




Diseases of the Poor in Texas

New innovations for a diseases of poverty : Globally and in Texas

Peter Hotez MD PhD

Sabin Vaccine Institute & Texas Children's Hospital Center for Vaccine Development

National School of Tropical Medicine

Baylor College of Medicine

"The Bottom 100 Million"
Latin American & Caribbean (LAC) Region

- **Total population of LAC is 578 million people**
  - 48 million people live on <US$1.25 per day (8%)
  - 99 million people live on <US$2 per day
  - 189 million "poor" according to CEPAL (UN Economic Commission for LAC)

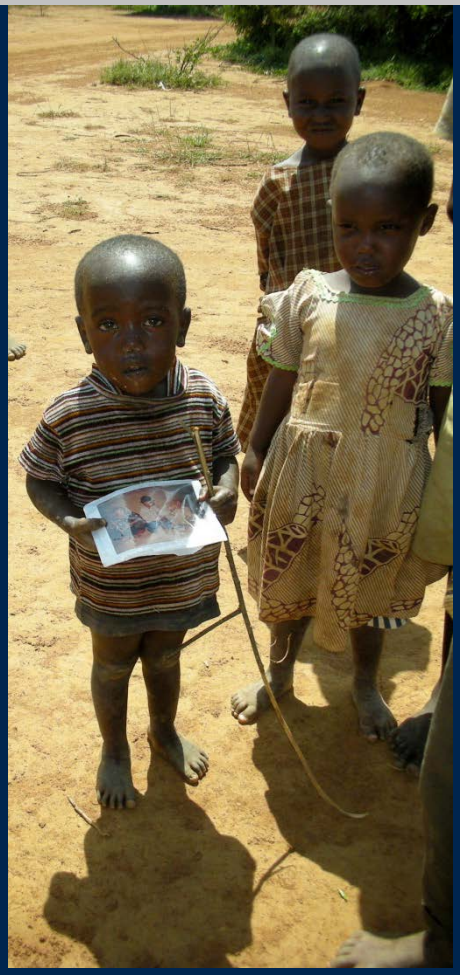
Hotez et al. 2012. Adv Exp Med Biol

Human Development Indices in LAC equivalent to Sub-Saharan Africa or Asia

Country	HDI	Comparator Countries
- Haiti	148	Sudan, Kenya
- Guatemala	121	South Africa, Gabon
- Nicaragua	120	South Africa, Gabon
- Honduras	117	Mongolia, Kyrgystan
- Bolivia	111	Egypt, Indonesia
- Guyana	110	Egypt, Indonesia
- El Salvador	101	Algeria, Cape Verde, Vietnam
- Paraguay	98	Sri Lanka, Iran

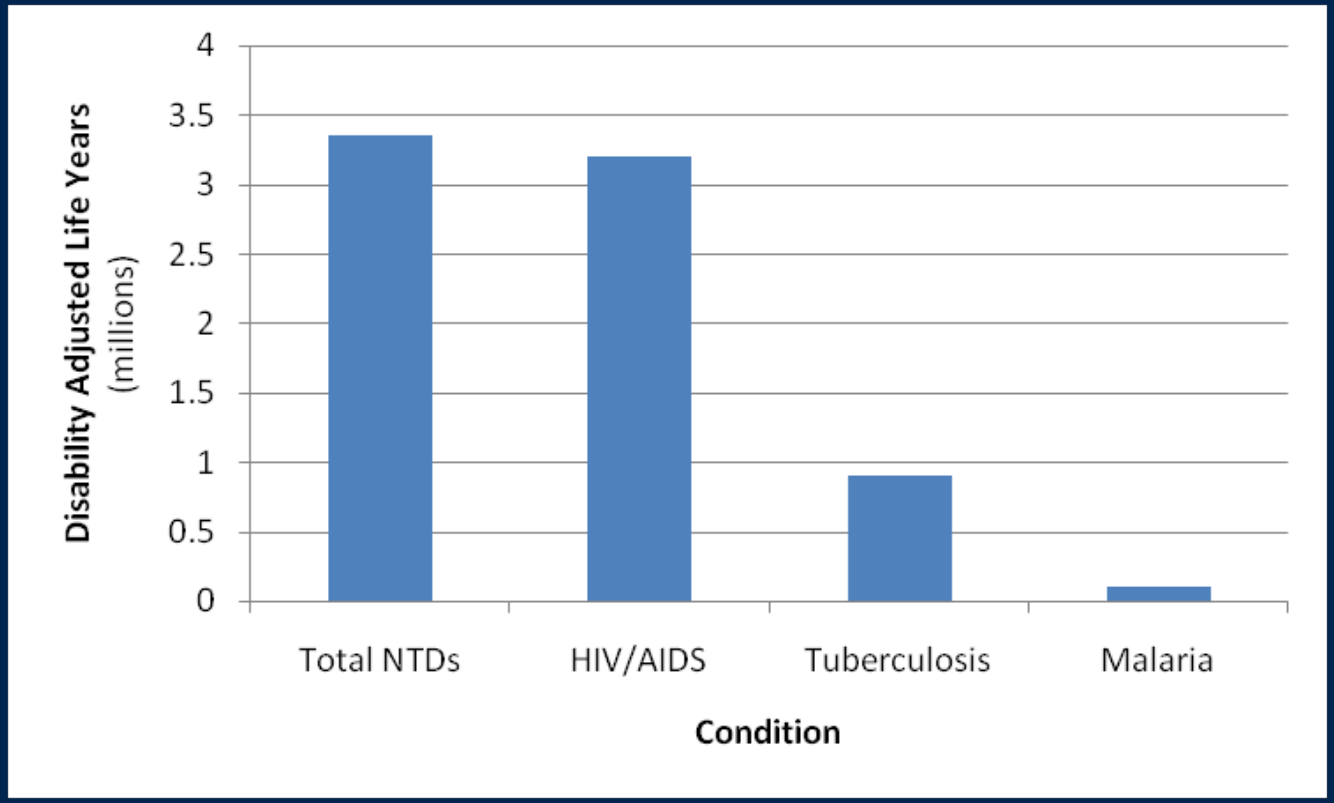
Hotez et al 2012
Adv. Exp. Biol. Med.

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.
6. Combat HIV/AIDS, malaria, and other diseases
7. Ensure environmental sustainability.
8. Develop a global partnership for development.

NTD Disease Burden in the Americas:
Higher than HIV/AIDS or Malaria?



Hotez, Bottazzi, et al. 2008. PLoS NTDs

The NTDs of LAC

Disease	DALYs	No. Cases	% Poor infected
- Hookworm	≤1.9 million	30 million	30%
- Ascariasis	≤1.1 million	85 million	85%
- Trichuriasis	≤1.1 million	71 million	71%
- Chagas	0.7 million	10 million	10%
- Schistosomiasis	0.1 million	2 million	2%
- Dengue	0.1 million	1 million	1%
- Leishmaniasis	0.1 million	<100,000	<1%
- LF	0.1 million	Not Determined	N.D.

NTDs
PROMOTE
POVERTY

NTDs and Poverty

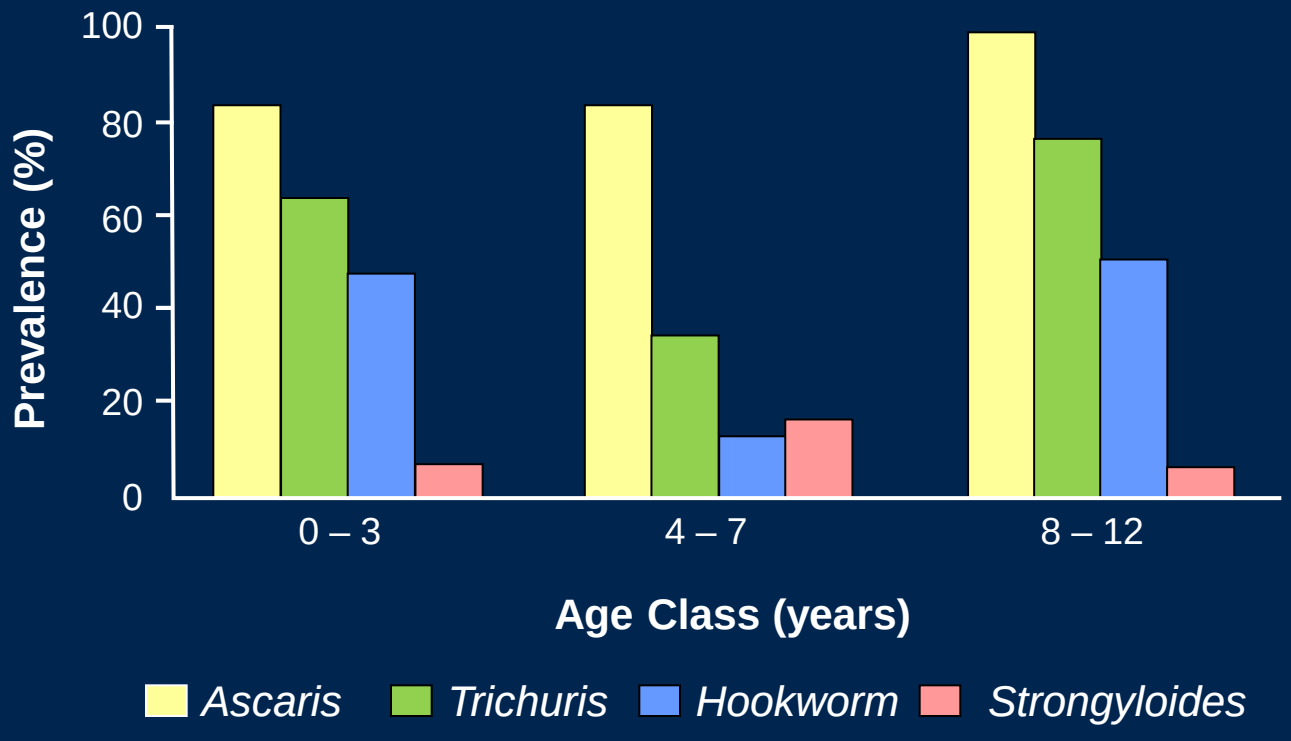
17 Chronic & Disabling Conditions

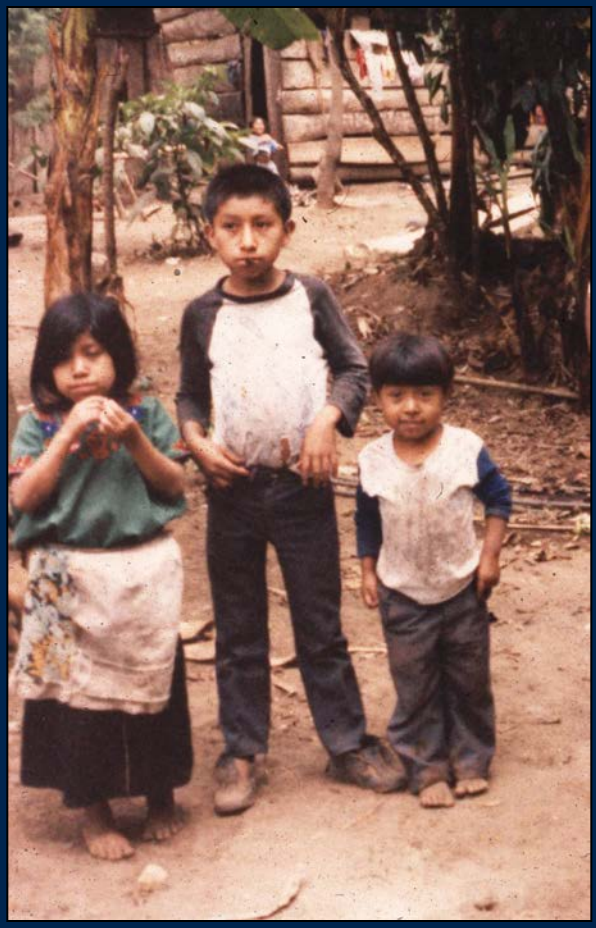
- **Reduce productive capacity**
- **Impair intellectual & physical development in children**
- **Cause adverse pregnancy outcomes**

Hotez PJ, Fenwick A, Savioli L Molyneux DH. Rescuing the bottom billion through control of neglected tropical diseases. *Lancet* 2009; 373: 1570-6

Intestinal Helminth Infections:
Ascariasis, Trichuriasis, Hookworm
The most common diseases of the Bottom Billion children

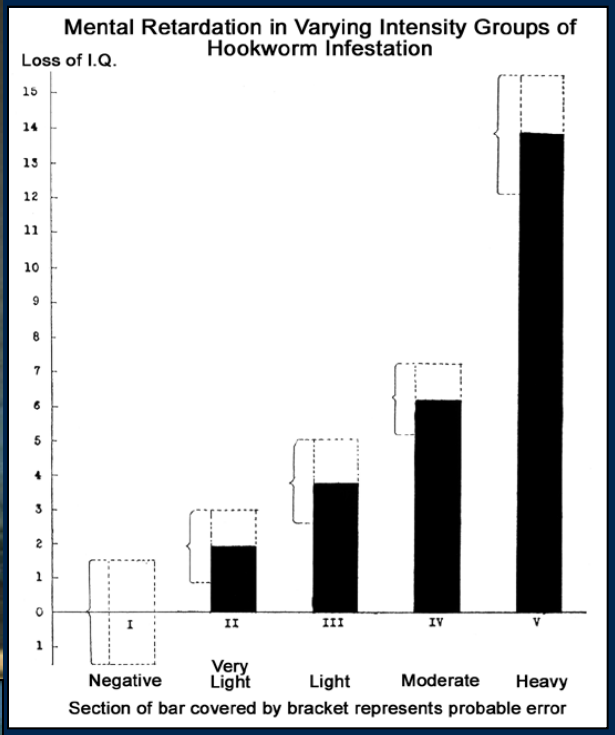
Village of Paquila, Guatemala

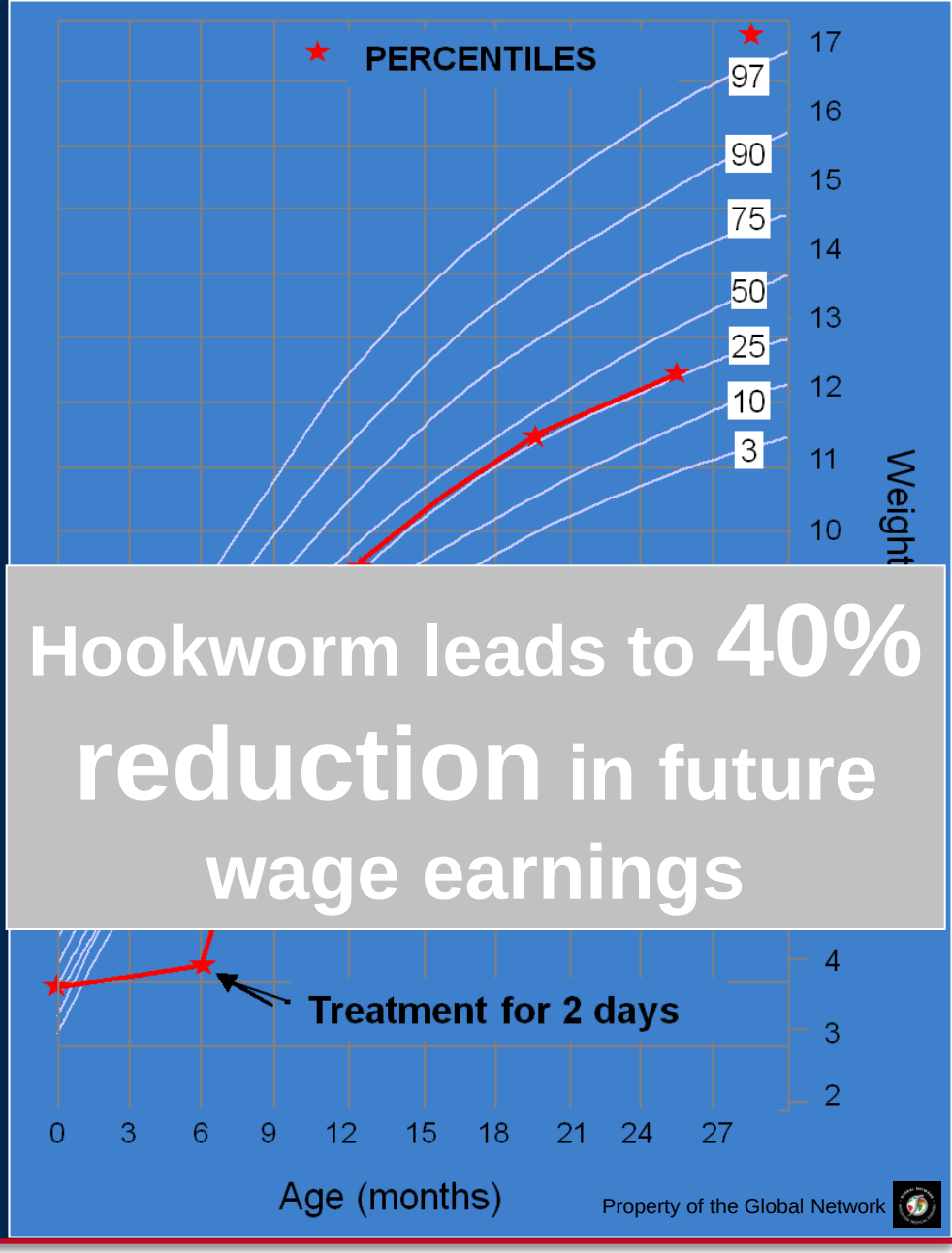




Child growth, development, and Education

Intestinal Worm Infections
Hookworm, Ascariasis



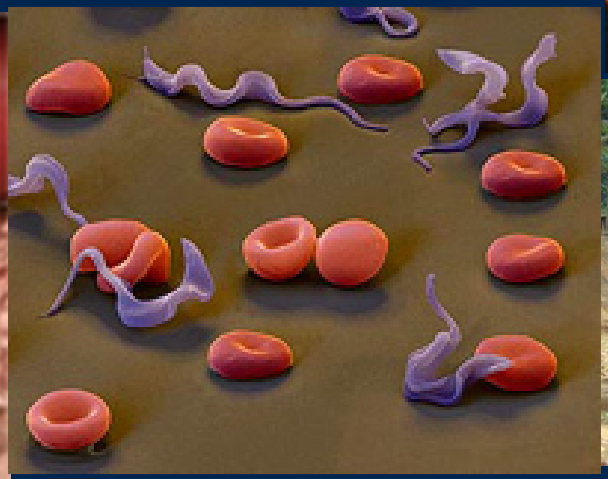


Hookworm leads to 40% reduction in future wage earnings

Chagas disease

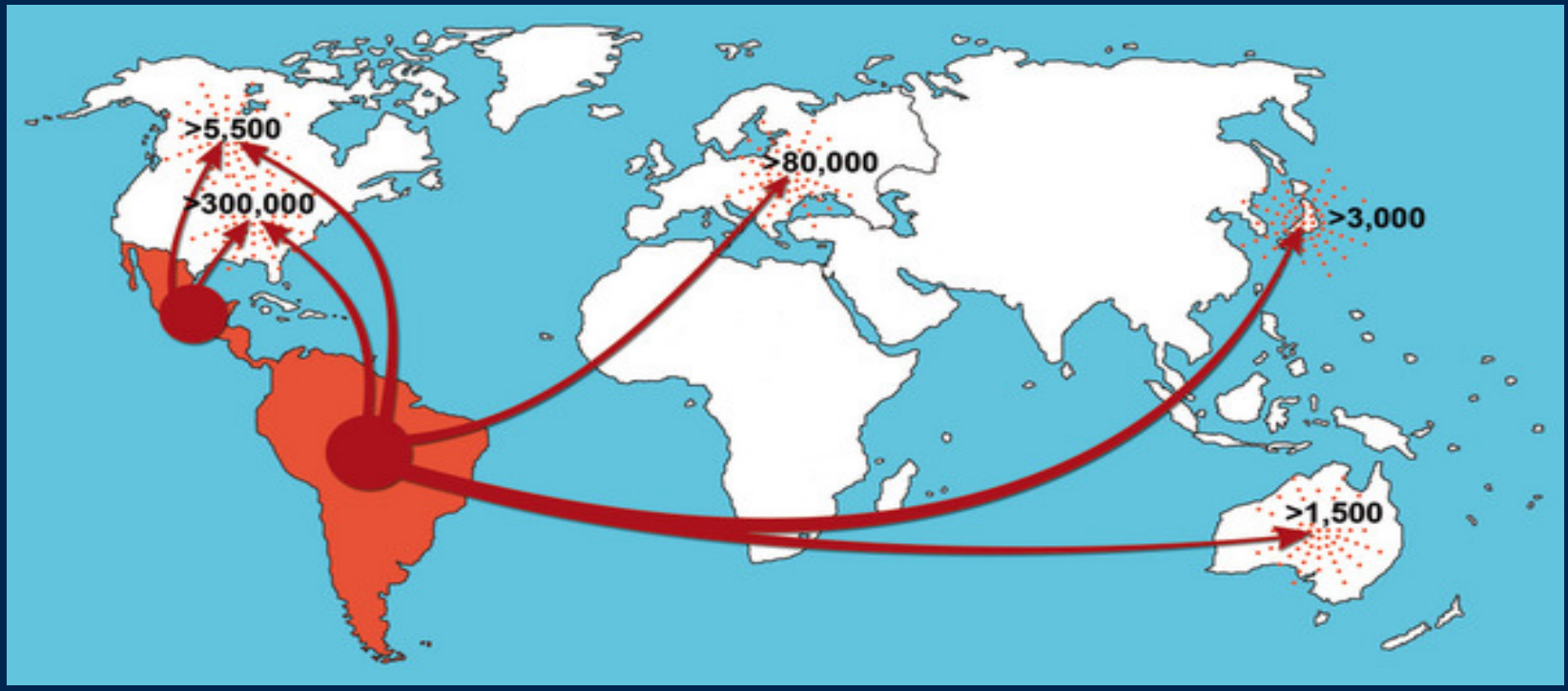
American Trypanosomiasis

- 10 million cases worldwide;
- 20,000 annual deaths
- >90% in Latin America
- $1.2 billion economic losses



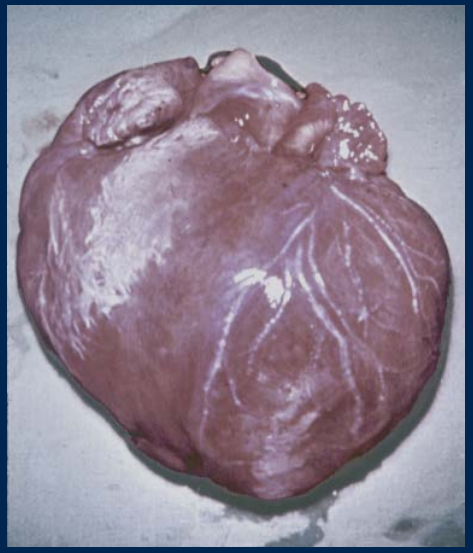
Geographic distribution of Chagas disease

Globalization of Chagas Disease



Chagasic Cardiomyopathy

- Develops in 20-30% of seroconverted pts
- Heart failure from persistence of Trypanosoma cruzi in the heart
  - •Conduction deficits (BBB)
  - •Aneurysms
  - •Thromboemboli
  - •Sudden death
- Rx fails in patients with cardiac disease (children do better)



Congenital Chagas disease

- 14,000-15,000 cases annually
    - 2,000 cases in North America including Mexico
- 300,000 pregnant women with Chagas disease
    - 40,000 in North America including Mexico
- 11% of pregnant women in Latin America
    - 34% of pregnant women in Bolivia
    - Pregnancy enhances parasitemia
    - Increased risk of miscarriage, preterm birth
- 5% (2-10%) transmission to infants
- Two major drugs contraindicated in pregnancy

Chagas disease: “The new American HIV/AIDS”?

10 million Chagas cases (6 million in North America)

- 2-3 million Chagasic cardiomyopathy
- >20,000 deaths annually
- 11% Pregnant women in Latin America
- Maternal-to-child transmission 5-10%
- Transfusion associated cases

1.6 million HIV/AIDS cases

- 3.2 million DALYs lost
- 105,000 deaths
- Maternal-to-child transmission 30%
- Transfusion associated cases

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PLoS NEGLECTED TROPICAL DISEASES

Editorial

Chagas Disease: “The New HIV/AIDS of the Americas”

Peter J. Hotez[1,2]*, Eric Dumonteil[3], Laila Woc-Colburn[2,4], Jose A. Serpa[2,4], Sarah Bezek[2,5], Morven S. Edwards[2,6], Camden J. Hallmark[2,7], Laura W. Musselwhite[8], Benjamin J. Flink[8], Maria Elena Bottazzi[1,2]

1 Departments of Pediatrics and Molecular Virology & Microbiology, and Sabin Vaccine Institute and Texas Children’s Center for Vaccine Development, Baylor College of Medicine, Houston, Texas, United States of America, **2** National School of Tropical Medicine, Baylor College of Medicine, Houston, Texas, United States of America, **3** Laboratorio de Parasitología, Centro de Investigaciones Regionales “Dr Hideyo Noguchi”, Universidad Autonoma de Yucatan, Merida, Yucatan, Mexico, **4** Section of Infectious Diseases, Department of Internal Medicine, Baylor College of Medicine, Houston, Texas, United States of America, **5** Department of Emergency Medicine, Baylor College of Medicine, Houston, Texas, United States of America, **6** Section of Infectious Diseases, Department of Pediatrics, Baylor College of Medicine, Houston, Texas, United States of America, **7** Houston Department of Health and Human Services, Houston, Texas, United States of America, **8** Duke University School of Medicine, Durham, North Carolina, United States of America

Endemic Chagas disease has emerged as an important health disparity in the Americas. As a result, we face a situation in both Latin America and the US that bears a resemblance to the early years of the HIV/AIDS pandemic.

Neglected tropical diseases (NTDs) are among the most common conditions afflicting the estimated 99 million people who live on less than US$2 per day in the Latin American and Caribbean (LAC) region [1]. Almost all of the “bottom 100 million” living in the Americas suffer from at least one NTD [1], and according to some estimates, the NTDs cause a burden of disease in the LAC region that closely approximates or even exceeds that resulting from HIV/AIDS [2]. Chagas disease (American trypanosomiasis) is a vector-borne disease and a leading cause of the deaths and disability-adjusted life years (DALYs) lost that result from NTDs in the LAC region [2]. With approximately 10 million people living with Chagas disease, this condition is one of the most common NTDs affecting the bottom 100 million in the region, a prevalence exceeded only by hookworm and other soil-transmitted helminth infections [1,2]. Moreover, among the NTDs in the Americas, Chagas disease ranks near the top in terms of annual deaths and DALYs lost [1,2].

While most of the world’s cases of Chagas disease occur in the LAC region, there is increasing recognition that many people with *Trypanosoma cruzi* infection also live in the US and Europe [3]. In practical terms, the “globalization” of Chagas translates to up to 1 million cases in the US alone, with an especially high burden of disease in Texas and along the Gulf coast [4,5], although other estimates suggest that there are approximately 300,000 cases in the US [6], in addition to thousands of cases documented in Canada, Europe, Australia, and Japan [3]. Among those living with Chagas disease around the world today, 20%–30% (roughly 2–3 million people) are either currently suffering from Chagasic cardiomyopathy or will develop this clinical sequela [7]. Chagasic cardiomyopathy is a highly debilitating condition characterized by cardiac arrhythmias, heart failure, and risk of sudden death from ventricular fibrillation or tachycardia or thromboembolic events [7]. Another estimate suggests that up to 5.4 million people living today will develop Chagasic cardiomyopathy [8,9]. Damage to the gastrointestinal tract can also produce debilitating megaesophagus and megacolon [7].

There are a number of striking similarities between people living with Chagas disease and people living with HIV/AIDS, particularly for those with HIV/AIDS who contracted the disease in the first two decades of the HIV/AIDS epidemic. Both diseases are health disparities, disproportionately affecting people living in poverty [1,2]. Both are chronic conditions requiring prolonged treatment courses: a lifetime of antiretroviral therapy for HIV/AIDS patients, and one to three months of therapy for those with Chagas disease [7]. Treatment for HIV/AIDS is lifesaving, although it seldom if ever results in cure, while for Chagas disease, the treatment has proven efficacy only for the acute stages of the infection or in children up to 12 years of age during the early chronic phase of the infection [10]. For both diseases the treatment is expensive in the case of Chagas disease, the expected cost of treatment per patient year is $1,028, with lifetime costs averaging $11,619 per patient [11]. Exacerbating costs, Chagas disease itself is a serious opportunistic infection of people living with HIV/AIDS, and is associated with meningoencephalitis, cerebral lesions, and high mortality [7]. As with patients in the first two decades of the HIV/AIDS epidemic, most patients with Chagas disease do not have access to health care facilities. A recent analysis indicates that many patients do not have access to the essential medicines for Chagas disease, in particular, the first line of therapy, the drug benznidazole [12]. According to Médecins Sans Frontières (MSF, Doctors Without Borders), many highly endemic countries, including Paraguay and Bolivia, face acute shortages of benznidazole, forcing thousands of newly diagnosed patients to postpone treatment [12]. Both diseases are also highly stigmatizing, a feature that for Chagas disease further complicates access to benznidazole and other essential medicines, as well as access to serodiagnosis and medical counseling. For some individuals with *T. cruzi* living in the US, immigration status presents an additional challenge to seeking care and prevention services. Just as stigma due to sexual orientation has been a barrier to HIV care and prevention, especially in the beginning of the epidemic, immigration status may function as a deterrent to Chagas disease care and prevention.

Citation: Hotez PJ, Dumonteil E, Woc-Colburn L, Serpa JA, Bezek S, et al. (2012) Chagas Disease: “The New HIV/AIDS of the Americas”. PLoS Negl Trop Dis 6(5): e1498. doi:10.1371/journal.pntd.0001498

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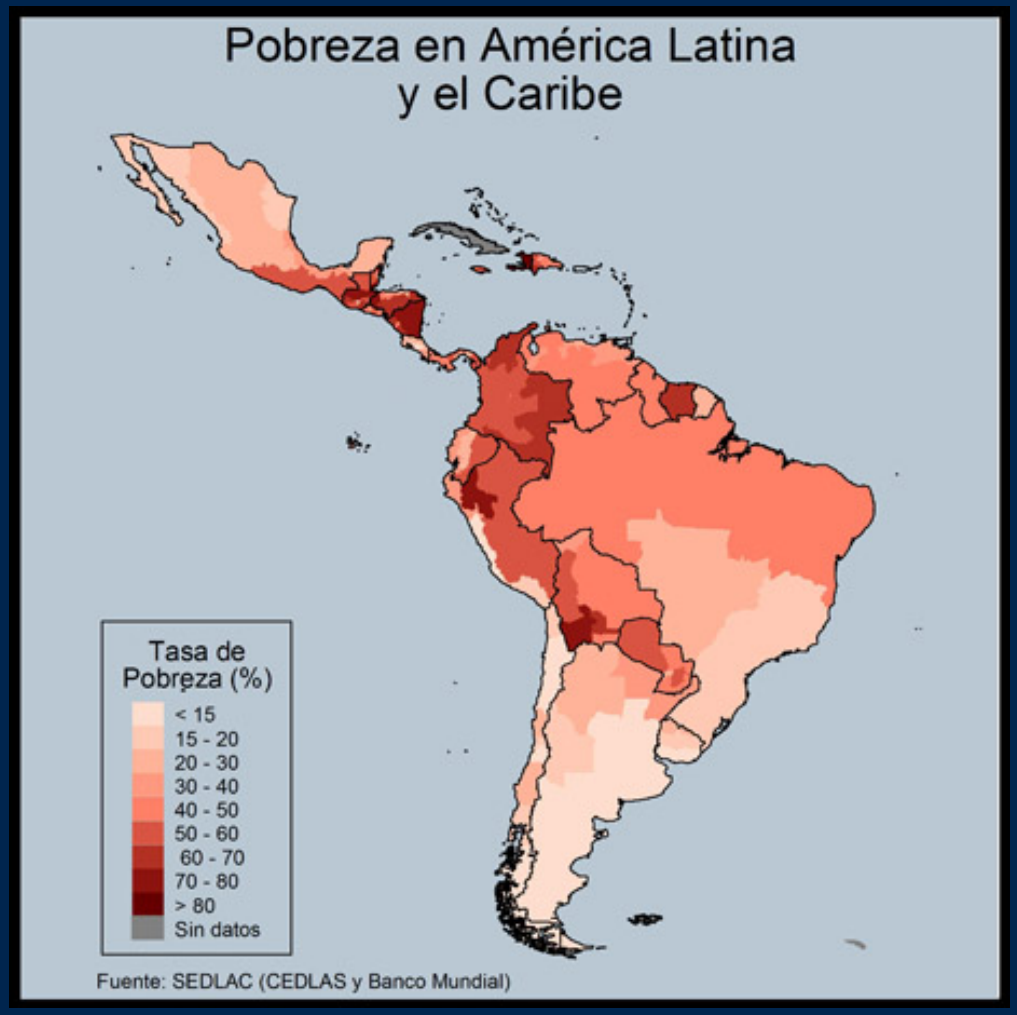
* E-mail: hotez@bcm.edu

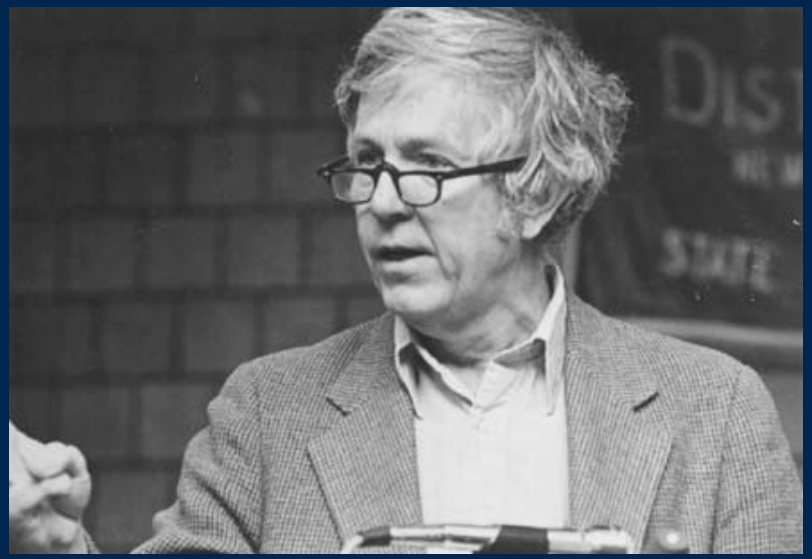
LAC poverty is not evenly distributed

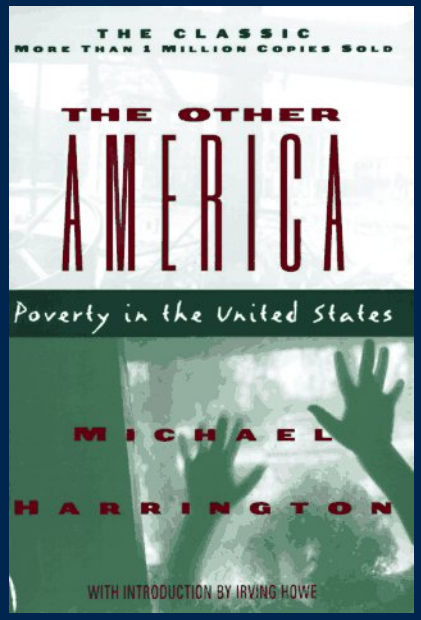
- Mesoamerica
  - Central America
  - Southern Mexico
- Northeastern Brazil
- Chaco
  - Bolivia/Paraguay
- Mountainous areas of Bolivia, Peru, Ecuador
- Caribbean
  - Haiti/Guyana



The Other America (1962)

To be sure, the other America is not impoverished in the same sense as those poor nations where millions cling to hunger as a defense against starvation. This country has escaped such extremes. That does not change the fact that tens of millions of Americans are, at this very moment, maimed in body and spirit, existing at levels beneath those necessary for human decency…They are without adequate housing and education and medical care.



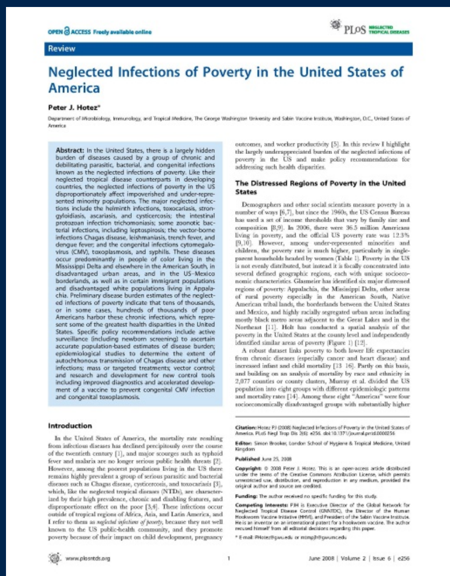


Poverty in the United States

United States

- 46 million Americans (15%) live below the poverty line
- 20 million Americans live in extreme poverty (<50% below poverty line)
- 1.46 million families (2.8 million children) on less than $2 per day
- Texas and the Gulf Coast have the highest rates of poverty

Poverty in the United States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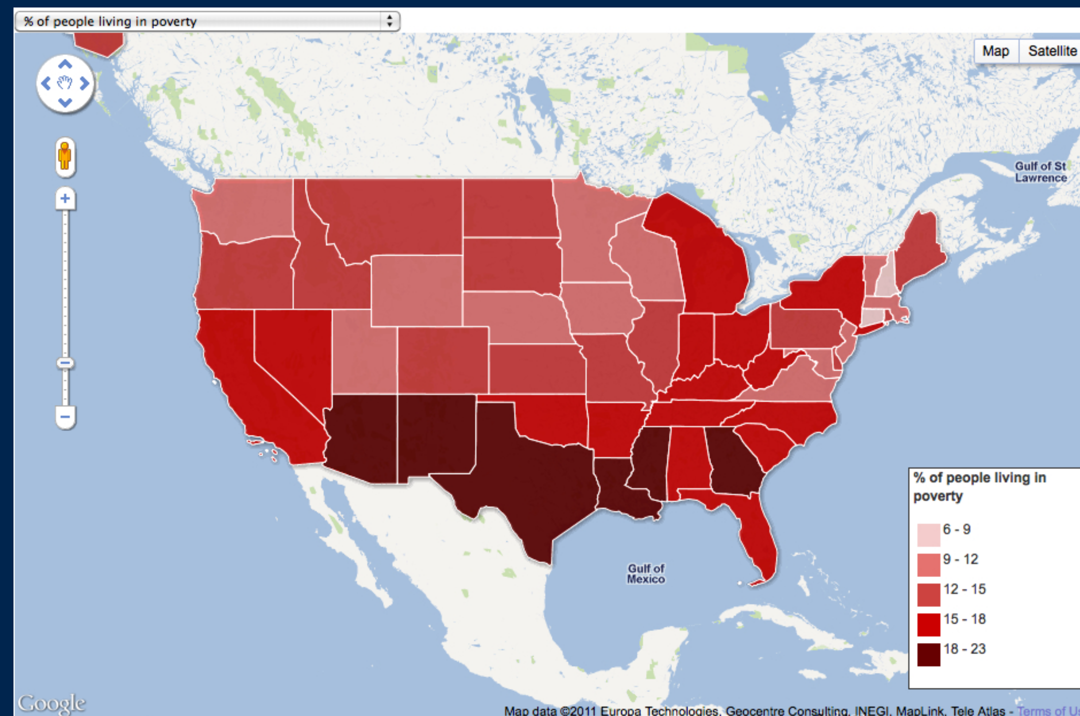
Review

Neglected Infections of Poverty in the United States of America

Peter J. Hotez



<u>5 million Americans with NTDs</u>

Toxocariasis 2.8 million

Chagas disease 1 million

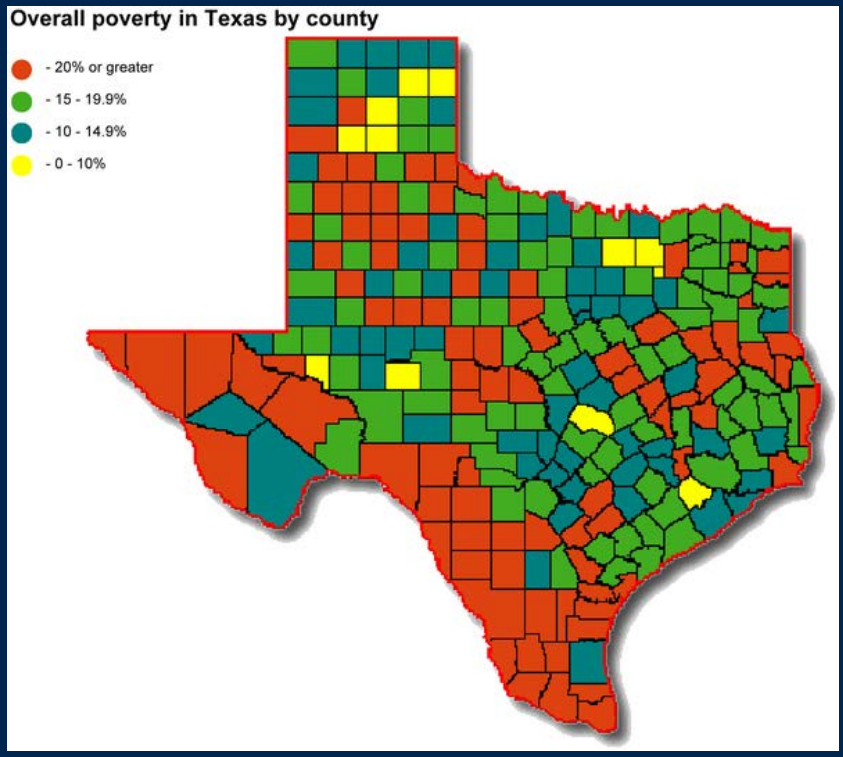
Trichomoniasis 0.8 million

Cysticercosis 0.2 million

Poverty in Texas

Texas

- Almost five million Texans live in poverty (most in U.S.)
- One in five Texans
- Poverty approaches 30% in South Texas counties of Zapata, Brooks, Starr
- “Colonias”



Hotez P. 2012. PLoS NTDs

Sharing a legacy of poverty and disease

- NTDs in Texas and Mexico
  - Chagas disease
  - Cysticercosis
  - Dengue
  - Leishmaniasis
  - Leprosy
  - Murine Typhus
  - West Nile virus infection

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PLoS NEGLECTED TROPICAL DISEASES

Editorial

Texas and Mexico: Sharing a Legacy of Poverty and Neglected Tropical Diseases

Peter J. Hotez[1*], Maria Elena Bottazzi[1], Eric Dumonteil[2], Jesus G. Valenzuela[3], Shaden Kamhawi[3], Jaime Ortega[4], Samuel Ponce de Leon Rosales[5], Miguel Betancourt Cravioto[6], Roberto Tapia-Conyer[6]

1 Sabin Vaccine Institute and Texas Children's Hospital Center for Vaccine Development, Section of Pediatric Tropical Medicine, Departments of Pediatrics and Molecular Virology & Microbiology, and National School of Tropical Medicine, Baylor College of Medicine, Houston, Texas, United States of America, 2 Laboratorio de Parasitología, Centro De Investigaciones Regional "Dr. Hideo Noguchi", Autonomous University of Yucatan (UADY), Merida, Mexico, 3 Vector Molecular Biology Section, Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, Maryland, United States of America, 4 Departamento de Biotecnología y Bioingeniería, Centro de Investigación y de Estudios Avanzados - Instituto Politécnico Nacional (CINVESTAV-IPN), Mexico City, Mexico, 5 Laboratorios de Biológicos y Reactivos de Mexico (BIRMEX), Mexico City, Mexico, 6 Instituto Carlos Slim de la Salud (ICSS), Mexico City, Mexico

A consortium of institutions from Texas and Mexico has launched a new initiative for developing vaccines and other tools to control and eliminate neglected tropical diseases in Mesoamerica.

The southern United States and northern Mexico not only share a border, they also share history, culture, and language. With its constant exchange of people and goods, the US Mexico border region (of which Texas represents a large proportion) can be considered a single, unique, epidemiological unit with its own difficulties and challenges. Although Mexico and Texas have benefited from widespread economic development and with it improvements in life expectancy and overall public health, many diseases in a group of infections known as the neglected tropical diseases (NTDs) still remain highly endemic on both sides of the Texas Mexico border. The NTDs are the most common infections of the poorest 120 million people in the Americas who live on less than US$2 per day [1]. They include ancient scourges such as hookworm and other soil-transmitted helminth infections, Chagas disease, amoebiasis, schistosomiasis, vivax malaria, leishmaniasis, and dengue [1]. Together, these NTDs produce a burden of disease in the western hemisphere that in certain regions even exceeds HIV/AIDS [1], while simultaneously trapping Latin America's "bottom 100 million" in poverty through their deleterious effects on child physical and intellectual development, pregnancy outcome, and worker productivity [2].

With the exception of schistosomiasis and lymphatic filariasis, most of the major NTDs found in Latin America are also endemic to Mexico [3] (Table 1). Because poverty is an overwhelming risk factor for exposure to NTDs, the estimated 52 million people (46% of the population) who live on less than 2,114 pesos (about US$180) per month in urban areas or 1,329 pesos in rural areas and who lack at least one basic social right suffer the highest rates of these infections. The estimated 11 million people (10% of the population) who live in extreme poverty (less than 978 pesos in urban areas, less than 684 pesos in rural areas) and lacking at least one social right [3] are especially vulnerable [4]. Most of the NTDs occur in Mexico's poorest states, led by the contiguous southern states of Chiapas, Guerrero, and Oaxaca [4]. Overall, these three southern states, in addition to neighboring Campeche, Quintana Roo, Veracruz, and Yucatan, exhibit the lowest human development indices in Mexico [5] (Figure 1). Soil-transmitted helminth infections are among the most common NTDs in Mexico, led by trichuriasis (18 million cases), ascariasis (9 million cases), hookworm infection (1 million cases), and toxocariasis (number of cases not determined) [1,6]. In rural Chiapas, *Necator americanus* hookworm infection is a significant cause of maternal-child anemia [7]. In addition, the incidence of cysticercosis, a soil-transmitted platyhelminth infection and a leading cause of epilepsy in Mexico, has been estimated at 0.4 per 100,000 people, with most of the cases in the southern states [5].

Equally important to Mexico are the major vector-borne NTDs, led by up to six million or more cases of Chagas disease (American trypanosomiasis caused by *Trypanosoma cruzi*), which are found primarily in the states of Chiapas, Oaxaca, Puebla, Veracruz, and Yucatan [8]. In addition to transmission by triatomine kissing bugs, both congenital infections and transfusion-related *T. cruzi* infections also occur [9]. Leishmaniasis is also endemic. Cutaneous leishmaniasis (CL) is responsible for 99% of the cases, mostly caused by *Leishmania mexicana* [5]. CL is hyperendemic in the state of Tabasco in association with the cocoa industry there. There are five possible vector species of the genus *Lutzomyia* responsible for the transmission of CL; *Lutzomyia olmeca* is the predominant species on the Yucatan peninsula and the incriminated vector in the state of Tabasco for CL [10]. Visceral leishmaniasis has also been reported

Citation: Hotez PJ, Bottazzi ME, Dumonteil E, Valenzuela JG, Kamhawi S, et al. (2012) Texas and Mexico: Sharing a Legacy of Poverty and Neglected Tropical Diseases. PLoS Negl Trop Dis 6(3): e1497. doi:10.1371/journal.pntd.0001497

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Competing Interests: Drs. Hotez and Bottazzi are principal investigators for vaccines against hookworm and schistosomiasis currently in development.

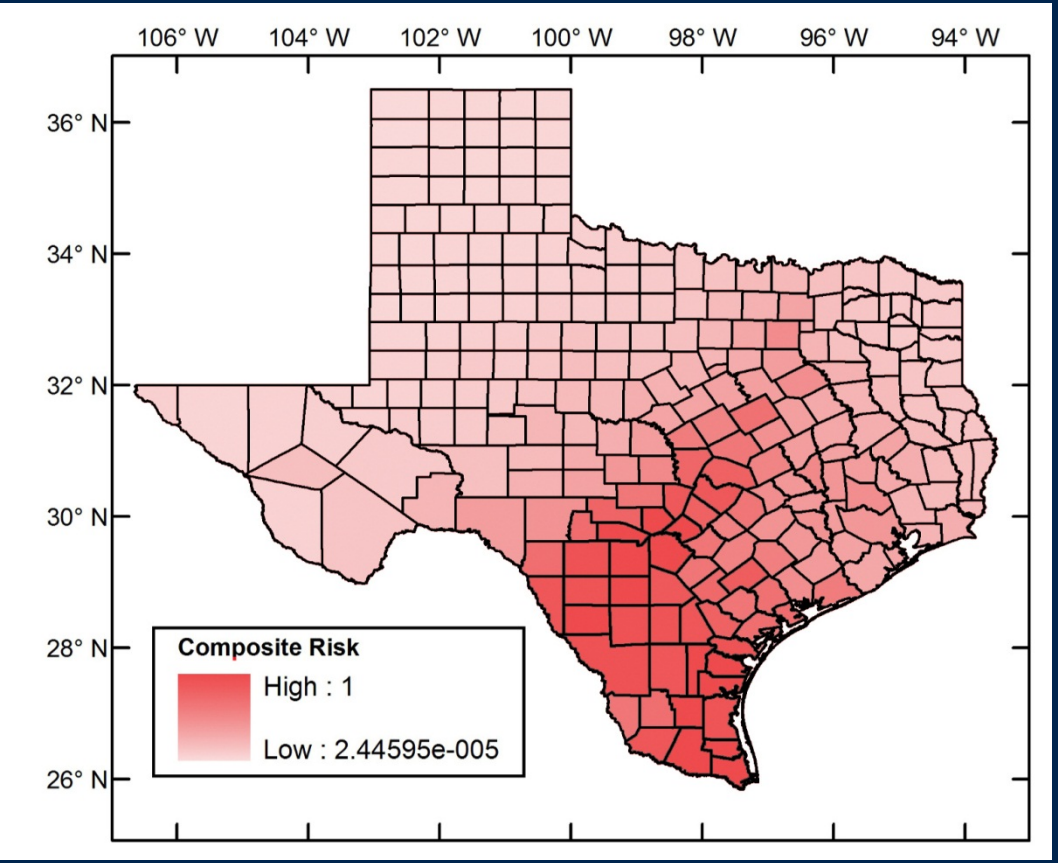
* E-mail: hotez@bcm.edu.

Peter Hotez, MD, PhD, and Maria Elena Bottazzi, PhD, are Dean and Associate Dean, respectively, of the National School of Tropical Medicine at Baylor College of Medicine, where they are also Professors of Pediatrics and Molecular Virology & Microbiology. Prof. Hotez is also the Texas Children's Endowed Chair of Tropical Pediatrics, President of the Sabin Vaccine Institute, and Co-Editor-in-Chief of *PLoS Neglected Tropical Diseases*. Eric Dumonteil, PhD, is Head of the Laboratorio de Parasitología, Centro de Investigaciones Regionales at UADY. Jesus Valenzuela, PhD, is Chief of the Vector Molecular Biology Section, Laboratory of Malaria and Vector Research at NIAID, NIH, and Shaden Kamhawi, PhD, is a Staff Scientist there. Jaime Ortega, PhD, is Professor in the Departamento de Biotecnología y Bioingeniería at CINVESTAV-IPN. Samuel Ponce de Leon Rosales, PhD, is Director General of Birmex. Miguel Betancourt Cravioto, MD, DrPH, is Director of Global Solutions at ICSS and Roberto Tapia Conyer, MD, PhD, is the Director General of ICSS.

PLoS NEGLECTED TROPICAL DISEASES

Chagas disease in Texas

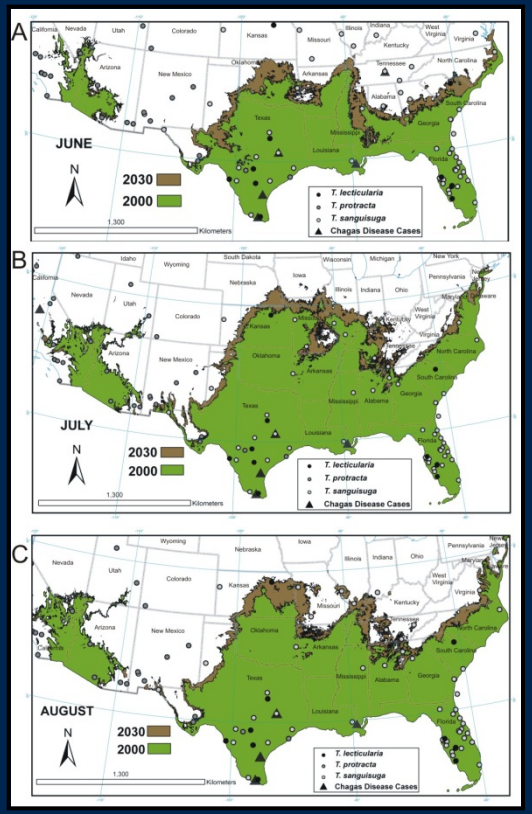
- Up to 267,000 human cases
- Endemic in dogs in South Texas (8%)
- Three major Triatoma spp
- Infected vectors in 82 of the 254 counties



Chagas Transmission in the U.S.

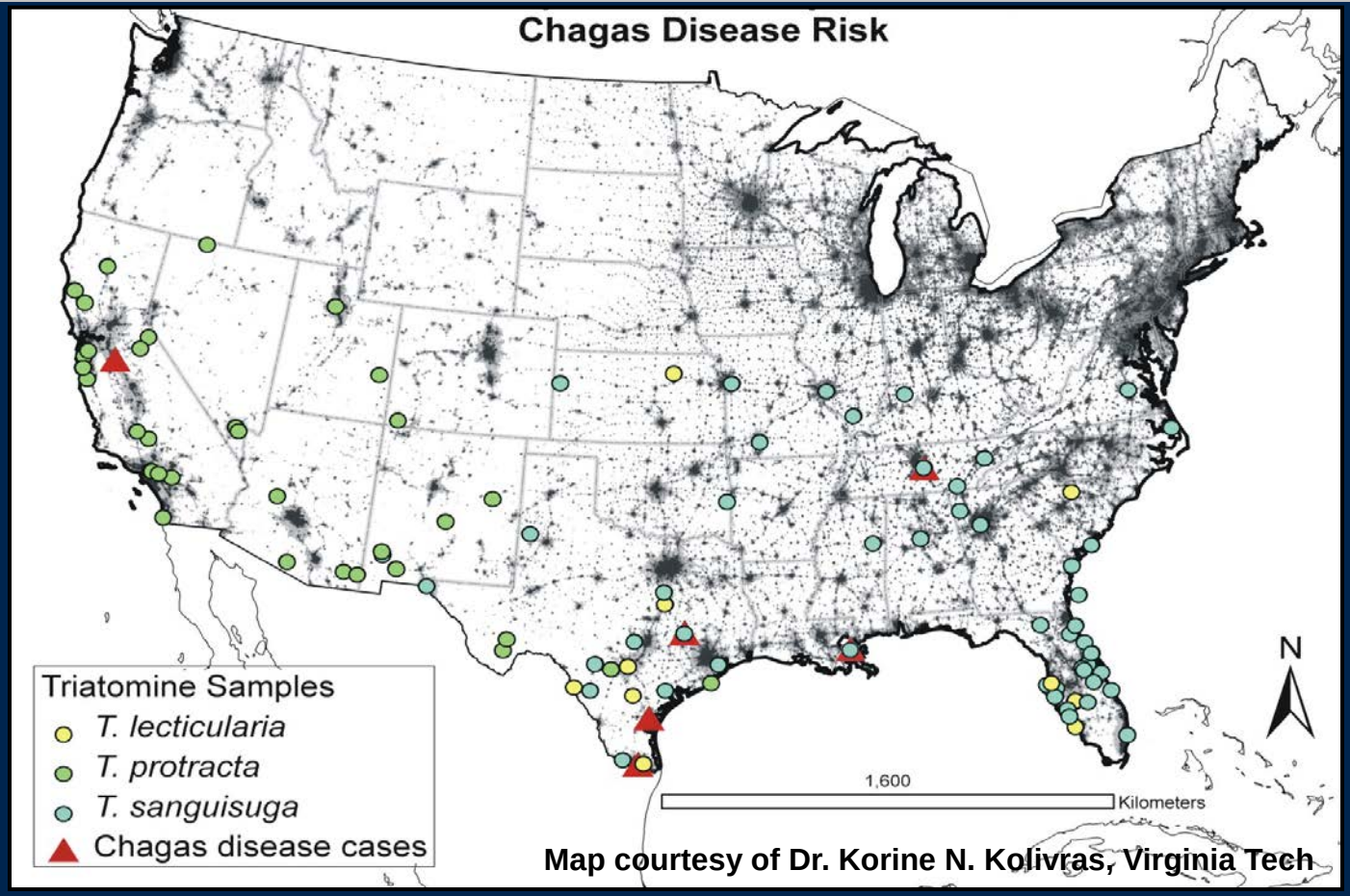
Risk Factors

- Triatomines in U.S.
  - 26 states
  - Generally sylvatic
  - *Triatoma sanguisuga* (6% *T. cruzi* infection rate)
  - *T. protracta* (20% *T. cruzi* infection rate)
  - *T. leticularia*
  - Delayed defecation by Triatomine species
  - Contaminated foods or mucous membranes
- Increased domesticity
- Zoonotic transmission from dogs
- Limited Physician Awareness
- Risk highest in lower latitudes in southern portion
  - Transmission 64-100ºF
  - Higher risk range upon 1.8ºF increase in temp by 2030



Lambert et al *Geospatial Health* 2008

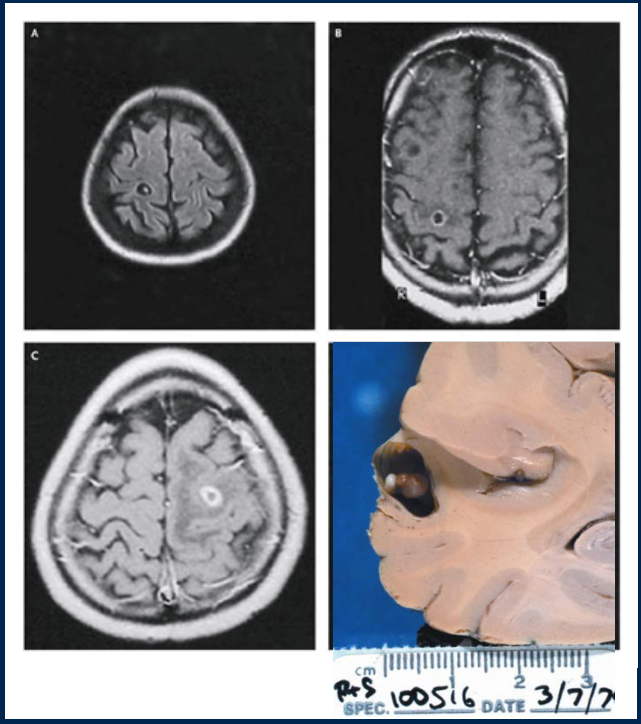
Triatomine vector has broad range in U.S.

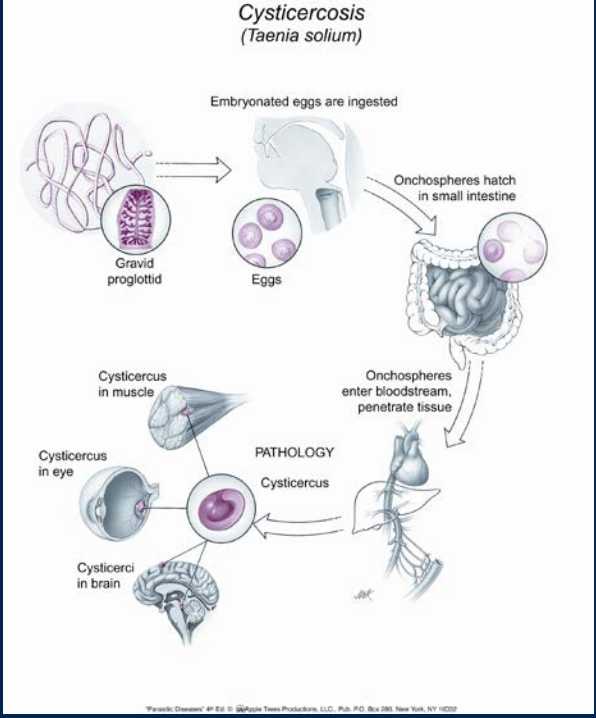


Map courtesy of Dr. Korine N. Kolivras, Virginia Tech

Cysticercosis *(Taenia solium)*

- Leading cause of epilepsy among Hispanic Americans
- (41,400-169,000 cases) based on 1.8% seroprevalence
- 10% of seizures presenting to ED in Los Angeles

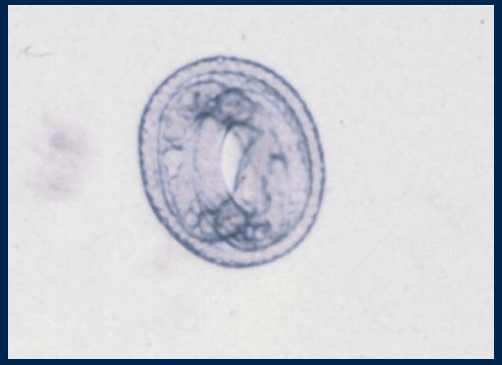


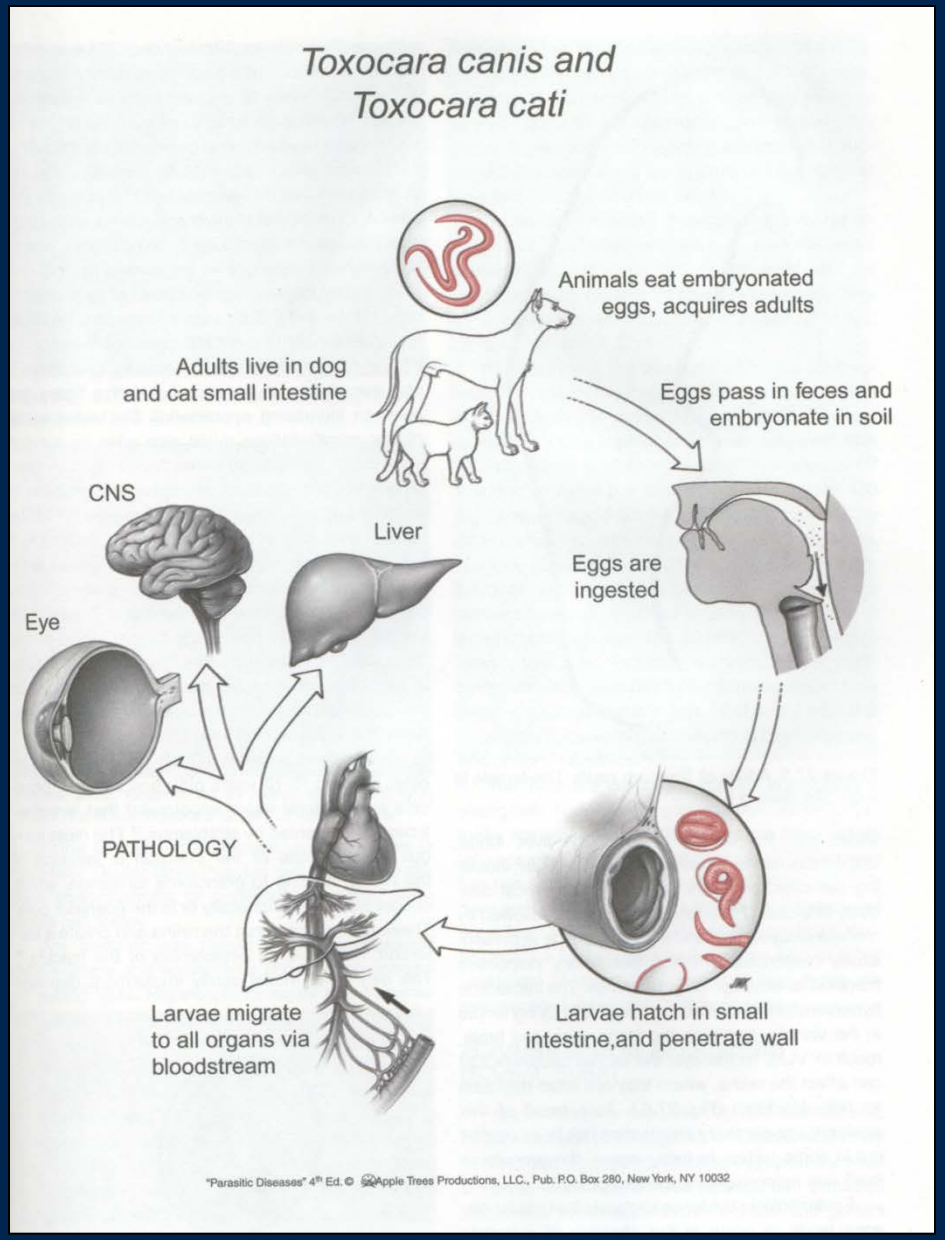


Toxocariasis in the American South

21% Seroprevalence among African Americans in poverty

‘Covert Toxocariasis:
Asthma
Developmental delays





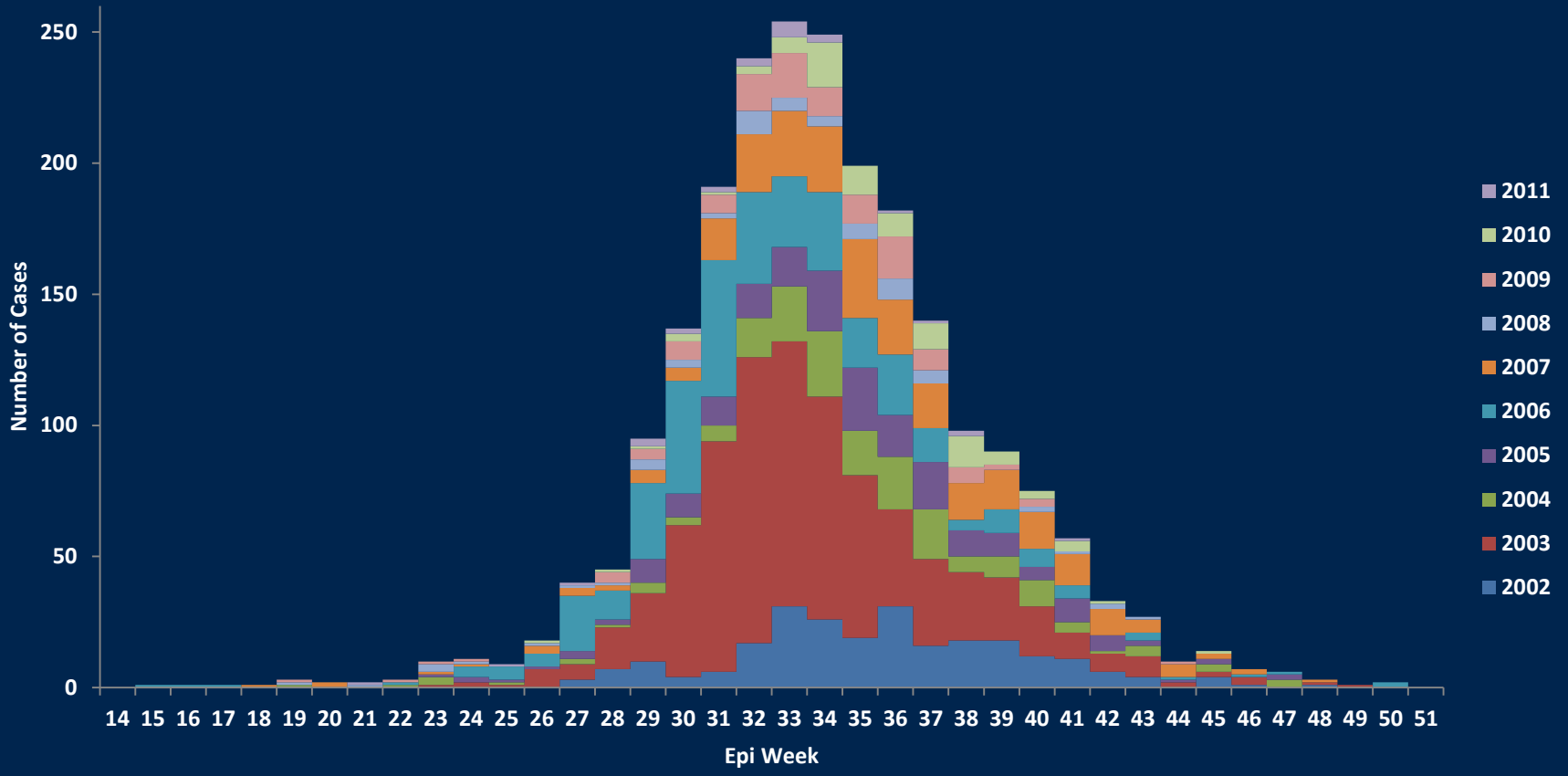
West Nile Virus Infection

One half of >1,000 WNV infections in Texas

A disease of poverty?

- Poverty positively associated with WNV incidence (Degroote & Sugumaran *Vector Borne Zoonotic Dis* 2012; 12: 657-65)
- Probability of fatal outcome depends on poverty rate (Tackett et al *Publ Health Res* 2006; 121: 666-73.
- Seroprevalence of 6.8% among homeless in Houston (Meyer et al *Emerg Infect Dis* 2007; 13: 1500-3)
- Homeless more likely to be hospitalized (Murray et al *Epidemiol Infect* 2006; 134: 1325-32)

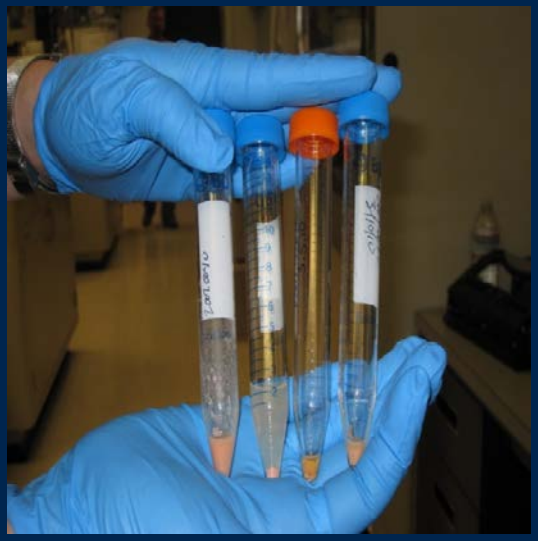
Epidemic Curve of all Texas WNV Cases

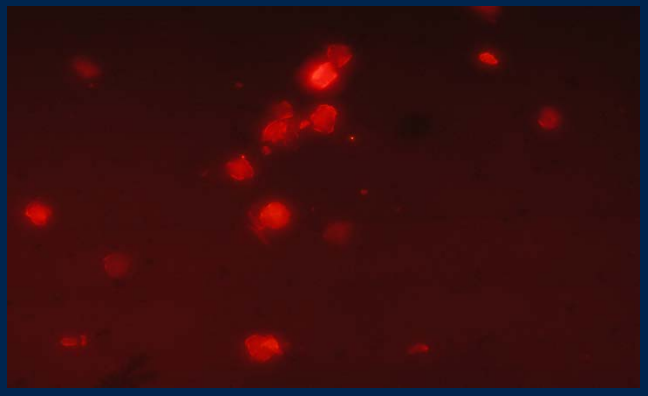


Viral Shedding in Urine

Further testing of the cohort : 45/131 (34%) patients shedding WNV RNA in the urine.

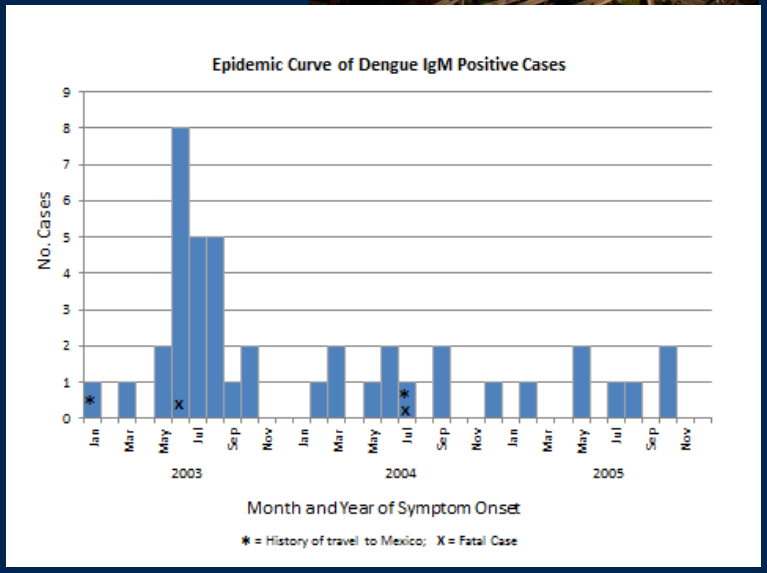
- 69% male, ages 19 to 87 years (median 54 yrs.)
- 27% had WNF or were asymptomatic
- 47% have proteinuria
- 80% have GFR< 90; 28% have GRF < 60
- Samples collected between 2 and 8 yrs. post infection





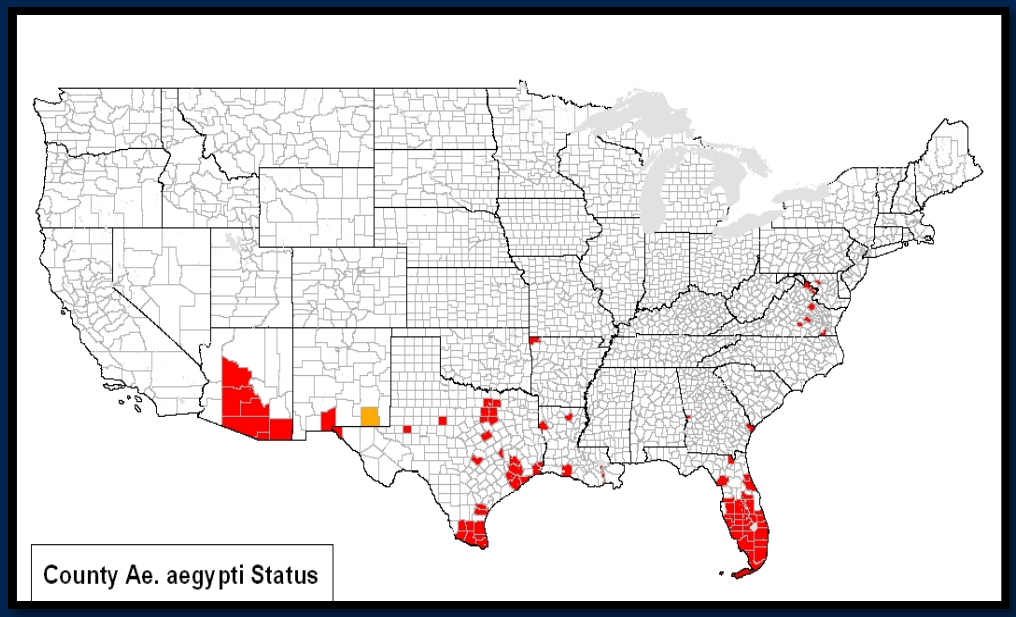
Houston: the Perfect Storm for Dengue

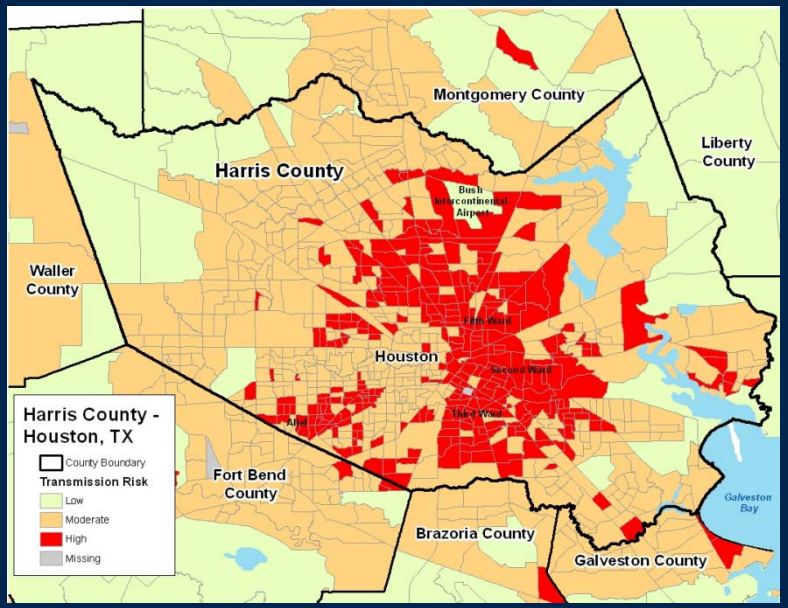
- Proximity to dengue-endemic areas
- Vast shipping; both air and ship travel entry points; NAFTA
- High proportion of its ~4 million residents who routinely travel to and from dengue-endemic areas
- Dense urban population
- Abundance of *Ae. aegypti* and *Ae. albopictus*
- Mild winters and year-round survival of mosquitoes
- Passive surveillance, lack of diagnostic testing available



Courtesy of Dr. Kristy Murray

Dengue in Houston, TX





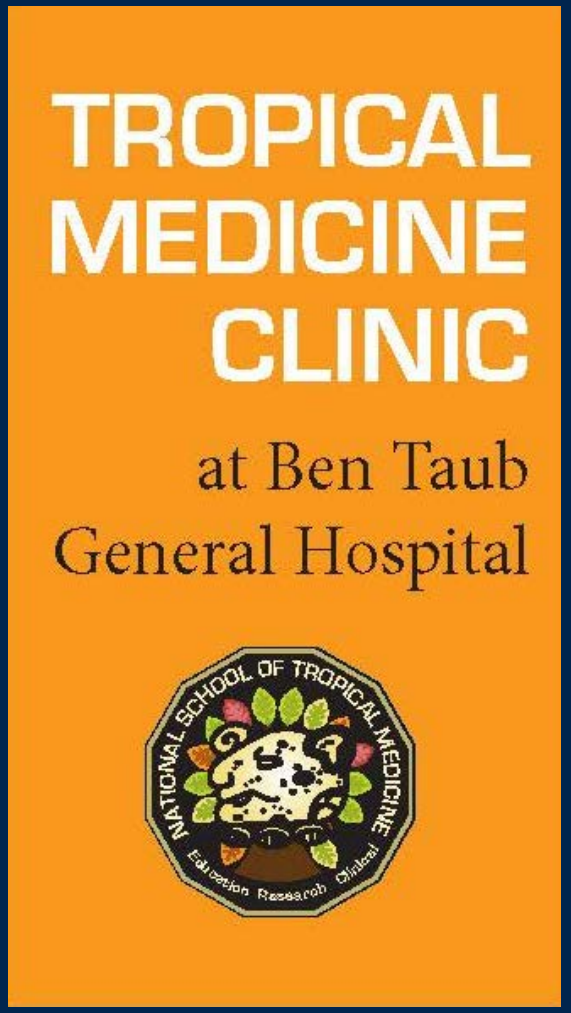
Aleisha Elliot MPH thesis

Tropical Medicine Clinic

Mission

To prevent, diagnose and treat common and neglected tropical diseases in the Houston metropolitan population and to improve occupational health for those working in regions where tropical diseases thrive.

The new clinic opened its doors Oct. 7, 2011



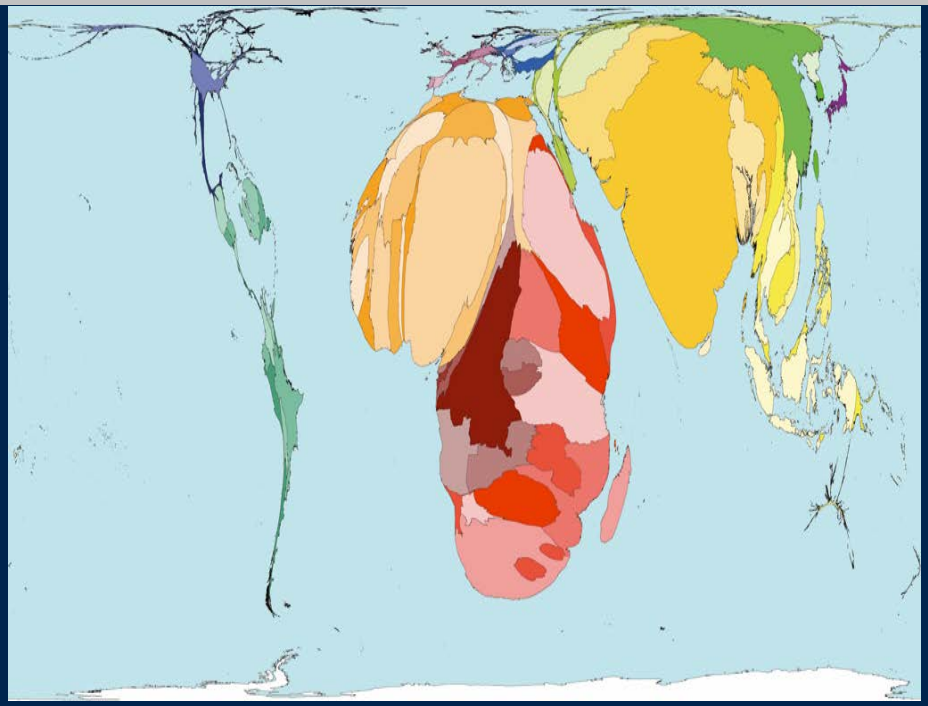
National School of Tropical Medicine
Baylor College of Medicine
Texas Medical Center, Houston, TX

A Call for the Decade of Vaccines (DoV)

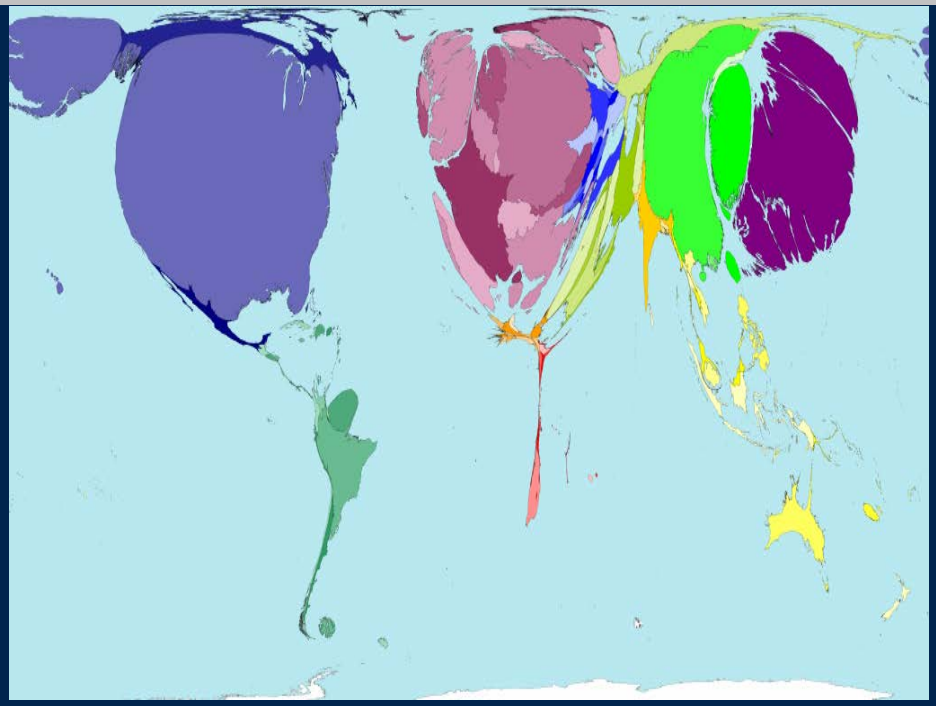
- The Bill & Melinda Gates Foundation asked donors, governments, the private sector and the general public to partner with them for action – everyone has a role
- Potential to save the lives of 6.4 million children with existing vaccines alone
- The foundation committed $10 billion towards the discovery, development and delivery of lifesaving vaccines
- This investment is not nearly sufficient to meet the needs for new vaccine research and delivery of existing vaccines

Bill and Melinda Gates' call to action re-energized and mobilized the vaccine community around an ambitious agenda

The “10/90 Gap”



Deaths from Infectious and Parasitic Diseases



Research & Development