Coming to a Shore Near You: Zika and other Emerging Infectious Diseases

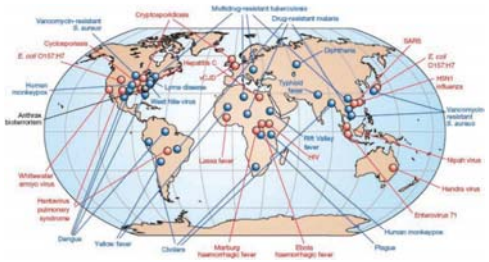
Doug Sider MD MSc FRCPC
Public Health Physician
Public Health Ontario

IPAC-SWO May 5, 2017

EIDs – Two Major Categories

Newly emerging:
- Newly recognized in human hosts

Remerging – have historically infected humans:
- Appear in new locations
- Appear in drug-resistant forms
- Reappear after control/elimination



Source: https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=FIGURE%205-2.%20Global%20examples%20of%20emerging%20and%20reemerging%20infectious%20diseases%2C%20some%20of%20which%20are%20discussed%20in%20the%20main%20text.&p=BOOKS&id=45714_ch5f5-2.jpg

But don't forget the following:

- MERS-CoV
- Chikungunya virus
- Influenza H7N9
- Ebola virus in West Africa
- Avian influenza H5N2 and others
- Zika virus
- Yellow fever (Angola, Brazil)

Factors in the Emergence of Infectious Diseases

1992
- Microbial adaptation and change
- Economic development and land use
- Human demographics and behavior
- International travel and commerce
- Technology and industry
- Breakdown of public health measures

2003
- **Microbial adaptation and change**
- Human susceptibility to infection
- Climate and weather
- Changing ecosystems
- **Human demographics and behavior**
- **Economic development and land use**
- **International travel and commerce**
- **Technology and industry**
- **Breakdown of public health measures**
- Poverty and social inequality
- War and famine
- Lack of political will
- Intent to harm

Source: IOM (2003).

Challenges of Newly Emerging Infections

Need to rapidly learn about:
- Transmission, e.g. incubation period, communicability
- Clinical presentations and consequences
- At-risk populations
- Treatments
- Prevention, e.g. vaccines
- IP&C measures

Risk assessment

Communication

Education, training

Our globally inter-connected reality

- The frontlines of infectious disease surveillance and response are not border-crossings/ports-of-entry.
- They are:
  - **Primary care/urgent care**
  - **Emergency departments/hospitals**
- EMS
- Community care
- LTC

Transmission and Incubation Period

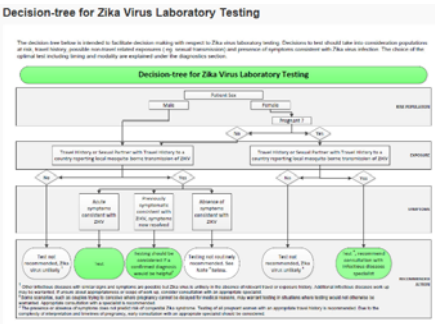
- Transmitted by *Aedes aegypti* mosquitos
- Incubation period - 3 to 12 days (may be up to 14 days)
- Usually causes a mild, self limiting illness
  - Maculopapular rash
  - Low grade fever
  - Conjunctivitis
  - Arthralgia

 Source: http://www.theyucatantimes.com/2015/11/deaths-from-dengue-rise-to-three-in-yucatan-three-cases-of-zika-reported-in-mexico/

Acute Zika Virus Infection: Clinical Management

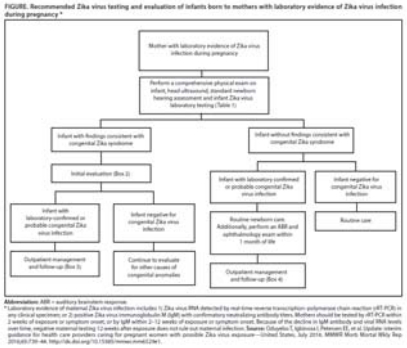
- Supportive management
  - No antiviral therapy available for Zika virus infection.
  - Rest, fluids to avoid dehydration
  - Antipyretics , analgesics
- Do not take aspirin and other non-steroidal anti-inflammatory drugs (NSAIDS) until dengue ruled out, and do not use them in pregnant patients.
- Avoid mosquito bites until a week after symptom onset (to prevent spread to others)

Decision-tree for Zika Virus Laboratory Testing



Source: http://www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm

FIGURE. Recommended Zika virus testing and evaluation of infants born to mothers with laboratory evidence of Zika virus infection during pregnancy*



Source: http://www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm

BOX 2. Initial clinical evaluation and management of infants with laboratory evidence of Zika virus infection and abnormalities consistent with congenital Zika syndrome

- Consultation with:
  - Neurologist for determination of appropriate neuroimaging and additional evaluation.
  - Infectious disease specialist for diagnostic evaluation of other congenital infections (e.g., syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection, and herpes simplex virus infection).
  - Ophthalmologist for comprehensive eye exam and evaluation for possible cortical visual impairment prior to discharge from the hospital or within 1 month of birth.
  - Endocrinologist for evaluation for hypothalamic or pituitary dysfunction.
  - Clinical geneticist to evaluate for other causes of microcephaly or other anomalies if present.
- Consider consultation with:
  - Orthopedist, physiatrist, or physical therapist for the management of hypertonia, club foot or arthrogryposic-like conditions.
  - Pulmonologist or otolaryngologist for concerns about aspiration.
  - Lactation specialist, nutritionist, gastroenterologist, or speech or occupational therapist for the management of feeding issues.
- Perform auditory brainstem response to assess hearing.
- Perform complete blood count and metabolic panel, including liver function tests.
- Provide family and supportive services.

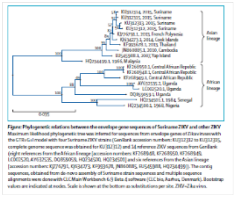
Testing Modalities Available

- Molecular detection: real-time RT-PCR (PHOL)
  - Blood/urine up to 14 days post-symptom onset
  - Combined with CHIKV and dengue PCRs if symptomatic
- Serology (NML)
  - ELISA IgM
  - Plaque reduction neutralization titre (PRNT)
- Antigen detection
  - Immunohistochemistry (CDC only)
  - Immunochromatographic tests
- Virus Culture

Zika virus IgM serology

- Zika virus IgM reactive specimens are considered indicative of a recent **flavivirus** infection.
- IgM antibodies against Zika, dengue, West Nile and other flaviviruses have strong cross reactivity in serological assays
- Current assays cannot reliably distinguish between Zika and dengue virus infections.
  - IgM reactive specimens will be further investigated by neutralization assays (PRNT).

Asian lineage detected in French Polynesia, 2014 and Suriname, 2015



Sources: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4047448/
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4777745/

Worldwide spread of Zika virus

Zika Virus in the Americas – Why now, why here?

- International spread eastward over past 10-12 years
- Immunologically naïve populations
- Ample competent mosquito vectors, especially *Ae. aegypti* + *Ae. albopictus*
- Socio-economic determinants:
  - Poverty
  - Population density
  - Housing
  - Heathcare/public health systems capacity/access
- Viral mutations – changes to transmissibility and/or virulence?
- Co-factors?
  - Previous/concurrent flavivirus infections, especially dengue
  - Environmental exposures
  - Bovine-like diarrheal virus (BVDV)

Challenges in Assessing/Understanding Emerging Zika Epidemiology

- Healthcare/public health system capacity in areas most affected
- Competing priorities in Zika-affected areas
- Concurrent epidemics of dengue fever and chikungunya virus infections
- Non-specific nature of clinical signs and symptoms:
  - Fever, rash, conjunctivitis, arthralgias

Challenges in Assessing/Understanding Emerging Zika Epidemiology

- Short period of viremia + capacity to detect via PCR
- Cross-reactivity of serological tests for antibodies with other flaviviruses:
  - Dengue
  - Yellow fever
  - West Nile virus
- High proportion of asymptomatic infections
- Evolving understanding of routes of transmission/clinical consequences

Figure 1. Countries and territories in the Americas with confirmed autochthonous (vector-borne) Zika virus cases, 2015 - 2017.

Figure 2. Distribution of suspected and confirmed Zika cases by epidemiological week and sub-region. Region of the Americas, 2016 – 2017 (as of EW 16).15

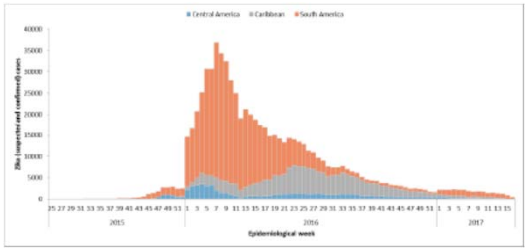


Figure 3. Distribution of suspected and confirmed Zika cases by EW. Bolivia (Plurinational State of), Brazil, Ecuador, and Peru, EW 25 of 2015 to EW 16 of 2017.

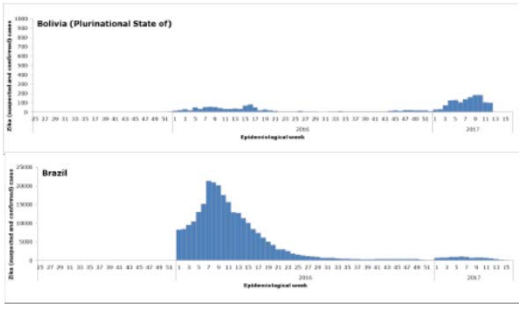
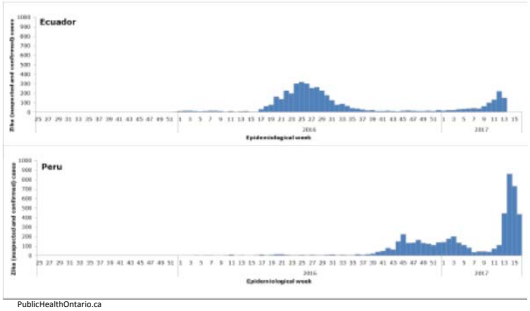


Figure 3. continued…



Source: http://www.haaretz.com/israel-news/science/1.699193

Source: http://dx.doi.org/10.1016/S0140-6736(16)30902-3

Articles

Congenital Zika virus syndrome in Brazil: a case series of the first 1501 livebirths with complete investigation

Giovanny V A Franca, Lavinia Schuler-Faccini, Wanderson K Oliveira, Claudia M P Henriques, Eduardo H Carmo, Vivineide D Pedi, Marilia L Nunes, Marcia C Castro, Suzanne Serruya, Marilengela F Silveira, Fernando C Barros, Cesar G Victora

Summary

Background In November, 2015, an epidemic of microcephaly was reported in Brazil, which was later attributed to congenital Zika virus infection. 7830 suspected cases had been reported to the Brazilian Ministry of Health by June 4, 2016, but little is known about their characteristics. We aimed to describe these newborn babies in terms of clinical findings, anthropometry, and survival.

Lancet 2016; 388: 891–97
Published Online June 25, 2016 http://dx.doi.org/10.1016/S0140-6736(16)30902-3

Source: *Lancet Infect Dis* 2016

Articles

Association between Zika virus infection and microcephaly in Brazil, January to May, 2016: preliminary report of a case-control study

Thalia Velho Barreto de Araújo, Laura Cunha Rodrigues, Ricardo Arraes de Alencar Ximenes, Demócrito de Barros Miranda-Filho, Ulisses Ramos Montarroyos, Ana Paula Lopes de Melo, Sandra Valongueiro, Maria de Fátima Pessoa Militão de Albuquerque, Wayner Vieira Souza, Cynthia Braga, Simoni Pinto Brandão Filho, Marli Tenório Cordeiro, Enrique Vazquez, Danielle Di Cavalcanti Souza Cruz, Cláudio Maierovitch Pessanha Henriques, Luciana Caroline Albuquerque Bezerra, Priscila Mayerlle da Silva Castanha, Rafael Dhalia, Ernesto Torres Azevedo Marques Júnior, Celina Maria Turchi Martelli, *on behalf of investigators from the Microcephaly Epidemic Research Group, the Brazilian Ministry of Health, the Pan American Health Organization, Instituto de Medicina Integral Professor Fernando Figueira, and the State Health Department of Pernambuco**

Summary

Background The microcephaly epidemic, which started in Brazil in 2015, was declared a Public Health Emergency of International Concern by WHO in 2016. We report the preliminary results of a case-control study investigating the association between microcephaly and Zika virus infection during pregnancy.

Lancet Infect Dis 2016
Published Online September 15, 2016

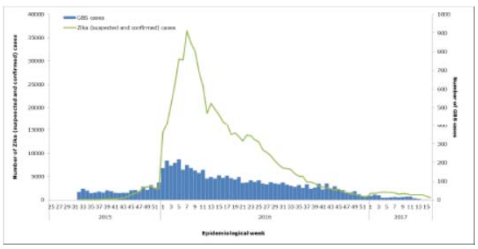
Early Growth and Neurologic Outcomes of Infants with Probable Congenital Zika Virus Syndrome

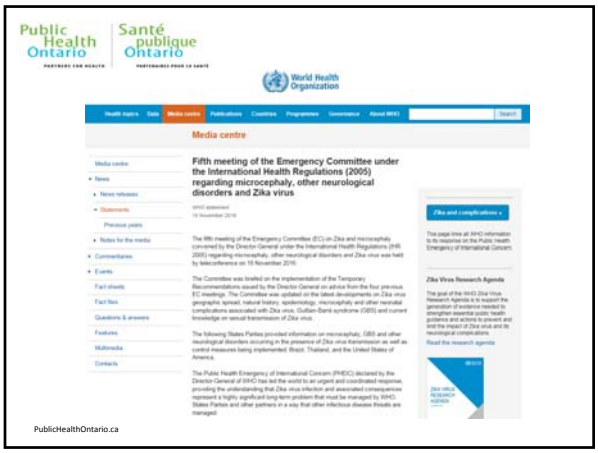
We report the early growth and neurologic findings of 48 infants in Brazil diagnosed with probable congenital Zika virus syndrome and followed to age 1–8 months. Most of these infants had microcephaly (86.7%) and craniofacial disproportion (95.8%). The clinical pattern included poor head growth with increasingly negative *z*-scores, pyramidal/extrapyramidal symptoms, and epilepsy.

Source: Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 22, No.11, November 2016.
DOI: http://dx.doi.org/10.3201/eid2211.160956

Source: http://wwwnc.cdc.gov/eid/article/23/1/16-1290_article

Figure 4. Distribution of suspected and confirmed cases of Zika and GBS by EW. Region of the Americas, 2015 – 2017 (as of EW 16).18





PublicHealthOntario.ca

The EC originally recommended a PHEIC in February 2016 on the basis of an extraordinary cluster of microcephaly and other neurological disorders reported in Brazil, following a similar cluster in French Polynesia and geographic and temporal association with Zika virus infection which required urgent and coordinated and research. Because research has now demonstrated the link between Zika virus infection and microcephaly, the EC felt that a robust longer-term technical mechanism was now required to manage the global response.

As a result, the EC felt that Zika virus and associated consequences remain a significant enduring public health challenge requiring intense action but no longer represent a PHEIC as defined under the IHR. Many aspects of this disease and associated consequences still remain to be understood, but this can best be done through sustained research. The EC recommended that this should be escalated into a sustained programme of work with dedicated resources to address the long-term nature of the disease and its associated consequences.

PublicHealthOntario.ca 32

PublicHealthOntario.ca Source: http://dx.doi.org/10.1016/S1473-3099(16)30270-5 33

Case Counts in the US

Zika virus disease is now a nationally notifiable condition. Cases are reported to CDC by state, territorial, and local health departments using standard case definitions. This webpage contains provisional data reported to ArboNET for **January 1, 2015 – April 26, 2017**.

US States

- 5,264 Zika virus disease cases reported
  - 4,963 cases in travelers returning from affected areas
  - 224 cases acquired through presumed local mosquito-borne transmission in Florida (N=218) and Texas (N=6)
  - 77 cases acquired through other routes, including sexual transmission (N=46), congenital infection (N=29), laboratory transmission (N=1), and person-to-person through an unknown route (N=1)

US Territories

- 36,575 Zika virus disease cases reported
  - 143 cases in travelers returning from affected areas
  - 36,432 cases acquired through presumed local mosquito-borne transmission
  - 0 cases acquired through other routes*

*Sexually transmitted cases are not reported for US territories because with local transmission of Zika virus it is not possible to determine whether infection occurred due to mosquito-borne or sexual transmission.

PublicHealthOntario.ca

Outcomes of Pregnancies with Laboratory Evidence of Possible Zika Virus Infection in the United States

Outcomes for Completed Pregnancies in the United States and District of Columbia, 2016-2017
*As of April 11, 2017

Completed pregnancies with or without birth defects	Liveborn infants with birth defects*	Pregnancy losses with birth defects**
1,367	58	7
Includes aggregated data reported to the US Zika Pregnancy Registry*	Includes aggregated data reported to the US Zika Pregnancy Registry*	Includes aggregated data reported to the US Zika Pregnancy Registry*

PublicHealthOntario.ca

Source: http://www.cdc.gov/zika/public-health-partners/zapss.html

PublicHealthOntario.ca 36

Public Health Ontario | Santé publique Ontario

Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016

Megan R. Reynolds, MPH[1]; Abbey M. Jones, MPH[1]; Emily E. Petersen, MD[2]; Ellen H. Lee, MD[3]; Marion E. Rice, MPH[1,4]; Andrea Bingham, PhD[5]; Sascha R. Ellington, MSPH[1,2]; Nicole Ewer, MS[6]; Sarah Reagan-Steiner, MD[7]; Titilope Oduyebo, MD[1]; Catherine M. Brown, DVM[8]; Stacey Martin, MSc[9]; Nina Ahmad, MD[10]; Julu Bhatnagar, PhD[7]; Jennifer Macdonald, MPH[11]; Carolyn Gould, MD[3]; Anne D. Fine, MD[3]; Kara D. Polen, MPH[1]; Heather Lake-Burger, MPH[1]; Christina L. Hillard, MA[1]; Noemi Hall, PhD[6,12]; Mahsa M. Yazdy, PhD[3]; Kamesha Slaughter MPH[1]; Jamie N. Sommer, MS[13]; Alys Adamski, PhD[1]; Meghan Rayeraft, MPH[1]; Shannon Fleck-Derderian, MPH[1,3]; Jyoti Gupta, MPH[11]; Kimberly Newsome, MPH[1]; Madelyn Baez-Santiago, PhD[1]; Sally Slavinski, DVM[1]; Jennifer L. White, MPH[13]; Cynthia A. Moore, MD, PhD[12]; Carrie K. Shapiro-Mendoza, PhD[2]; Lyle Petersen, MD[2]; Coleen Boyle, PhD[14]; Denise J. Jamieson, MD[2]; Dana Meaney-Delman, MD[13]; Margaret A. Honein, PhD[1]; U.S. Zika Pregnancy Registry Collaboration

On April 4, 2017, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

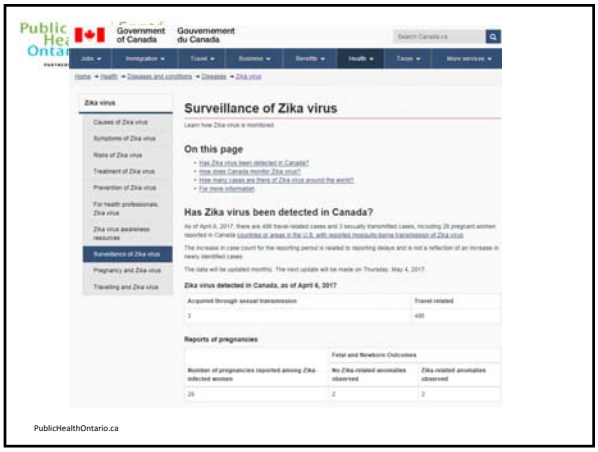
Abstract

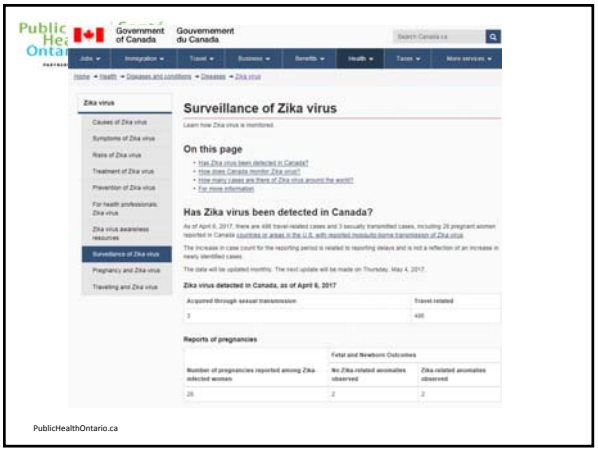
Background: In collaboration with state, tribal, local, and territorial health departments, CDC established the U.S. Zika Pregnancy Registry (USZPR) in early 2016 to monitor pregnant women with laboratory evidence of possible recent Zika virus infection and their infants.

Methods: This report includes an analysis of completed pregnancies (which include live births and pregnancy losses, regardless of gestational age) in the 50 U.S. states and the District of Columbia (DC) with laboratory evidence of possible recent Zika virus infection reported to the USZPR from January 15 to December 27, 2016. Birth defects potentially associated with Zika virus infection during pregnancy include brain abnormalities and/or microcephaly, eye abnormalities, other consequences of central nervous system dysfunction, and neural tube defects and other early brain malformations.

Public Health Ontario | Santé publique Ontario

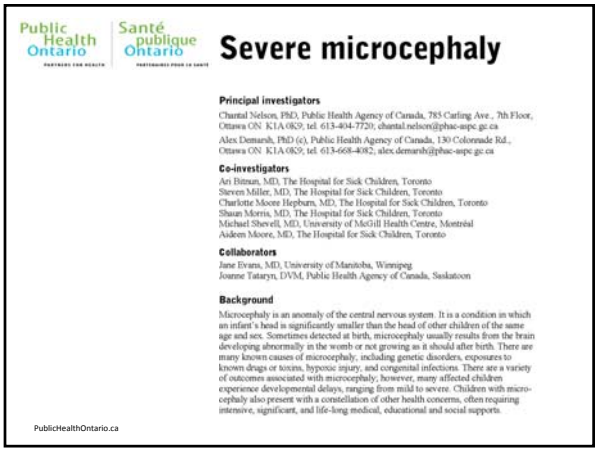
Results: During the analysis period, 1,297 pregnant women in 44 states were reported to the USZPR. Zika virus–associated birth defects were reported for 51 (5%) of the 972 fetuses/infants from completed pregnancies with laboratory evidence of possible recent Zika virus infection (95% confidence interval [CI] = 4%–7%); the proportion was higher when restricted to pregnancies with laboratory-confirmed Zika virus infection (24/250 completed pregnancies [10%, 95% CI = 7%–14%]). Birth defects were reported in 15% (95% CI = 8%–26%) of fetuses/infants of completed pregnancies with confirmed Zika virus infection in the first trimester. Among 895 liveborn infants from pregnancies with possible recent Zika virus infection, postnatal neuroimaging was reported for 221 (25%), and Zika virus testing of at least one infant specimen was reported for 585 (65%).

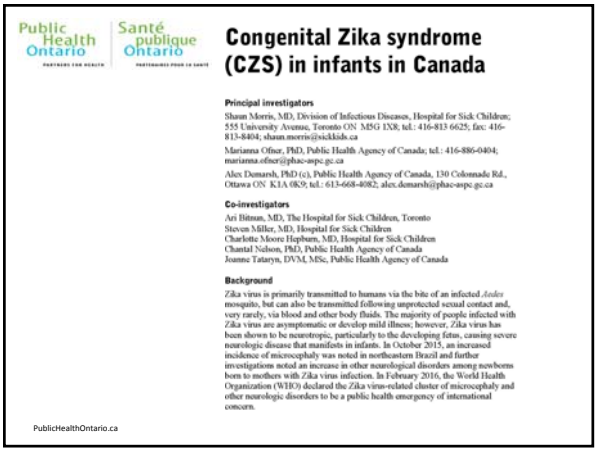


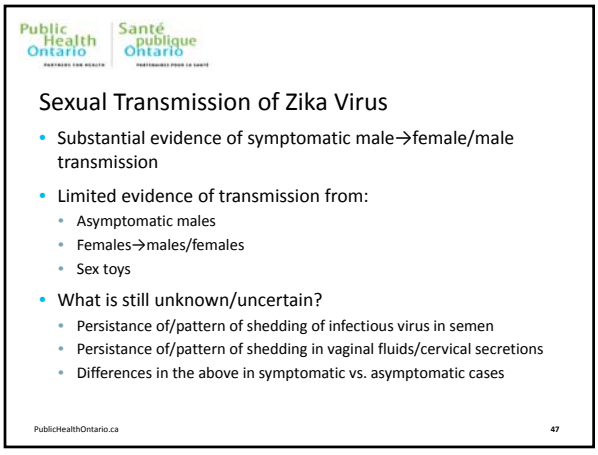


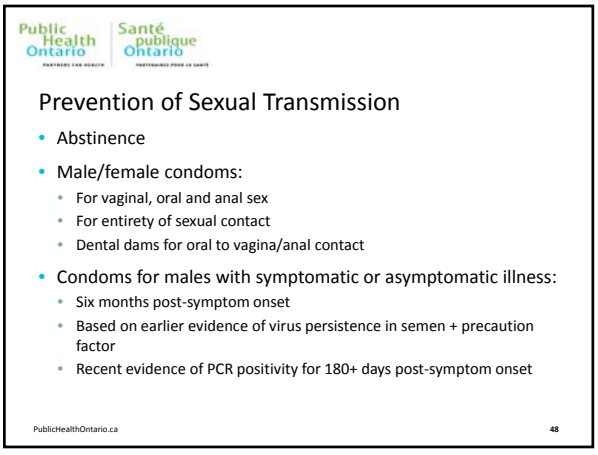

Public Health Ontario
Santé publique Ontario
Government of Canada
Gouvernement du Canada
Recommendations on the Prevention and Treatment of Zika Virus for Canadian health care professionals
An Advisory Committee Statement (ACS)
Committee to Advise on Tropical Medicine and Travel (CATMAT)
Table of contents
PublicHealthOntario.ca


Public Health Ontario
Santé publique Ontario
Surveillance report of Zika virus among Canadian travellers returning from the Americas
Andrea K. Boggild MD, Jennifer Geduld MHSc, Michael Libman MDCM, Cedric P. Yansouni MD, Anne E. McCarthy MD, Jan Hajek MD, Wayne Ghesquiere MD, Yazdan Mirzanejad MD, Jean Vincelette MD, Susan Kuhn MD, Pierre J. Plourde MD, Sumontra Chakrabarti MD, David O. Freedman MD, Kevin C. Kain MD
ABSTRACT
PublicHealthOntario.ca


Public Health Ontario
Santé publique Ontario
Severe microcephaly
Principal investigators
Chantal Nelson, PhD, Public Health Agency of Canada, 785 Carling Ave., 7th Floor, Ottawa ON K1A 0K9; tel. 613-404-7720; chantal.nelson@phac-aspc.gc.ca
Alex Demarsh, PhD (c), Public Health Agency of Canada, 130 Colonnade Rd., Ottawa ON K1A 0K9; tel. 613-668-4082; alex.demarsh@phac-aspc.gc.ca
Co-investigators
Ari Bitnun, MD, The Hospital for Sick Children, Toronto
Steven Miller, MD, The Hospital for Sick Children, Toronto
Charlotte Moore Hepburn, MD, The Hospital for Sick Children, Toronto
Shaun Morris, MD, The Hospital for Sick Children, Toronto
Michael Shevell, MD, University of McGill Health Centre, Montréal
Aideen Moore, MD, The Hospital for Sick Children, Toronto
Collaborators
Jane Evans, MD, University of Manitoba, Winnipeg
Joanne Tataryn, DVM, Public Health Agency of Canada, Saskatoon
Background
PublicHealthOntario.ca


Public Health Ontario
Santé publique Ontario
Congenital Zika syndrome (CZS) in infants in Canada
Principal investigators
Shaun Morris, MD, Division of Infectious Diseases, Hospital for Sick Children; 555 University Avenue, Toronto ON M5G 1X8; tel.: 416-813 6625; fax: 416-813-8404; shaun.morris@sickkids.ca
Marianna Ofner, PhD, Public Health Agency of Canada; tel.: 416-886-0404; marianna.ofner@phac-aspc.gc.ca
Alex Demarsh, PhD (c), Public Health Agency of Canada, 130 Colonnade Rd., Ottawa ON K1A 0K9; tel.: 613-668-4082; alex.demarsh@phac-aspc.gc.ca
Co-investigators
Ari Bitnun, MD, The Hospital for Sick Children, Toronto
Steven Miller, MD, Hospital for Sick Children
Charlotte Moore Hepburn, MD, Hospital for Sick Children
Chantal Nelson, PhD, Public Health Agency of Canada
Joanne Tataryn, DVM, MSc, Public Health Agency of Canada
Background
PublicHealthOntario.ca


Public Health Ontario
Santé publique Ontario
Sexual Transmission of Zika Virus
• Substantial evidence of symptomatic male→female/male transmission
• Limited evidence of transmission from:
◦ Asymptomatic males
◦ Females→males/females
◦ Sex toys
• What is still unknown/uncertain?
◦ Persistance of/pattern of shedding of infectious virus in semen
◦ Persistance of/pattern of shedding in vaginal fluids/cervical secretions
◦ Differences in the above in symptomatic vs. asymptomatic cases
PublicHealthOntario.ca
47


Public Health Ontario
Santé publique Ontario
Prevention of Sexual Transmission
• Abstinence
• Male/female condoms:
◦ For vaginal, oral and anal sex
◦ For entirety of sexual contact
◦ Dental dams for oral to vagina/anal contact
• Condoms for males with symptomatic or asymptomatic illness:
◦ Six months post-symptom onset
◦ Based on earlier evidence of virus persistence in semen + precaution factor
◦ Recent evidence of PCR positivity for 180+ days post-symptom onset
PublicHealthOntario.ca
48

Prevention of Sexual Transmission

- Symptomatic or asymptomatic females require 8 weeks of transmission precautions:
  - Shorter duration of viral persistence in vaginal fluids/cervical secretions
- Avoid sharing of sex toys

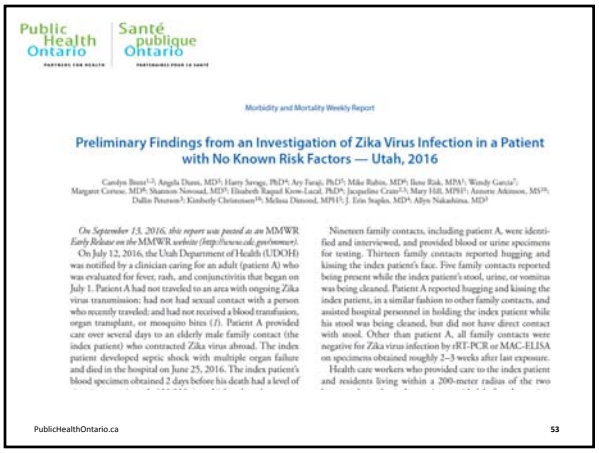
Other Potential Exposures/Modes of Transmission

- Urine:
  - No reports of transmission
  - Use of routine practices
- Breastmilk:
  - No reports of transmission
  - No restrictions on breastfeeding
- Saliva/tears:
  - No reports of transmission
  - Use of routine practices
- Blood screening/blood supply:
  - CBS donor deferral for 21 days

Reportability of Zika Virus Infection

- Zika virus infection not designated reportable in Ontario
- Limited data elements from PHO laboratories collected by/shared with CMOH/PHAC
- Why isn't Zika reportable?
  - Limited PH actions requiring reporting/collection of personal health info
  - Prevention of sexual transmission via public education vs. case/contact follow-up
  - Priorities for lab testing → dependence on clinical diagnosis/reporting
  - Non-specific clinical signs and symptoms → ? Zika, ? chikungunya, ? dengue, ? other
  - High proportion of asymptomatic infections
- Pregnancy complications/CZS reporting/assessment via PHAC/CPS voluntary system

Inactivation and Environmental Stability of Zika Virus



Morbidity and Mortality Weekly Report

Preliminary Findings from an Investigation of Zika Virus Infection in a Patient with No Known Risk Factors — Utah, 2016

CDC Centers for Disease Control and Prevention

Zika Virus

Interim Guidance for Managing Occupational Exposures to Zika Virus for Healthcare Personnel

Introduction

Managing Occupational Exposures

- No documented evidence to date of transmission to HCWs, one lab transmission via needlestick injury
- Use of routine practices
- If exposed, within 8 wks of source patient exposure?
- If risk factors, testing of source patient
- Initial testing/counselling re. Zika symptoms
- If transmission occurs, pregnancy/sexual transmission follow-up
- No exclusion from work

Rapid risk assessment: Zika virus

August 12, 2016

Summary

Event information summary:

Zika virus (ZIKV) infection is a mosquito-borne illness that is usually mild and resolves without treatment. This outbreak was first documented in Brazil in early 2015. Since then, ZIKV infection has spread rapidly throughout Central and South America and the Caribbean, with local transmission recently documented in two counties in Florida. The World Health Organization (WHO) has concluded that ZIKV is a causative agent of congenital malformations and neurological complications.

Figure 1: Core questions in risk assessment for communicable diseases

Assessing likelihood of transmission:

1. Is human exposure and transmission likely within Ontario?
2. Is the population highly susceptible?
3. Is the agent highly infectious?

Assessing probability of impact:

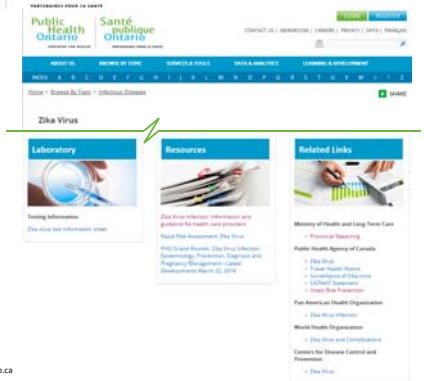
4. Is the agent likely to cause severe disease?
5. Will a significant proportion of the population be affected?
6. Are effective treatments and/or control measures available?

Rapid Risk Assessment: The risk of Zika virus to Canadians (third update) – Appendix 1

Table 3: Working definitions for confidence levels

Level	Definition	Examples of information/evidence
Low	Little or poor-quality evidence, significant uncertainty, conflicting views amongst experts, no experience with similar incidents. Further research is likely to have significant impact on the results of the assessment.	Individual case reports Grey literature
	Further research is very likely to change the results of the assessment and the confidence in the assessment and the information used.	Individual, non-expert opinion
Medium	Adequate quality of evidence, including consistent results, reliable source(s), and assumptions made on analogy. Agreement between experts or opinions of two trusted experts. Further research may necessitate some changes to the assessment.	Non-peer-reviewed published studies/reports Observational studies
	Further research is likely to have an impact on the confidence in the assessment and information used. It may change the results of the assessment.	Surveillance reports Outbreak reports Individual, expert opinion
High	Good-quality evidence, multiple reliable sources, verified, multiple expert opinions concur; experience with previous and similar events. Further research is unlikely to change the results of the assessment.	Peer reviewed published studies where design and analysis reduce bias (i.e. systematic reviews, RCT, outbreak report)
	Further research is unlikely to change the confidence in the assessment.	Textbooks regarded as definitive sources. Expert group risk assessment, or specialized expert knowledge, or consensus opinion of experts.

 Source: http://www.healthycanadians.gc.ca/publications/diseases-conditions-maladies-affections/risks-zika-virus-risques/index-eng.php



Zika Virus Infection:
Information and guidance for health care providers

(Updated October 5, 2016)

Public Health Ontario has been working with the Ontario Ministry of Health and Long-Term Care, the Public Health Agency of Canada (PHAC) and other partners on monitoring and assessing the epidemiology, clinical impacts, prevention and control of Zika virus (ZIKV) infection. Where possible, PHO refers to the latest advice from the Committee to Advise on Tropical Medicine and Travel (CATMAT). PHO also refers to the Centers for Disease Control and Prevention (CDC), Pan American Health Organization (PAHO) or the European Centre for Disease Prevention and Control (ECDC) when more up-to-date guidance is available.

PAHO and Zika Risk Communication

- With uncertain health risks, what is known, what not?
- Timely, transparent, accurate, accessible information
- Coordinating messages across health organizations
- Prioritize the messages → those with greatest impact
- Adapt information for different audiences
- Avoid over-interpretation and over-confidence
- Things will change as more is learned
- Link with/mobilize community leaders/educators
- Keep media informed

Journal of Clinical Virology 83 (2016) 66–71
Contents lists available at ScienceDirect
Journal of Clinical Virology
journal homepage: www.elsevier.com/locate/jcv

Simultaneous detection of Zika, Chikungunya and Dengue viruses by a multiplex real-time RT-PCR assay

Kanti Pabbaraju[a,*], Sallene Wong[a], Kara Gill[a], Kevin Fonseca[a,b], Graham A. Tipples[a,c], Raymond Tellier[a,b]

[a] Provincial Laboratory for Public Health, Calgary, Alberta, Canada
[b] Department of Microbiology, Immunology and Infectious Diseases, University of Calgary, Alberta, Canada University of Calgary, Alberta, Canada
[c] Department of Pathology and Laboratory Medicine, University of Alberta, Edmonton, Alberta, Canada

Zika Virus Commercial Assays

altona DIAGNOSTICS

Press Release

altona Diagnostics launches worldwide first commercially available CE-IVD real-time PCR test for detection of Zika Virus

Hamburg, January 27, 2016 The RealStar® Zika Virus RT-PCR Kit 1.0 is an in vitro diagnostic assay based on real-time Reverse Transcriptase/Polymerase Chain Reaction (RT-PCR) technology, for the identification of Zika virus. RealStar® Kits are reliable CE-IVD marked assays for detection and quantification of various viruses, bacteria and parasites. The assays meet all requirements of the IVD Directive 98/79/EC. With the development of the RealStar® Zika Virus RT-PCR Kit 1.0, altona Diagnostics enlarges its panel of CE-IVD marked ready-to-use kits for tropical pathogens.

altona DIAGNOSTICS

RealStar®
Zika Virus RT-PCR Kit 1.0
01/2016

fast-track DIAGNOSTICS
TRUE POSITIVES. TRUE NEGATIVES.

Manual
FTD Zika virus

32 reactions (catalog no. FTD-77-32)

64 reactions (catalog no. FTD-77-64)

WHO PREQUALIFICATION TEAM: DIAGNOSTICS
World Health Organization

Invitation to manufacturers of in vitro diagnostics for Zika virus to submit an application for emergency use assessment and listing by WHO (originally issued 10 February 2016)

Source: http://www.who.int/diagnostics_laboratory/eual-zika-virus/160211invitation_to_mx_of_Zika_virus_diagnostics_v2.pdf?ua=1

Contents lists available at ScienceDirect
International Journal of Infectious Diseases
journal homepage: www.elsevier.com/locate/ijid

Editorial

Zika virus outbreak and the case for building effective and sustainable rapid diagnostics laboratory capacity globally

Keywords:
Zika virus
Emerging pathogens
laboratory
diagnostics
surveillance
public health

New and re-emerging pathogens with epidemic potential have threatened global health security for the past century.[1] As with the recent Ebola Virus Disease (EVD) epidemic, the Zika Virus (ZikV) outbreak has yet again surprised and overwhelmed the international health community with an unexpected event for which it might have been better prepared.

ZikV was first identified in Uganda in 1947, was also found in Gabon in 2007 and may be endemic in much of tropical Africa without receiving much attention.[2] The current ZIKV epidemic facing the Americas,[3] was declared a "Public Health Emergency of International Concern (PHEIC)" by the World Health Organization on 1st February 2016.[4,5] Preceding the declaration of a Global Public Health Emergency by 4 days was the release of the United Nations report "Protecting Humanity from Future Health Crises. Report of the High-level Panel on the Global Response to Health

The present ZIKV outbreak again exposes an unprepared global public health system.

Surveillance of infections is based on reporting cases of illness, often syndromic reporting of CNS or pulmonary infections among others, but unspecified brief febrile illnesses are rarely reported, even in pregnant women. In addition, assigning a possible diagnosis to syndromic surveillance requires suitable laboratory tests to be readily available for the causative agent and require a considerable laboratory capacity. During the first six months of the Ebola virus disease (EVD) epidemic in West Africa, the weak diagnostic laboratory capacity in the affected countries was an important factor in the rapid spread of the outbreak.[6] As a result of intense international efforts, over 27 laboratories were established to provide rapid in-country testing for Ebola virus. These laboratories included both mobile and temporary laboratories equipped to do molecular diagnostic testing and several laboratories to provide local genomic sequencing of the virus to help in contact tracing. However, since the laboratories were mostly run by Non Governmental Organizations and volunteers from overseas public health laboratories, most of these efforts provided only a temporary solution, rather than a long-term sustainable solution. Furthermore these laboratories were focused on a single, known infection.

PLOS | NEGLECTED TROPICAL DISEASES

FROM INNOVATION TO APPLICATION

OpenZika: An IBM World Community Grid Project to Accelerate Zika Virus Drug Discovery

Sean Ekins[1*], Alexander L. Perryman[2*], Carolina Horta Andrade[3*]

1 Collaborations Pharmaceuticals, Inc., Fuquay-Varina, North Carolina, United States of America, 2 Department of Pharmacology, Physiology and Neuroscience, Rutgers University New Jersey Medical School, Newark, New Jersey, United States of America, 3 LabMol Laboratory for Molecular Modeling and Drug Design, Faculdade de Farmácia, Universidade Federal de Goiás, Goiânia, Goiás, Brasil

* ekinssean@yahoo.com (SE); Alex.L.Perryman@rbms.rutgers.edu (ALP); carolina@ufg.br (CHA)

Abstract

The Zika virus outbreak in the Americas has caused global concern. To help accelerate this fight against Zika, we launched the OpenZika project. OpenZika is an IBM World Community Grid Project that uses distributed computing on millions of computers and Android devices to run docking experiments, in order to dock tens of millions of drug-like compounds against crystal structures and homology models of Zika proteins (and other related flavivirus targets). This will enable the identification of new candidates that can then be tested in vitro, to advance the discovery and development of new antiviral drugs against the Zika virus. The docking data is being made openly accessible so that all members of the global research community can use it to further advance drug discovery studies against Zika and other related flaviviruses.

OPEN ACCESS

Source: Ekins S, Perryman AL, Horta Andrade C (2016) OpenZika: An IBM World Community Grid Project to Accelerate Zika Virus Drug Discovery. PLoS Negl Trop Dis 10(10): e0005023. doi:10.1371/journal.pntd.0005023

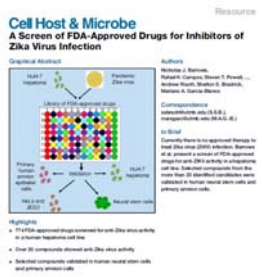
Source: http://www.nature.com/nm/journal/v22/n8/full/nm0816-824.html

A second look:

Efforts to repurpose old drugs against Zika cast a wide net

By Ellie Kincaid

Source: http://dx.doi.org/10.1016/j.chom.2016.07.004



Cell Host & Microbe

A Screen of FDA-Approved Drugs for Inhibitors of Zika Virus Infection

ARTICLES

nature medicine

Identification of small-molecule inhibitors of Zika virus infection and induced neural cell death via a drug repurposing screen

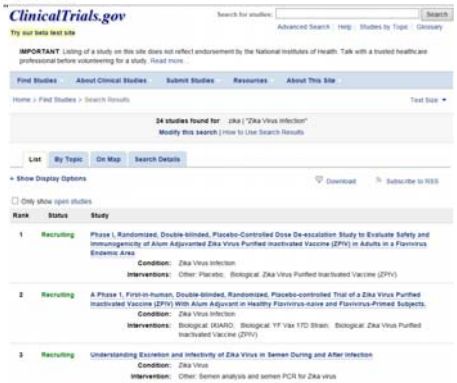
Miao Xu[1,2,16], Emily M Lee[3,16], Zhexing Wen[4–7,16], Yichen Cheng[8], Wei-Kai Huang[7,9], Xuyu Qian[7,9], Julia TCW[10], Jennifer Kouznetsova[1], Sarah C Ogden[3], Christy Hammack[3], Fadi Jacob[7,11], Ha Nam Nguyen[7,12], Misha Itkin[1], Catherine Hanna[1], Paul Shinn[1], Chase Allen[1], Samuel G Michael[1], Anton Simeonov[1], Wenwei Huang[1], Kimberly M Christian[7,12], Alison Goate[10], Kristen J Brennand[7,13], Ruili Huang[1], Menghang Xia[1], Guo-li Ming[7,9,11,12,14,15,17], Wei Zheng[1,17], Hongjun Song[7,9,11,12,15,17] & Hengli Tang[3,17]

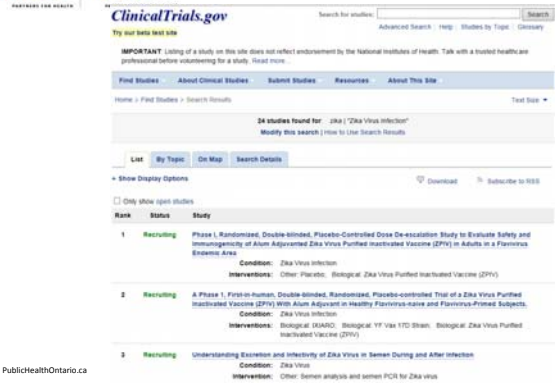
In response to the current global health emergency posed by the Zika virus (ZIKV) outbreak and its link to microcephaly and other neurological conditions, we performed a drug repurposing screen of ~6,000 compounds that included approved drugs, clinical trial drug candidates and pharmacologically active compounds; we identified compounds that either inhibit ZIKV infection or suppress infection-induced caspase-3 activity in different neural cells. A pan-caspase inhibitor, emricasan, inhibited ZIKV-induced increases in caspase-3 activity and protected human cortical neural progenitors in both monolayer and three-dimensional organoid cultures. Ten structurally unrelated inhibitors of cyclin-dependent kinases inhibited ZIKV replication. Niclosamide, a category B anthelmintic drug approved by the US Food and Drug Administration, also inhibited ZIKV replication. Finally, combination treatments using one compound from each category (neuroprotective and antiviral) further increased protection of human neural progenitors and astrocytes from ZIKV-induced cell death. Our results demonstrate the efficacy of this screening strategy and identify lead compounds for anti-ZIKV drug development.

From Drug Re-Purposing to Clinical Treatments

- In-vitro studies re. mechanism of action, toxicity
- Prioritization among drug candidates
- Phase 1, 2 and 3 clinical trials:
  - Clinical end-points: infection, transmission, protection of fetus?
  - Dose, route, duration of treatment?
  - Capacity to set-up/undertake vs. competing priorities?
- Drug approvals
- Manufacturing, distribution, clinical guidelines
- Phase 4 post-marketing capacity

Source: http://www.paho.org/zika-research/



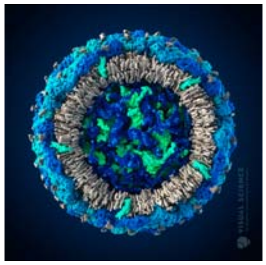


Public Health Ontario | Santé publique Ontario

ZIKV Vaccines

Options for vaccine development:

- Inactivated whole virus
- Subunit vaccines
- Live attenuated →
  - ?? with pregnant women
- Chimeras, using existing viral platforms
- DNA vaccines → virus-like particles



PublicHealthOntario.ca 73

Public Health Ontario | Santé publique Ontario

Source: http://www.who.int/immunization/research/meetings_workshops/WHO_Zika_vaccine_TPP.pdf

WHO/UNICEF Zika Virus Vaccine Target Product Profile for Emergency use: July 2016

World Health Organization   unicef

WHO Zika Virus (ZIKV) Vaccine Target Product Profile (TPP):
Vaccine to protect against congenital Zika virus syndrome for use during an emergency

The purpose of this document:

This document is a TPP that describes the preferred and minimal product characteristics for vaccines aimed at protecting against congenital ZIKV syndrome during the ongoing Public Health Emergency of International Concern (PHEIC), or future emergency situations. With that public health objective, this TPP is primarily aimed at vaccines for use in women of childbearing age, with men as a secondary target population if resources permit. The TPP has been drafted by an independent WHO working group of subject matter experts with diverse areas of expertise, and focuses on the product attributes. It has undergone public consultation, and discussion in various fora. As the TPP is based on currently available information in the context of emerging data on ZIKV epidemiology and pathogenesis, the TPP should be considered as living document, and it may undergo adaptation, as knowledge on ZIKV evolves.

PublicHealthOntario.ca 74

Public Health Ontario | Santé publique Ontario

Issues in ZIKV Vaccine Development

Challenges of developing/testing a vaccine for women in reproductive years/pregnant:

- outcomes of Zika in pregnancy not fully characterized
- ethical challenges – risks vs. benefits mother/fetus, consent
- research design – vaccination prior to/early pregnancy
- baseline outcome rates (e.g. miscarriage), across geographies

Potential vaccine complications:

- association of GBS with ZIKV infection
- antibody-dependent enhancement with previous dengue infections
- phase 3 and 4 detection/monitoring

PublicHealthOntario.ca 75

Public Health Ontario | Santé publique Ontario

Issues in ZIKV Vaccine Development (cont'd)

- Testing in animal models, phase 1, 2 and 3 studies
- WHO Emergency Assessment and Listing procedure for the use of experimental products during an epidemic:
  - accelerated assessment process
  - ensure products meet acceptable levels of quality, safety and efficacy, even if evaluation fast-tracked
- Regulatory approvals, manufacturing and distribution
- Funding, education, infrastructure, delivery, Phase 4 capacity

PublicHealthOntario.ca 76

Public Health Ontario | Santé publique Ontario

Source: https://www.nih.gov/news-events/news-releases/nih-begins-testing-investigational-zika-vaccine-humans

Health Information | Grants & Funding | News & Events | Research & Training | Institutes at NIH | About NIH

NEWS RELEASES

NIH begins testing investigational Zika vaccine in humans

Institute/Center

Contact

Connect with Us

PublicHealthOntario.ca 77

Public Health Ontario | Santé publique Ontario

World Health Organization

Immunization, Vaccines and Biologicals

WHO vaccine pipeline tracker

WHO Vaccine Pipeline Tracker

Candidate vaccine name	Developer / Collaborators	Disease / Pathogen
BBV121	Bharat Biotech International Ltd. India	ZIKV
	Bio-Manguinhos in house development and Sanofi Pasteur/WRAIR	ZIKV
	Bio-Manguinhos partnership	ZIKV
	Bio-Manguinhos / Aggeu Magalhaes (FIOCRUZ)	ZIKV
	Brazilian MoH agreement with UTMB and IEC/SVS/MS	ZIKV
Butantan ZIKV	Butantan	ZIKV
Butantan attenuated ZIKV	Butantan	ZIKV
ZIKV	Emergent BioSolutions	ZIKV

PublicHealthOntario.ca

PublicHealthOntario.ca Source: http://www.statnews.com/2016/03/16/us-cities-local-zika-transmission/ 79

Source: http://news.nationalgeographic.com/2016/02/160225-zika-virus-brazil-mosquitoes-microcephaly-pictures/

PublicHealthOntario.ca 80

Mosquito Vector Control

- Personal protection measures → acceptability? compliance? effectiveness?
- Larviciding → myriad breeding sites
- Adulticiding:
  - Magnitude of applications
  - *Aedes* lives/feeds indoors
  - Reduction of adult mosquito populations
  - Impact on disease transmission/impacts?
  - Cost/sustainability

PublicHealthOntario.ca 81

Sources:
http://memoria.ebc.com.br/agenciabrasil/sites/_agenciabrasil/files/imagecache/300x225/gallery_assist/29/gallery_assist664106/prev/13062010-FOTO11217.jpg ;
http://memoria.ebc.com.br/agenciabrasil/sites/_agenciabrasil/files/gallery_assist/27/gallery_assist737964/Demolicao_RJ_0382.jpg

PublicHealthOntario.ca 82

Mosquito Vector Control (cont'd)

- Eradication of breeding sites:
  - El Nino and rainfall patterns
  - Scale of what would be required, given *Aedes* breeding capacity
  - Huge community capacity/compliance
- Release of genetically-modified adult male mosquitoes:
  - WHO-supported
  - Evidence of impact on mosquito populations
  - Impact on incidence and complications, especially pregnancy-related?
  - Scale up, sustainability, cost-effectiveness?
  - Potentially part of the answer, not THE answer

Emergence of/need to monitor for insecticide resistance

- Resistance to permethrins – impregnated clothing

PublicHealthOntario.ca 83

PublicHealthOntario.ca Source: https://www.statnews.com/2016/10/26/mosquitoes-wolbachia-bacteria-virus/ 84

Source: Zika: CDC Interim Response Plan, August 2016

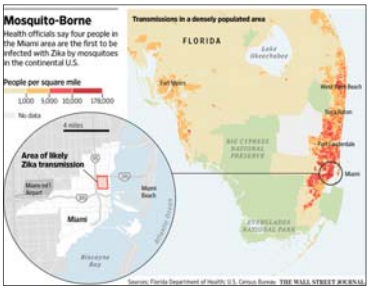
ZIKA
CDC Interim Response Plan

CDC and partners will support and assist states in the key activity areas listed below as different stages in this continuum are reached.

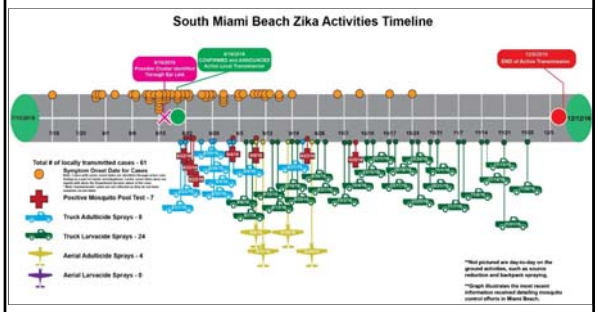
Stage	Phase Level[1]	Transmission Risk Category
Pre-incident	0	**Preparedness —** vector present or possible in the state
	1	**Mosquito Season** — *Aedes aegypti* or *Aedes albopictus* mosquito biting activity. Introduced travel-related, sexually, or other bodily fluid transmitted cases
Suspected/Confirmed Incident	2	**Confirmed Local Transmission** — single, locally acquired case, or cases clustered in a single household and occurring <2 weeks apart
Incident/Response	3	**Confirmed Multiperson Local Transmission** — Zika virus illnesses with onsets occurring ≥2 weeks apart but within an approximately 1 mile (1.5 km) diameter

Local Zika virus transmission, Florida

- Local transmission started in June 2016
- 285 confirmed cases in 2016
- *Aedes aegypti* responsible
- Intensive management program put in place

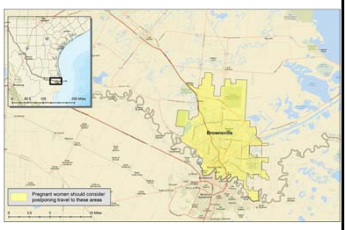


Zika virus management, Florida



Local Zika virus transmission, Texas

- First evidence of local transmission at end of November 2016
- 6 confirmed cases
- Likely *Aedes aegypti* is vector
- Intensive management program initiated
- Active testing of residents near index case



As Zika Season Nears, States Brace for an End to CDC Funding

Aedes albopictus – pre 2016, Ontario

- 2005 – Ottawa, August 28
- 2005 – Peel, September 1
- 2005 – Toronto, August 10
- 2012 – Windsor-Essex, June 12
- Likely detected from adventitious individuals hitching ride in vehicles from south
- WNV surveillance not designed to detect these mosquitoes, but if there is a local population, our traps will detect it

Aedes albopictus detected in Ontario

- Late September and early October 2016
- Adult mosquitoes collected in CDC traps at single location in Windsor (index site)
- Mid-October, intense collection of eggs, larvae and pupae from container habitats near index site
- BGS traps set up to collect adults, designed specifically for *Aedes albopictus* and *Aedes aegypti*
- Results:
  - Immature forms reared to adulthood identified as *Aedes albopictus* and *Aedes aegypti*
  - Female and male adult *Aedes albopictus* collected by BGS traps

Aedes sampling, Windsor: 2016


Sampling for *Aedes* mosquitoes, Windsor: 2016

Sampling for *Aedes* mosquitoes with BGS trap, Windsor: 2016

Guidance For Managing Ethical Issues In Infectious Disease Outbreaks

Public Health Ontario | Santé publique Ontario

Table of Contents

Foreword 3
Acknowledgements 4
Introduction 7
Guidelines 12
1. Obligations of governments and the international community 13
2. Involving the local community 15
3. Situations of particular vulnerability 17
4. Allocating scarce resources 20
5. Public health surveillance 23
6. Restrictions on freedom of movement 25
7. Obligations related to medical interventions for the diagnosis, treatment, and prevention of infectious disease 28
8. Research during infectious disease outbreaks 30
9. Emergency use of unproven interventions outside of research 35
10. Rapid data sharing 38
11. Long-term storage of biological specimens collected during infectious disease outbreaks 39
12. Addressing sex- and gender-based differences 41
13. Frontline response workers' rights and obligations 43
14. Ethical issues in deploying foreign humanitarian aid workers 47

Public Health Ontario | Santé publique Ontario

Source: http://thelancet.com/journals/langlo/issue/vol4no7/PIIS2214-109X(16)X0008-3

Public Health Ontario | Santé publique Ontario

Source: www.thelancet.com/lancetgh

Editorial

The right(s) approach to Zika

"The face of Zika is not often seen in the air-conditioned shopping malls of upscale Rio neighbourhoods or on the beaches of Ipanema. Rio has its fair share of cases, but so far the heaviest burden has been borne by the northeast region of Brazil, where poverty, poor infrastructure, and lack of access to health services are rampant, and the penetration of Aedes aegypti is high. A large proportion of the population in that region is of African descent—indeed, the face of Zika is often that of a darker-skinned person. And because most cases are asymptomatic, and the most dramatic signs of the disease appear through congenital Zika syndrome, the face of Zika is that of a woman or a small child. That is at least what we are able to outline, because in spite of the need for disaggregated epidemiological data to understand transmission patterns and evaluate interventions in vulnerable populations, there is no reliable count of Zika cases by sex and ethnicity."

Public Health Ontario | Santé publique Ontario

Source: https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-0036-1593411

Public Health Ontario | Santé publique Ontario

A gendered human rights analysis of Ebola and Zika: locating gender in global health emergencies

SARA E. DAVIES AND BELINDA BENNETT*

Globally, gender remains a key determinant of health.[1] Alcohol consumption, violence, deaths related to road injuries and sexually transmitted infections may be accounted for by the intersecting gendered inequalities and gender norms that determine the health of both men and women. Any attempt to address the gendered dimensions of health faces complex challenges that go beyond sex-specific health needs based on biological difference to understandings of health as socially and economically determined.[2]

 Source: *International Affairs* **92**: 5 (2016) 1041–1060

Public Health Ontario | Santé publique Ontario

Source: http://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(16)30332-2.pdf

Comment

Zika virus and global health security

A recent poll found that 77% of the US public is not seriously concerned about Zika virus.[1] Congress went on summer recess without authorising President Obama's US$1·8 billion emergency Zika appropriation request. By Aug 30, 2016, the US Centers for Disease Control and Prevention had spent $194 million of the $222 million allocated to respond to the Zika virus outbreak.[2] WHO's $122 million strategic plan for response, to be implemented until December, 2017, grossly underestimates the resources required. Still worse, WHO has raised only $14·2 million in direct contributions for a worldwide response.[3] WHO's emergency contingency fund has a meagre balance of $31·5 million, spread thinly among ongoing health threats.[4] Consequences of Care Act. These policies make reproductive, maternal, and health services unaffordable or inaccessible. Poor women often have long waits for Zika virus testing, maternal, and other health services.

Up to 6% of Zika-virus-infected pregnant women will miscarry or have stillborn deliveries.[5] Actual rates might be even higher. Surviving infants have as much as a 13% chance of Zika-virus-related microcephaly and associated mental, ocular, and hearing impairments.[6] Recent studies suggest that Zika virus infection can cause severe joint damage and genitourinary, cardiac, and digestive complications among affected infants.[7] Many could be impaired in less obvious ways, with disabilities appearing later in a child's development.

Zika and Global Health Security – Some Facts

WHO strategic response plan needs until end-2017	$122 million!!!
International funds raised by WHO to mid-August 2016	$14.5 million
WHO emergency contingency fund for all health threats	$31.5 million
World Bank estimates of economic losses, Latin America, to date	$3.5 billion
World Bank offsetting loans to mid-August 2016	$155 million
CDC spending on Zika response activities by end-August 2016	$194 million of $222 million allocated

UNDP Report Conclusions

- The current Zika epidemic will have a long-term impact, and countries will incur high direct and indirect costs as a result.
- There is a profound equity challenge at the core of the Zika epidemic. The impact is disproportionate on the poorest countries of the region, as well as on the poorest and most vulnerable groups, especially poor women in peri-urban communities.
- Regional and national preparedness and response strategies require strengthening and must involve communities.

UNDP Report Recommendations

Given that Zika is likely to become endemic, budgetary plans should be established accordingly.

Integrate efforts aimed at multiple mosquito-borne viruses, allowing room to tailor approaches to each disease's unique effects.

Put equity considerations at the forefront of Zika strategies and provide adequate social protection mechanisms for those affected.

Promote public policies that support gender equality and promote sexual and reproductive health and rights, targeting affected communities.

Develop a multi-sectoral approach to mosquito-borne diseases both nationally and regionally.

PLOS | MEDICINE

ESSAY

Make Data Sharing Routine to Prepare for Public Health Emergencies

Jean-Paul Chretien[1]*, Caitlin M. Rivers[2], Michael A. Johansson[3]

1 Integrated Biosurveillance Section, Armed Forces Health Surveillance Branch, Defense Health Agency, Silver Spring, Maryland, United States of America, 2 Epidemiology and Disease Surveillance, US Army Institute of Public Health, Aberdeen Proving Ground, Maryland, United States of America, 3 Dengue Branch, Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, San Juan, Puerto Rico, United States of America

Source: Chretien J-P, Rivers CM, Johansson MA (2016) Make Data Sharing Routine to Prepare for Public Health Emergencies. PLoS Med 13(8): e1002109. doi:10.1371/journal.pmed.1002109

Figure 1. Timeline for the development and implementation of standardized research protocols for ZIKV

Source: WHO/Institut Pasteur Draft

Public Health Ontario | Santé publique Ontario

Our globally inter-connected reality

- The frontlines of infectious disease surveillance and response are not border-crossings/ports-of-entry.
- They are:
  - **Primary care/urgent care**
  - **Emergency departments/hospitals**
- EMS
- Community care
- LTC