Texas Task Force on Infectious Diseases Preparedness & Response

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From the MDGs to the SDGs

2000-15 MDGs

2016 SDGs
The Millennium Development Goals

1. Eradicate extreme poverty and hunger.
2. Achieve universal primary education.
3. Promote gender equality and empower women.
4. Reduce child mortality.
5. Improve maternal health.
7. Ensure environmental sustainability.
8. Develop a global partnership for development.
The Global Burden of Disease Study

Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010

The Global Burden of Disease 2013

Expanded use of vaccines
- 83% reduction in measles deaths
- 82% reduction in tetanus deaths
- 57% reduction in diphtheria/pertussis deaths
- 45% reduction in Hib deaths

Development new vaccines
- Pneumococcal disease (36% reduction in deaths)
- Rotavirus (63% reduction in deaths)

2.5 million childhood lives saved through these initiatives
• Texas ranks at the bottom of fully immunized children
• 45,000 Personal Belief Exemptions in Texas
Patches of Disorganization in the Neocortex of Children with Autism

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ABSTRACT

BACKGROUND

Autism involves early brain overgrowth and dysfunction, which is most strongly evident in the prefrontal cortex. As assessed on pathological analysis, an excess of neurons in the prefrontal cortex among children with autism signals a disturbance in prenatal development and may be concomitant with abnormal cell type and...
The Millennium Development Goals

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Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

• 19 million lives saved from AIDS
• 30% reduction in Malaria
Global Health Whack-a-Mole

NCDs

HIV/AIDS + Malaria
“Other Diseases”
The Neglected Tropical Diseases

- 13-14 tropical infections:
  - Highly prevalent among the poor
  - Endemic in rural areas of low-income countries
  - Ancient afflictions
  - Chronic
  - Disabling (growth delays, blindness or disfigurement)
  - Stigmatizing
  - Poverty promoting
NTDs Global Burden Disease Study 2013-14

- Ascariasis 804.4 million
- Trichuriasis 477.4 million
- Hookworm Disease 471.8 million
- Schistosomiasis 290.6 million
- Food-borne Trematodiases 80.2 million
- Dengue 58.4 million
- Lymphatic Filariasis 43.8 million
- Onchocerciasis 17.0 million
- Chagas disease 9.4 million
- Leishmaniasis 4.0 million
- Zika 4.0 million*
- Trachoma 2.4 million
- Cysticercosis 1.0 million
- Echinococcosis 0.8 million
- Ebola 28,000
- Rabies 23,500
- African Trypanosomiasis 19,700
- Yaws Not determined
- Buruli ulcer Not determined
USAID NTD Program

>450 million People Rx
Emergence of Dengue, Zika, and Chikungunya
Zika is an arbovirus and a flavivirus

**FLAVIVIRUSES (ss +RNA)**
- Dengue Virus
- Yellow Fever Virus
- Japanese Encephalitis Virus
- West Nile Virus
- St. Louis Encephalitis Virus
- Zika Virus

**TRANSMITTED BY AEDES MOSQUITOES**
- Dengue, YF but NOT WNV
Aedes mosquitoes including *Aedes aegypti* (*humans*) and *Ae. albopictus* (*mammals, birds*) in New World.
Origins in the Zika Forest of Uganda

Zika means “Overgrowth”  
*Aedes africanus* vector

Found in 1947  
Virus Isolation published in 1952  
First human case in Nigeria in 1954  
14 cases in Africa
Zika Path: Explosive Pacific Outbreaks
What made Zika spread so quickly?

• Hypothesis 1: Something uniquely Zika*
  - “Pandemic strain” of Zika vs. African strain
  - Codon usage of NS1 gene
  - Increases fitness for replication in human host without changes in protein sequence
  - Codon usage by pandemic strains is optimized for replication in human cells
  - Higher viremias and increased infectivity for mosquitoes
  - Evolutionary strain

*Maj Gen Philip K Russell MD
Asian vs African Lineage

Nucleotide sequences from 41 strains were included in the analysis: 30 human isolates (including two newly reported here), ten mosquito isolates, and one monkey isolate.

From Mosquitos to Humans: Genetic Evolution of Zika Virus.
Pre-M Protein

PrM protein of ZIKV shows significant structural alterations

PrM forms a heterodimer with the main viral surface protein, E, in the neutral pH of the lumen of the endoplasmic reticulum (ER)

The role of prM in viral pathogenesis has been under extensive investigation over the past few years. It has been shown that prM plays a critical role in viral assembly, maturation, heterodimer formation with the E protein, particle secretion, and virulence

From Mosquitos to Humans: Genetic Evolution of Zika Virus.
What made Zika spread so quickly?

• Hypothesis 2: Immune enhancement*
  - Previous flavivirus epidemics – dengue or chikungunya
  - Non-neutralizing cross reactive antibodies
  - Penetration of cells through Fc receptor
  - Increased virus replication
  - Zika virus enhanced in culture by heterologous flaviviruses
  - Dengue overlap

*Maj Gen Philip K Russell MD
What made Zika spread so quickly?

• Hypothesis 3:

• Zika is going by the same playbook used by dengue and chikungunya

• Part of a general expansion of insect and snail-transmitted diseases into the Americas and Europe
Same thing happening in Southern Europe, Why?
The Anthropocene is a proposed epoch that begins when human activities started to have a significant global impact on Earth's geology and ecosystems.
Anthropocene forces promoting NTDs

- Poverty
- Deforestation
- Conflict and Political Destabilization
- Urbanization and Human Migrations
- Climate Change
POVERTY: “Blue Marble Health”

- Neglected diseases of the poor living amidst wealth
- A new framework for global science policy and the poverty-related diseases
Blue Marble Health:
The poor living among the wealthy (G20 + Nigeria)

G20 + Nigeria = 54% Population and 86% Global Economy

WHO + GBD 2013
• 73-78% Leprosy
• 61-78% Chagas
• 60-61% Dengue
• 57-60% TB
• 45-67% VL
• 50-52% Helminths

- STH
- Schistosomiasis
- Lymphatic Filariasis
- Onchocerciasis

http://www.plosntd.org/article/info:doi/10.1371/journal.pntd.0002570
Brazil and Blue Marble Health

Introduction to Brazil

LARGEST Economy in Latin America

5th Largest country by land mass + population

7th Largest economy by nominal GDP

Member MERCOSUL Member BRICS

Poverty & Disease NE Brazil:
Schistosomiasis, Leishmaniasis, Chagas, Dengue
Zika Microcephaly cases in NE Brazil

Updated as of Epidemiological Week 48
(Nov 29 - Dec 5, 2015)

Microcephaly rates by state in Brazil, 2015
(cases per 100,000 live births)
- 1
- 10
- 100

Microcephaly rates by state in Brazil, 2010-2014
(cases per 100,000 live births)
- 1
- 5
- 10

Countries with Zika confirmed cases
- in 2015
- in 2014
- Country limits
- Brazil state boundaries

One case of autochthonous transmission of Zika virus infection in Easter Island, Chile, 2014. The presence of the virus was reported until June of the same year and was not detected later.

Data Source:
Reported from the IHR National Focal Points and through the Ministry of Health websites.

Map Production:
PAHO-WHO AC/CHA IR/00
Poverty in Northeastern Brazil

Recife

Salvador de Bahia
The Most Vulnerable

Predicted locations of the yellow fever mosquito, which transmits the Zika virus and other diseases.

Source: Marcia U. G. Kraemer et al., eLife Sciences; Simon Hay, University of Oxford

By The New York Times
Poverty in Houston TX

Houston’s Historic Wards

Anna Grove Photographer
>12 million Americans with NTDs
Toxocariasis 3 million
Chagas disease 1 million
Trichomoniasis 7 million
Cysticercosis 0.2 million
Toxoplasmosis 1 million
Dengue 0.1 million
Chagas disease in Texas

New CDC Estimates

- 36,977 cases
- Not including undocumented

One Health Interactions of Chagas Disease Vectors, Canid Hosts, and Human Residents along the Texas-Mexico Border
Zoonotic Helminth Infections & Brain: Toxocariasis & Cysticercosis in Texas
WAR & POLITICAL DESTABILIZATION: Ebola

Data are based on reported cases up to the end of 13 September 2014 for Guinea and Sierra Leone. Data for Liberia are based on reported cases up to the end of 9 September 2014. The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
ISIS-Occupied Syria, Iraq, Libya
Yemen

- Measles/Polio
- Leishmaniasis
- Schistosomiasis
- Brucellosis
- MERS CoV
- Dengue
- Malaria/TB
- Rift Valley Fever
Clinical Zika

Fever
Maculopapular Rash (pruritic)
Headache
Conjunctivitis
Retroorbital pain
3 Schematic of the course of human and mosquito infection.

Justin Lessler et al. Science 2016;science.aaf8160

Published by AAAS
Guillain-Barre syndrome

- Recent history of zika (within 6 days)
- Zika IgM/IgG
- 1/3 respiratory assistance
- Anti-glycolipid antibody (GA1)
- Guillain Barre
  1/1,000 French Polynesia
  554 cases in Brazil
  Increase in El Salvador
MICROCEPHALY

Abnormal size of the head, a congenital condition associated with Zikia and other pathogens. Zika Virus, transmitted by Aedes Aegypti mosquitoes, can lead to microcephaly, which is mainly seen in South America.
The fetal brain disruption sequence is a recognizable pattern of defects that includes moderate to profound microcephaly, overlapping sutures, occipital bone prominence, and scalp rugae. The condition is postulated to arise from partial brain disruption…with subsequent fetal skull collapse resulting from decreased intracranial hydrostatic pressure. Recognition of this phenotype is critical because the condition has a uniformly poor prognosis for infants but the recurrence risk in future pregnancies is low.

IS ZIKA MICROCEPHALY RESTRICTED TO BRAZIL?

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Zika Cases</th>
<th>Microcephaly Cases</th>
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<tbody>
<tr>
<td>Brazil</td>
<td>196,976</td>
<td>2,001</td>
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<tr>
<td>Colombia</td>
<td>95,639</td>
<td>42</td>
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<td>Venezuela</td>
<td>58,212</td>
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<td>Martinique</td>
<td>36,445</td>
<td>12</td>
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</table>
PAHO/WHO Mosquito Eradication Campaign 1947-1962
US has no track record in *Aedes aegypti* control

- US did not participate in PAHO Eradication Program
- Began in 1965 halted in 1969
GMO Aedes Mosquitoes “The company's scientists genetically alter the male mosquitoes so that any offspring they father don't develop properly. These genetically modified males mate with the females, which lay dud eggs.”
Zika Vaccine Development Timeline

2016
- DNA vaccine candidate (NIAID VRC): Preclinical Discovery
- Zika purified inactivated vaccine candidate (WRAIR/NIAID/BARDA and Sanofi Pasteur): Preclinical Discovery
- Live-attenuated Zika/dengue chimeric virus (NIAID intramural/Butantan): Preclinical Discovery
- Vesicular Stomatitis Virus vectored vaccine (NIAID extramural): Preclinical Discovery/ Tech Transfer
- mRNA vaccine candidate (NIAID VRC, GSK): Preclinical Discovery

2017
- DNA vaccine candidate (NIAID VRC): Phase 1
- Zika purified inactivated vaccine candidate (WRAIR/NIAID/BARDA and Sanofi Pasteur): Phase 1/2
- Live-attenuated Zika/dengue chimeric virus (NIAID intramural/Butantan): Phase 1
- Vesicular Stomatitis Virus vectored vaccine (NIAID extramural): Phase 1
- mRNA vaccine candidate (NIAID VRC, GSK): Phase 1

2018
- DNA vaccine candidate (NIAID VRC): Long term follow up
- Zika purified inactivated vaccine candidate (WRAIR/NIAID/BARDA and Sanofi Pasteur): Phase 2b
- Live-attenuated Zika/dengue chimeric virus (NIAID intramural/Butantan): Phase 2/2b
- Vesicular Stomatitis Virus vectored vaccine (NIAID extramural): Phase 2
- mRNA vaccine candidate (NIAID VRC, GSK): Phase 3

AS Fauci/NIAID

Legend:
- Blue: Intramural NIAID and partnerships
- Red: Extramural NIAID and partnerships
Sabin PDP Pipeline and Disease Portfolio

2000 to 2004
- Built structure
- Launched Hookworm Program

2004 to 2011
- Expanded Hookworm Program
- Schisto Program
- Relocated to TMC

2011 to 2015
- Added 7 additional programs
- Expansion of capabilities

Programs:
- Hookworm
- Schistosomiasis
- Leishmaniasis
- Chagas Disease
- Trichuriasis
- Ascarisiasis
- West Nile
- SARS
- Onchocerciasis
Therapeutic Chagas Disease Vaccine

Figure 9: Immune response of chronically infected female ICR mice vaccinated therapeutically. IFNγ and IL-4 release from acutely infected and therapeutically vaccinated ICR splenocytes restimulated in vitro with 100µg/mL Tc24 protein.

Increased Ag-specific IFNγ
Decreased T. cruzi burden
Decreased Cardiac fibrosis
Leishmaniasis Vaccine

• Bivalent recombinant vaccine
  - NH36
  - Sandfly antigens: LJM19 LJM143
  - GLA or CpG
U.S. Science Envoy Program

Office of Science and Technology Policy

Texas Children's Hospital