

2012 Demystifying Medicine Lecture Series

Emerging and Re-emerging Infectious Diseases: The Perpetual Challenge to Global Health



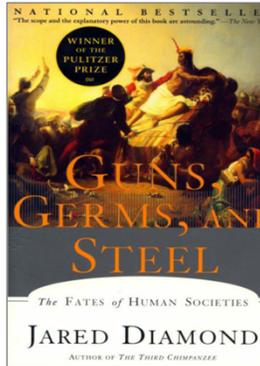
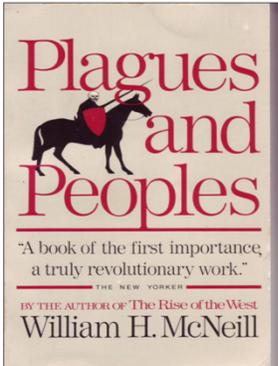
Anthony S. Fauci, M.D.
Director
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
January 10, 2012



Examples of Epidemic Emerging Infections

		Causal Agent	Deaths (est.)
430-426 BC	Plague of Athens	Unknown	40,000
1340s	Black death (plague)	<i>Yersinia pestis</i>	~50 million
1520-21	Smallpox in Aztec Empire	<i>Variola major</i>	3.5 million
1793-98	The American plague	Yellow fever virus	~25,000
1918-19	Spanish influenza	H1N1 influenza virus	>50 million
1981 →	AIDS pandemic	HIV	~30 million

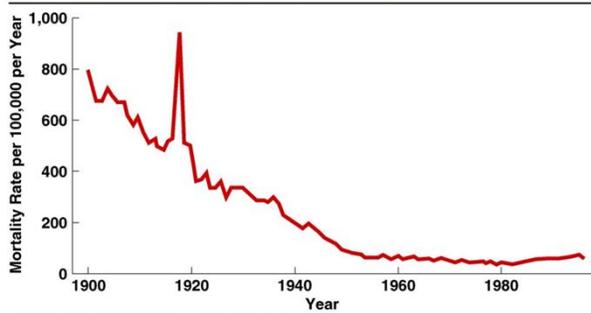
Source: Morens, Folkers, Fauci; *Lancet Infect Dis*, 2008; UNAIDS, 2011



Progress in the Control of Infectious Diseases

- Recognition that microbes causes many serious diseases
- Improvements in sanitation, hygiene, vector control
- Discovery and development of antimicrobials
- Development of vaccines and implementation of vaccination programs
- Advances in detecting and monitoring infectious diseases

Crude Infectious Disease Mortality Rate, United States, 1900 to 1996



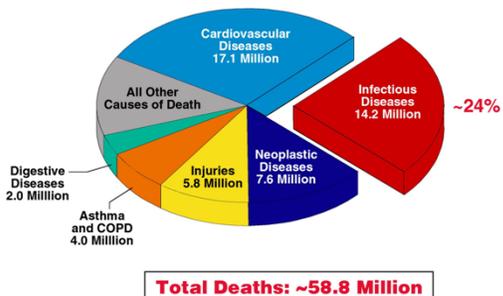
A Premature Declaration of Victory Over Infectious Diseases

"We can look forward with confidence to a considerable degree of freedom from infectious diseases at a time not too far in the future. Indeed... it seems reasonable to anticipate that within some measurable time... all the major infections will have disappeared."

- Aidan Cockburn, *The Evolution and Eradication of Infectious Diseases*, 1963.

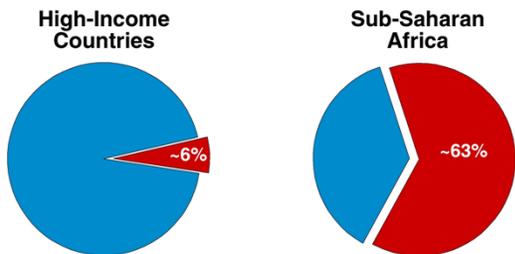
A Failure to Look Beyond our Borders

Infectious Diseases Cause ~24% of All Deaths Worldwide



Source: WHO, 10/2008

Proportion of Deaths Due to Infectious Diseases



Source: Disease Control Priorities Project, 2006

Global Health and Infectious Diseases

Established Infectious Diseases

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Emerging and Re-Emerging Infectious Diseases

Global Health and Infectious Diseases

Established Infectious Diseases

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Emerging and Re-Emerging Infectious Diseases

Selected Established Infectious Diseases of Global Public Health Importance

	Estimated Annual Deaths
Respiratory Infections	4.0 million
HIV/AIDS	1.8 million
Diarrheal Infections	1.8 million
Tuberculosis	1.7 million
Vaccine Preventable Childhood Diseases (measles, pertussis, tetanus, etc.)	1.1 million
Hepatitis (B and C)	950,000
Malaria	655,000
Neglected Tropical Diseases	547,000

Sources: WHO; Hotez et al., *Lancet* 373:1570, 2009

Global Health and Infectious Diseases

Established Infectious Diseases

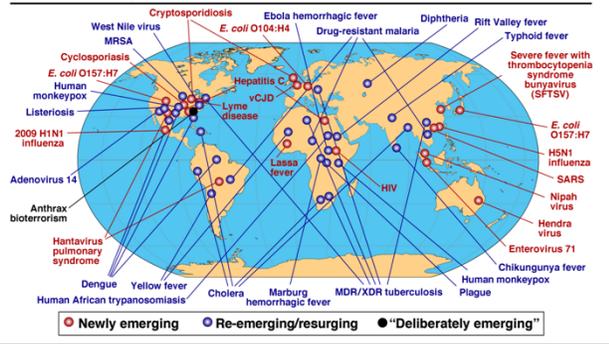
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Emerging and Re-Emerging Infectious Diseases



“In the global human population, we report the emergence of 335 infectious diseases between 1940 and 2004.”

Global Examples of Emerging and Re-Emerging Infectious Diseases



Factors Contributing To Infectious Disease Emergence

- International travel, trade and commerce
- Human demographics and behaviour
- Human susceptibility to infection
- Poverty, social inequality, war, lack of political will
- Breakdown of public-health measures
- Technology and industry
- Ecological and environmental factors
- Microbial adaptation and change
- Economic development and land use

DM Morens, GK Folkers, AS Fauci, Lancet Infect Dis 2008

~75 Percent of Emerging Pathogens are Zoonotic

Examples:

- HIV
- Influenza
- Human monkeypox
- Nipah virus
- BSE/vCJD
- SARS
- Ebola

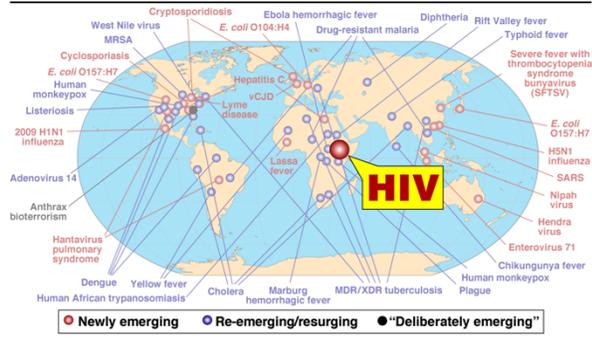
Source: Taylor et al., 2001; WHO

Emerging Infectious Diseases

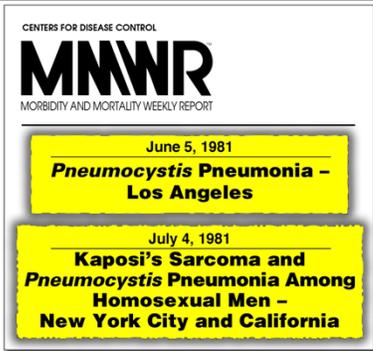
Newly Emerging

Re-emerging or Resurging

Global Examples of Emerging and Re-Emerging Infectious Diseases



30 Years of AIDS





Origin of HIV-1 in the chimpanzee *Pan troglodytes troglodytes*

Feng Gao et al. *Nature* 1999;397:436-41

The Scope of the Global HIV/AIDS Pandemic

- Cumulative HIV infections 65 million
- People living with HIV/AIDS 34 million
- New HIV infections in 2010 2.7 million
- Deaths due to AIDS in 2010 1.8 million
- Cumulative AIDS deaths ~30 million

UNAIDS estimates, 11/2011



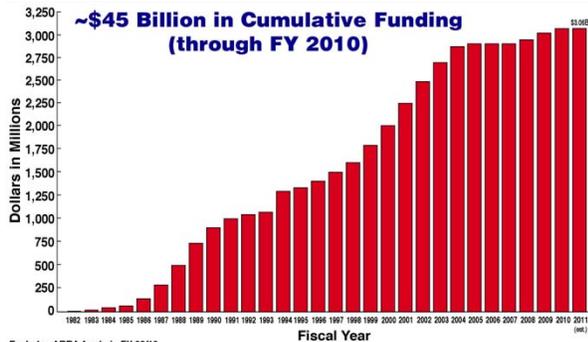
HIV/AIDS in the United States - Latest Estimates

- 594,496 cumulative deaths
- ~1.2 million living with HIV, 20% unaware of their infection
- ~50,000 new infections/yr.
 - 61% male-to-male sexual contact, 27% heterosexual contact
 - incidence rates among blacks >7 times higher than whites

Source: CDC, 2011. Includes 50 States and District of Columbia.

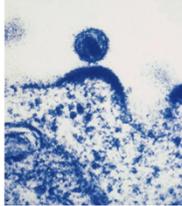


NIH HIV/AIDS Research Funding



Advances in HIV Science

- Etiology
- Diagnosis
- Molecular Virology and Epidemiology
- Natural History
- Pathogenesis
- Treatment
- Prevention
- Vaccine Development

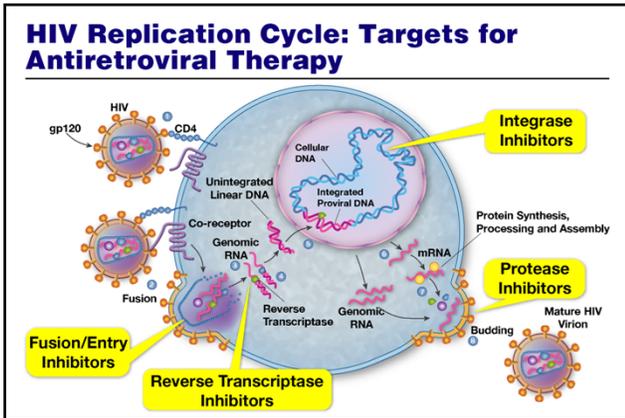


Treatment of the HIV-Infected Individual

Rounding on AIDS Ward, NIH Clinical Center, Early 1980s



- Median survival of AIDS patients: ~6-8 months



- ### FDA-Approved Antiretroviral Drugs
- | | | |
|--|---|--|
| NRTI <ul style="list-style-type: none"> ■ Zidovudine ■ Didanosine ■ Zalcitabine ■ Stavudine ■ Lamivudine ■ Abacavir ■ Tenofovir ■ Emtricitabine | PI <ul style="list-style-type: none"> ■ Saquinavir ■ Ritonavir ■ Indinavir ■ Nelfinavir ■ Amprenavir ■ Lopinavir ■ Atazanavir ■ Fosamprenavir ■ Tipranavir ■ Darunavir | Entry Inhibitor <ul style="list-style-type: none"> ■ Maraviroc |
| NNRTI <ul style="list-style-type: none"> ■ Nevirapine ■ Delavirdine ■ Efavirenz ■ Etravirine ■ Rilpivirine | Fusion Inhibitor <ul style="list-style-type: none"> ■ Enfuvirtide (T-20) | Integrase Inhibitor <ul style="list-style-type: none"> ■ Raltegravir |
| Combinations <ul style="list-style-type: none"> ■ 6 available, combining 2 or 3 drugs | | |
- 



Life Expectancy of Recently Diagnosed Asymptomatic HIV-infected Patients Approaches that of Uninfected Individuals

A. van Sighem et al. on behalf of the ATHENA National Observational Cohort Study

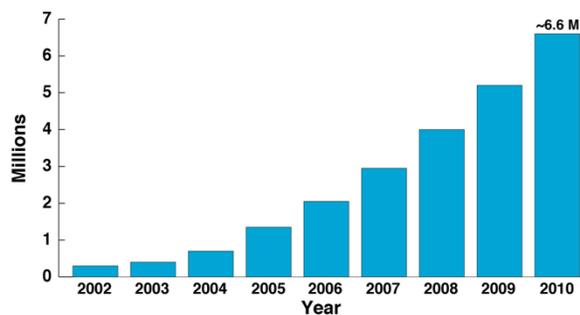
- **Life expectancy** for HIV-infected patients (without AIDS) aged 25 yrs at six months postinfection
 - Men: an additional 52.7 yrs** (versus 53.1 yrs in general population)
 - Women: an additional 57.8 yrs** (versus 58.1 yrs in general population)

Examples of Programs Providing HIV/AIDS Prevention, Treatment and Care to Developing Nations

- President's Emergency Plan for AIDS Relief (PEPFAR)
- Global Fund to Fight AIDS, Tuberculosis and Malaria
- Philanthropies and NGOs (e.g. Gates Fdtn., Clinton Fdtn., MSF)



Number of People Receiving Antiretrovirals in Low- and Middle-Income Countries



Source: UNAIDS, 2011

Major Challenges Globally in the Treatment of HIV Disease

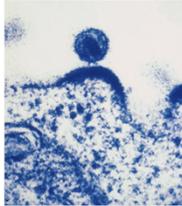
- 47% of people in need of ARV therapy in low- and middle-income countries are receiving it
- For every person put on ARV therapy in 2010, about 2 others were newly infected with HIV



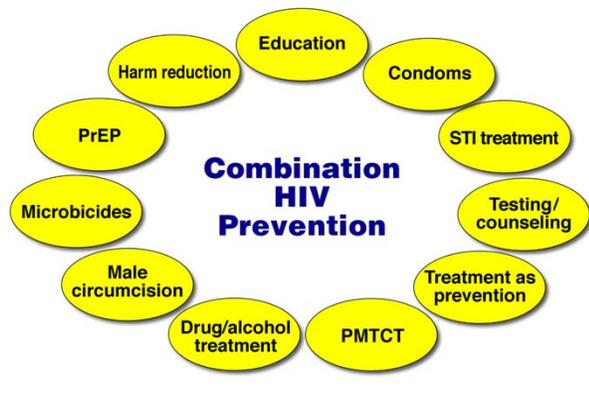
UNAIDS estimates, 11/2011

Advances in HIV Science

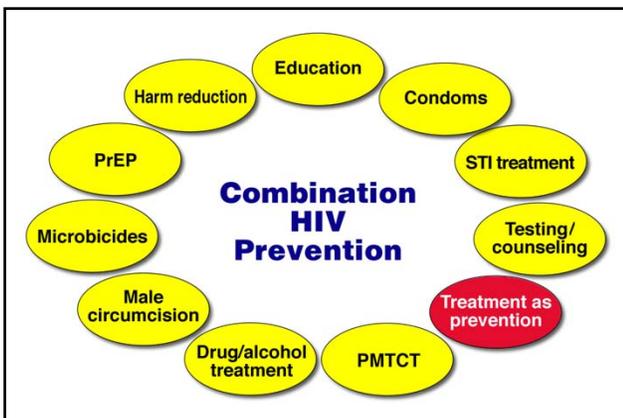
- Etiology
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- Vaccine Development

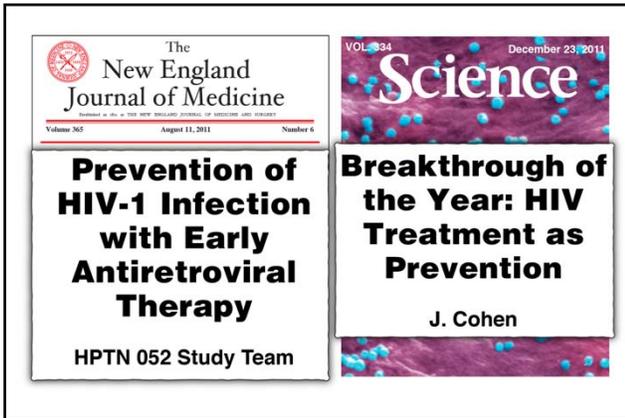


Combination HIV Prevention

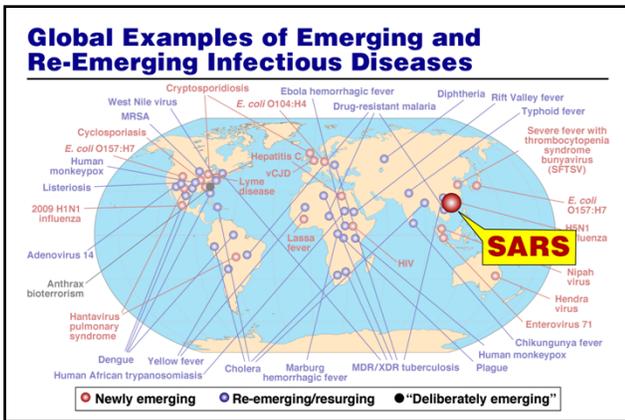


Combination HIV Prevention









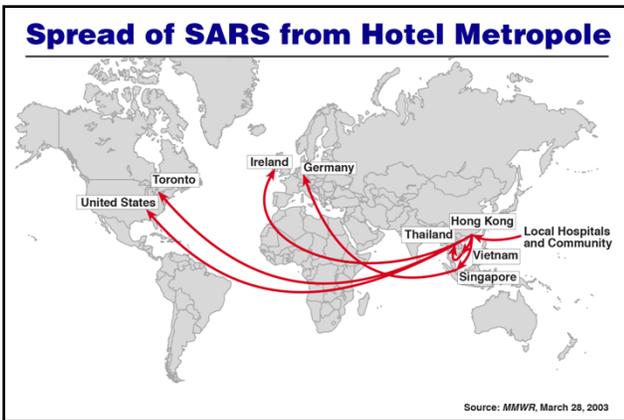
SARS: A New Challenge to Global Health



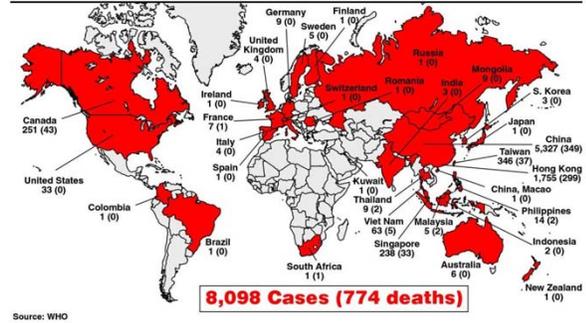
Early Cases of SARS: Guangdong Province, China



Spread of SARS from Hotel Metropole



Cumulative Reported Cases of Severe Acute Respiratory Syndrome (SARS), Sept. 26, 2003

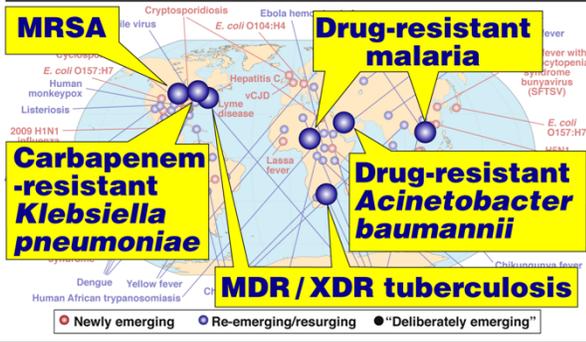


Emerging Infectious Diseases

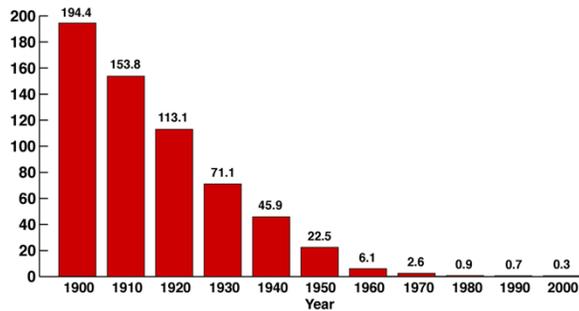
Newly Emerging

Re-emerging or Resurging

Global Examples of Emerging and Re-Emerging Infectious Diseases



Death Rate for Tuberculosis, United States, 1900-2000 (per 100,000 population)



The Global Burden of Tuberculosis

- One-third of the world's population is infected with *Mycobacterium tuberculosis* (Mtb)
- In 2010
 - 8.8 million new cases, incl. 1.1 million among HIV+
 - 1.45 million deaths, incl. 350,000 among HIV+
 - 650,000 prevalent cases of MDR-TB
 - XDR-TB reported in ~70 countries



Source: WHO, 10/2011

Image: CDC

Major Challenges in the Control of Tuberculosis

- Standard **diagnostics** are antiquated, insensitive and slow
- Current **drug regimens** are complex and lengthy
- Available **vaccine** not effective in preventing adult pulmonary TB
- Our understanding of TB **pathogenesis** is limited

The Global Burden of Malaria, 2010

- ~655,000 malaria deaths, 91% in Africa
- ~216 million malaria cases
- Malaria present in 106 countries and territories
 - Half the world's population is at risk
- Every 60 seconds a child dies from malaria



Credit: S. Hollyman

Source: WHO, World malaria report 2011

December 1, 2009
Volume 200
Number 11

The Journal of Infectious Diseases

Malaria Control, Elimination, and Eradication: The Role of the Evolving Biomedical Research Agenda

B. Fenton Hall and Anthony S. Fauci

“The final challenge is to ensure the vigor and sustainability of the substantial biomedical research efforts that will be required to eliminate and ultimately eradicate malaria.”



The
New England
Journal of Medicine

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

Published Online October 18, 2011

First Results of Phase 3 Trial of RTS,S/AS01 Malaria Vaccine in African Children

The RTS,S Clinical Trials Partnership

- Initial report on efficacy, safety, and immunogenicity in the first 6,000 children, age 5 to 17 months
- Vaccine prevented about half of malaria infections

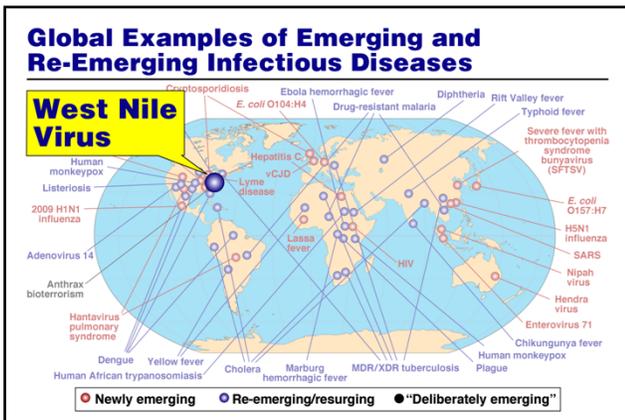
December 7, 2011

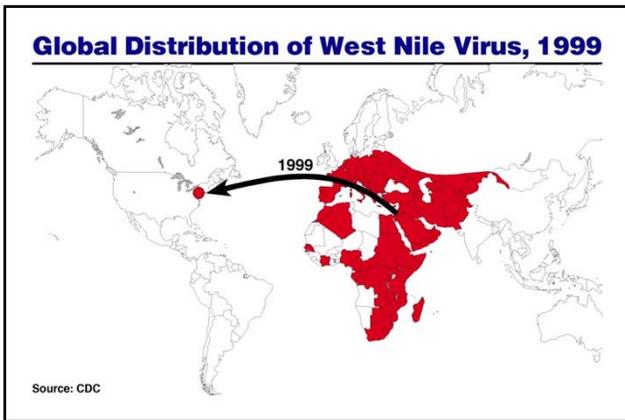
TIME

Top 10 Medical Breakthroughs of 2011

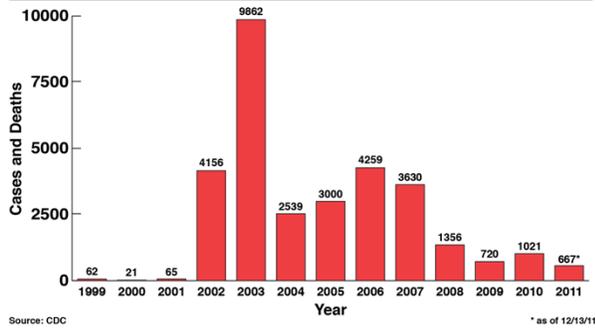
#2. A First-Ever Malaria Vaccine



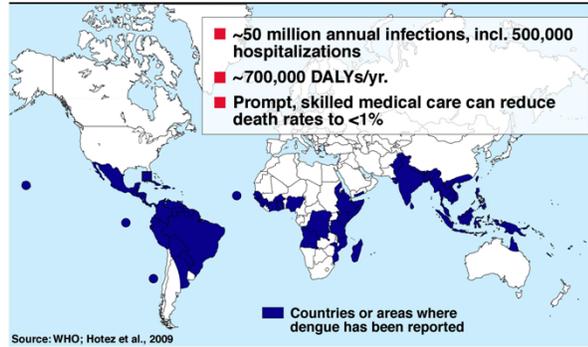




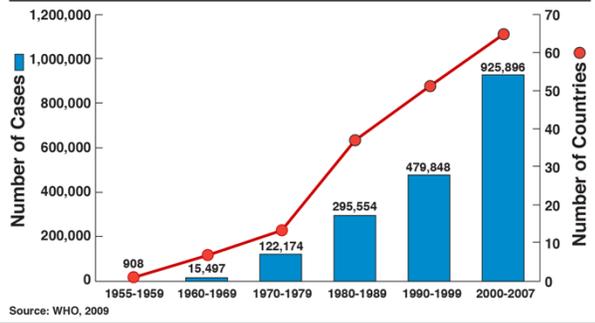
Reported Human Cases of West Nile Virus Infection, USA, 1999-2011

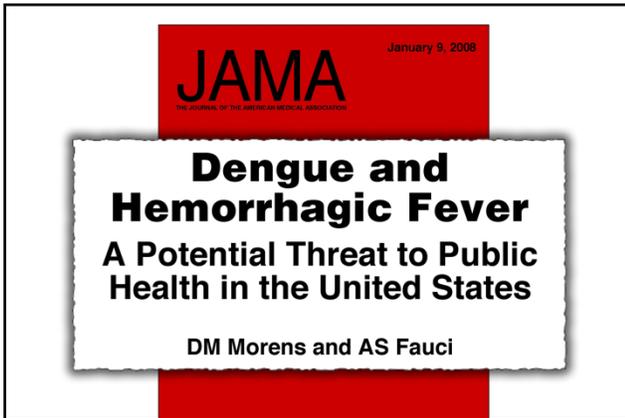


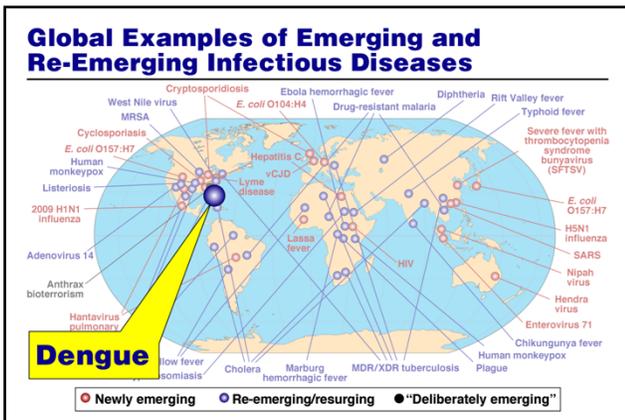
Dengue: 2.5 Billion People at Risk



Average Annual Number of Cases and Countries Reporting Dengue Fever and Dengue Hemorrhagic Fever







28 Cases of Locally Acquired Dengue in Key West, 2009-2010

Locally Acquired Dengue -- Key West, Florida, 2009--2010

"Clinicians should include dengue in the differential diagnosis of acute febrile illnesses in patients who live in or have recently traveled to subtropical areas of the United States or to the tropics."

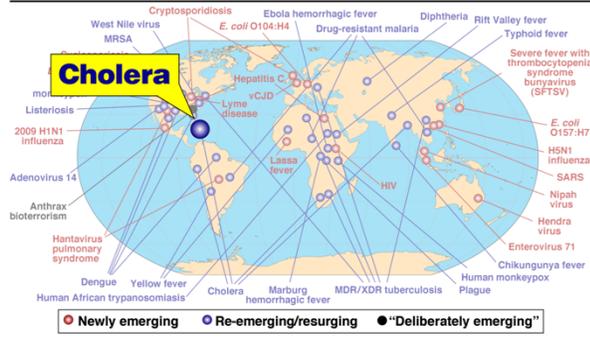
The Miami Herald

September 28, 2011

Second Case of Locally Acquired Dengue Fever Found in Miami-Dade

Miami-Dade health officials announced a second case of locally acquired dengue fever this year, and urged residents to drain standing water and wear protective clothing and mosquito repellent.

Global Examples of Emerging and Re-Emerging Infectious Diseases



The New York Times

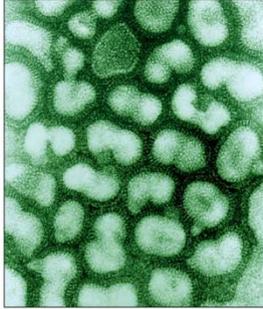
October 26, 2010

Amid Cholera Outbreak in Haiti, Fear and Misery



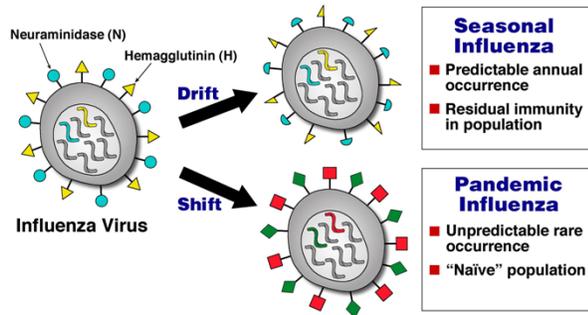
- First large cholera outbreak in Haiti in >100 years
- 473,649 cases and 6,631 deaths (PAHO, November 7, 2011)

Influenza

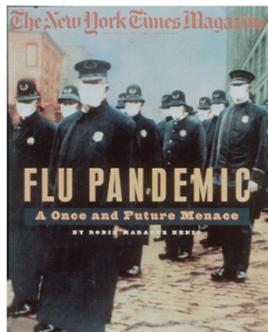


- Re-emerging disease (seasonal influenza)
- Newly emerging disease (pandemic influenza)

Seasonal vs. Pandemic Influenza

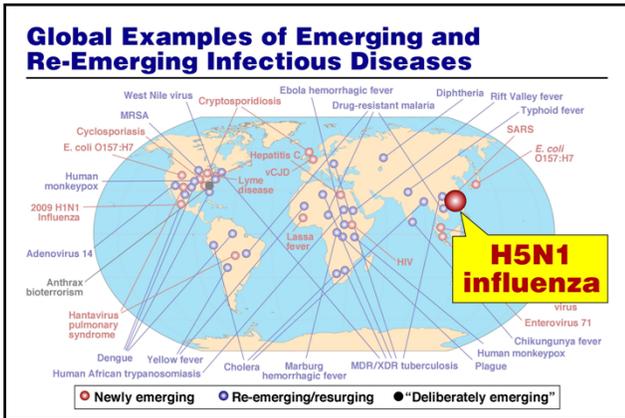


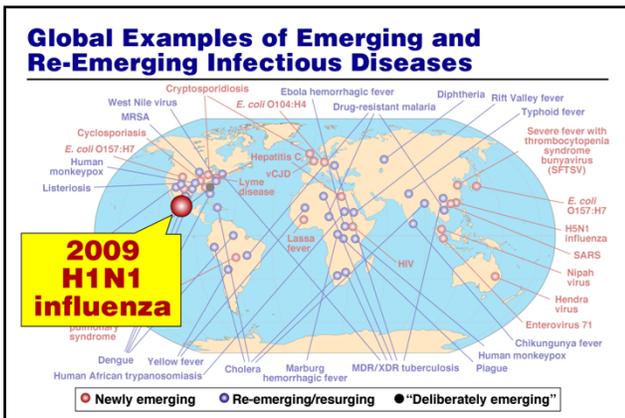
The Influenza Pandemic of 1918-1919

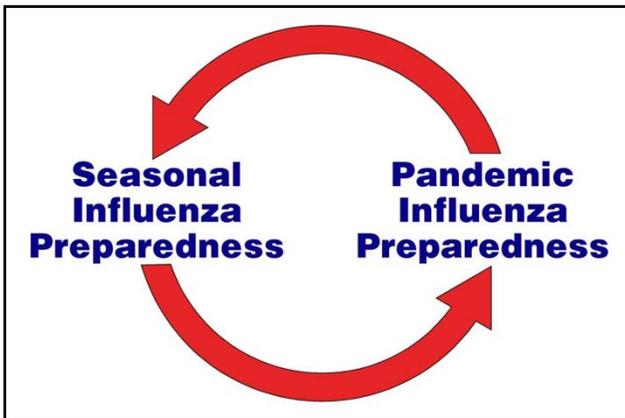


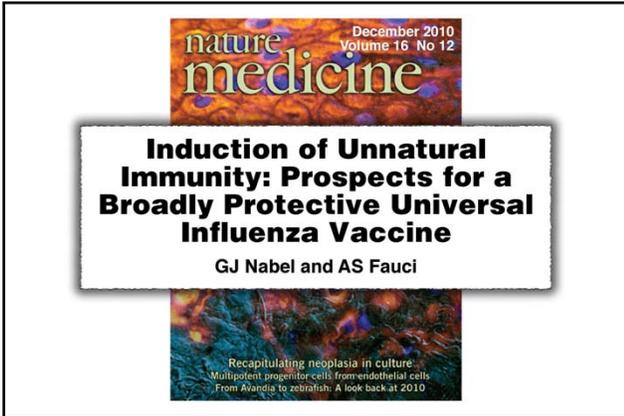
- 25-30% of world's population (~500 million people) fell ill
- > 50 million deaths worldwide; ~60 percent in people ages 20-45
- > 500,000 deaths in United States; 196,000 in October, 1918 alone

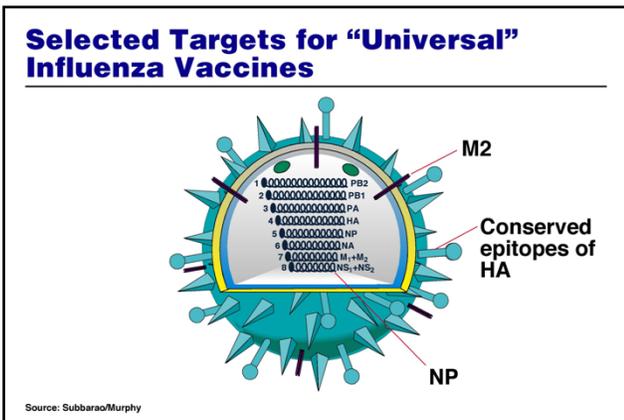
Source: WHO, 1/2005

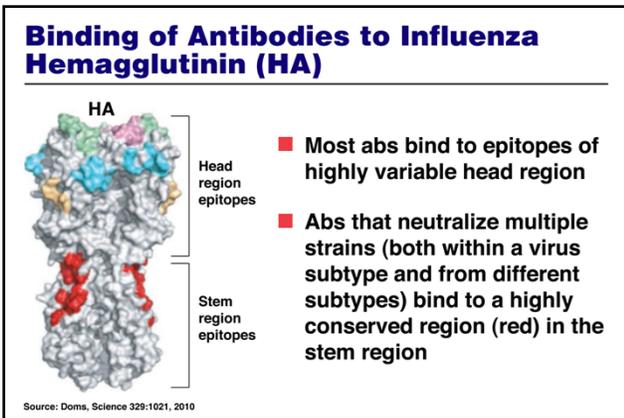












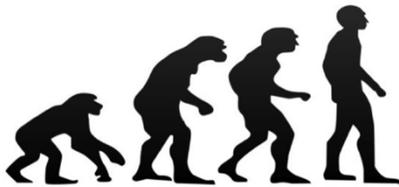
Emerging and Re-emerging Infectious Diseases – A Delicate Balance

**The Extraordinary
Capability of
Microbial Pathogens
to Change, Adapt,
Emerge,
Re-Emerge, and Persist**

**Public Health
Measures,
Biomedical
Research, and
Countermeasure
Development**



Microorganisms versus Man



Homo sapiens
~8 million years
2% genome change



Human virus
<one day
2% genome change

“The future of humanity and microbes likely will unfold as episodes of a suspense thriller that could be titled *Our Wits Versus Their Genes.*”

--Joshua Lederberg, *Science*, April 14, 2000
