World Medical Association Assembly

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
October 14, 2017

White House Holds Disaster-Response Exercise with Trump Officials

Testimony before the House Appropriations Subcommittee for NIH – 1980s

Global Examples of Emerging and Re-Emerging Infectious Diseases

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Five Administrations and Emerging Infectious Diseases

William J. Clinton 1993-2001
George W. Bush 2001-2009
Barack H. Obama 2009-2017

HIV/AIDS


"...because we do not know the cause of this syndrome, any assumption that the syndrome will remain restricted to a particular segment of our society is truly an assumption without scientific basis."

"SILENCE = DEATH"
Rounds at NIH Clinical Center, Early 1980s – AIDS Patient

- Median survival of AIDS patients: ~6-15 months

FDAC-Approved Antiretroviral Drugs

<table>
<thead>
<tr>
<th>NRTI</th>
<th>PI</th>
<th>Pharmacokinetic Enhancers</th>
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<tbody>
<tr>
<td>Stavudine, Didanosine, Lamivudine</td>
<td>Nelfinavir, Saquinavir, Tipranavir</td>
<td>Cobicistat, Ritonavir</td>
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<td>Abacavir, Didanosine, Lamivudine</td>
<td>Atazanavir, Darunavir, Ritonavir</td>
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<tr>
<td>Emtricitabine</td>
<td>Indinavir</td>
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<table>
<thead>
<tr>
<th>NNRTI</th>
<th>Multi-Class Combinations</th>
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<tbody>
<tr>
<td>Delavirdine, Nevirapine, Etravirine</td>
<td>Atazanavir, Darunavir, Indinavir</td>
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<tr>
<td>Etiravirine</td>
<td>Lopinavir/ritonavir, Nelfinavir</td>
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</tbody>
</table>

Integrase Inhibitors

- Dolutegravir, Raltegravir, Eptinezivir

Fusion Inhibitor

- Enfuvirtide

Entry Inhibitor

- Maraviroc

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

Source: A. Montan et al., AIDS 2016.

Combination HIV Prevention

- HIV Testing/Counseling
- Treatment as Prevention
- Medical Male Circumcision
- PrEP
- Blood Supply Screening
- STI Treatment
- Condoms
- Clean Syringes
- Education/Behavior Modification
- Treatment/Prevention of Drug/Alcohol Abuse
- Microbicides

HIV/AIDS
West Nile Virus
H5N1 Influenza
Antimicrobial Resistance

Meeting at the White House to Discuss AIDS Research, Dec. 3, 1996

Commencement Address by President Clinton at Morgan State University, Baltimore, May 18, 1997

"If America commits to find an AIDS vaccine and we enlist others in our cause, we will do it... Today I'm pleased to announce the National Institutes of Health will establish a new AIDS vaccine research center dedicated to this crusade."

VRC Research: From HIV to Zika

HIV
West Nile virus
Chikungunya
Ebola/Marburg
Influenza
Malaria
MERS-CoV
RSV
Tuberculosis
Venezuelan, Eastern, and Western equine encephalitis viruses
Zika

Global Examples of Emerging and Re-Emerging Infectious Diseases

Global Distribution of West Nile Virus, 1999
**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.”

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**Newsday**

November 18, 2001

**The Worst Bioterrorist May Be Nature Itself**

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**The New England Journal of Medicine**

**REVIEW ARTICLE**

Avian Influenza A (H5N1) Infection in Humans

The Writing Committee of the World Health Organization (WHO) Consultation on Human Influenza A/H5

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**Pandemic Influenza Preparedness Strategy and Implementation**

- International Surveillance
- Domestic Surveillance
- Vaccines
- Antivirals
- Communications
- State and Local Preparedness

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**The Birth of the President’s Emergency Plan for AIDS Relief (PEPFAR)**
Addressing HIV/AIDS: Visits to 11 Countries in Sub-Saharan Africa

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

State of the Union Address, January 28, 2003

- President Bush announces the President’s Emergency Plan for AIDS Relief (PEPFAR)
SARS Characterization and Vaccine Development

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

Global Examples of Emerging and Re-Emerging Infectious Diseases

Beginning of Global H1N1 Influenza as of March, 2009

Barack H. Obama
2009-2017

- H1N1 Pandemic influenza
- MERS
- Chikungunya
- Ebola
- Zika
- Antimicrobial Resistance

Source: WHO
Global H1N1 Influenza Cases, as of April 29, 2009

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

Reported Ebola Virus Disease Cases in Guinea, Liberia, and Sierra Leone, 2014-2016
First Case Diagnosed in the U.S.: Timeline

Sept 19: Subject departs Monrovia
Sept 20: Arrives and departs Brussels, Belgium
Sept 23: Patient transferred by ambulance, admitted
Sept 24: Develops symptoms
Sept 26: Presents to ER, sent home
Oct 5: Patient dies

First Two Ebola Transmissions Within the U.S.

The New York Times
October 12, 2014

Texas Health Worker Tests Positive for Ebola
2nd Ebola Case in U.S. Stokes Fears of Health Care Workers

USA TODAY
October 14, 2014

Fear Spreads Faster than Ebola: Our View
By USA Today Editorial Board

NIH Special Clinical Studies Unit: Designated Ebola Treatment Facility

As of Oct. 2014, three designated Ebola treatment facilities existed in the U.S.

The Washington Post
October 25, 2014

Nina Pham, Nurse Who Contracted Ebola, is Now Free of Virus and Leaves NIH

CNN
March 12, 2015

U.S. Ebola Patient Headed to NIH
Patient Admitted With Ebola Virus Disease Discharged From NIH Clinical Center
Zika Virus Spread, 1947-2017

Symptoms of Zika Virus Infection
- 4 in 5 individuals asymptomatic
- Incubation: 3-12 days
- Mild symptoms: 2-7 days
- Rash
- Headache/Malaise
- Non-purulent conjunctivitis/Conjunctival hyperemia
- Elevated body temperature (Above 99°F)
- Arthralgia/Myalgia
- Peripheral edema/gastrointestinal disturbance have also been observed

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

Marked Increase in Microcephaly Cases in Brazil

Baby Born With Microcephaly

Congenital Zika Syndrome is a Pattern of Birth Defects in Babies Infected with Zika During Pregnancy

Source: CDC
NIH Zika Vaccine Candidates

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

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VRC DNA Vaccines for Emerging Infections

<table>
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<tr>
<th>Sequence Selection to 1st Human Injection</th>
<th>Months</th>
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<tbody>
<tr>
<td>SARS (6-14-2003)</td>
<td>6</td>
</tr>
<tr>
<td>2005 H5N1 (2-11-2006)</td>
<td>11</td>
</tr>
<tr>
<td>2009 H1N1 (4-27-2009)</td>
<td>4</td>
</tr>
<tr>
<td>ZIK (4-28-2016)</td>
<td>3.25</td>
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Phase 2 Zika Vaccine Trial Begins in U.S. and Central and South America

Study Will Evaluate NIH’s Experimental DNA Vaccine

- Enrollment target: at least 2,490 individuals in the continental United States, Puerto Rico, Brazil, Peru, Costa Rica, Panama and Mexico
Five Administrations and Emerging Infectious Diseases

William J. Clinton 1993-2001
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Six Administrations and Emerging Infectious Diseases

William J. Clinton 1993-2001
George W. Bush 2001-2009
Barack H. Obama 2009-2017
Donald J. Trump 2017-present

What’s Next?

Health Officials Brace for Return of Zika

Examples of Recently Emergent Influenza Viruses

Oropouche Virus Could Emerge and Cause a Public Health Problem

Vesiculovirus is no longer confined to villages in the Amazon but is spreading to major cities throughout Brazil, researcher warns
Five Waves of Human H7N9 Influenza Infections in China, February 2013-present

- 1,589 confirmed human cases, 616 deaths
- 5th wave: >50% of cumulative cases

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Induction of Unnatural Immunity: Prospects for a Broadly Protective Universal Influenza Vaccine

GJ Nabel and AS Fauci

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Health Affairs Blog

February 9, 2017

What Three Decades Of Pandemic Threats Can Teach Us About The Future

Anthony S. Fauci

“If history has taught us anything, it is that the new administration is likely to experience at least one infectious disease crisis of significance.”

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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”

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Emerging Infections: A Perpetual Challenge

DM Morens, GK Folkers & AS Fauci