



Emerging and Re-emerging Infectious Diseases: From AIDS to Zika

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**National Institute of Allergy and
Infectious Diseases**

National Institutes of Health

May 4, 2018



**THE
HILL**

January 13, 2017

**White House Holds
Disaster-Response
Exercise with
Trump Officials**



Five Administrations and Emerging Infectious Diseases

Ronald W. Reagan 1981-1989



George H.W. Bush 1989-1993



William J. Clinton 1993-2001



George W. Bush 2001-2009



Barack H. Obama 2009-2017





■ HIV/AIDS

Ronald W. Reagan
1981-1989

CENTERS FOR DISEASE CONTROL

MNWRTM

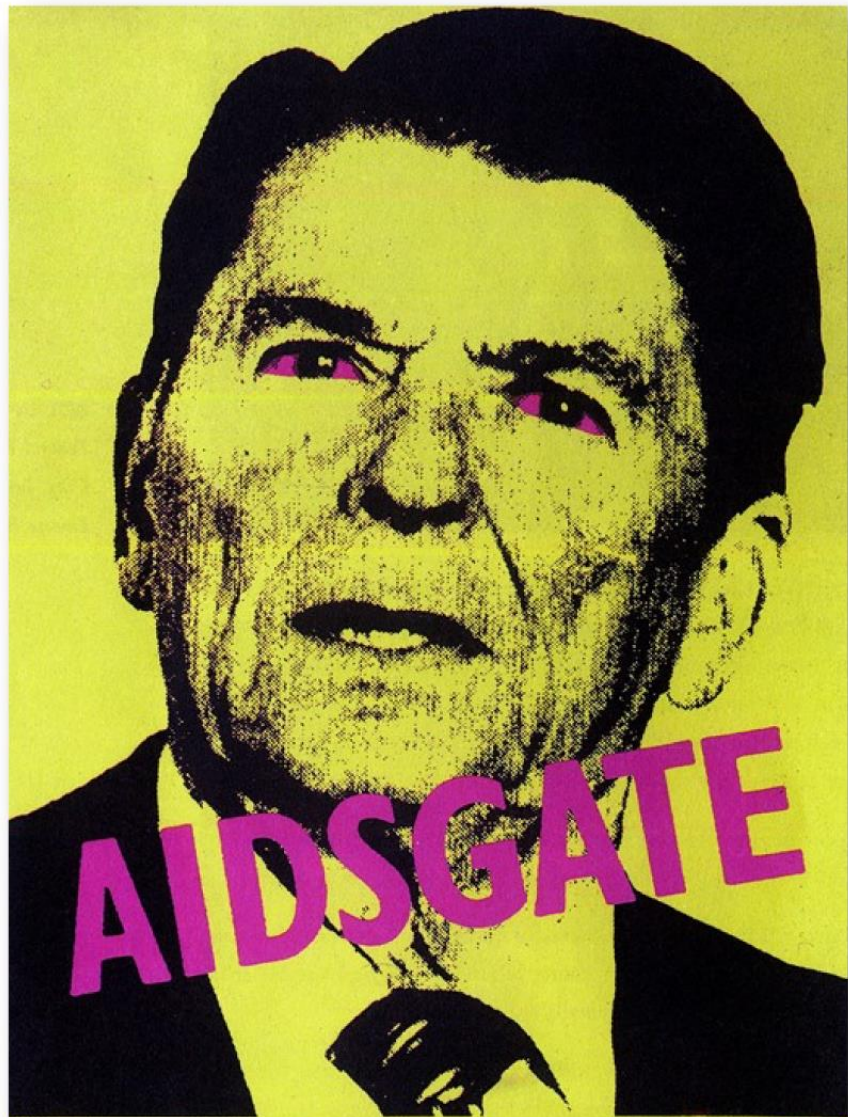
MORBIDITY AND MORTALITY WEEKLY REPORT

June 5, 1981

***Pneumocystis Pneumonia -
Los Angeles***

July 3, 1981

***Kaposi's Sarcoma and
Pneumocystis Pneumonia
Among Homosexual Men -
New York City and California***



This Political Scandal Must Be Investigated!

54% of people with AIDS in NYC are Black or Hispanic... AIDS is the No. 1 killer of women between the ages of 24 and 29 in NYC...

By 1991, more people will have died of AIDS than in the entire Vietnam War... What is Reagan's real policy on AIDS?

Genocide of all Non-whites, Non-males, and Non-heterosexuals?...

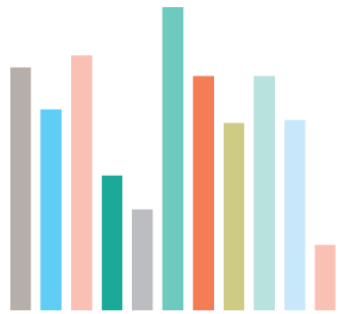
SILENCE = DEATH



UNAIDS Global AIDS Update, 2017

UNAIDS 2017 | REFERENCE

UNAIDS DATA 2017



■ In 2016:

- 36.7 million living with HIV
- 1.8 million infected with HIV
- 1.0 million deaths from AIDS-related illnesses

■ Since start of the pandemic

- 76.1 million infected with HIV
- 35.0 million deaths from AIDS-related illnesses



■ **HIV/AIDS**

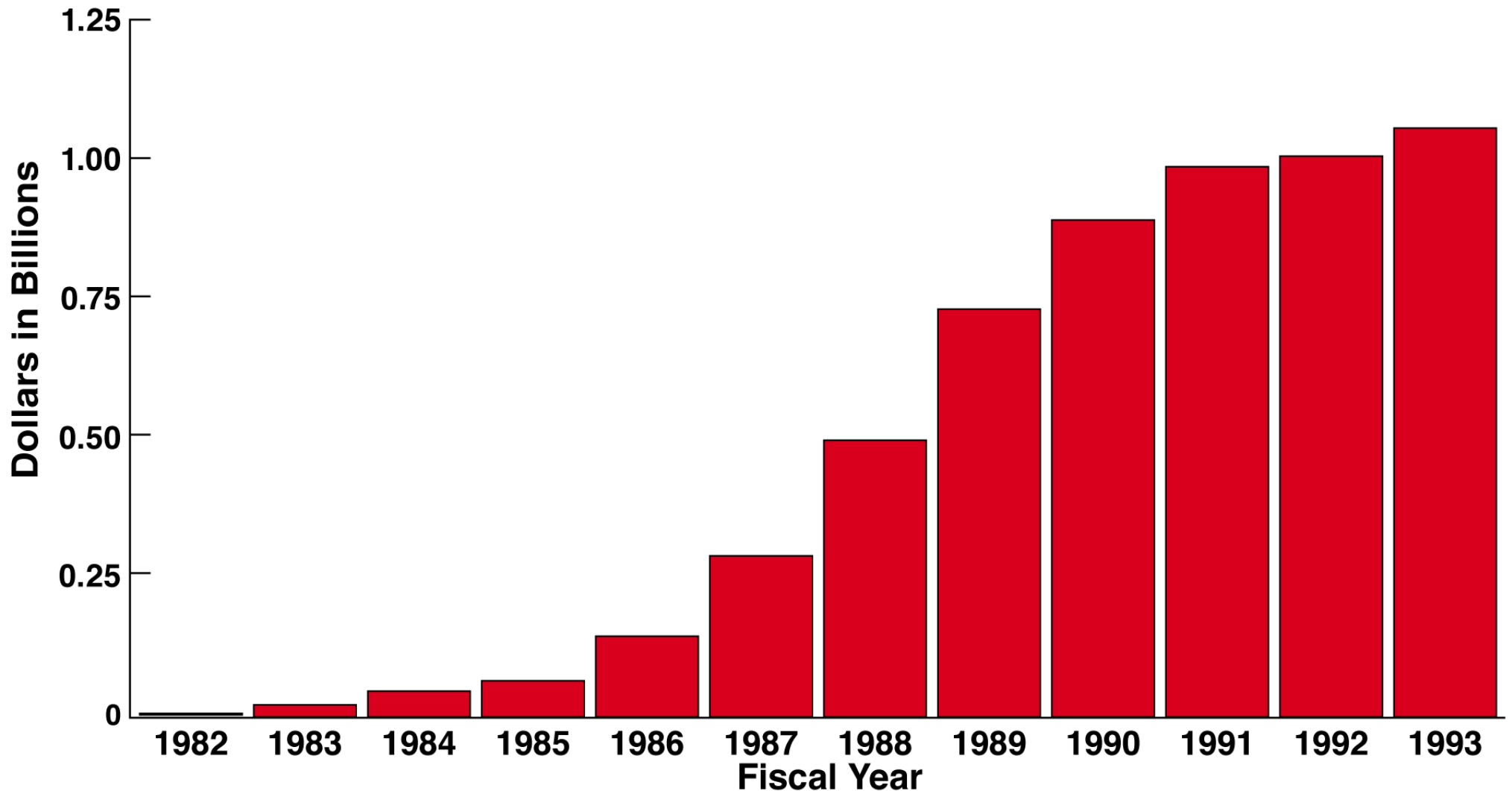
George H. W. Bush
1989-1993

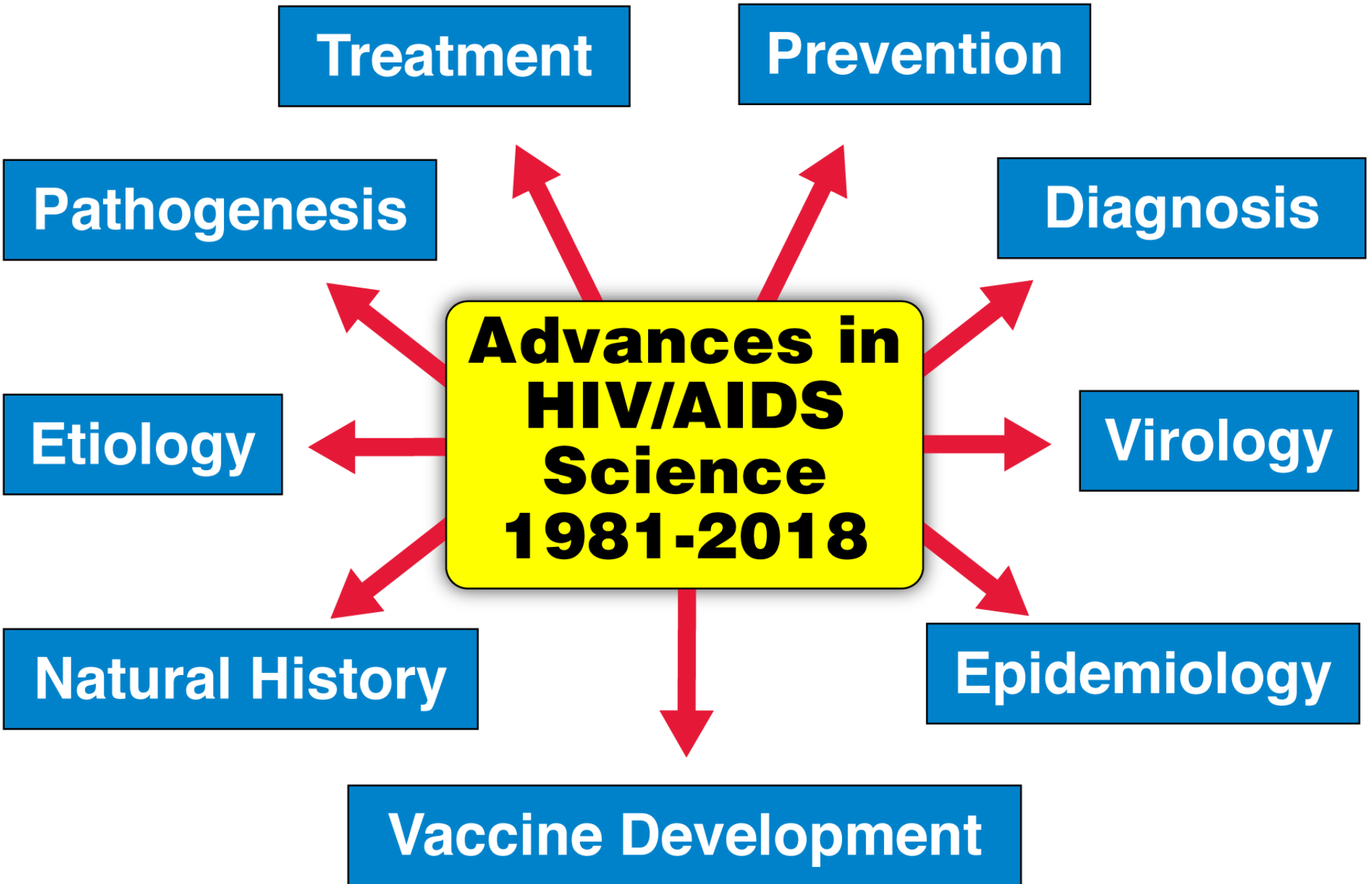






NIH HIV/AIDS Research Funding, FY 1982 to FY 1993





Treatment

Prevention

Pathogenesis

Diagnosis

Etiology

Virology

Natural History

Epidemiology

Vaccine Development

**Advances in
HIV/AIDS
Science
1981-2018**

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graph TD; A[Advances in HIV/AIDS Science 1981-2018] --> B[Treatment]; A --> C[Prevention]; A --> D[Pathogenesis]; A --> E[Diagnosis]; A --> F[Etiology]; A --> G[Virology]; A --> H[Natural History]; A --> I[Epidemiology]; A --> J[Vaccine Development];
```

Rounds at NIH Clinical Center, Early 1980s – AIDS Patient



■ Median survival of AIDS patients: ~8-15 months



The
New England
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

VOLUME 317

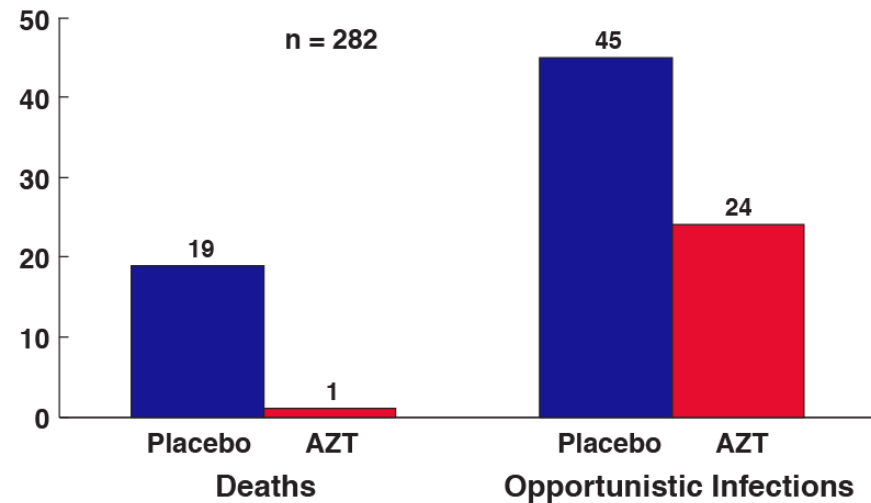
July 23, 1987

NUMBER 4

**The Efficacy of
Azidothymidine (AZT)
in the Treatment of
Patients with AIDS
and AIDS-Related
Complex: A Double-
Blind, Placebo-
Controlled Trial**

MA Fischl et al.

**BW 002: 24-Week Study of AZT vs.
Placebo in Patients with AIDS or ARC**



Antiretroviral Therapy Among First Uses of Accelerated Approval Pathway



The Use of Plasma HIV RNA as a Study Endpoint in Efficacy Trials of Antiretroviral Drugs

JS Murray, KA Struble et al.

FDA-Approved Antiretroviral Drugs

NRTIs

- 7 multi-drug combinations
- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir (TDF, TAF)
- Zidovudine

NNRTIs

- Delavirdine
- Efavirenz
- Etravirine
- Nevirapine
- Rilpivirine

Integrase Inhibitors

- Bictegravir
- Dolutegravir
- Elvitegravir
- Raltegravir

Post-Attachment Inhibitor

- Ibalizumab

Pharmacokinetic Enhancers

- Cobicistat
- Ritonavir

PIs

- Atazanavir
- Darunavir
- Fosamprenavir
- Indinavir
- Lopinavir/Ritonavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

Entry Inhibitor

- Maraviroc

Multi-Class Combinations

- Atripla
- Biktarvy
- Complera
- Genvoya
- Juluca
- Odefsey
- Stribild
- Symfi
- Symfi Lo
- Triumeq

Fusion Inhibitor

- Enfuvirtide

Life Expectancy for 20-Year-Old Newly Diagnosed with HIV, 1980s and Today

**1980s
(no ART)**



**1-2 years from
AIDS diagnosis**

**Today
(on ART)**



**~53
years**

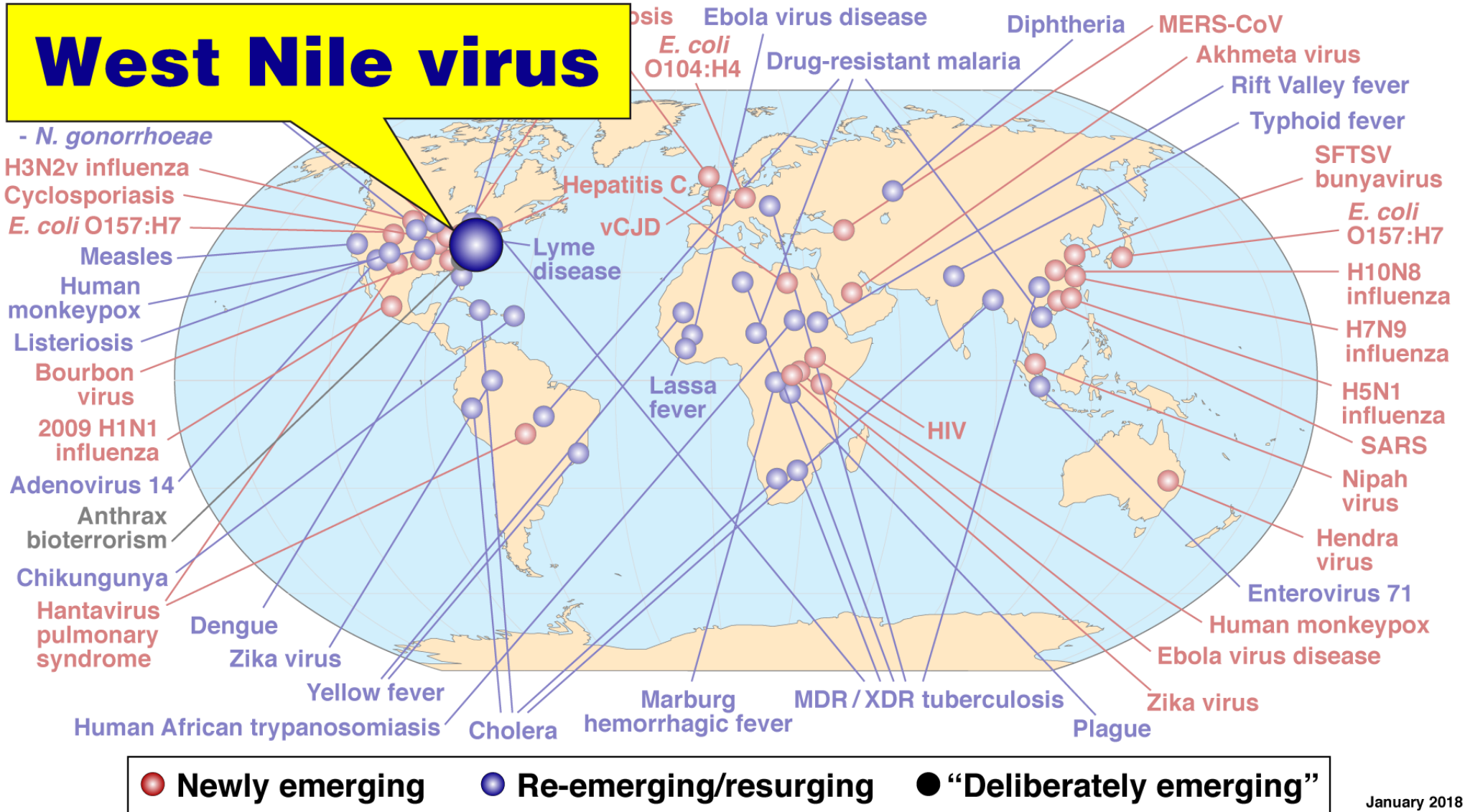


William J. Clinton
1993-2001

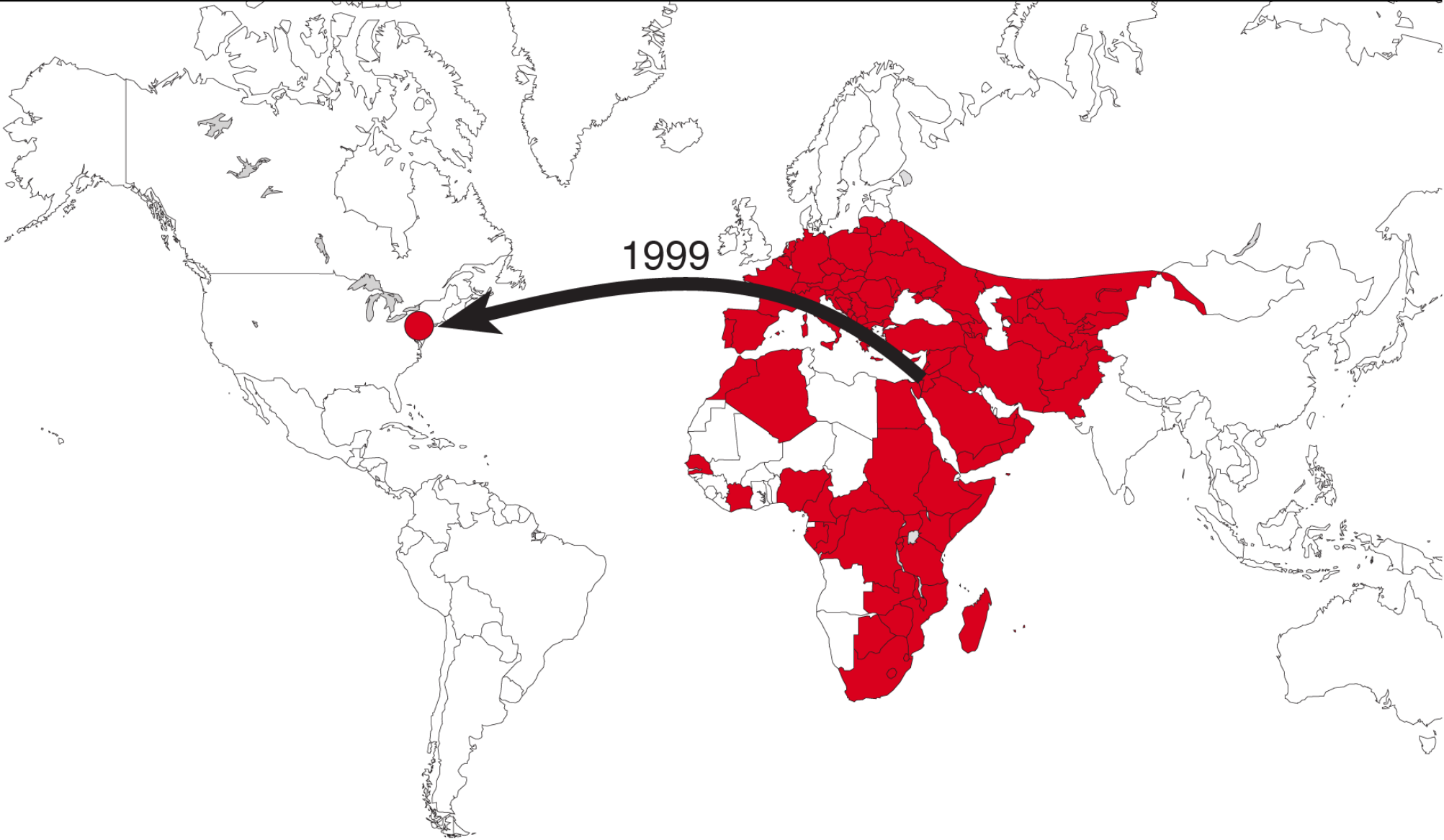
- **HIV/AIDS**
- **West Nile Virus**
- **H5N1 Influenza**
- **Antimicrobial Resistance**

Global Examples of Emerging and Re-Emerging Infectious Diseases

West Nile virus

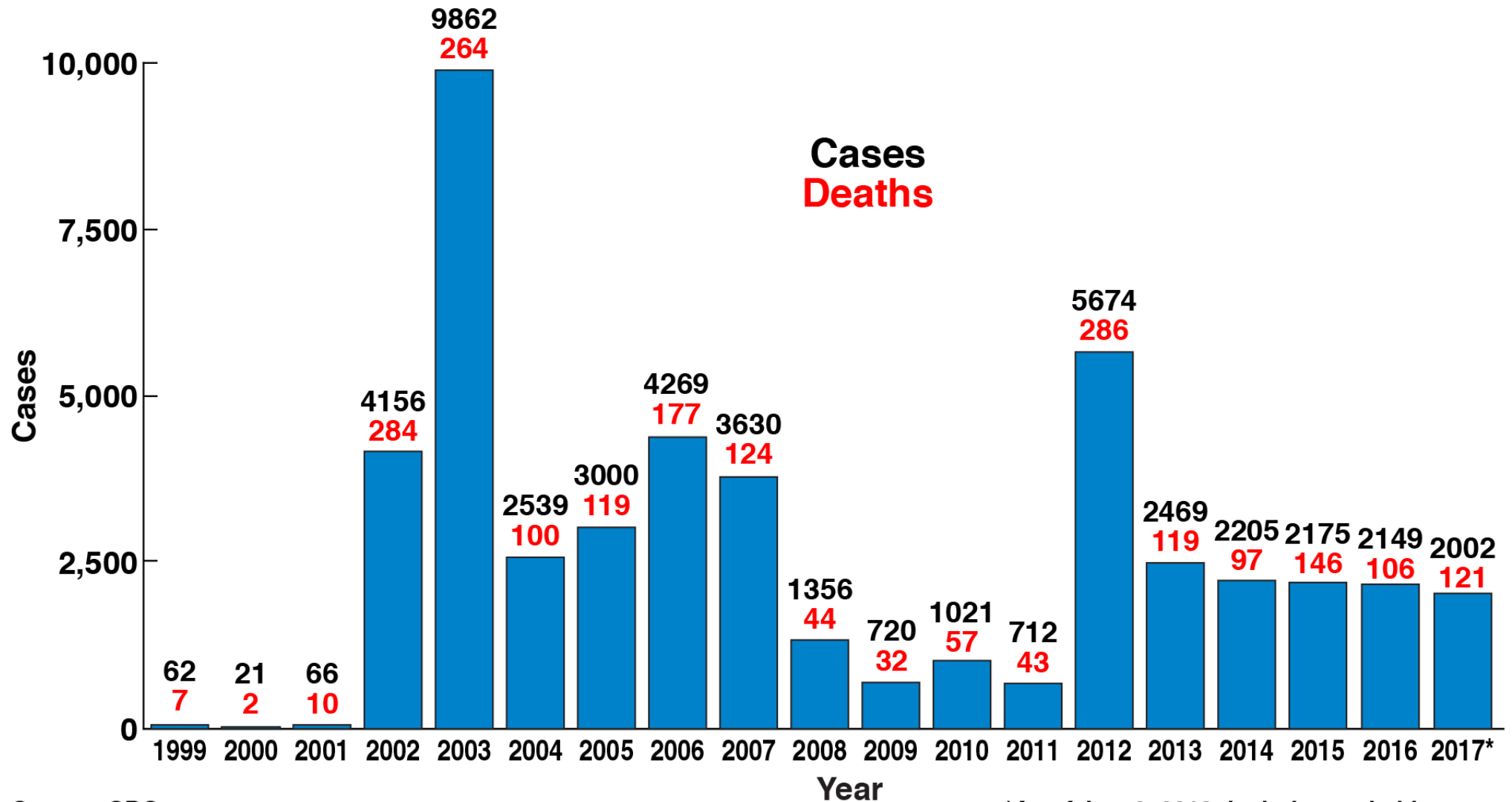


Global Distribution of West Nile Virus, 1999



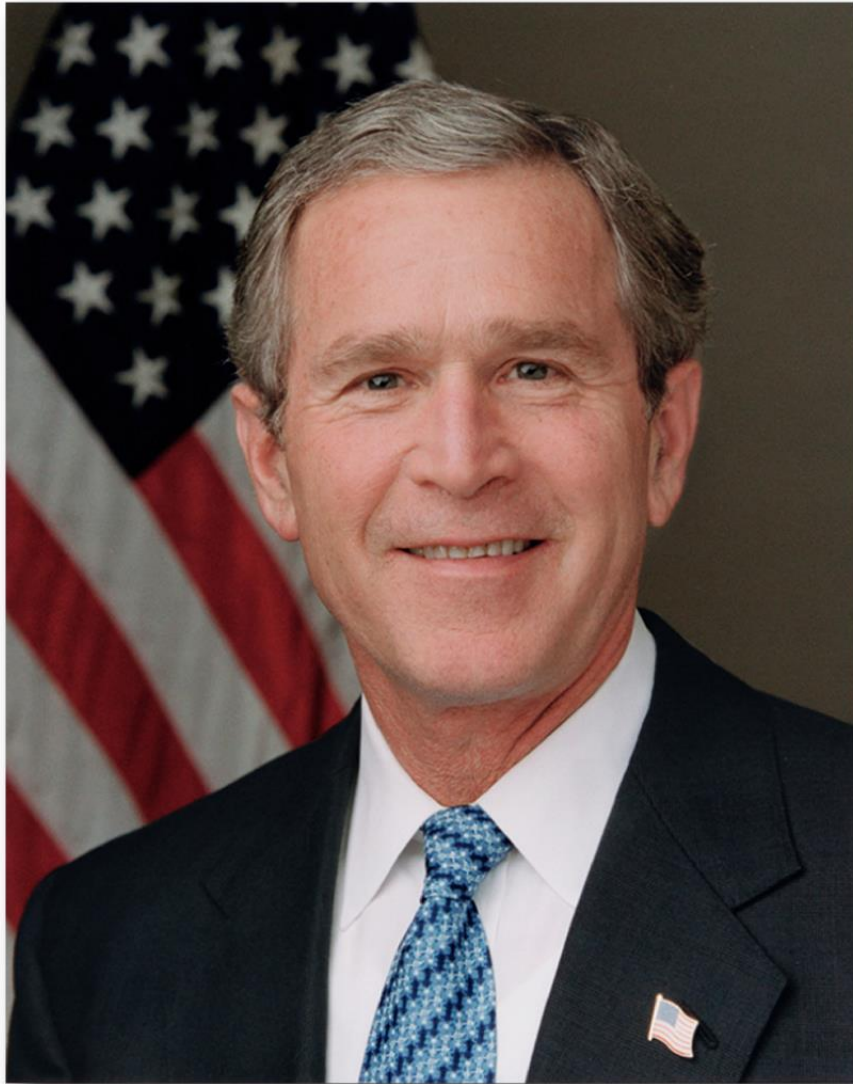
Source: CDC

U.S. West Nile Virus Cases & Deaths, 1999-2017



Source: CDC

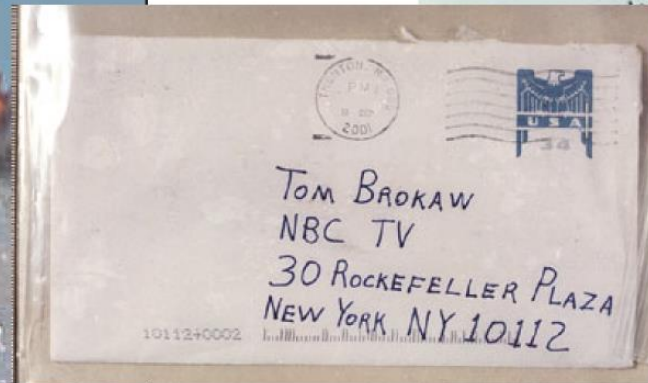
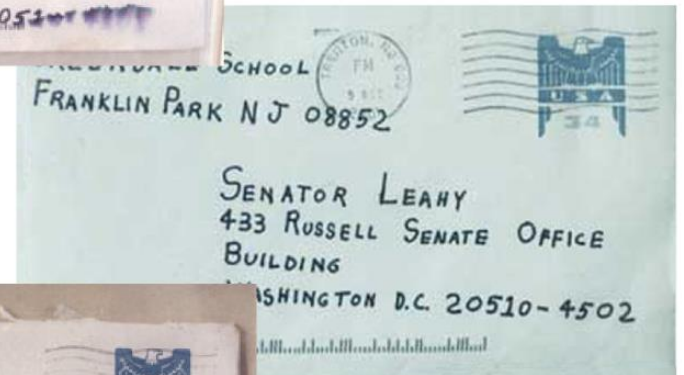
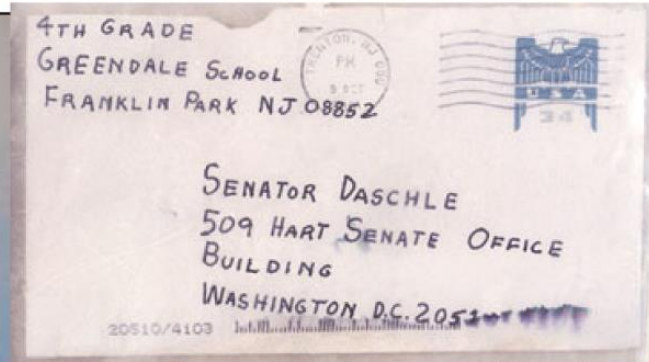
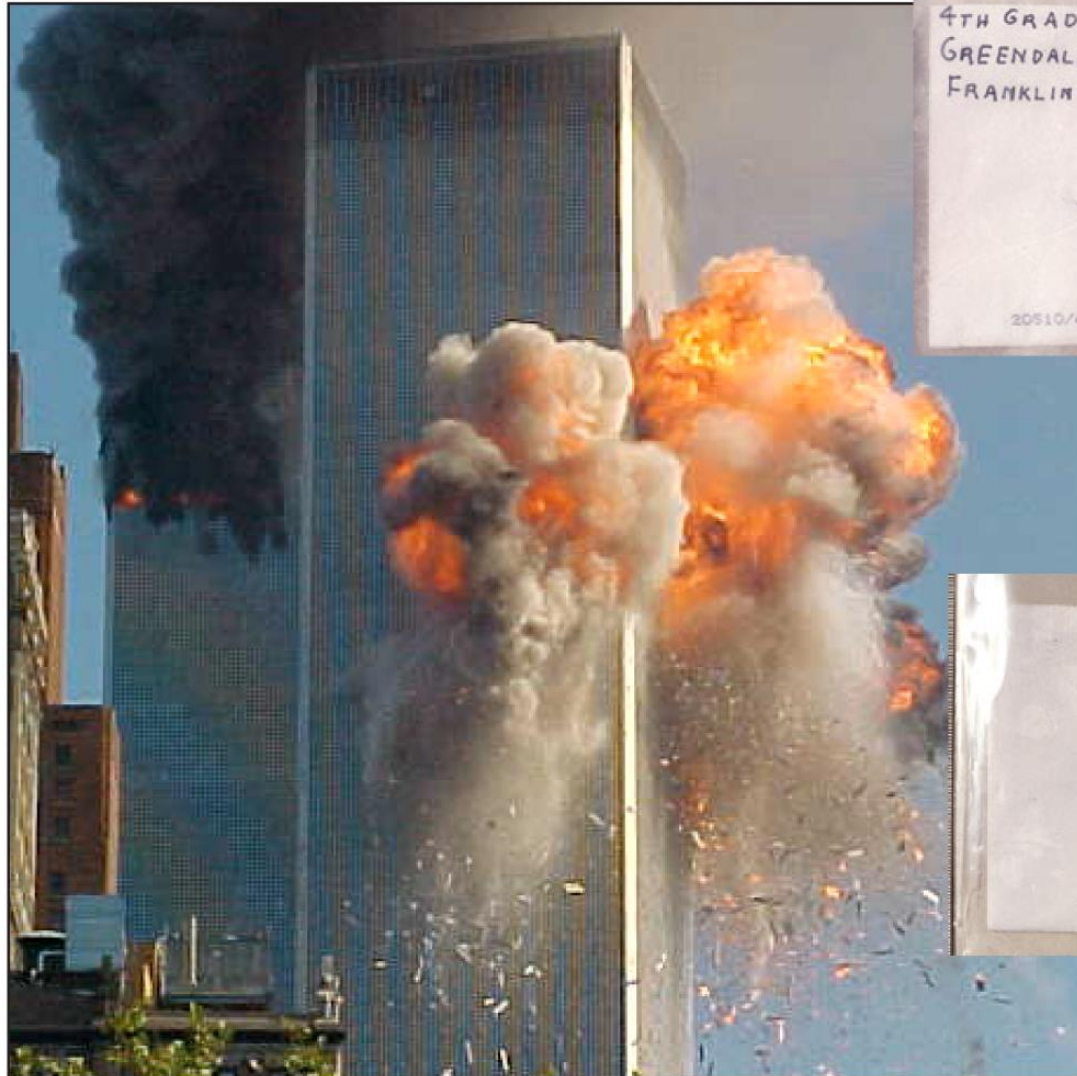
*As of Jan. 9, 2018; includes probable cases



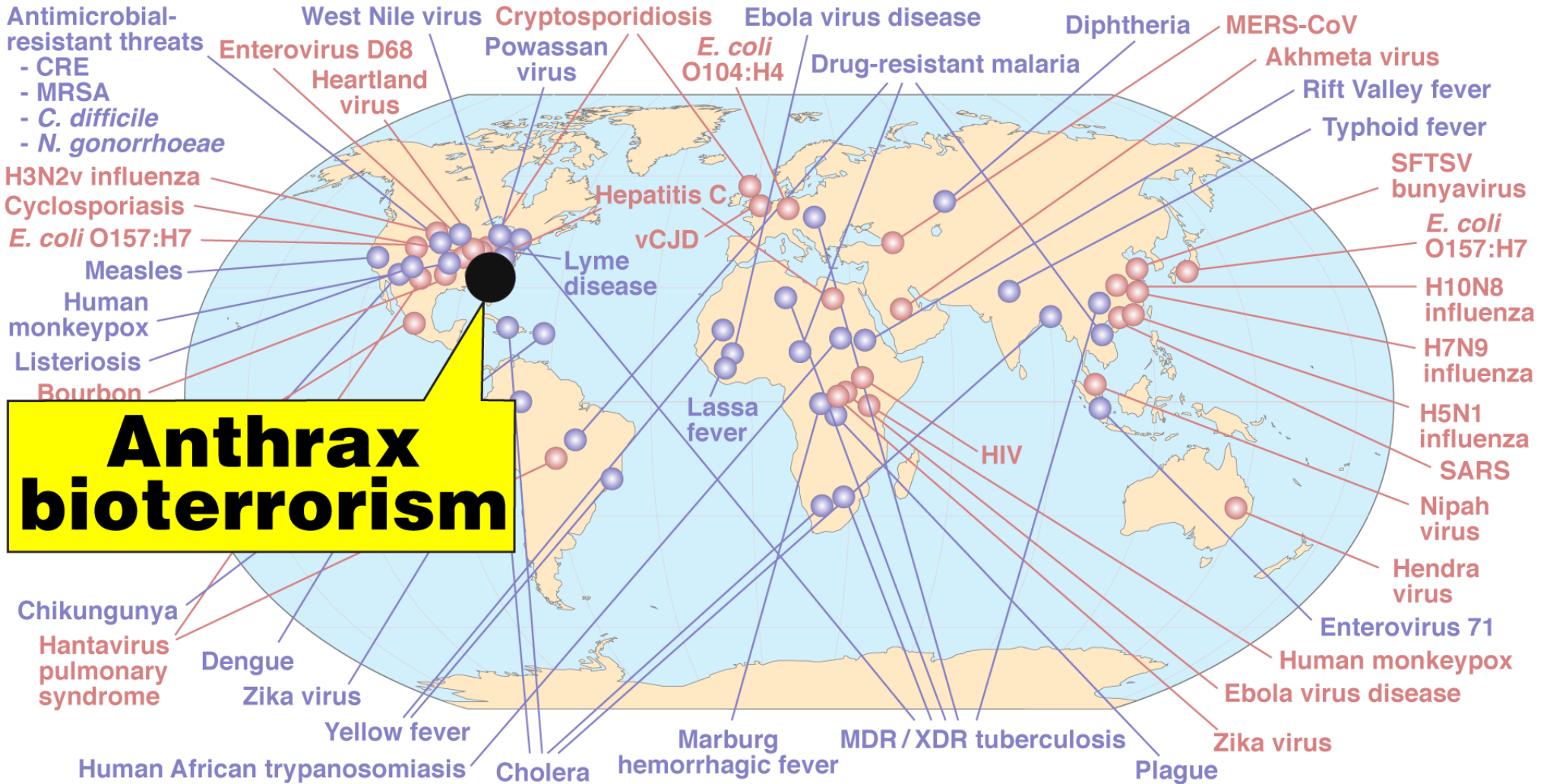
**George W. Bush
2001-2009**

- **HIV/AIDS**
- **Anthrax**
- **H5N1 Influenza**
- **SARS**

Juxtaposition of Events of September 11, 2001 and the Deliberate Release of Anthrax



Global Examples of Emerging and Re-Emerging Infectious Diseases



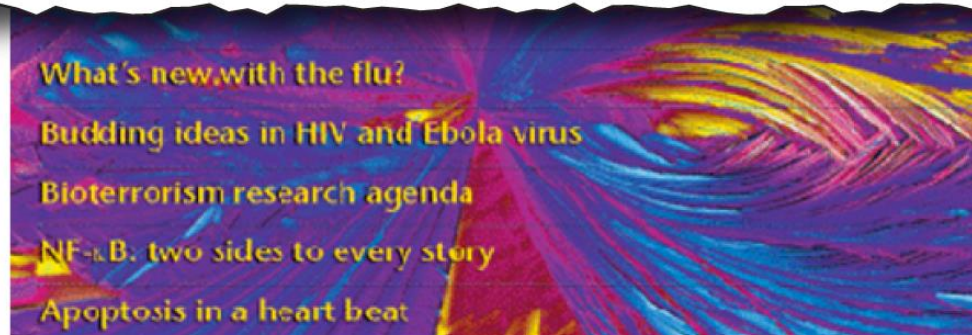
Anthrax bioterrorism

● Newly emerging ● Re-emerging/resurging ● "Deliberately emerging"



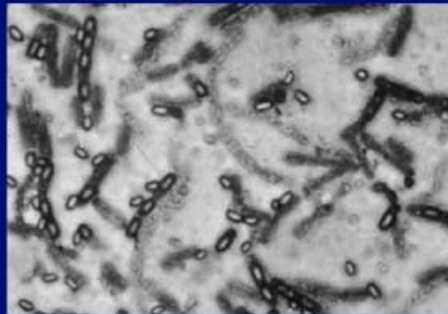
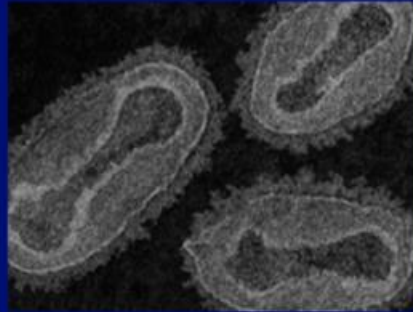
Bioterrorism: A Clear and Present Danger

HC Lane, J La Montagne and AS Fauci



February 2002

NIAID Strategic Plan for Biodefense Research



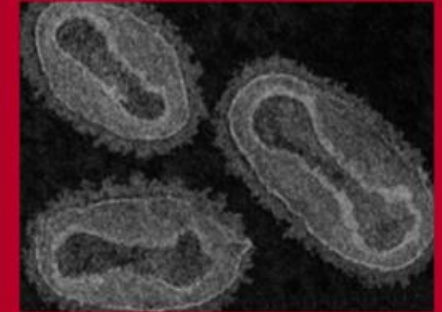
Responding
Through
Research



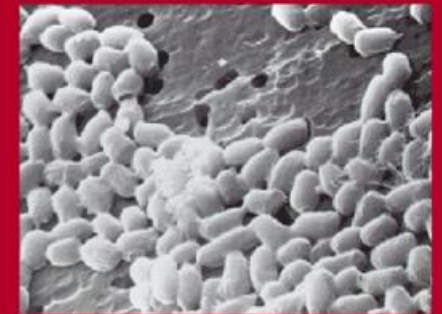
National Institute of Allergy and Infectious Diseases
NATIONAL INSTITUTES OF HEALTH

February 2002

NIAID Biodefense Research Agenda for CDC Category A Agents



Responding
Through
Research

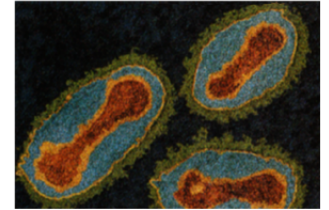


National Institute of Allergy and Infectious Diseases
NATIONAL INSTITUTES OF HEALTH

Category A Select Agents: Key Achievements

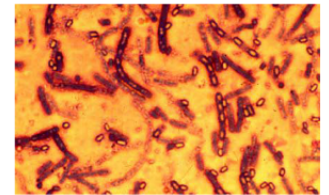
■ Smallpox

– Dryvax; MVA; antivirals



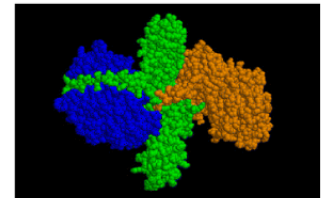
■ Anthrax

– Next-generation vaccines; antitoxins



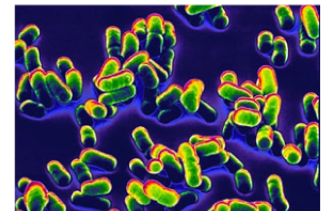
■ Botulinum

– Antitoxins; mAbs



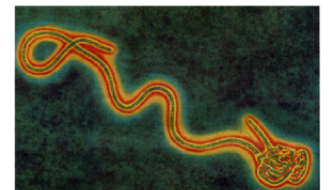
■ Plague

– Antibiotics



■ Ebola

– First human vaccine trials; therapeutics; diagnostics



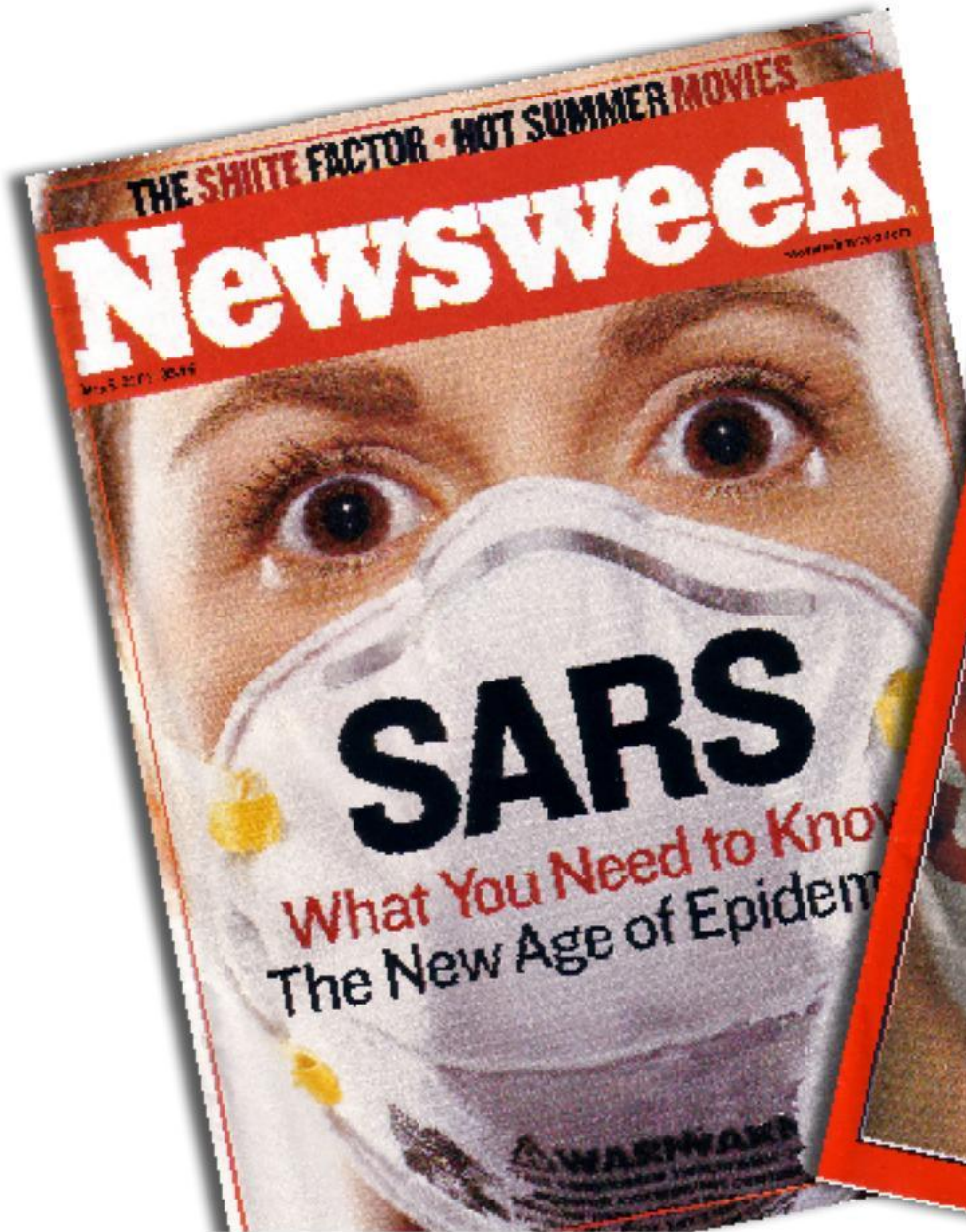
February 5, 2002



President GW Bush: “Tony, what scares you the most among potential microbial threats that a terrorist might use?”

Fauci: “Mr. President, I worry more about the natural occurrence of an influenza pandemic and the ongoing plague of HIV than I do about a bioterror attack.”

SARS: A New Challenge to Global Health



Early Cases of SARS: Guangdong Province, China

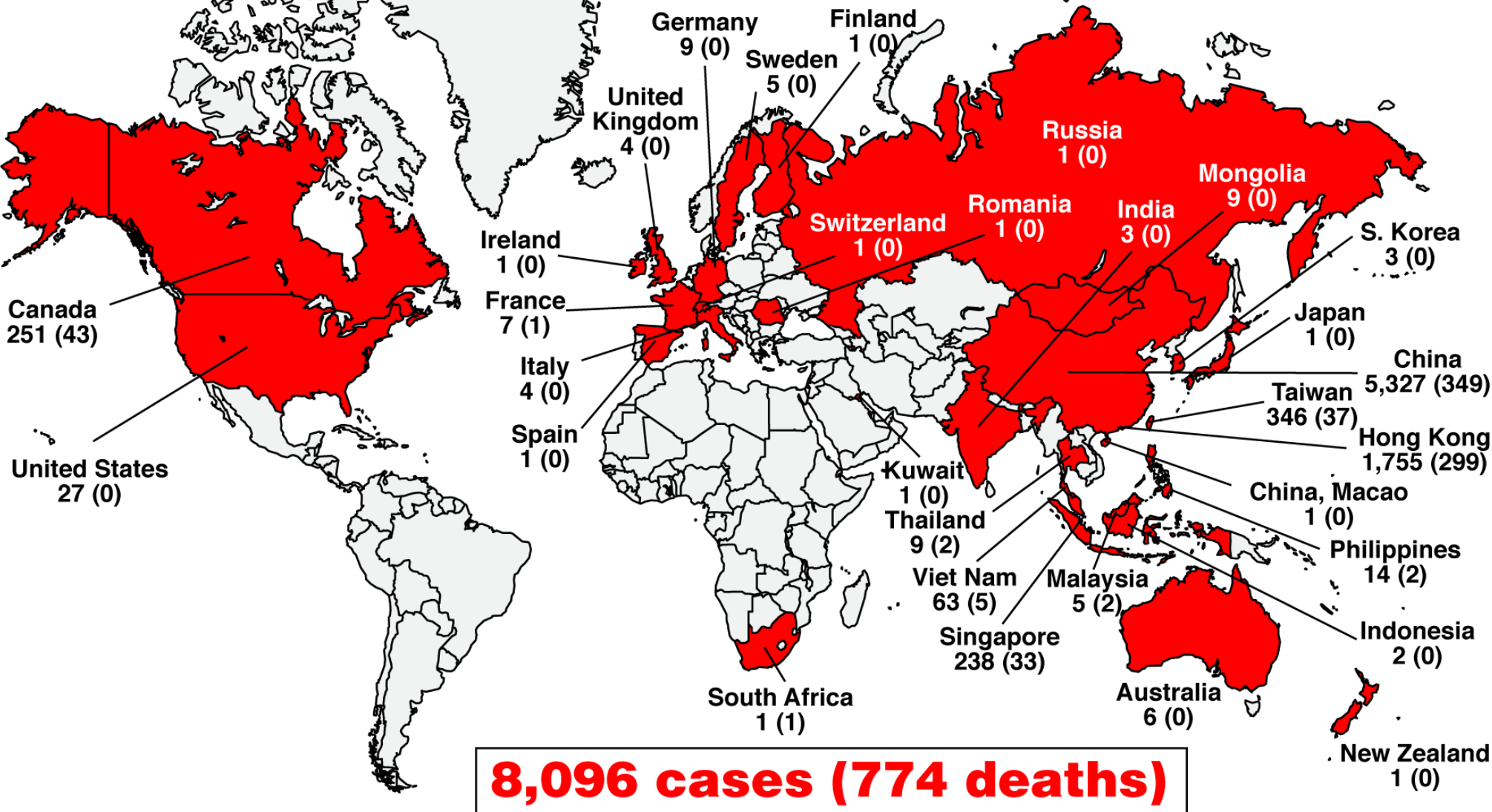


2003 Spread of SARS from Hotel Metropole in Hong Kong



Sources: *MMWR*, March 28, 2003; WHO, 2003

Cumulative Reported Cases of SARS November 1, 2002 to July 31, 2003



Source: WHO

OTTAWA



CITIZEN

July 6, 2003

**WHO Declares Victory
over SARS: Taiwan Last
Country to Be Taken off
List of Infected Areas**

The Birth of the President's Emergency Plan for AIDS Relief (PEPFAR)



State of the Union Address, January 28, 2003

- **President Bush announces the President's Emergency Plan for AIDS Relief (PEPFAR)**

The President's Emergency Plan for AIDS Relief – \$15B Over 5 Years

Goals:

- Prevent 7 million new infections
- Treat 2 million HIV-infected people
- Care for 10 million HIV-infected people, orphans and other vulnerable children



Selected PEPFAR Accomplishments

As of Sept. 30, 2017,

- **13.3 million** people on antiretroviral therapy
- **2.2 million** perinatal HIV infections averted
- **85.5 million** received HIV testing in FY 2017
- **25-40% decline** in new HIV diagnoses among adolescent girls/young women through DREAMS partnership



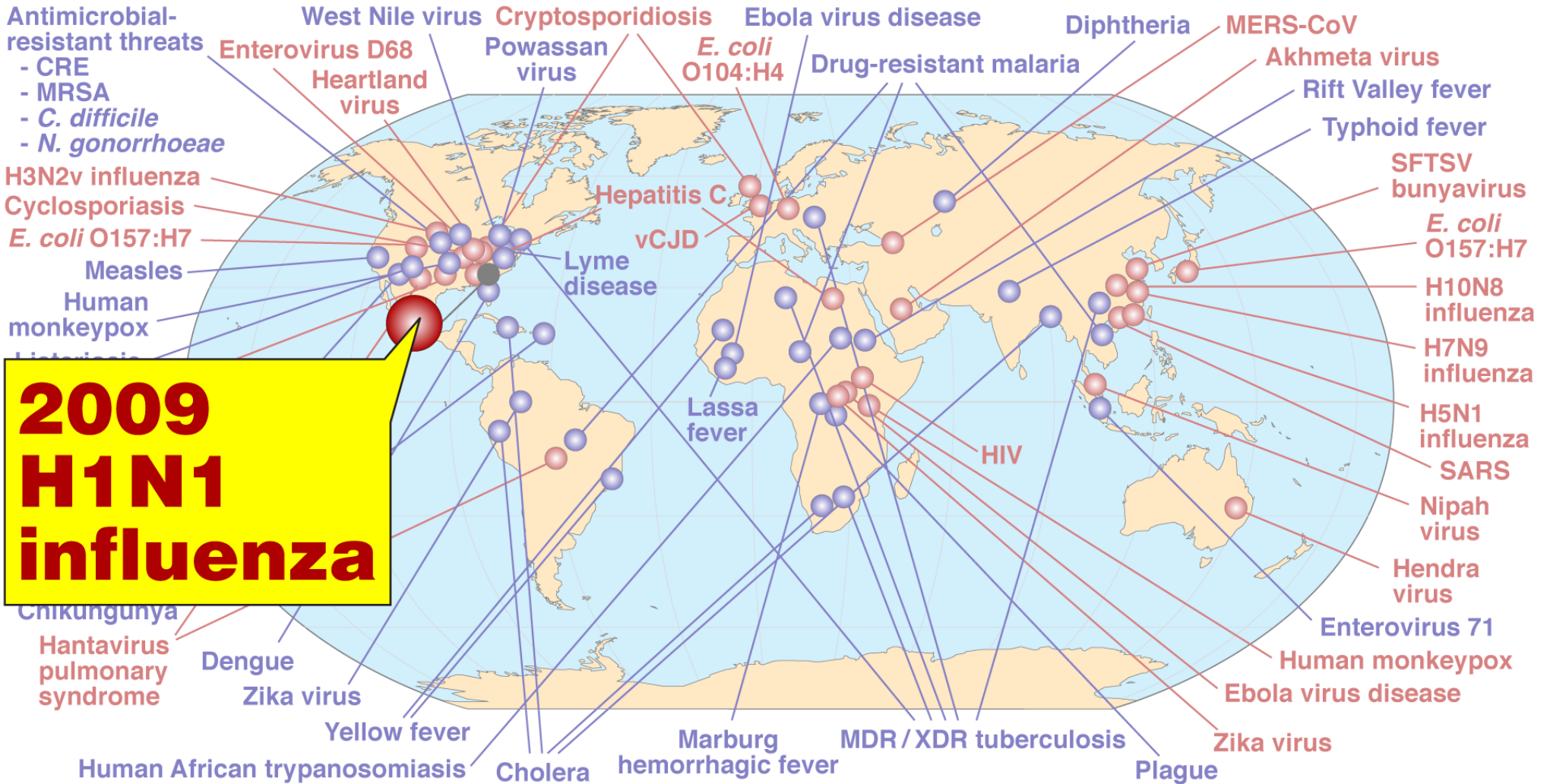


**Barack H. Obama
2009-2017**

- **H1N1
Pandemic
Influenza**
- **MERS**
- **Chikungunya**
- **Ebola**
- **Zika**
- **Antimicrobial
Resistance**



Global Examples of Emerging and Re-Emerging Infectious Diseases



● Newly emerging ● Re-emerging/resurging ● “Deliberately emerging”

Beginning of Global H1N1 Influenza Outbreak in March 2009



Global H1N1 Influenza Cases, as of April 29, 2009

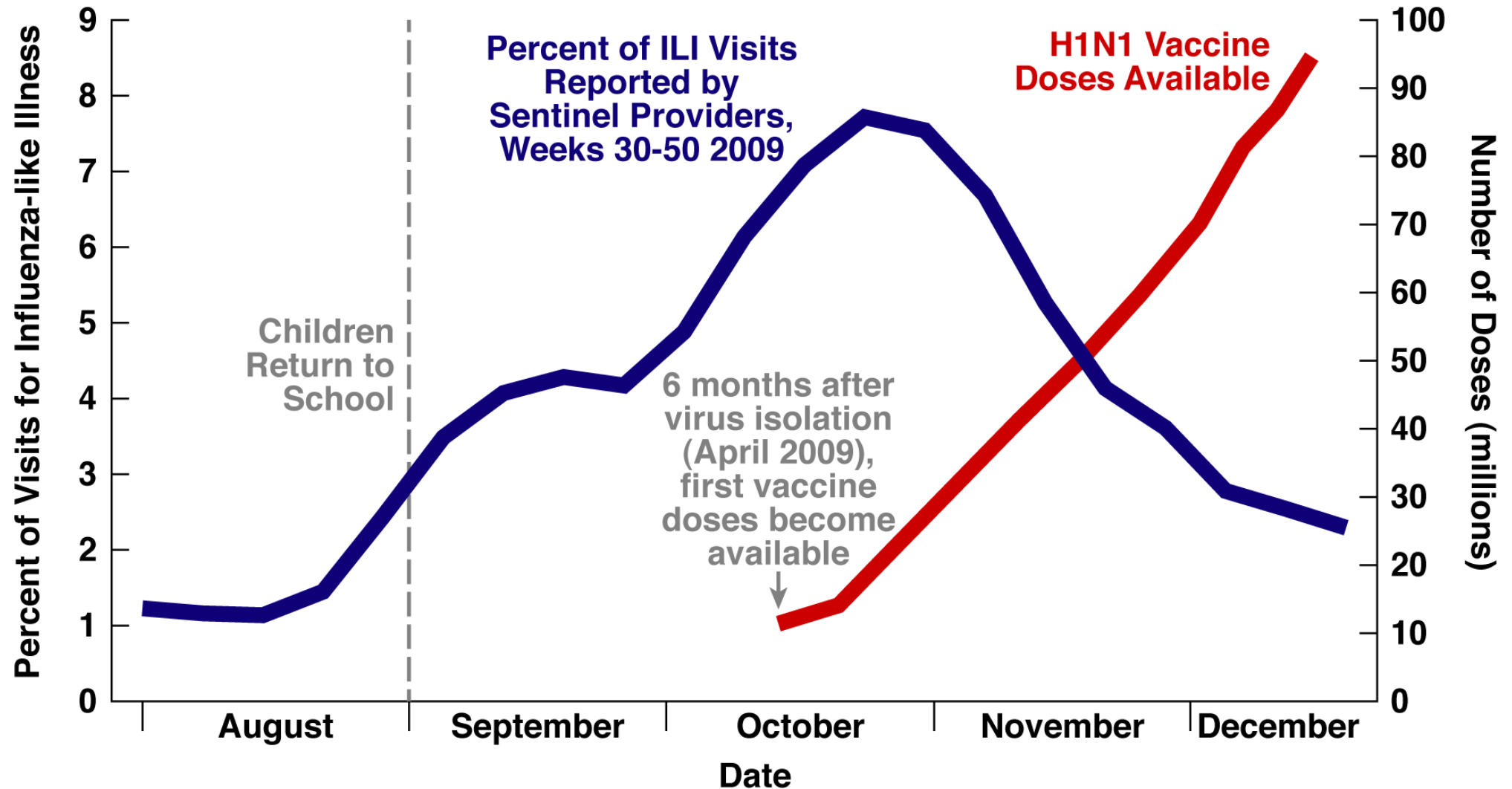


Source: WHO

Senate Appropriations Subcommittee Hearing on H1N1 Influenza, April 28, 2009



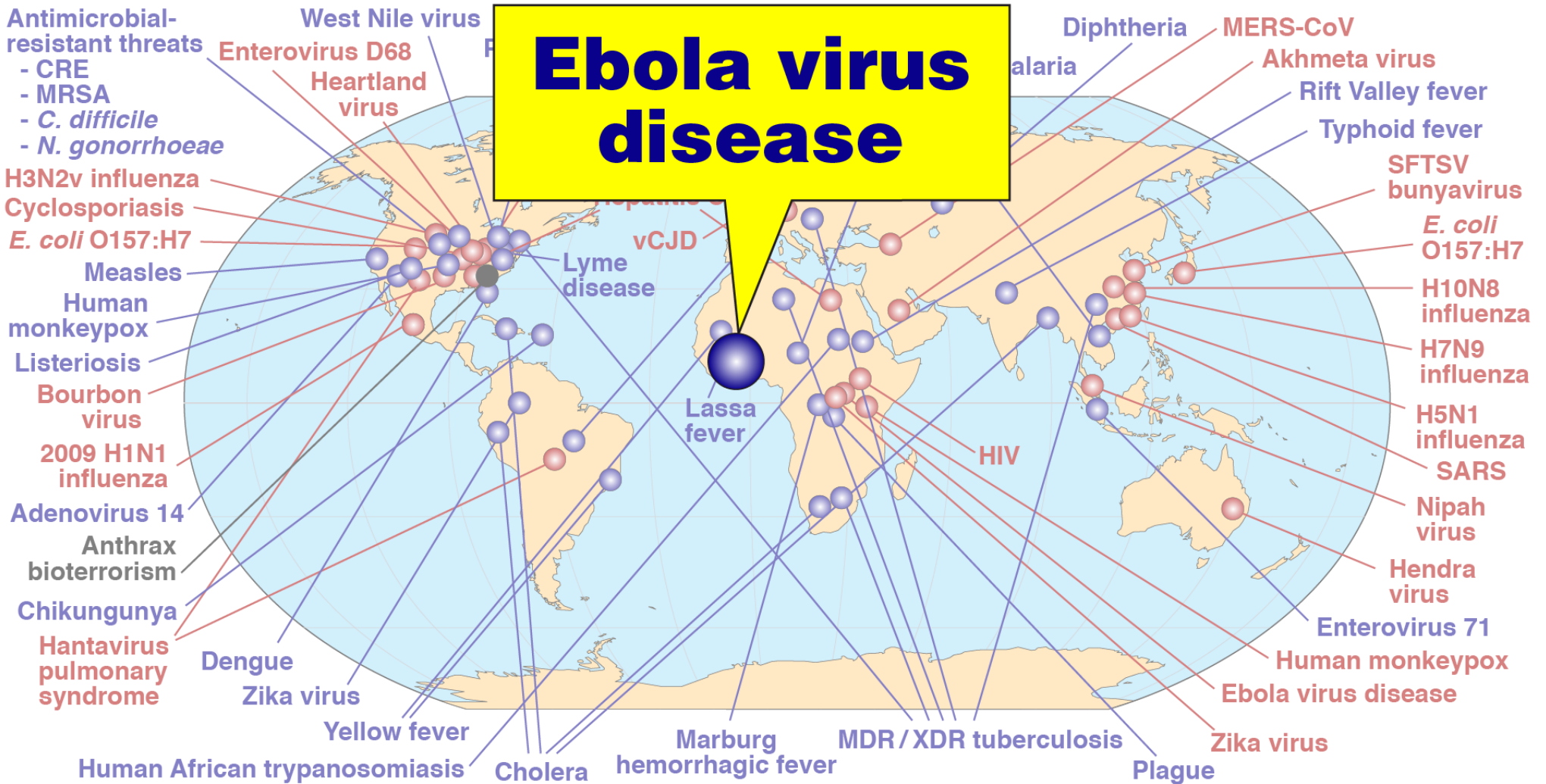
Vaccine Lags Behind 2009 H1N1 Influenza Pandemic



House Oversight and Government Reform Committee Hearing on H1N1 Influenza Vaccines, Sept. 29, 2009



Global Examples of Emerging and Re-Emerging Infectious Diseases



● Newly emerging ● Re-emerging/resurging ● "Deliberately emerging"

Reported Ebola Virus Disease Cases in Guinea, Liberia, and Sierra Leone, 2014-2016

Guinea
3,814 cases / 2,544 deaths

Sierra Leone
14,124 cases / 3,956 deaths

Liberia
10,678 cases / 4,810 deaths



Total*:
28,616 cases
11,310 deaths

40% mortality

*Confirmed, probable and suspected cases

Source: WHO, 12/2016



The
New England
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Volume 376

March 9, 2017

Number 10

Chimpanzee Adenovirus Vector Ebola Vaccine

JE Ledgerwood, BS Graham et al. for the VRC 207 Study Team



National Institute of Allergy and Infectious Diseases

Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.

News Release

August 28, 2014

NIH to Launch Human Safety Study of Ebola Vaccine Candidate

Phase I Trial Timeline for cAd3 (Before and After Outbreak)

Planned (pre-outbreak)



August 2013
Pre-IND Meeting

March-April 2015
Forecasted
Launch Phase I

Actual

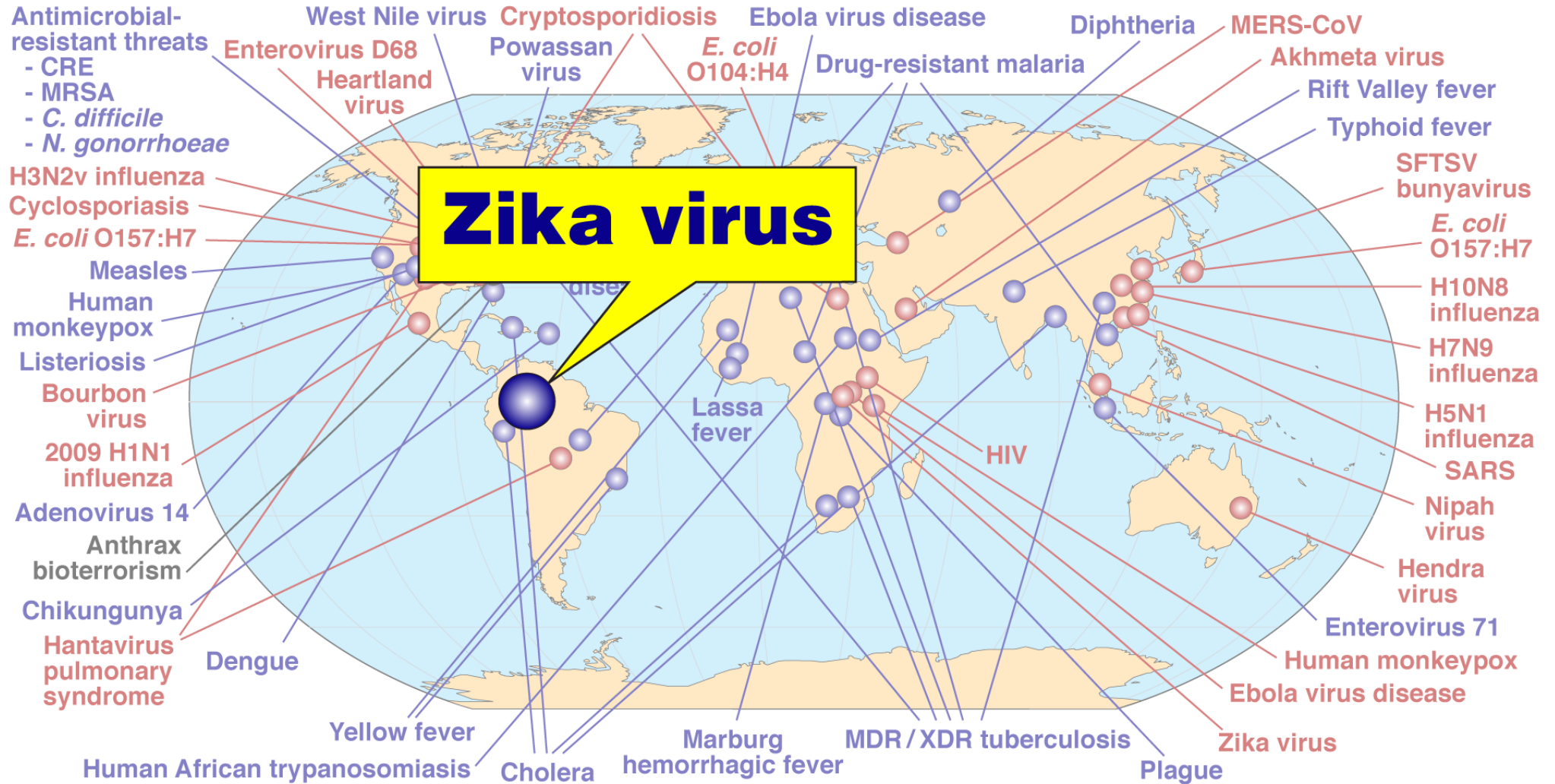


August 2013
Pre-IND Meeting

Sept 2, 2014
Phase I launches

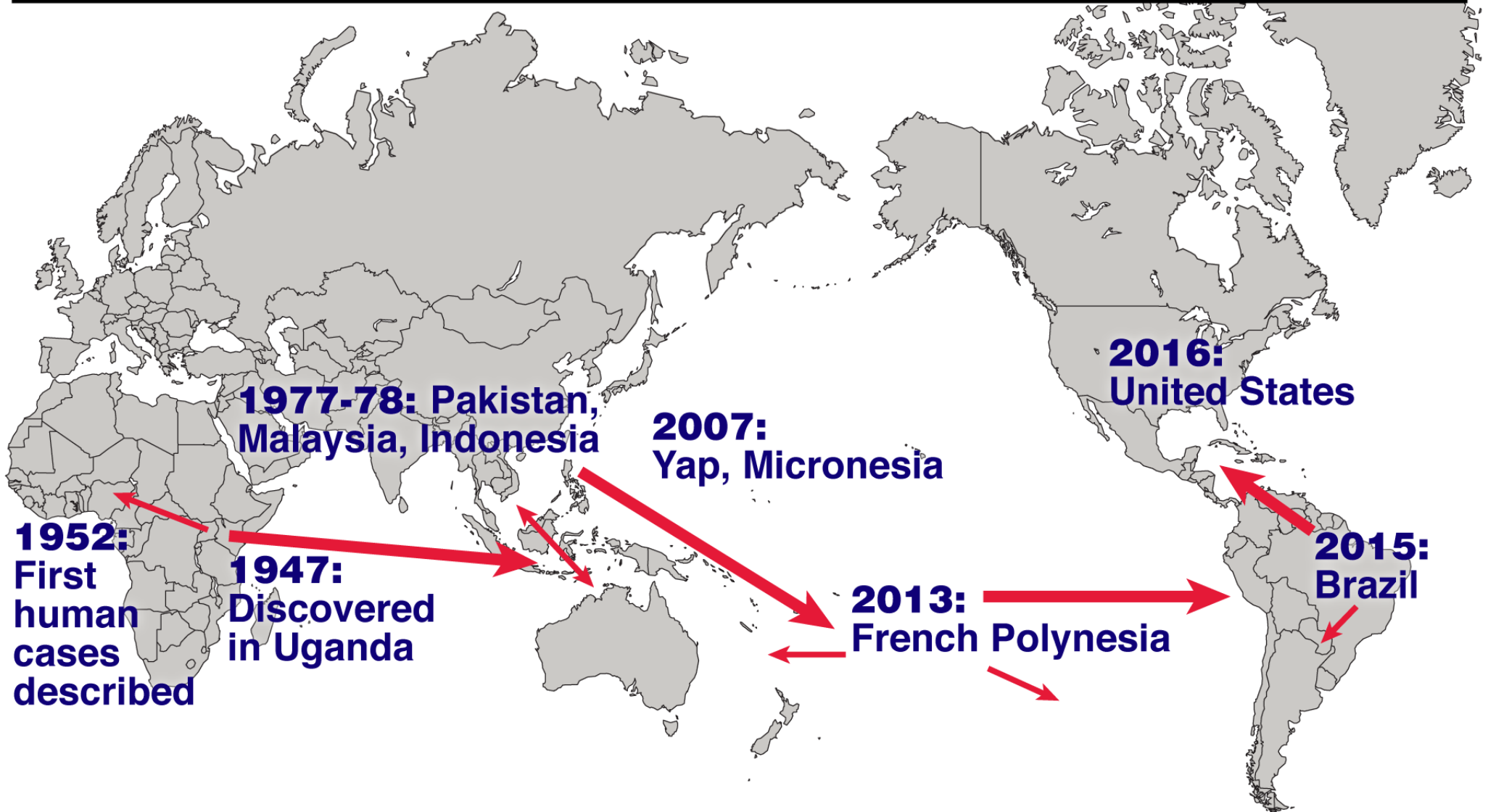
Timeline
compressed by
7 months

Global Examples of Emerging and Re-Emerging Infectious Diseases



● Newly emerging
 ● Re-emerging/resurging
 ● “Deliberately emerging”

Zika Virus Spread, 1947-2018

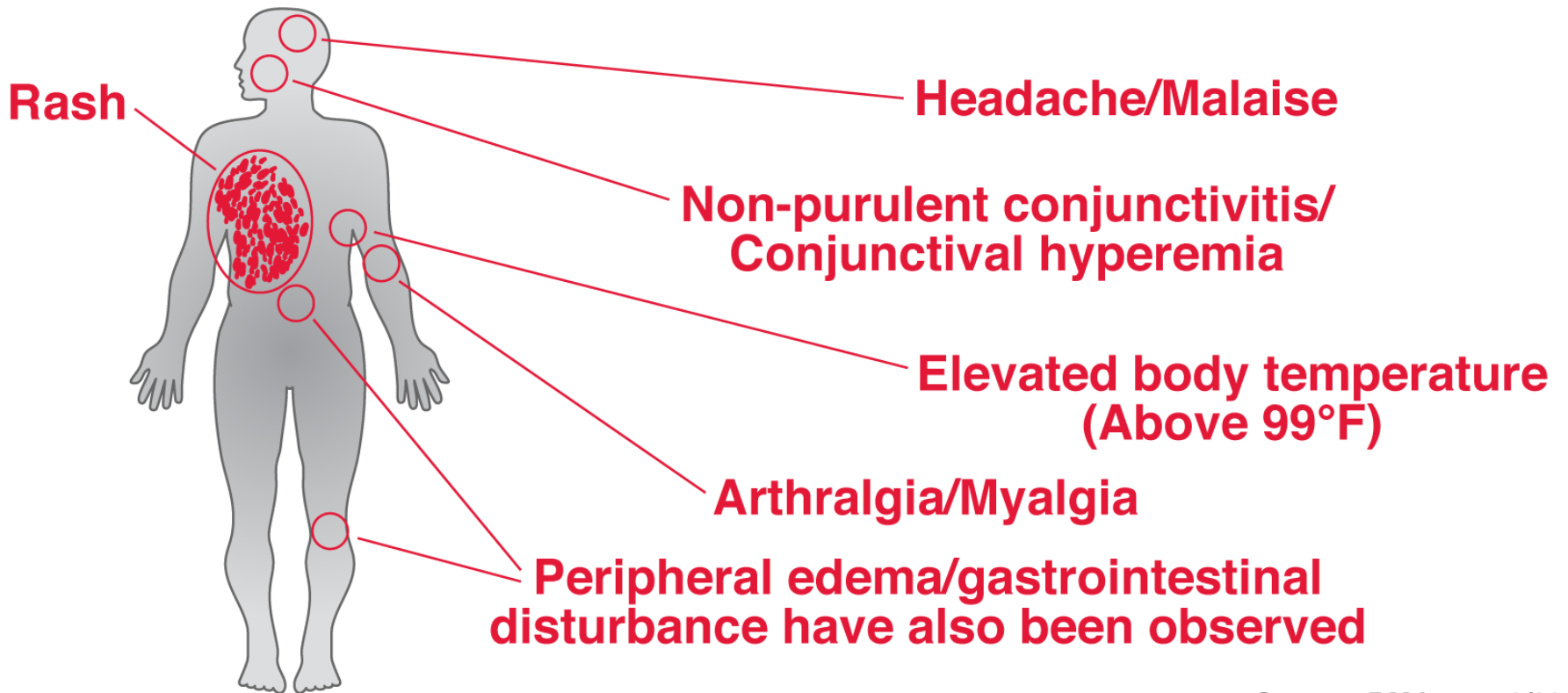


Symptoms of Zika Virus Infection

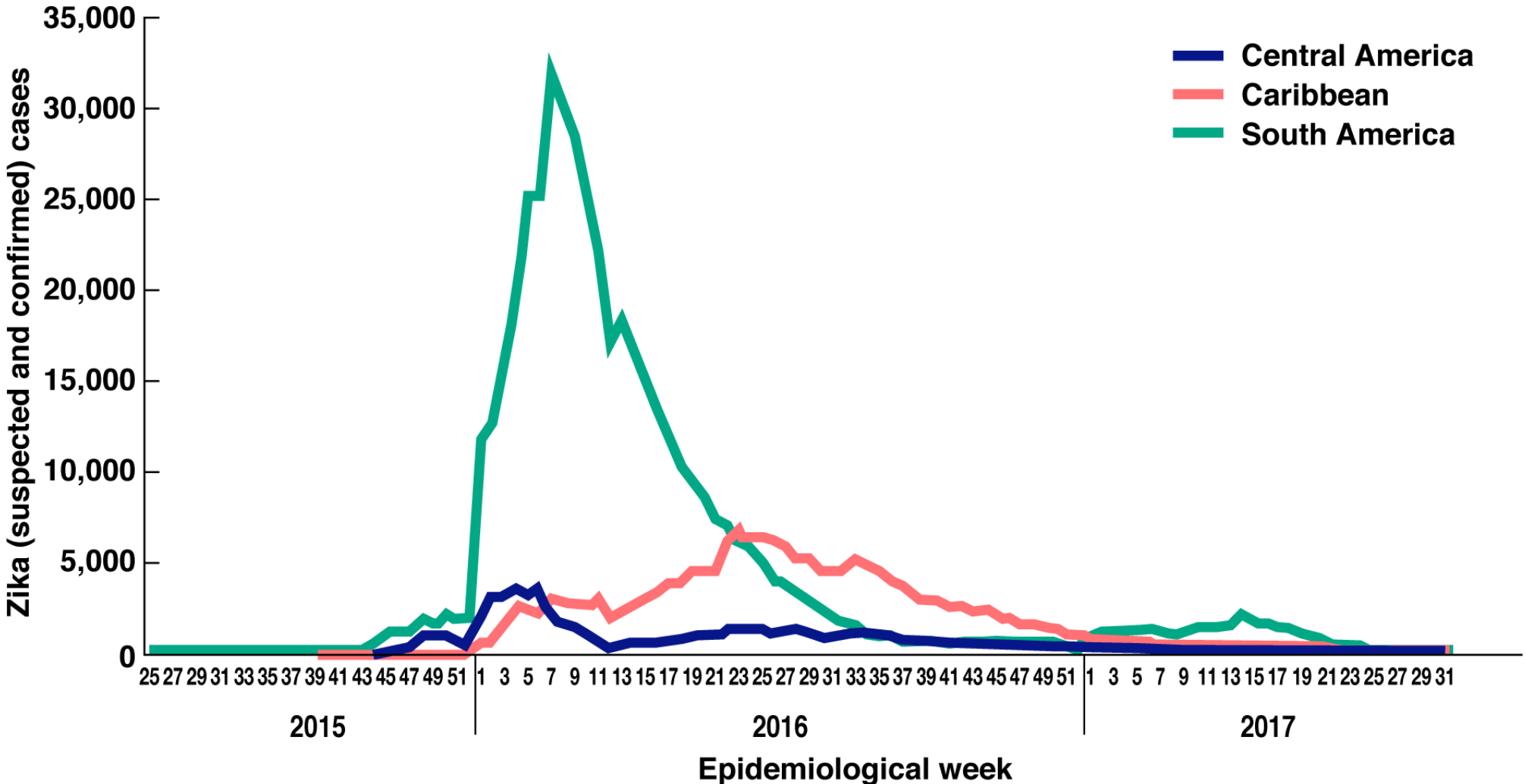
■ 4 in 5 individuals *asymptomatic*

Incubation
3-12 days

Mild symptoms
2-7 days



Suspected and Confirmed Zika Cases in the Americas, 2015-2017



Source: PAHO, 8/25/2017.

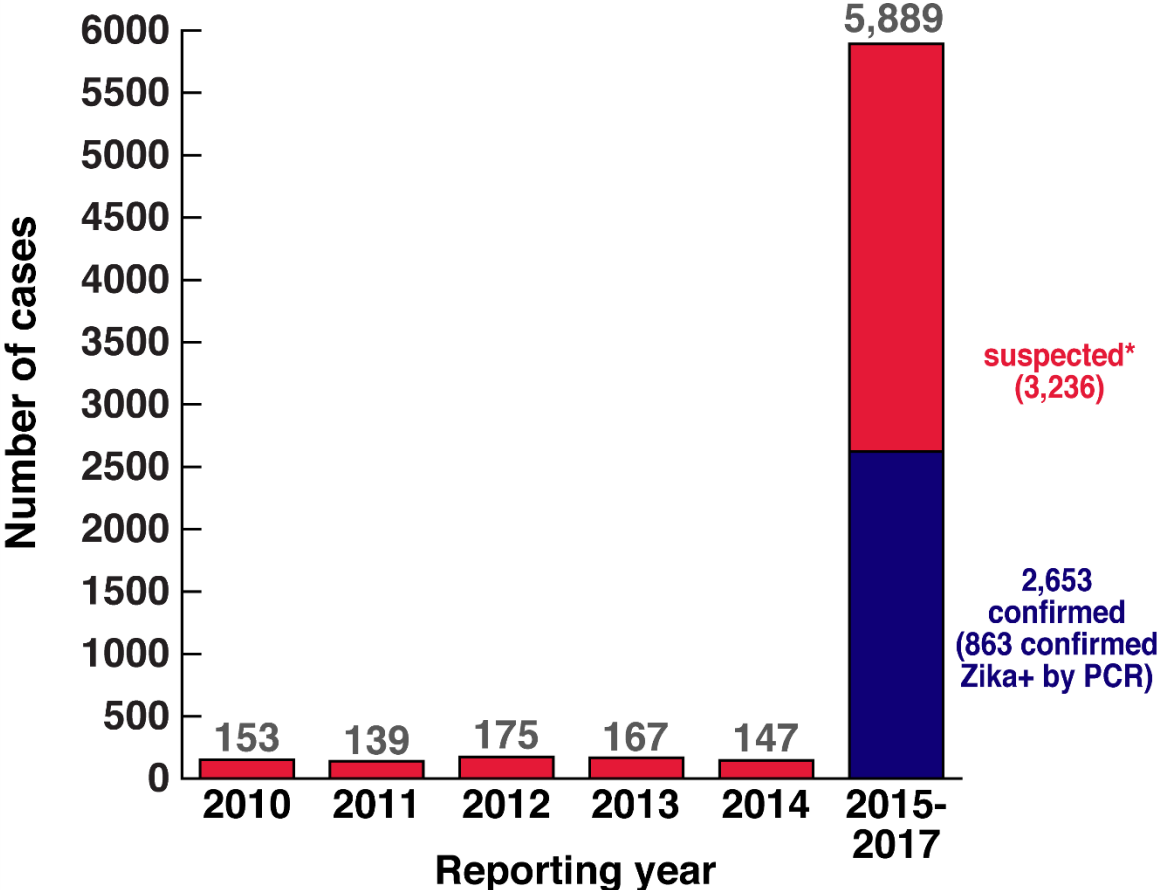
Marked Increase in Microcephaly Cases in Brazil

Associated Press

November 30, 2015

Brazil Links Mosquito-Borne Zika Virus to Microcephaly Birth Defect

Microcephaly cases in Brazil 2010-14; suspected/confirmed cases 2015-2017



*does not include cases investigated and discarded

Baby Born With Microcephaly

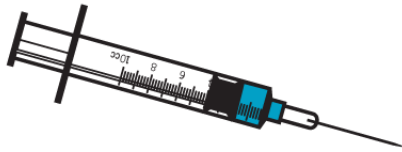




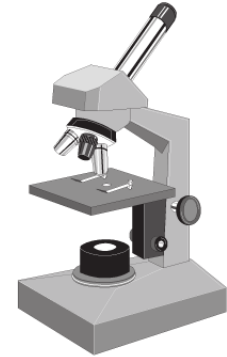
Therapeutics



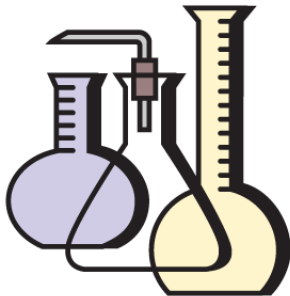
Novel Vector Control



Vaccines



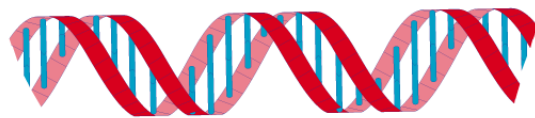
Diagnostics



Basic Research



**Expansion of
Research
Capacity**



Genomics



**Clinical
Research**

**NIH Zika
Countermeasure
Research and
Development**

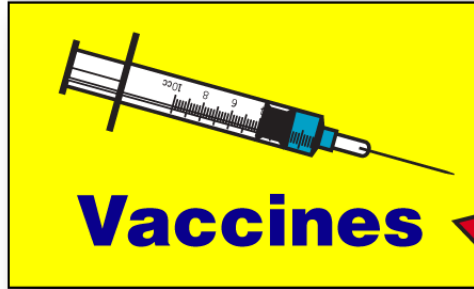




Therapeutics

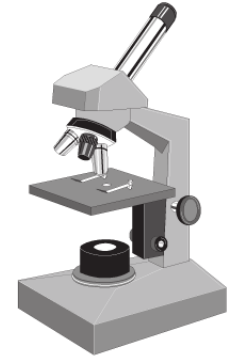


Novel Vector Control

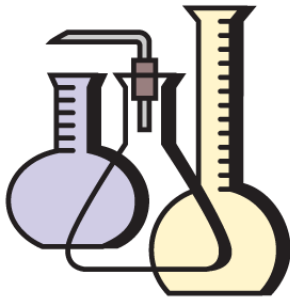


Vaccines

**NIH Zika
Countermeasure
Research and
Development**



Diagnostics



Basic Research



**Expansion of
Research
Capacity**



Genomics



**Clinical
Research**

Phase 2/2b Clinical Trial of VRC Zika DNA Vaccine

■ Part A (non-placebo controlled)

- Launched 3/31/2017
- Fully enrolled – n=90

■ Part B (placebo-controlled)

- Launched 7/19/2017
- Target n=2,400 to 5,000



Immune Correlates and Surrogates for Zika Vaccine Development



March 7-8, 2018

5601 Fishers Lane
Conference Room 1D13
Rockville, MD

**Organized by
FDA, NIAID and
WHO**

Five Administrations and Emerging Infectious Diseases

Ronald W. Reagan 1981-1989



George H.W. Bush 1989-1993



William J. Clinton 1993-2001



George W. Bush 2001-2009



Barack H. Obama 2009-2017



Six Administrations and Emerging Infectious Diseases

Ronald W. Reagan 1981-1989



George H.W. Bush 1989-1993



William J. Clinton 1993-2001



George W. Bush 2001-2009



Barack H. Obama 2009-2017



Donald J. Trump 2017-present



What's Next?

Lessons Learned from Previous Pandemics

- **Global surveillance**
- **Transparency and communication**
- **Infrastructure and capacity building**
- **Coordinated and collaborative basic and clinical research**
- **Adaptable platform technologies for vaccines, diagnostics and therapeutics**
- **Stable funding mechanism – “Public Health Emergency Fund”**

Volume 8, Issue 11

November 2008

THE LANCET Infectious Diseases



Emerging Infections: A Perpetual Challenge

DM Morens, GK Folkers & AS Fauci

