmission

- Male to female; male to male
- High viral load \(10^{8.6}/\text{ml vs. blood/urine } 10^{3}/\text{ml}\)
  - 100k increase in semen
- Infectious during incubation period through up to 62 d
  - Atkinson et al EID 2016

Late sexual transmission of Zika virus related to persistence in the semen

Jean Marie Turmel JM et al. Lancet 2016
Prevention of Sexual Transmission of Zika post - travel

- **Sexual partners of pregnant women** - safe sex or abstain from sexual activity for duration of pregnancy
- **Men with Zika virus-like symptoms** - wait 6 months + before attempting conception
- **Asymptomatic men** - wait at least 8 weeks before attempting conception
- **Asymptomatic and symptomatic women** - wait at least 8 weeks before attempting conception

CDC Guidelines 2016

**ROLE OF LAB TESTING OF RETURNING TRAVELLERS??**
Management of pregnant women with suspected Zika?

- Symptomatic pregnant women (and asymptomatic) with exposure to Zika virus - PCR testing of serum and urine is recommended up to 2 weeks after symptom onset

- Microcephaly is most easily diagnosed by ultrasound late in the second trimester or early in the third trimester of pregnancy - many challenges
Caused by a virus spread by the day biting Aedes mosquitoes.

Over Head Tank  Coconut Shell  Air Conditioner  Tyres  Vessels  Banana Tree

This Aedes Mosquito develops in clean water. Destroy and remove water stagnation in your house.
‘Singapore will be releasing an army of bacteria-infected mosquitoes on Tuesday in a bid to suppress the *Aedes aegypti* mosquito population as the country battles with an outbreak of Zika’.

The National 19th October 2016

- ‘Vietnam’s Dr Dracula and the dengue-busting mosquitoes’

Genetically modified mosquitoes
Zika vaccine trials

There are new and familiar challenges in the race for timely and effective vaccines

By Marc Lipsitch1 and Benjamin J. Cowling2

Promising data for candidate vaccines against Zika virus infection reported by Abbink et al. (1) on page 1129 of this issue raise hopes that one or more Zika virus vaccines may soon be ready for efficacy trials. Recent years have seen a barrage of emerging infectious diseases, including those caused by new pathogens such as Middle East respiratory syndrome (MERS) coronavirus, and those that are newly salient because of increased geographic spread, higher incidence, or genetic change, such as influenza A(H1N1)pdm09, Ebola virus, and Zika virus. Developing effective vaccines is a central goal for such pathogens.

Repeatedly, emerging infectious diseases have caught us by surprise, with no vaccine candidate or only very early-stage candidates available. Human safety and immunogenicity must be established...