Columbia University
MAILMAN SCHOOL
OF PUBLIC HEALTH

Emerging Infections

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GHP 350 (Epidemiology)
Princeton University
November 18, 2008

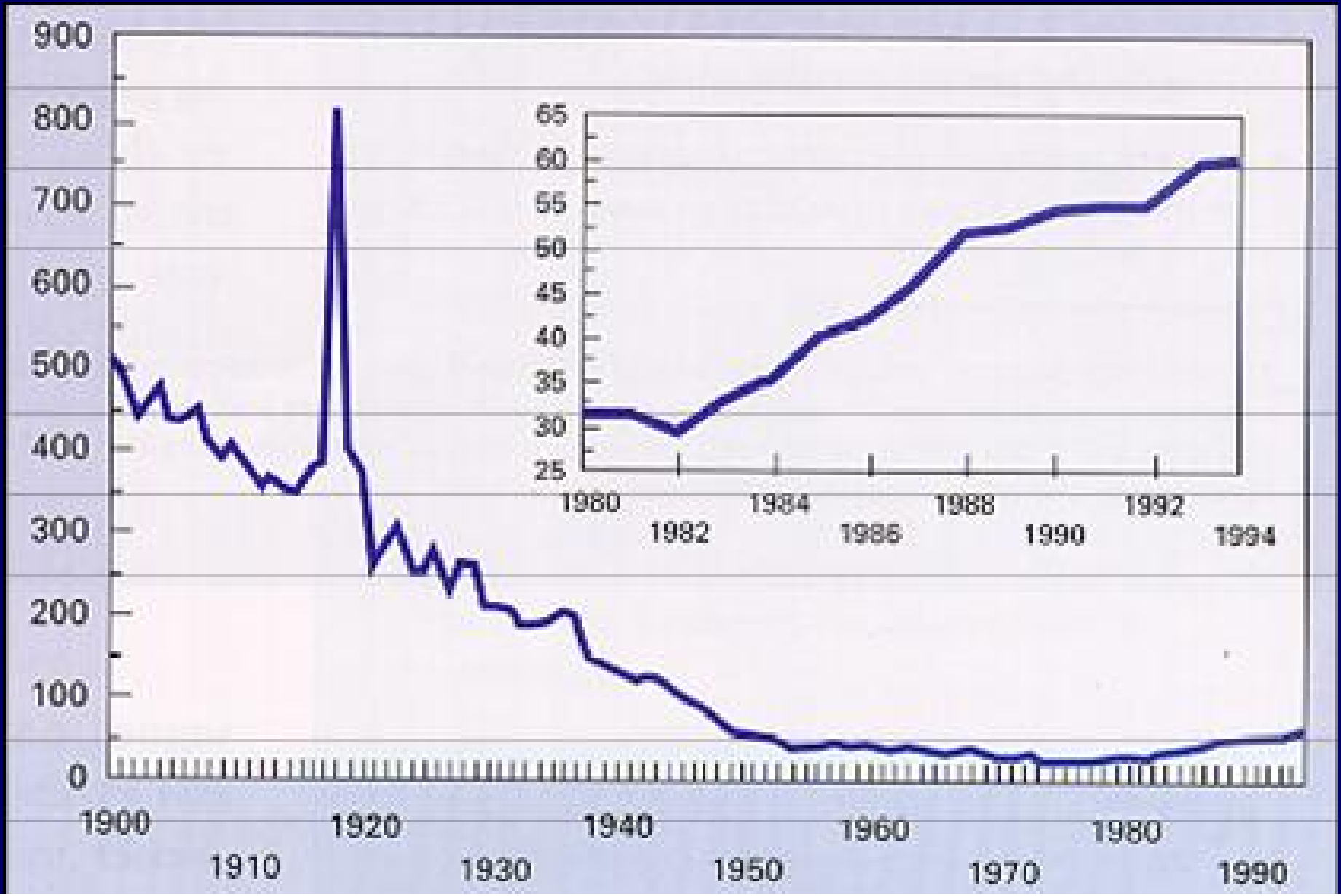
Some Famous Microbial Invaders in History

- The Black Death (plague, 1348)
- Smallpox
- “The Columbian Exchange”? (smallpox, syphilis)
- Cholera (19th Century and after)
- 1918 Influenza

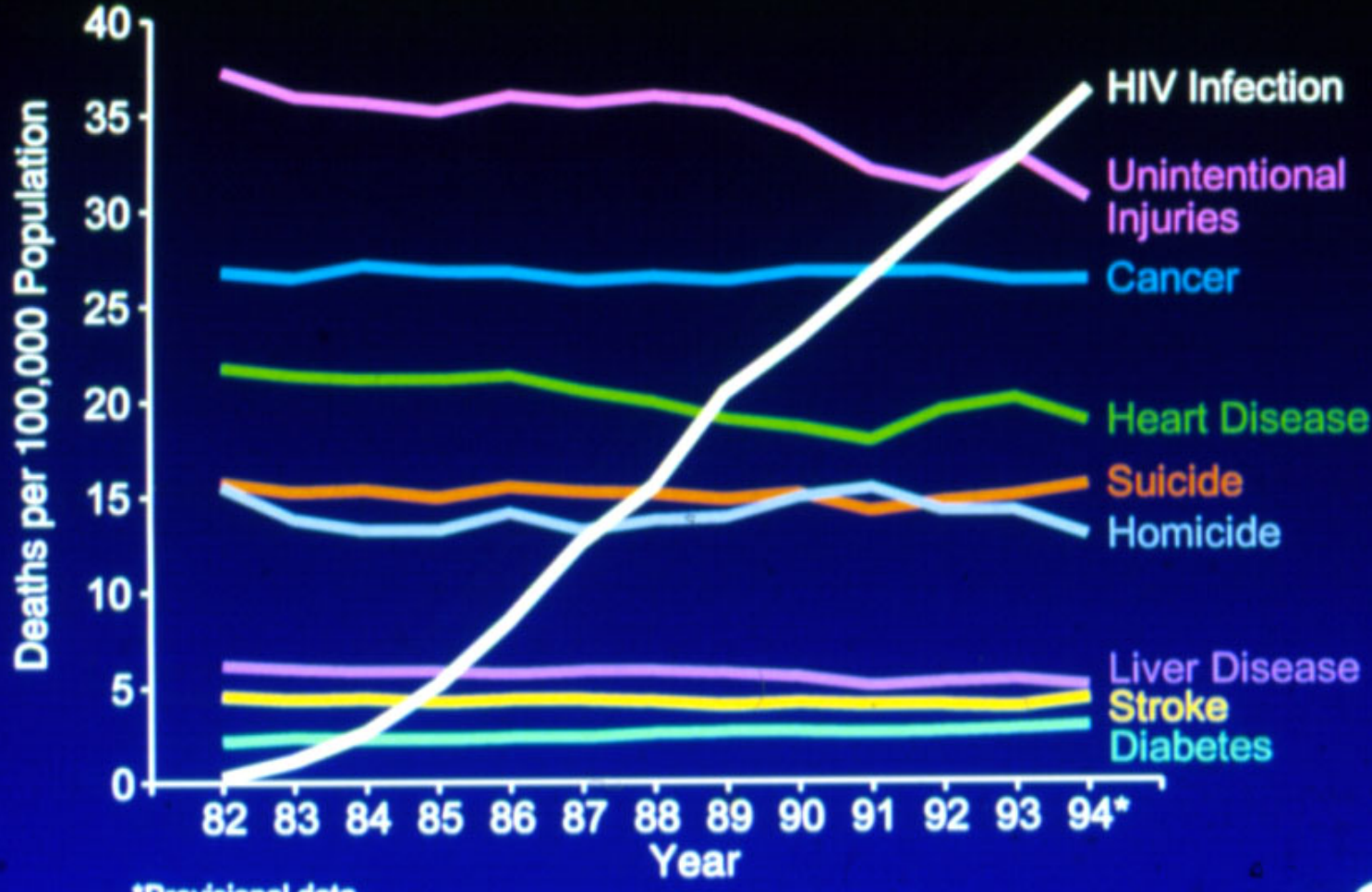
Infectious Diseases in the Present

- In much of the world, infectious diseases remain major causes of disease and death
- Infections not previously recognized also appear (“Emerging infections”)
- Forgotten infections reappear (“Re-emerging infections”)

US Mortality Rates, Infectious Diseases, 1900-1994



Death Rates from Leading Causes of Death in Persons Aged 25-44 Years, USA, 1982-1994

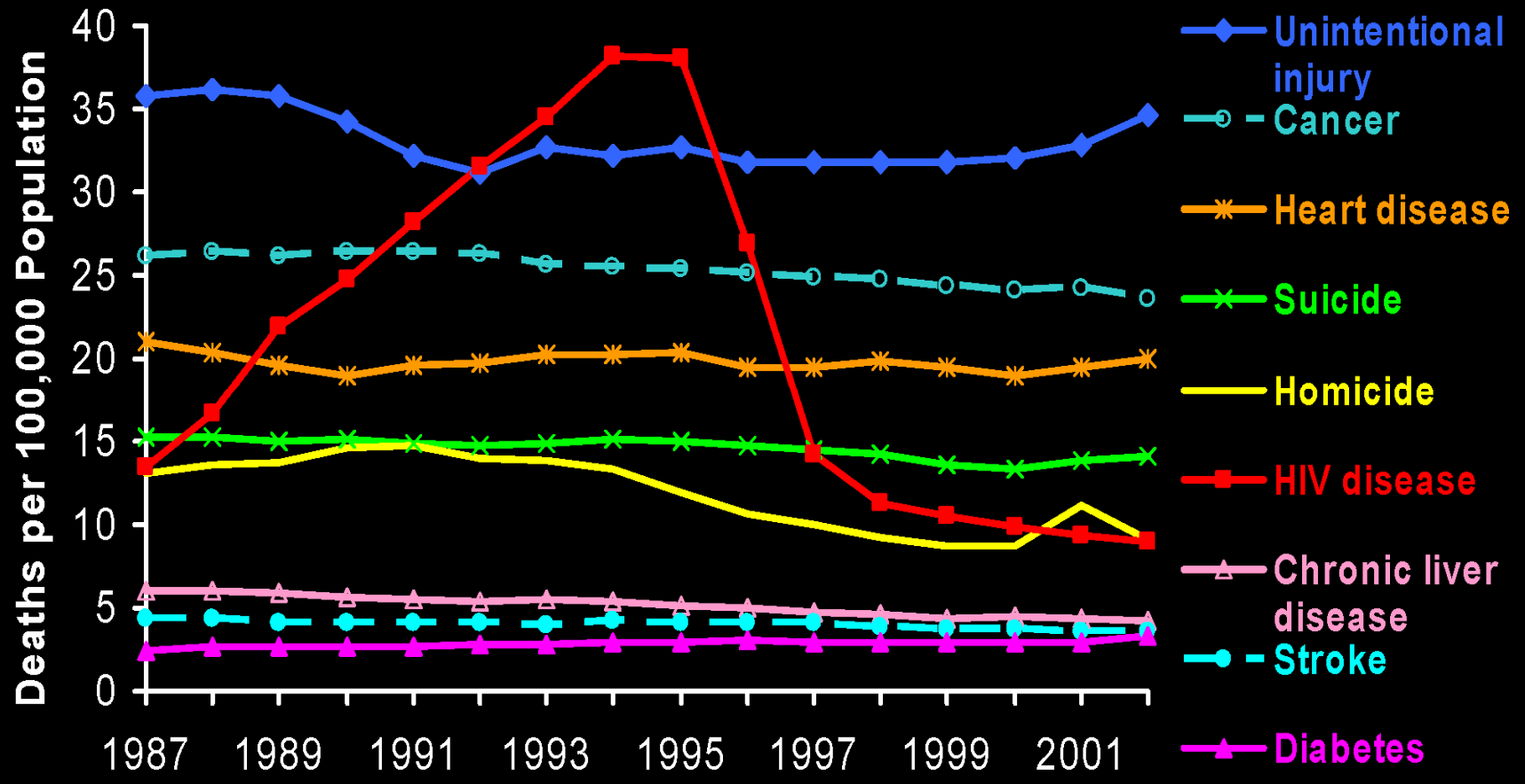


*Provisional data

SOURCE: National Vital Statistics

CDC

Trends in Annual Rates of Death due to the 9 Leading Causes among Persons 25–44 Years Old, USA, 1987–2002

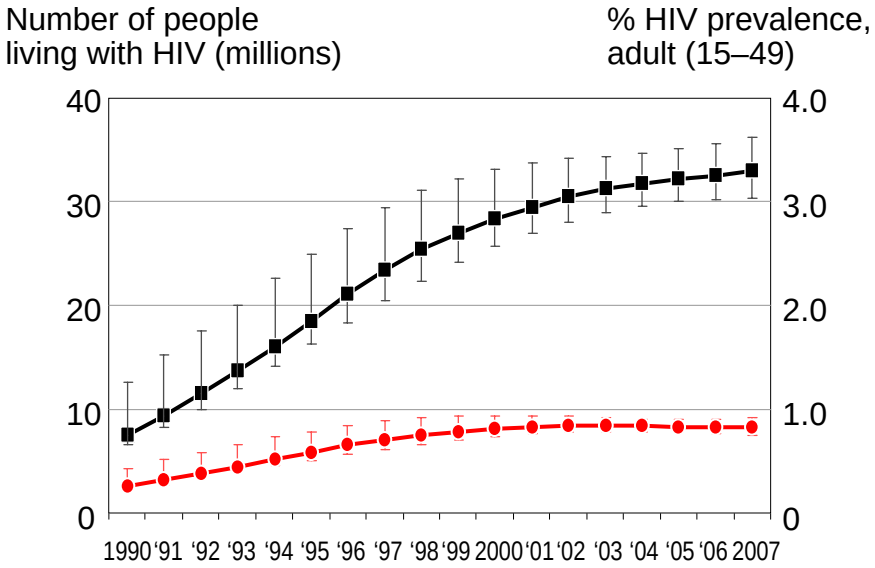


Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for *ICD-10* rules instead of *ICD-9* rules.

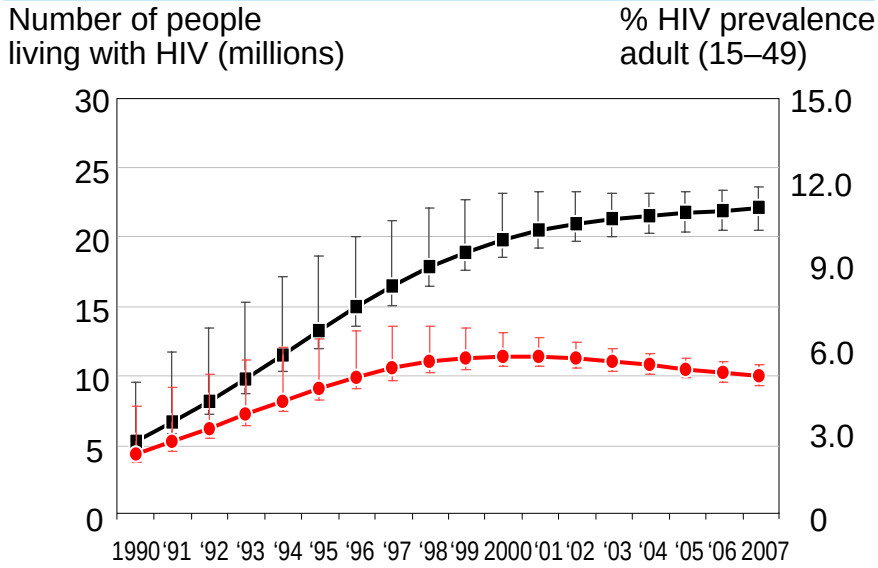
Courtesy Michael Marco

Estimated number of people living with HIV, and adult HIV prevalence

Global HIV epidemic, 1990–2007



HIV epidemic in Sub-Saharan Africa, 1990–2007



Number of people living with HIV

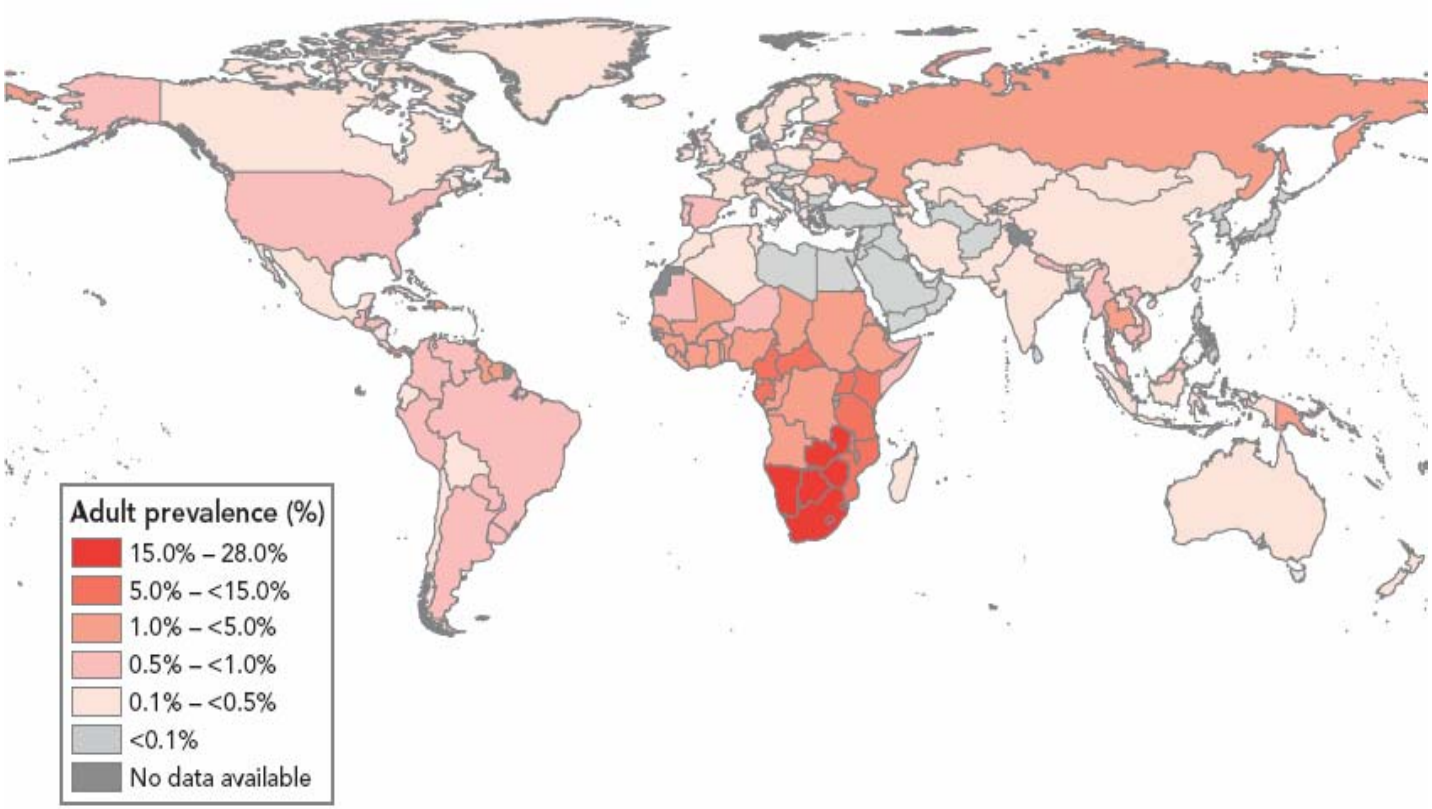
% HIV prevalence, adult (15–49)

These bars indicate the range around the estimate

NOTE: Even though the HIV prevalence stabilized in Sub-Saharan Africa, the actual number of people infected continues to grow because of ongoing new infections and increasing access to antiretroviral therapy.

A global view of HIV infection

33 million people [30–36 million] living with HIV, 2007



2.2 UNAIDS

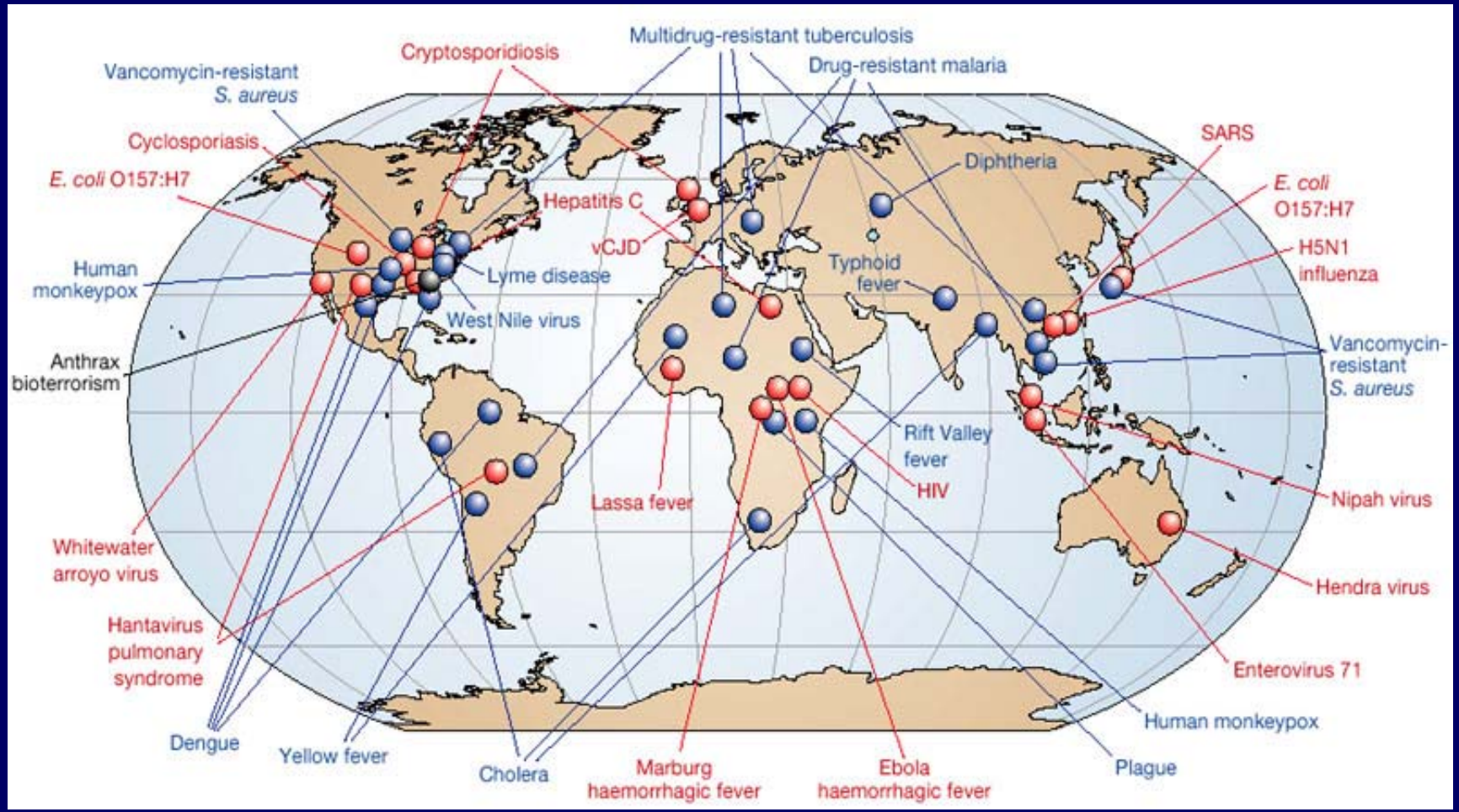
Emerging Infections

- Those rapidly increasing in incidence (number of new cases) or geographic range
- Often novel (a previously unrecognized disease)
- Anthropogenic causes often important in emergence

EMERGING INFECTIONS: SOME RECENT EXAMPLES

- Ebola, 1976 –
- HIV/AIDS
- BSE & Variant CJD, ca. 1986 –
- Hantavirus pulmonary syndrome, 1993
- Hemolytic uremic syndrome, 1990's –
- Nipah, 1998 –
- West Nile, US, multistate, 1999 –
- SARS 2003 –
- Influenza (including H5 in Asia 2003 –)

Global Examples of Emerging and Re-Emerging Infectious Diseases



Courtesy NIAID (Drs. David Morens & Anthony Fauci)

The Emerging Infections “Two-Step”

Step 1: Introduction

Step 2: Establishment/Dissemination

The Emerging Infections Two-Step

Opportunities increasing for both steps:

- Changes in land use
- Rural to urban migration
- Internal displacement
- Globalization of people and goods, travel, international migration
- Medical technologies

The Emerging Infections Two-Step

Step 1: Introduction

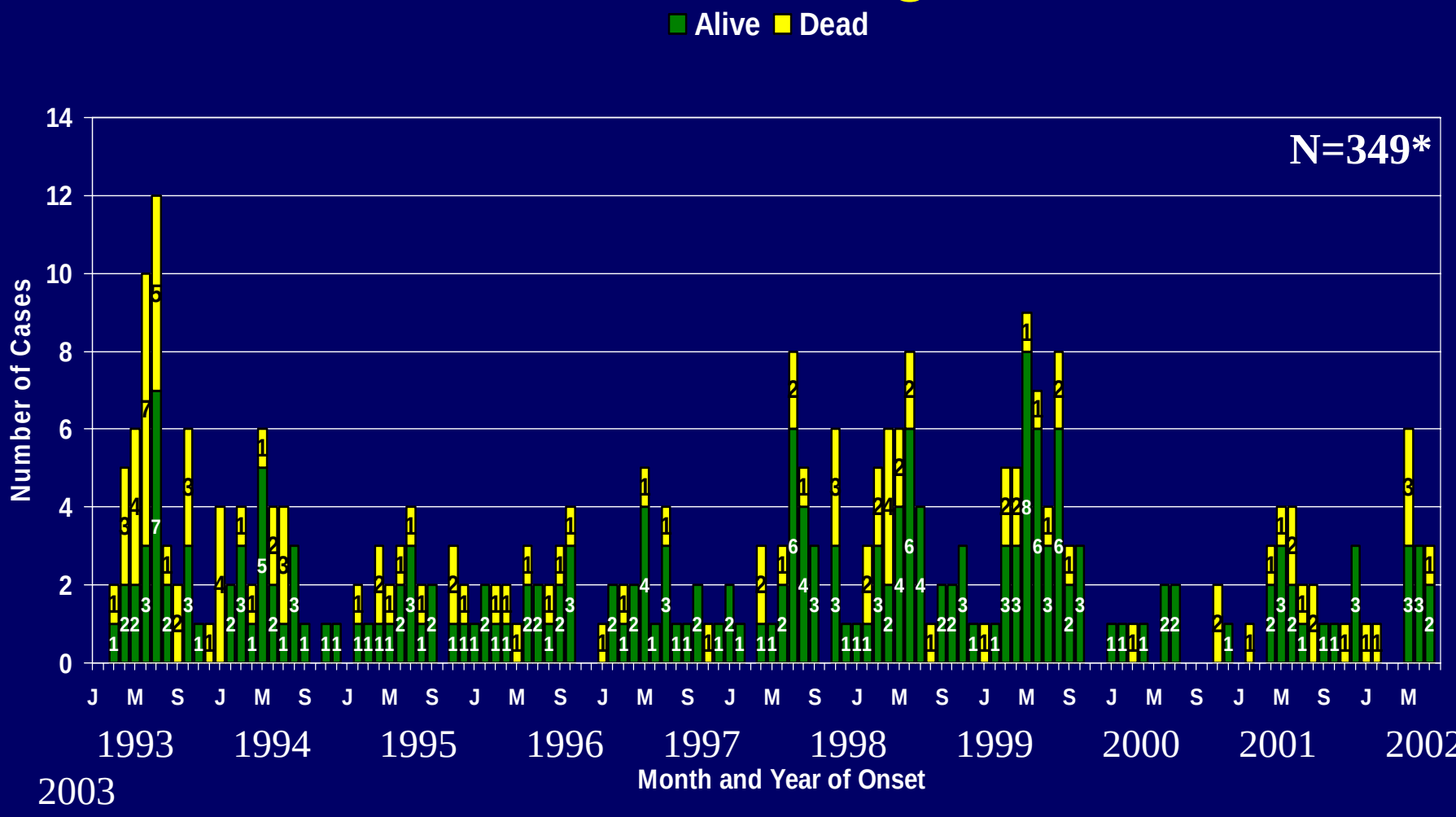
- Many are zoonotic
- The “zoonotic pool” is a rich source of potential emerging pathogens
- Changes in environment may increase contact, with greater chance or frequency of introduction
- Role of food animals as well as wildlife

New Opportunities for Pathogens: Ecological Changes

Agriculture	Hantaan, Argentine Hemorrhagic Fever, Nipah, West Nile (Israel), possibly pandemic influenza
Food handling practices	SARS, H5N1 influenza, HIV?, Enteropathogenic *E. coli*
Dams, changes in water ecosystems	Rift Valley Fever, other vector borne diseases, Schistosomiasis
Deforestation, reforestation	Kyasanur Forest, Lyme disease
Climate changes	HPS, vector borne diseases

Case Study: Hantavirus Pulmonary Syndrome, US, 1993

Hantavirus Pulmonary Syndrome Cases by Outcome
United States, as of August 27,2003

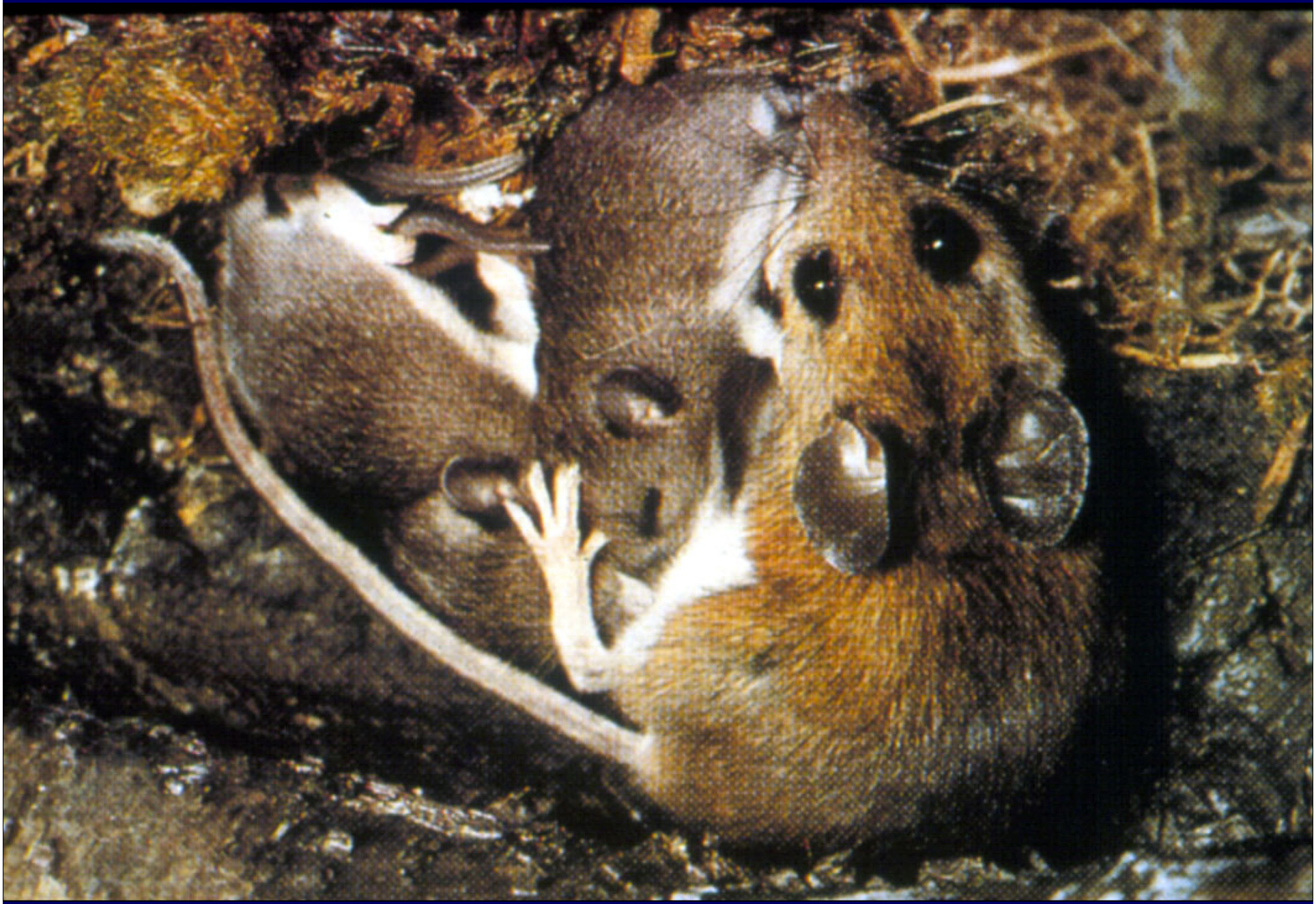


*Thirty-two additional cases (nineteen deceased) with onset before 1993 not shown.

COMPARISON OF SEROLOGIC & GENETIC TESTS OF ANIMALS

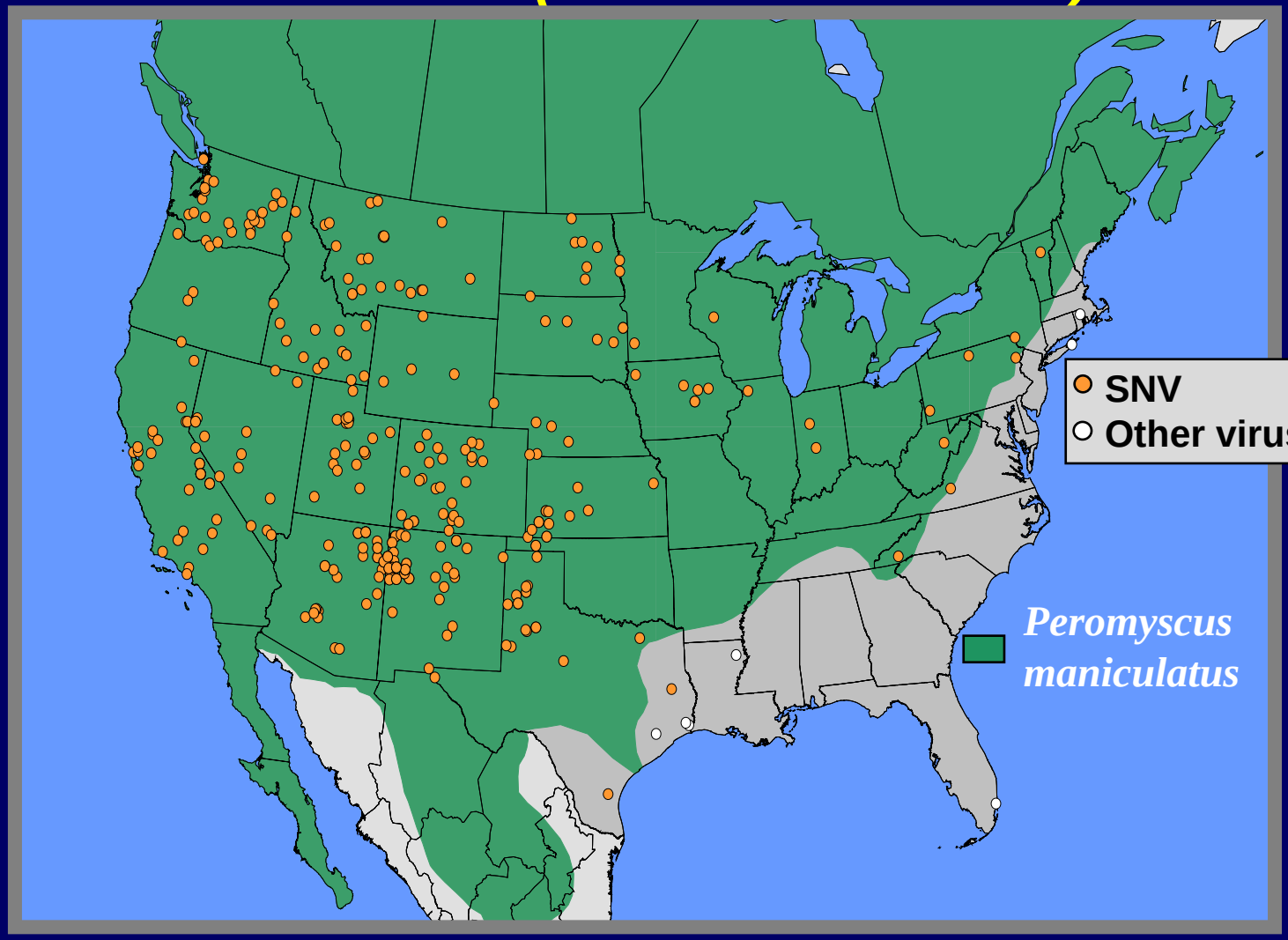
SPECIES	PHV pos	RT-PCR pos	% Concordance
P. maniculatus	61	59	96.7
P. truei	23	16	69.6
P. boylii	4	2	50.0
T. dorsalis	6	2	33.3
T. quadrivittatus	7	2	28.6
M.. musculus	2	1	50.0
R. megalotis	2	0	0.0
S.variegatus	1	0	0.0
N. albigula	2	0	0.0
Sylvilagus audoboni	1	0	0.0

CDC - DVRD - SPB



Distribution* of *Peromyscus maniculatus* and Location of HPS Cases as of August 27, 2003

Total Cases (N=349 in 31 States)



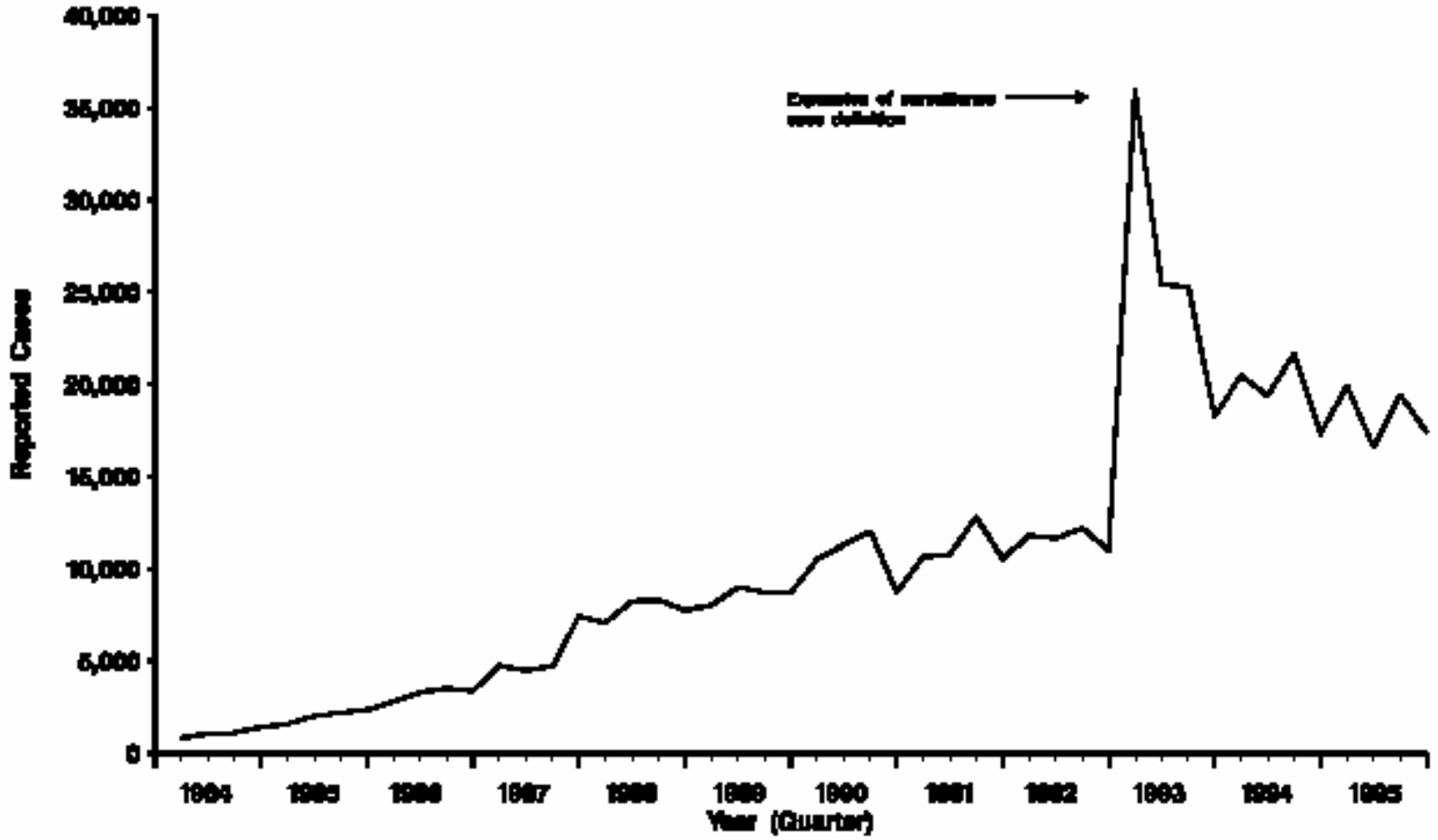
*Rodent distributions from: Burt WH, Grossenheider RP. A Field Guide to the Mammals. 3rd ed. New York, New York. Houghton Mifflin Company. 1980

STEPS IN OUTBREAK INVESTIGATION

1. Prepare for field work
2. Confirm the existence of an epidemic
3. Verify the diagnosis
4. Identify and count cases
- *Widen net (active case finding)*
- *Create a case definition (**very important**)*
- *Develop a line listing*
5. Descriptive epidemiology:
- *Person, place, and time*
- *Characterize the cases and population at risk (Epidemic curve, maps, etc.)*
6. Formulate hypotheses (about source of infection, mode of transmission)
7. Analytic epidemiology:
- *Test hypotheses (e.g., case-control studies)*
8. Plan additional studies as necessary
9. Implement and evaluate control and preventive measures
10. Initiate surveillance
11. Communicate findings

From: CDC-EIS Case Study, “An Outbreak of Hemorrhagic Fever in Africa” (ATPM/New England Epidemiology Inst., 1992), p. 17.

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) — reported cases, by quarter, United States,* 1984–1995



*Includes Guam, Puerto Rico, the U.S. Pacific Islands, and the U.S. Virgin Islands.

The number of AIDS cases reported during 1995 was lower than the number reported in 1994 or in 1993. This decrease reflects the waning effect of the expansion, in 1993, of the AIDS case definition used for surveillance.

Roles of Evolution

- Leads to the biodiversity of pathogens existing in nature
- Adaptation to new hosts and environments (through variation and selection)
- Including selection for antimicrobial resistance

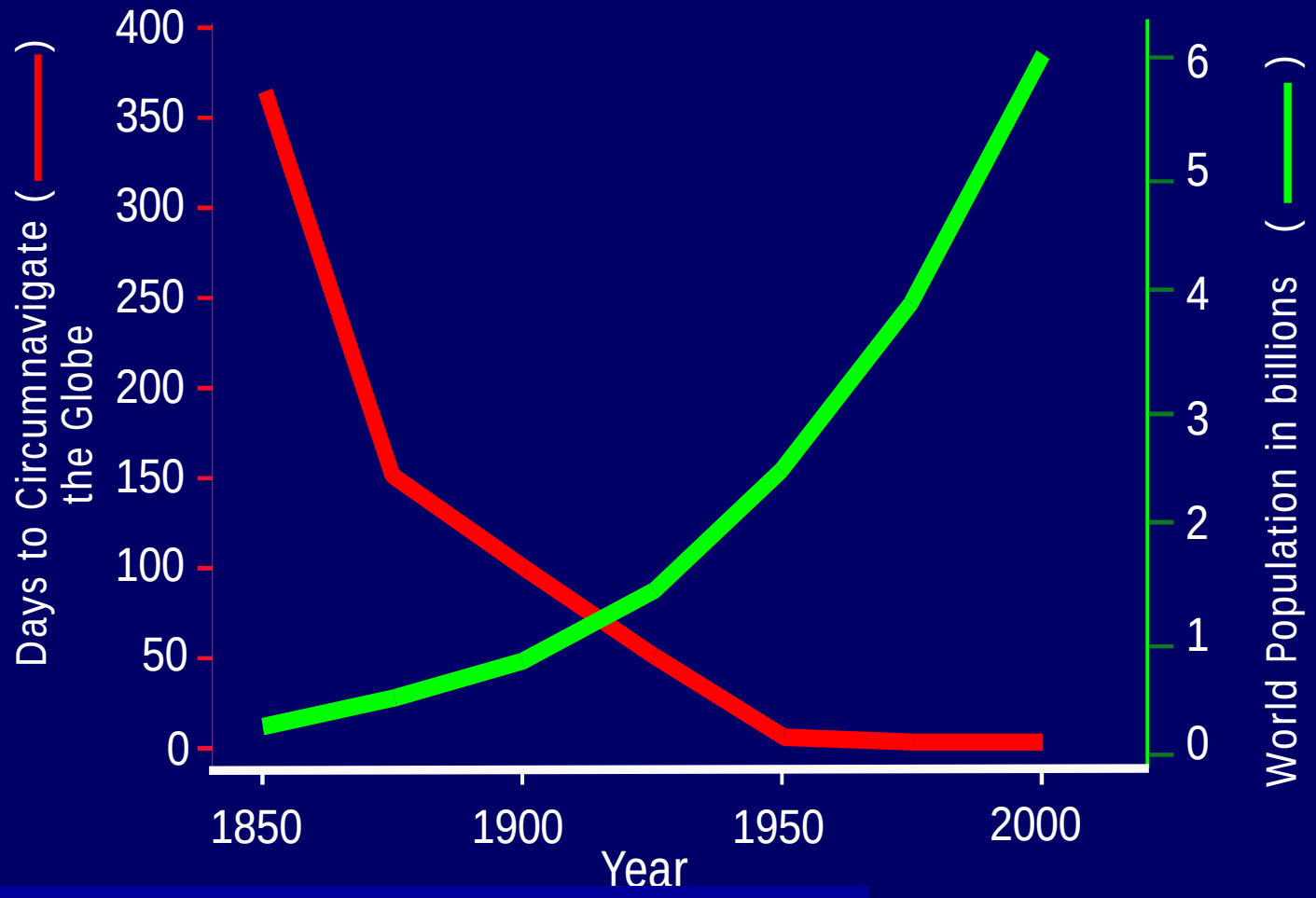
New World Hantaviruses

Slide courtesy of Dr. C.J. Peters **(Virus Names in Orange are Associated with Human Disease)**

Step 2: Establishment & Dissemination

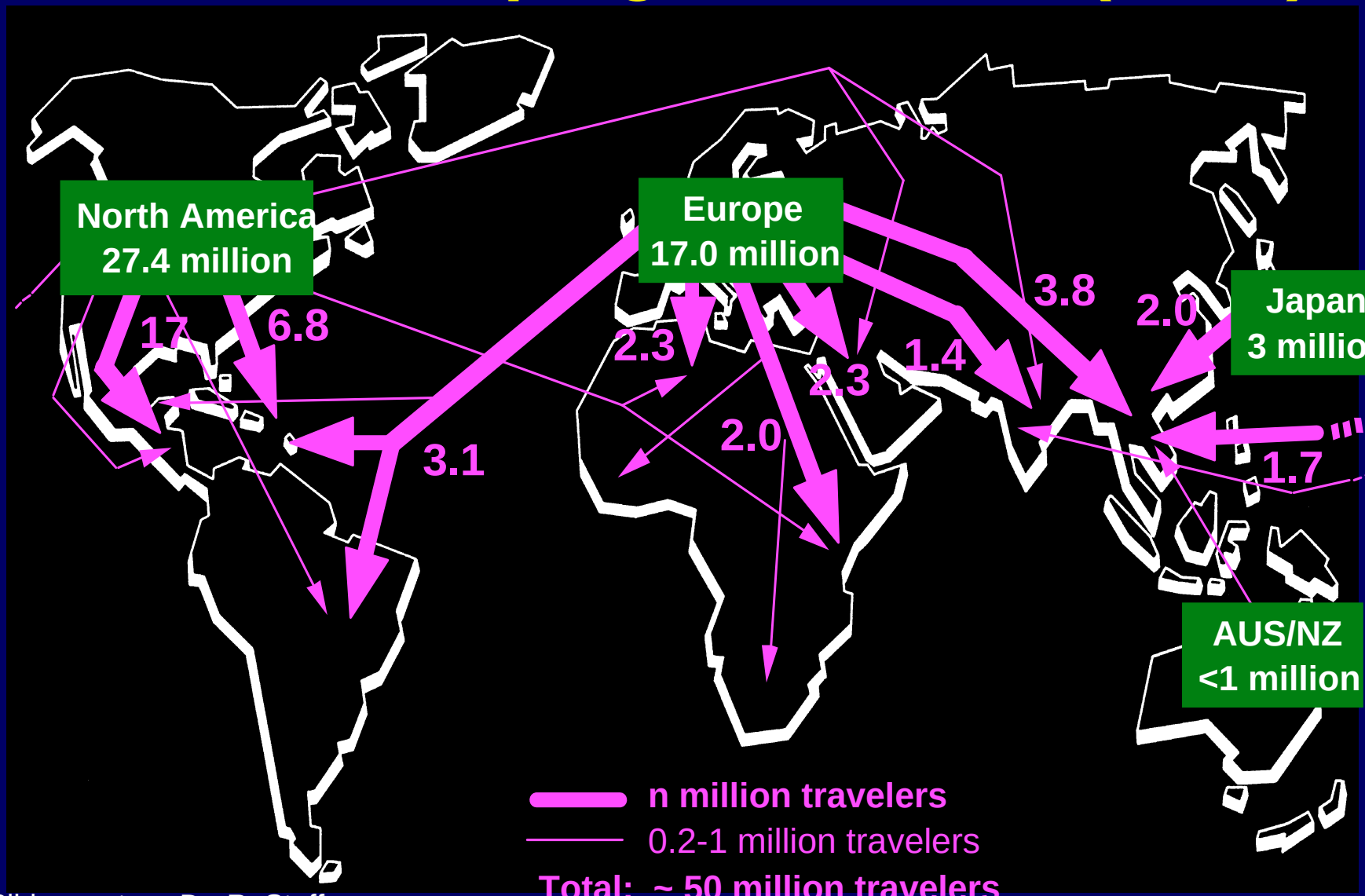
- Luckily for us, many candidates but relatively few are successful
- Human activities, including migration or travel, may disseminate a localized infection
  - Highways for “microbial traffic” to new areas
- Environmental changes may spread a natural host or vector

Speed of Global Travel in Relation to World Population Growth



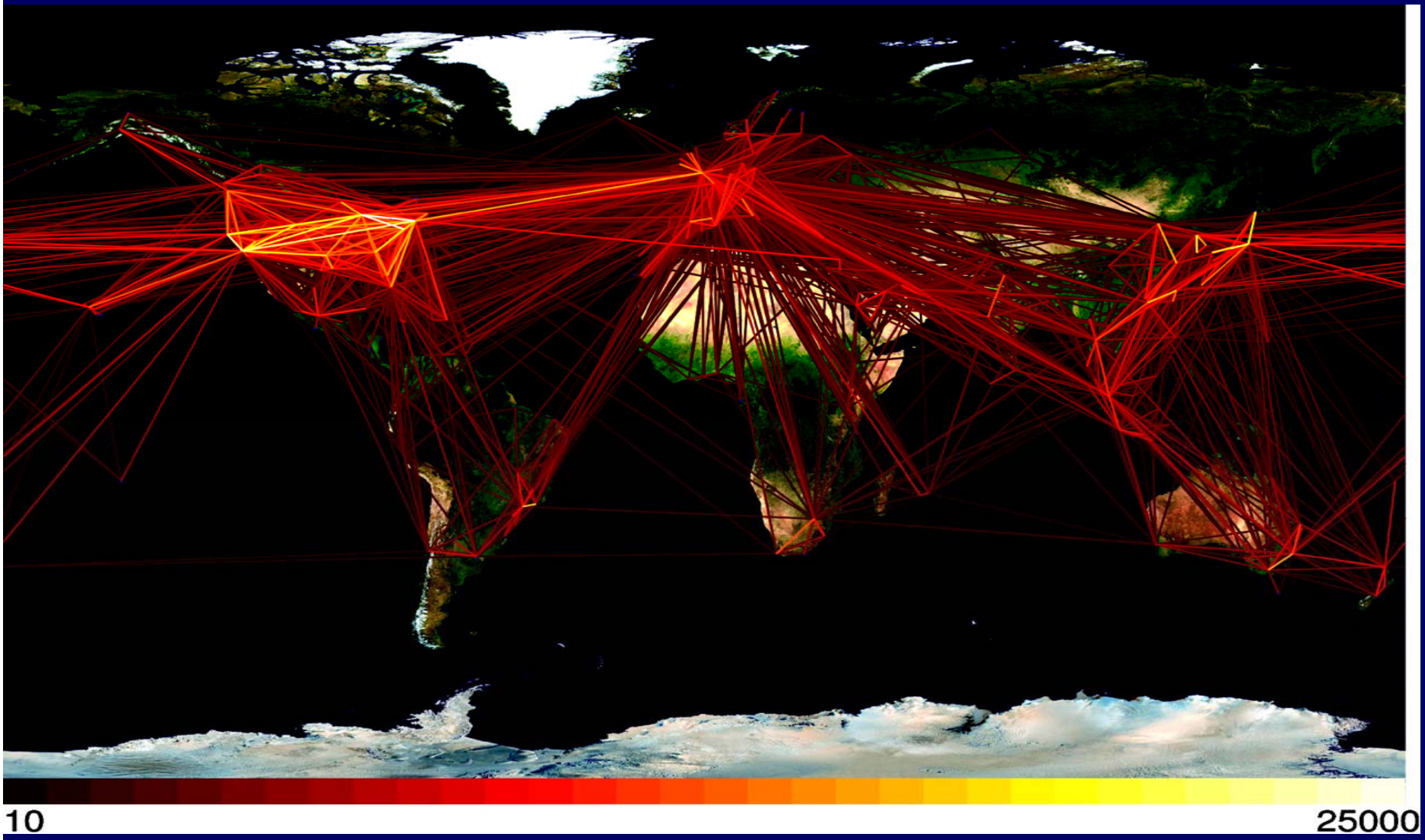
Courtesy CDC. From: Murphy and Nathanson. Semin. Virol. 5, 87, 1994

Travelers from industrialized areas to developing areas 1993 (WTO)



Slide courtesy Dr. R. Steffen

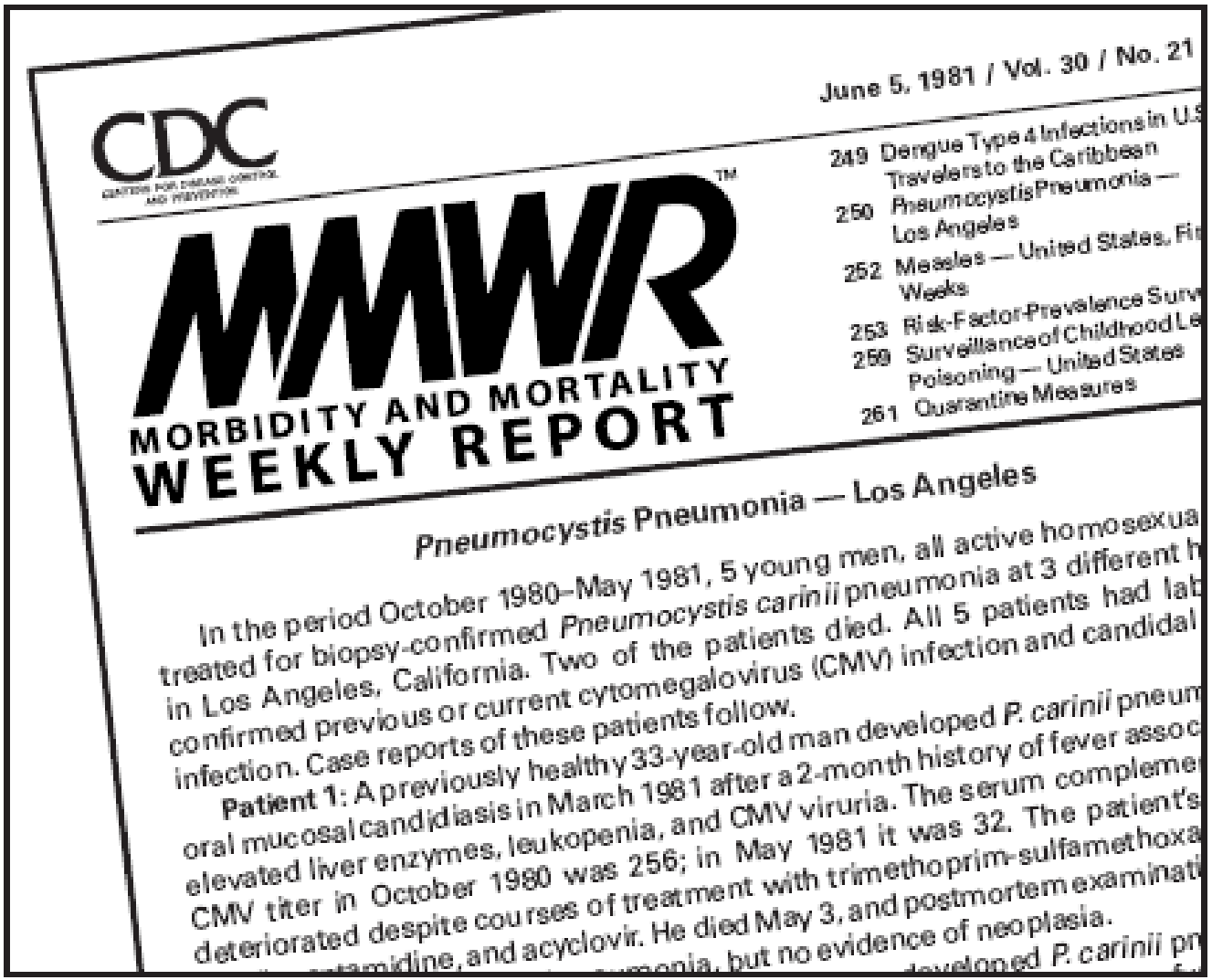
Global aviation network



Hufnagel, L. et al. (2004) Proc. Natl. Acad. Sci. USA 101, 15124-15129

PNAS

FIGURE. *MMWR* report on *Pneumocystis* pneumonia in five previously healthy young men in Los Angeles — June 5, 1981



June 5, 1981 / Vol. 30 / No. 21

CDC

MMWR™

MORBIDITY AND MORTALITY WEEKLY REPORT

***Pneumocystis* Pneumonia — Los Angeles**

In the period October 1980–May 1981, 5 young men, all active homosexua treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different h in Los Angeles, California. Two of the patients died. All 5 patients had lab confirmed previous or current cytomegalovirus (CMV) infection and candidal infection. Case reports of these patients follow.

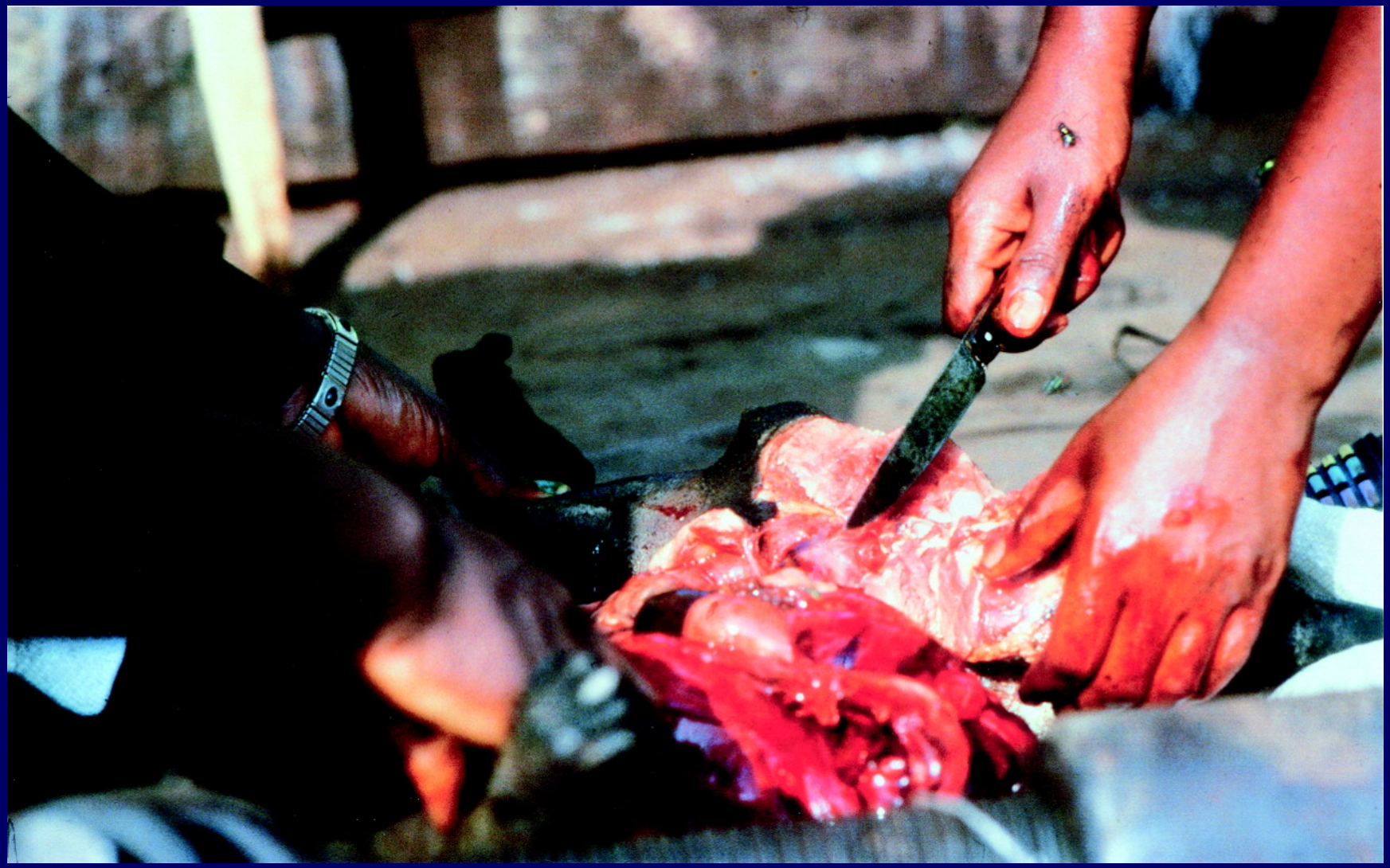
Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneum oral mucosal candidiasis in March 1981 after a 2-month history of fever assoc elevated liver enzymes, leukopenia, and CMV viruria. The serum compleme CMV titer in October 1980 was 256; in May 1981 it was 32. The patient's deteriorated despite courses of treatment with trimethoprim-sulfamethoxa pentamidine, and acyclovir. He died May 3, and postmortem examinati pneumonia, but no evidence of neoplasia. developed *P. carinii* pn

Courtesy Michael Marco

Geography of HIV-2

Photo: courtesy Preston Marx

The “Bushmeat” Trade



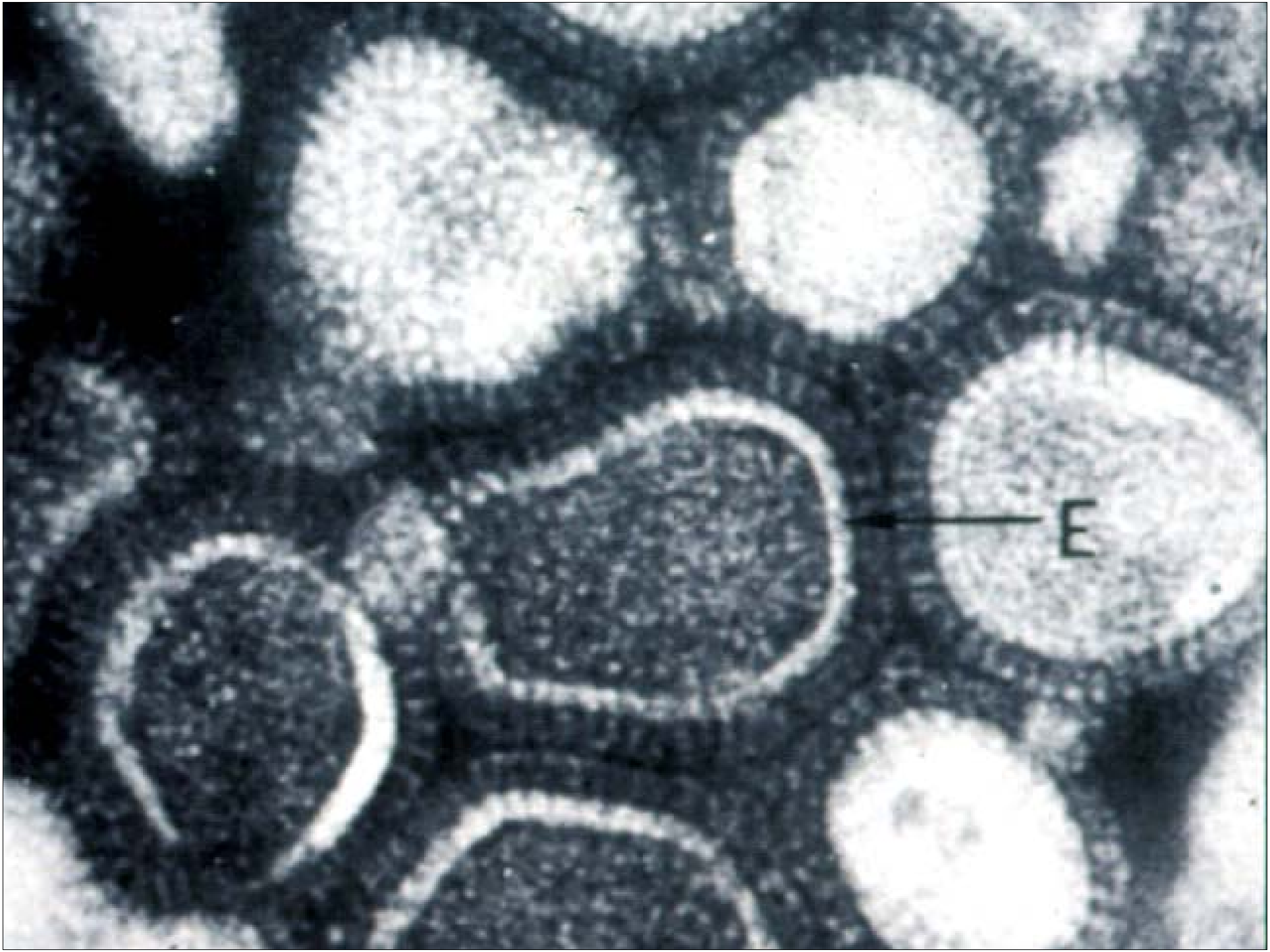
Photograph: Karl Ammann; from Hahn et al., 2000

Hospitals as Amplifiers

Ebola	Secondary cases through contaminated injection equipment
HIV	Transfusion, contaminated injection equipment
Lassa Fever	Secondary cases through contact with infected individuals
SARS	Secondary cases through contact with infected individuals

What About Respiratory Viruses?

- Many historical examples (influenza, measles, smallpox)
- Possibility of rapid spread, high morbidity
- Some may have high case-fatality rates
- Possibility of nosocomial infection, healthcare workers (e.g., SARS)
- Limited control measures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WHAT IS PANDEMIC INFLUENZA?

- An influenza epidemic so large it essentially involves the entire world
- Requires a “novel” influenza subtype (unfamiliar to humans) …
- … And that can also spread well from person to person

Influenza pandemics and recent outbreaks, 1918–2003

Year	*Colloquial name & subtype*	*Affected ages*	*No. deaths*
Pandemics:			
1918	**Spanish flu (H1N1)**	**all ages**	**20-40 million**
1957	**Asian flu (H2N2)**	**> 65 and under five ***	
1968	**Hong Kong flu (H3N2)**	**> 65 and under five ***	
	* Est. 4.5 M total deaths for 1957 + 1968		
Other outbreaks of interest:			
1976	Swine flu (H1N1)	all ages	2
1997	Avian flu (H5N1)	all ages	18
2003--	Avian flu (H5N1)	all ages	64

Data: David Heymann, WHO

Influenza Pandemic, 1918

Influenza Pandemic 1918 at Camp Funston (Kansas)

What Are the Rules for Influenza?

- What we thought we knew:
  - In past, human infections from H1, H2, H3 subtypes
  - Mild human infections with H7
  - Avian influenzas caused serious disease in poultry but not in humans
- BOTTOM LINE:
  - We really don’t know!
  - Influenza A remains highly variable and unpredictable

AVIAN INFLUENZA H5

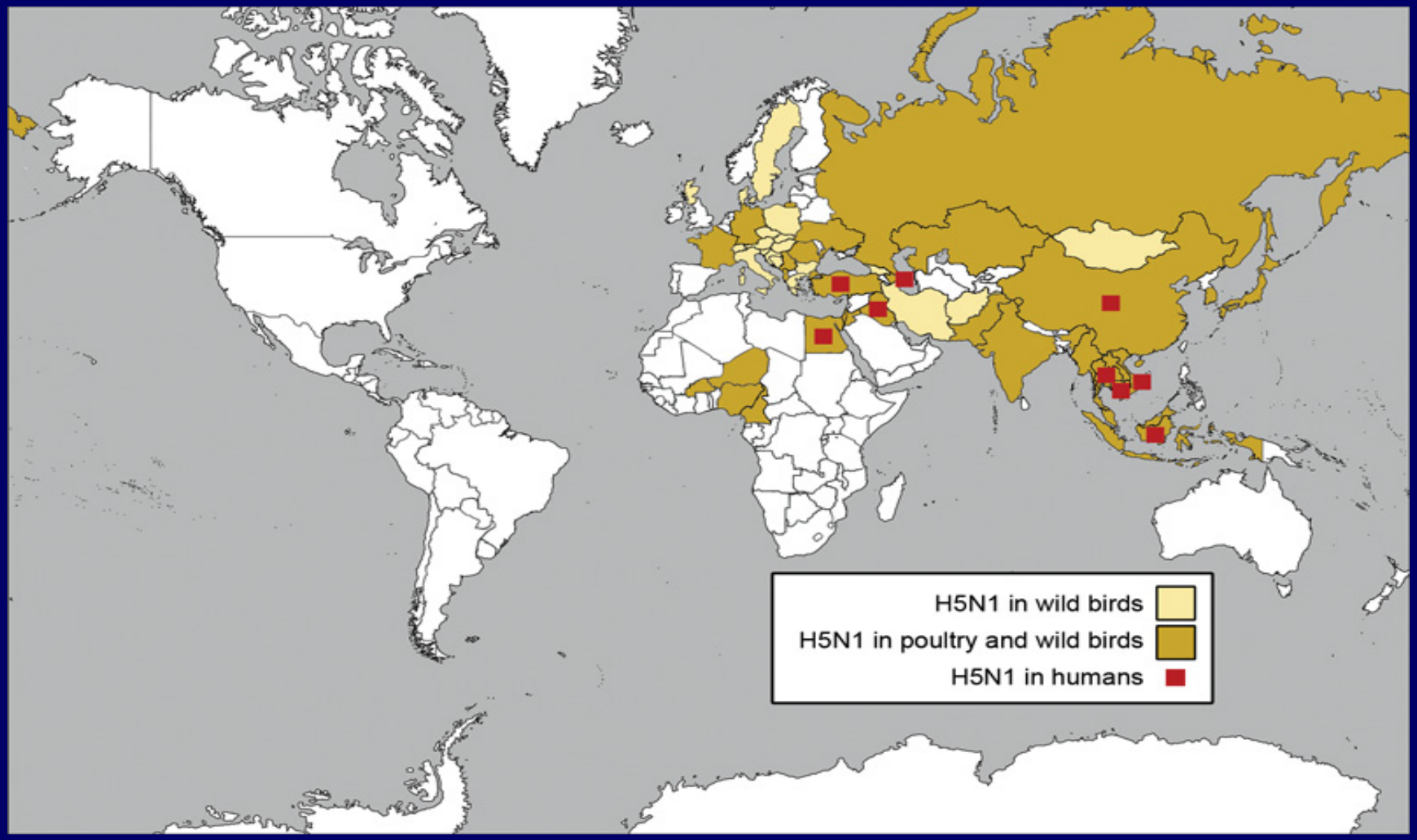
First human cases:
Hong Kong, 1997
18 cases with 4 deaths

Avian flu: Is it for the birds?

(By Barry Blitt, from The New Yorker)

“PANDEMIC” and
“AVIAN FLU”
are NOT synonymous!

Nations With Confirmed Cases H5N1 Avian Influenza (April 19, 2006)

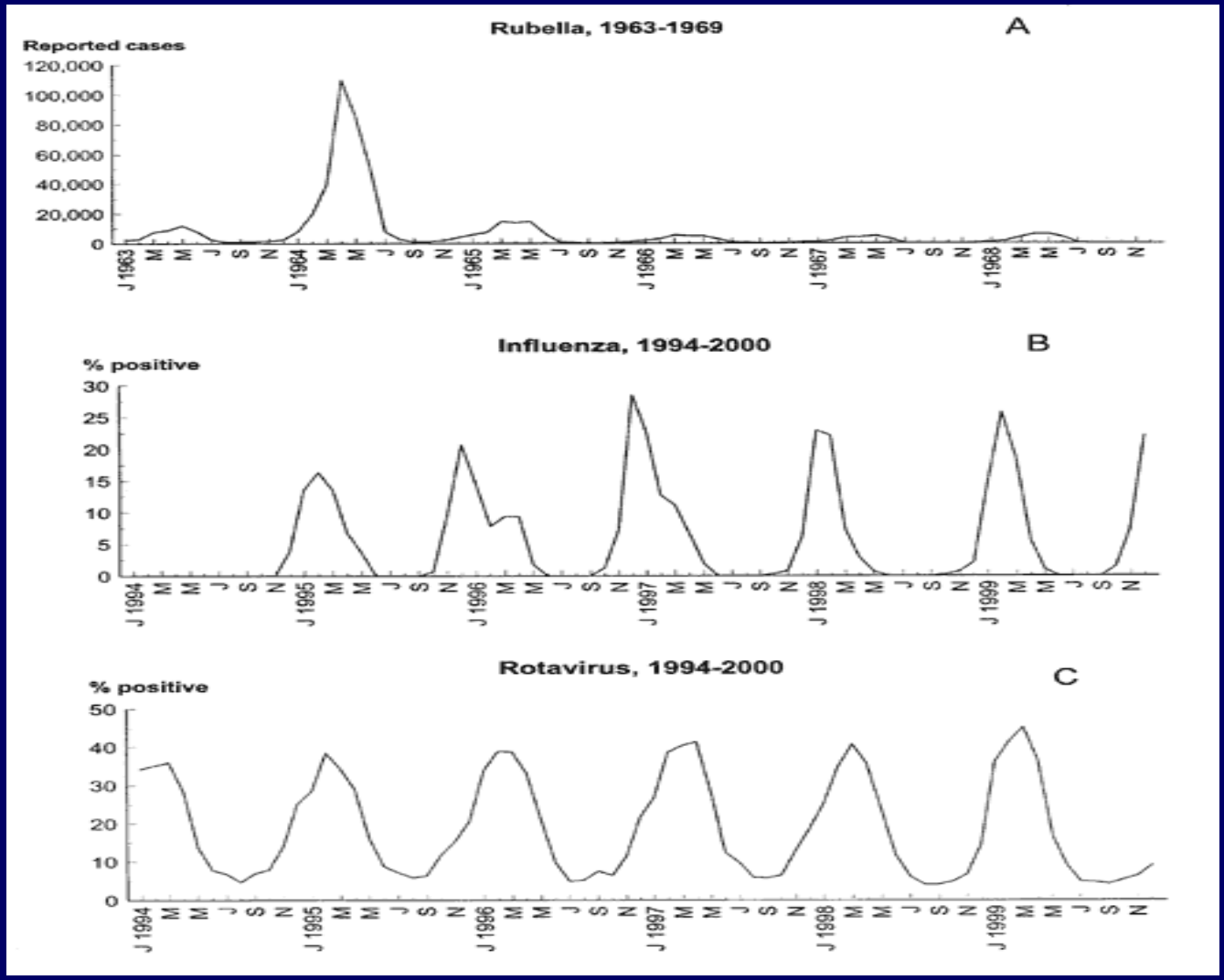


CDC

Human Cases of Avian Influenza A/(H5N1), WHO, 10 Sept. 2008

COUNTRY	CASES (DEATHS)
Azerbaijan	8 cases, incl. 5 deaths
Bangladesh	1 (0)
Cambodia	7 (7)
China	30 (20)
Djibouti	1 (0)
Egypt	50 (22)
Indonesia	137 (112)
Iraq	3 (2)
Laos	2 (2)
Myanmar (Burma)	1 (0)
Nigeria	1 (1)
Pakistan	3 (1)
Thailand	25 (17)
Turkey	12 (4)
Viet Nam	106 (52)
TOTAL	**387 (245)**

Seasonality of Influenza and Other Viruses in U.S.

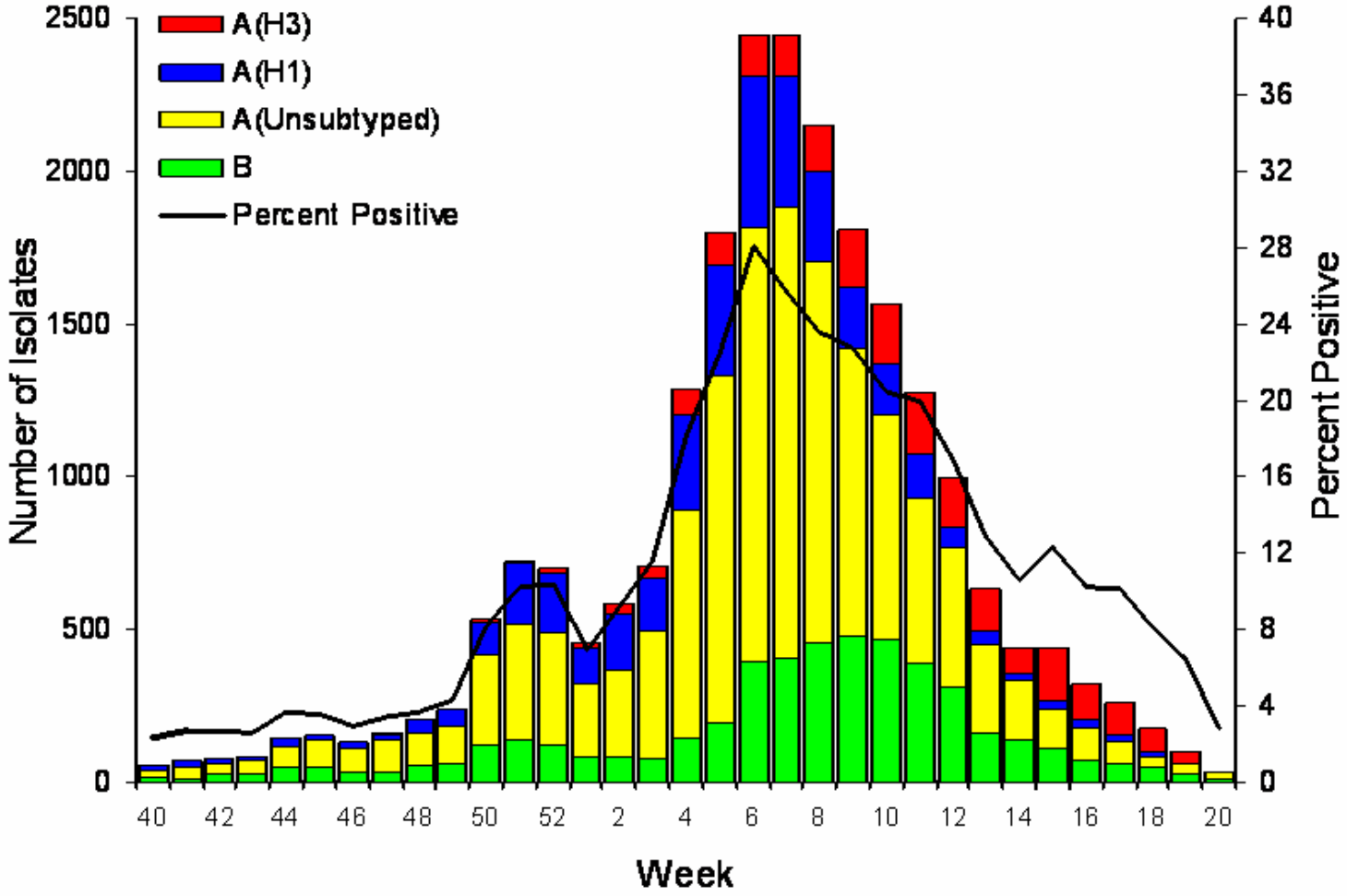


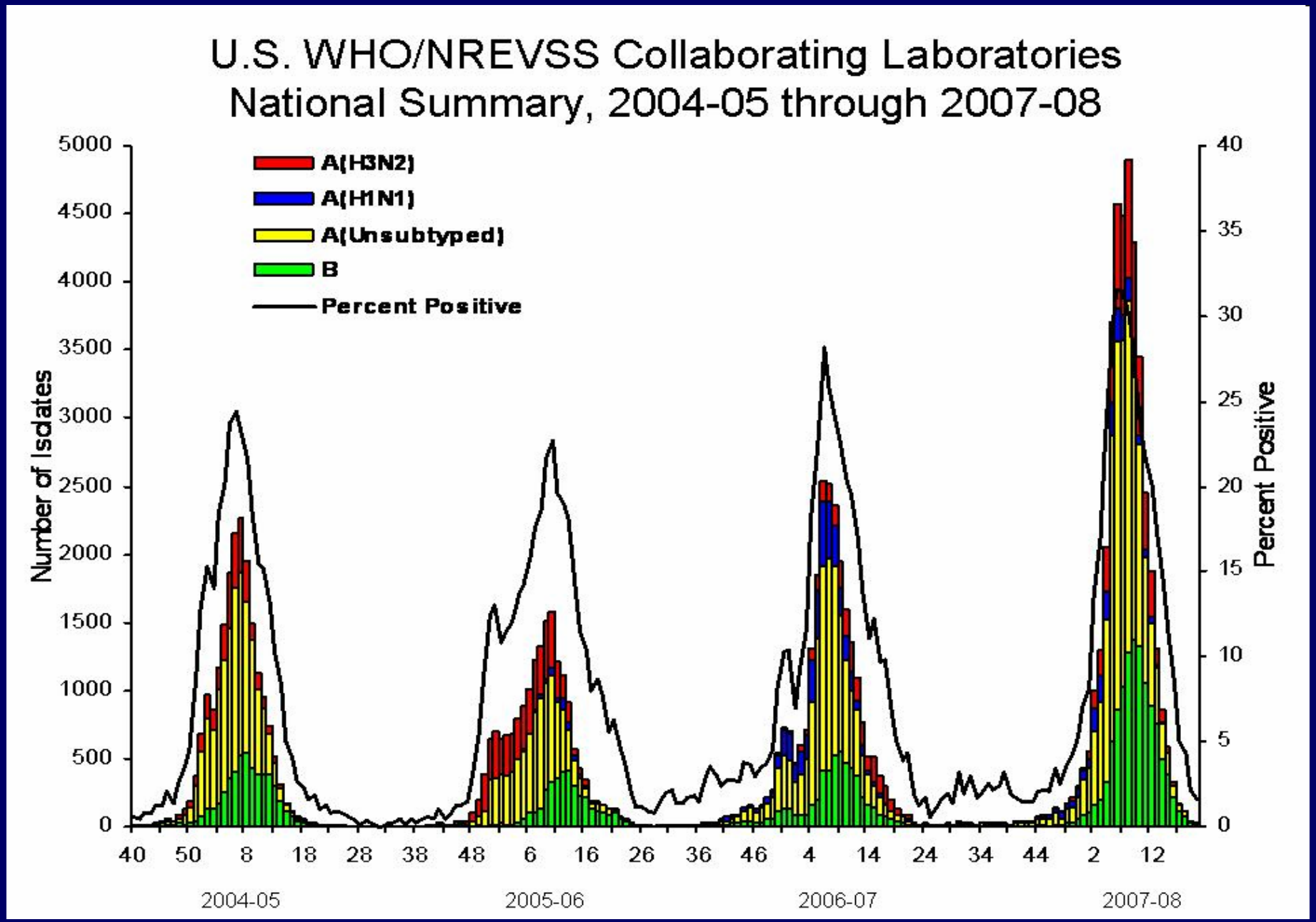
Dowell, Emerg Infect Dis, 7(3), May–Jun 2001

What Accounts for the Seasonality of Infections?

- Generally not well understood
- Especially poorly understood for influenza
  - Winter disease in temperate zones
  - Two peaks usually (winter and summer) in subtropical areas
  - In tropics, may be year round or show two peaks

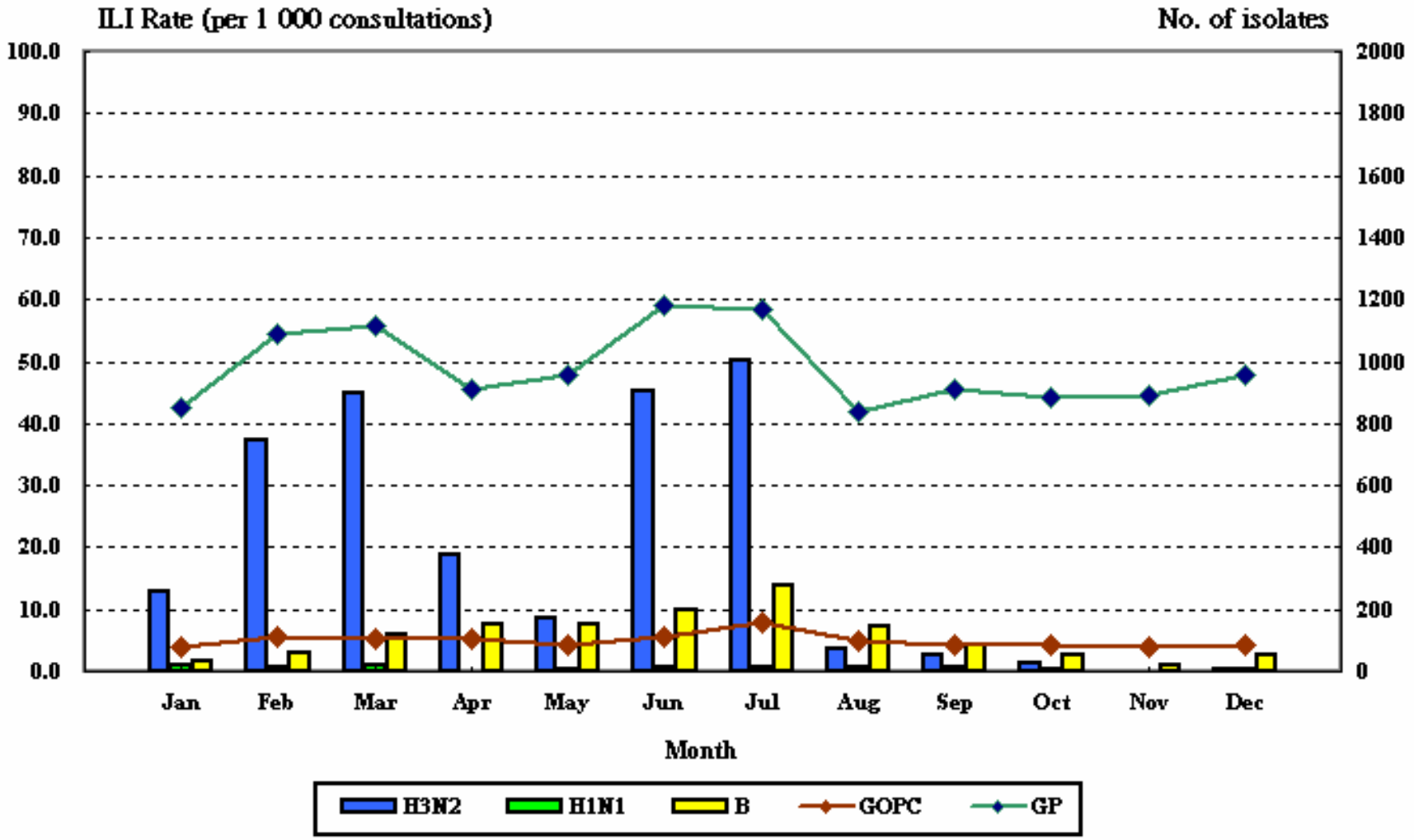
U.S. WHO/NREVSS Collaborating Laboratories Summary, 2006-07





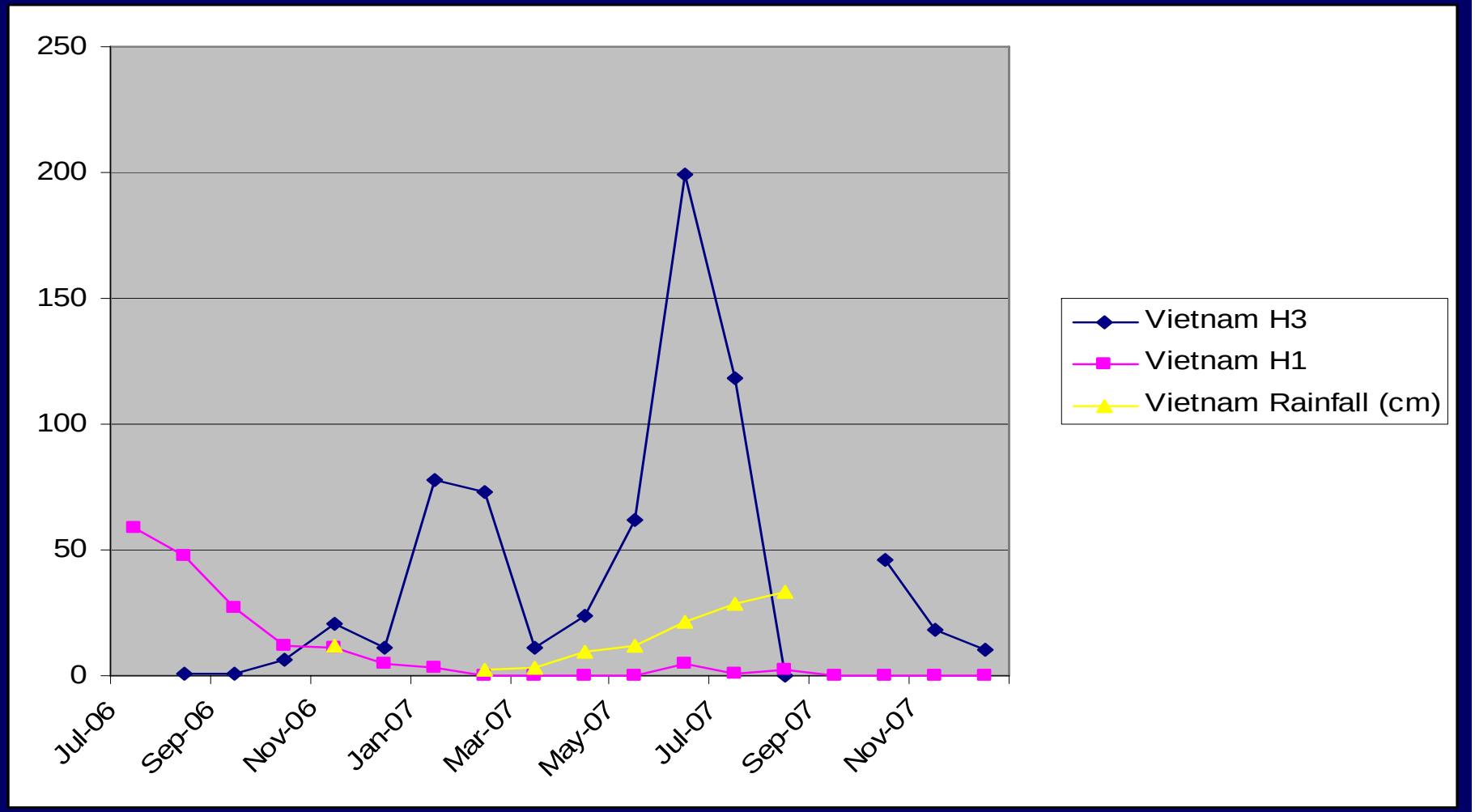
Source: CDC (http://www.cdc.gov/flu/weekly/weeklyarchives2007-2008/07-08summary.htm

Influenza Activity, Hong Kong, 2007



Hong Kong Department of Health, Centre for Health Protection

Vietnam Influenza H3/H1 incidence and rainfall, July 2006 – December 2007



Michelle Waste, MPH 2008

How Might Climate Affect Influenza?

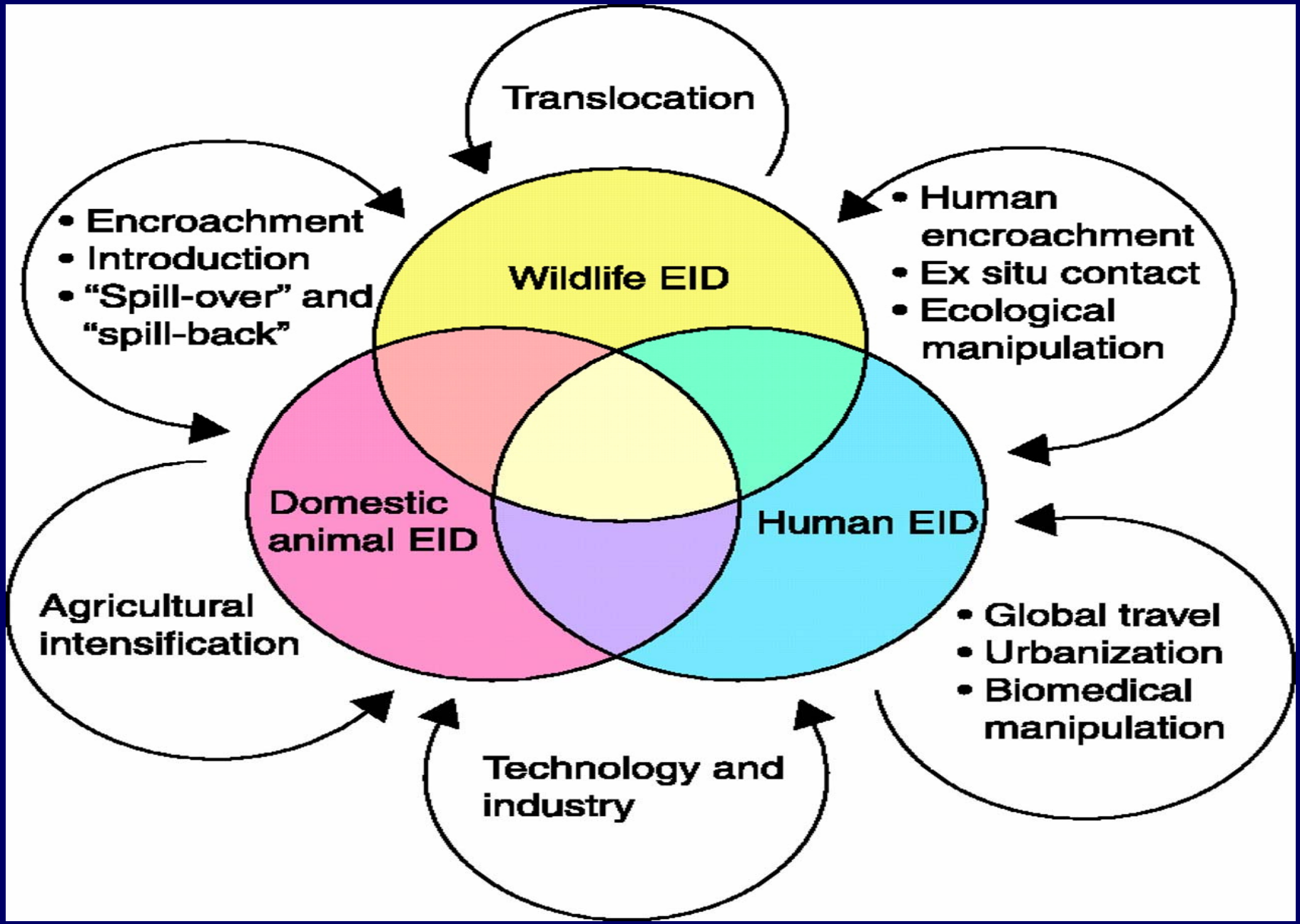
- A warming climate could convert influenza from a wintertime disease to a 2 peak (winter and summer) or year-round infection
- Effect of climate on mutation rate is unknown
- Interactions between wild waterfowl and domestic poultry may increase
- Husbandry, farmers' interactions with poultry will change
- Export of poultry may be affected

Climate and Health/Infectious Diseases: For More Information

- McMichael AJ, Woodruff RE, Hales S (2006). Climate change and human health: present and future risks. *Lancet* **367**(9513): 859-69.
- Patz JA, Campbell-Lendrum D, Holloway T, Foley JA (2005). Impact of regional climate change on human health. *Nature* **438** (7066):310-317.
- Jonathan Patz J, Diarmid Campbell-Lendrum D, Holly Gibbs H, Rosalie Woodruff R (2008). Health impact assessment of global climate change: Expanding on comparative risk assessment approaches for policy making. *Annu Rev Public Health* **29**:27-39.
- Fisman DN (2007). Seasonality of infectious diseases. *Annu Rev Public Health* **28**:127-143.
- AIBS Symposium 2008, "Climate, Environment, and Infectious Diseases. Available at: **http://www.aibs.org/media-library/**

Factors in Infectious Disease Emergence

- Ecological Changes
  - Including economic development, land use
- Human Demographics, Behavior
- International Travel and Trade
- Technology and Industry
  - Food processing
  - Health care
- Microbial Adaptation and Change
- Breakdown in Public Health Measures ("Re-Emerging Diseases")



Peter Daszak *et al.,* Science **287**:443-449 (2000)

‘One Health’ Initiative

- **Vision Statement: One Health (formerly called One Medicine) is dedicated to improving the lives of all species—human and animal—through the integration of medicine and veterinary medicine.**

- **Mission Statement: Recognizing that human and animal health and mental health (via the human-animal bond phenomenon) are inextricably linked, One Health seeks to promote, improve, and defend the health and well-being of all species by enhancing cooperation and collaboration between physicians and veterinarians, and by promoting strengths in leadership and management to achieve these goals.**

Prepared by Laura H. Kahn, MD, MPH, MPP; Bruce Kaplan, DVM; Thomas P. Monath, MD

Endorsed by AMA, AVMA, ASM, many other health organizations

One Health Initiative - One World One Medicine One Health - Mozilla Firefox

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one health initiative

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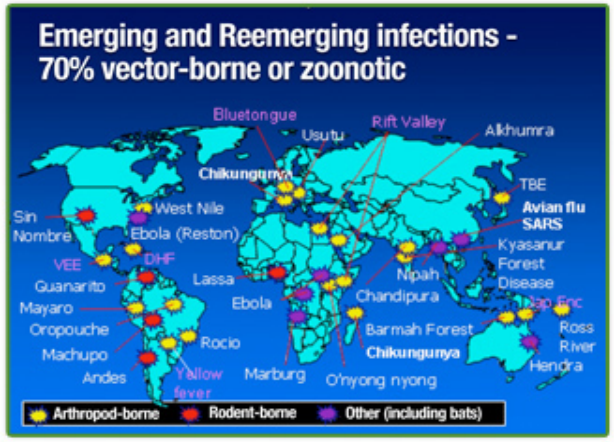
One Health Initiative will unite human and veterinary medicine

The One Health Initiative, a movement to forge co-equal, all inclusive collaborations between physicians, veterinarians, and other scientific-health related disciplines, has been endorsed by various major medical organizations and health agencies, including the American Veterinary Medical Association, the American Medical Association, the American Society of Tropical Medicine and Hygiene, the American Society for Microbiology and the Centers for Disease Control and Prevention (CDC). Additionally, more than 350 prominent scientists, physicians and veterinarians worldwide have endorsed the initiative.

> more about one health



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Latest News

Upcoming Events

Recent Publications

Done

start One Health Initiative ... 1:41 PM

What Can We Do?

Research:

- Ecology of infectious disease
  - Especially at key animal-human interfaces
  - Better predictive approaches: Epidemiology, patterns of movement and spread (“microbial traffic”), predictive modeling
- Pathogenesis, host interactions
- Understanding barriers and enablers for successful cross-species transmission (at molecular level)
- Better understanding of the biological basis of transmissibility

What Can We Do?

Lab capacity:

- For diagnosis

Public Health:

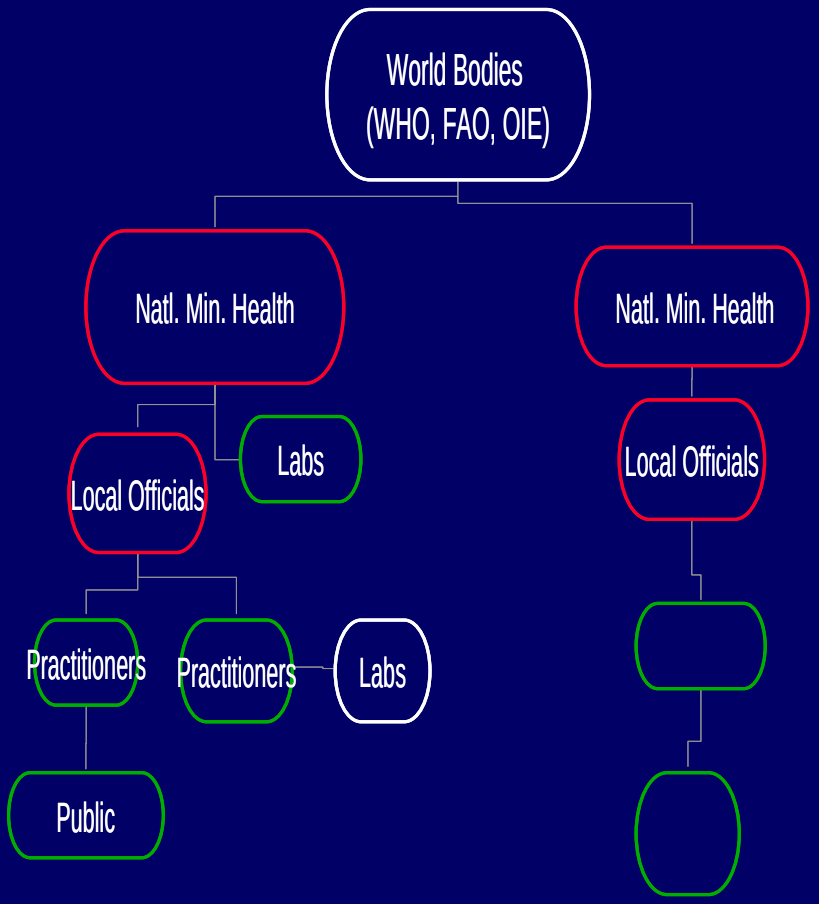
- Preparedness
  - Planning, training, drills and exercises
  - “Expecting the unexpected”
- Surveillance (Early Warning Systems)
  - Newly enacted WHO International Health Regulations
- Public Health Response (Disease Control)
- “Medical Countermeasures” (Vaccines, Therapeutics)

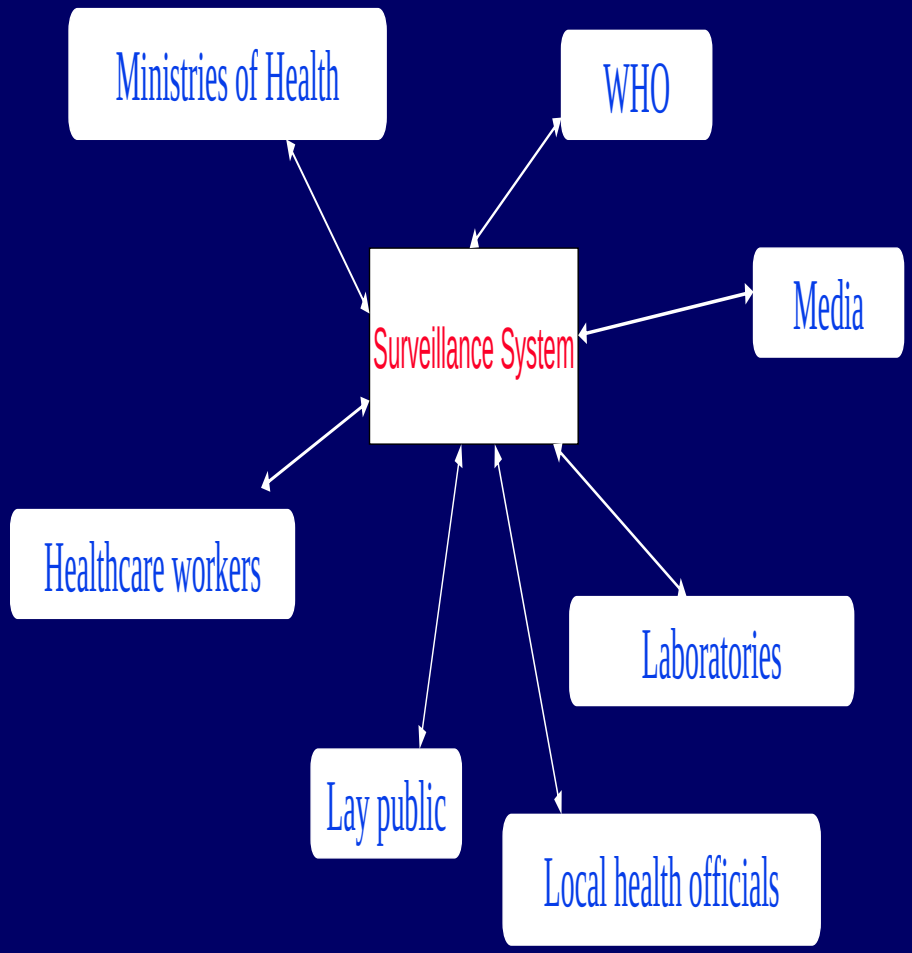
ProMED-mail: A Prototype Outbreak Reporting System

ProMED-mail:
www.promedmail.org

- **Moderated listserv**
- **Free to all**
- **Started 1994**
- **Approximately 30,000 subscribers in >155 countries**

Traditional vs. “All-Source” Surveillance





A Compliment?

"The popular ProMED-mail e-list offers a daily update on all the known disease outbreaks flaring up around the world, which surely makes it the most terrifying news source known to man."

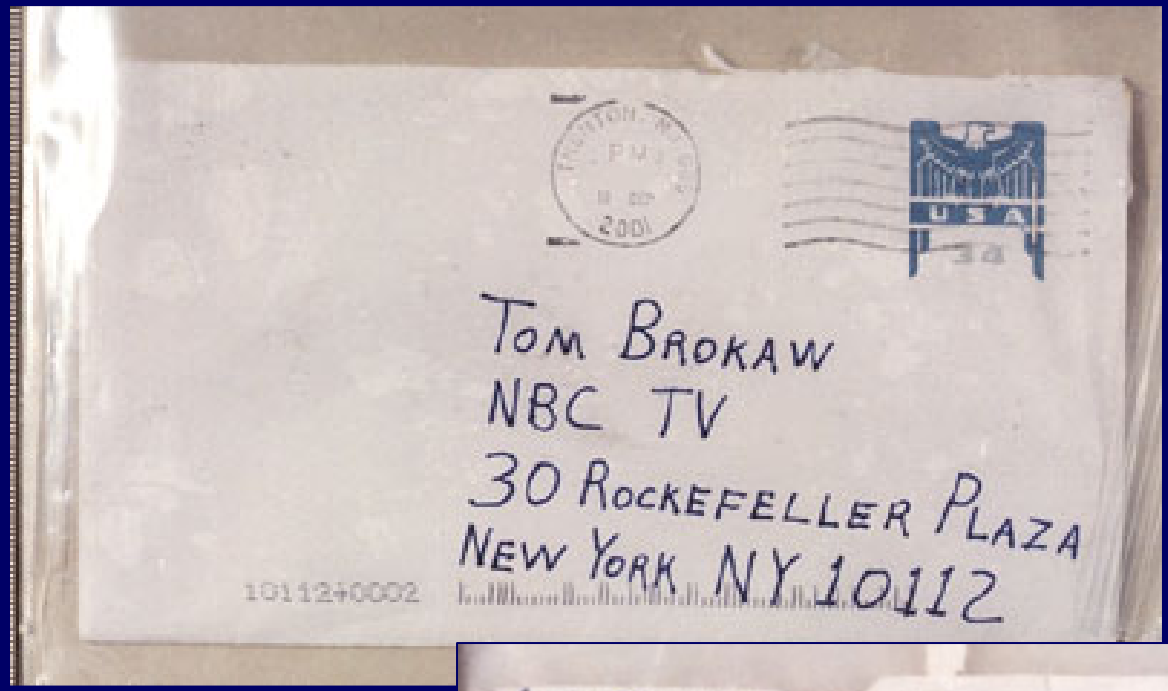
– Steven Johnson

"The Ghost Map", p. 219

Riverhead Books/Penguin, 2006

New Frontiers?

- Bioterrorism
- Infectious causes of chronic disease
  - E.g.: *Helicobacter pylori* and ulcers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NEW YORK NY 10112
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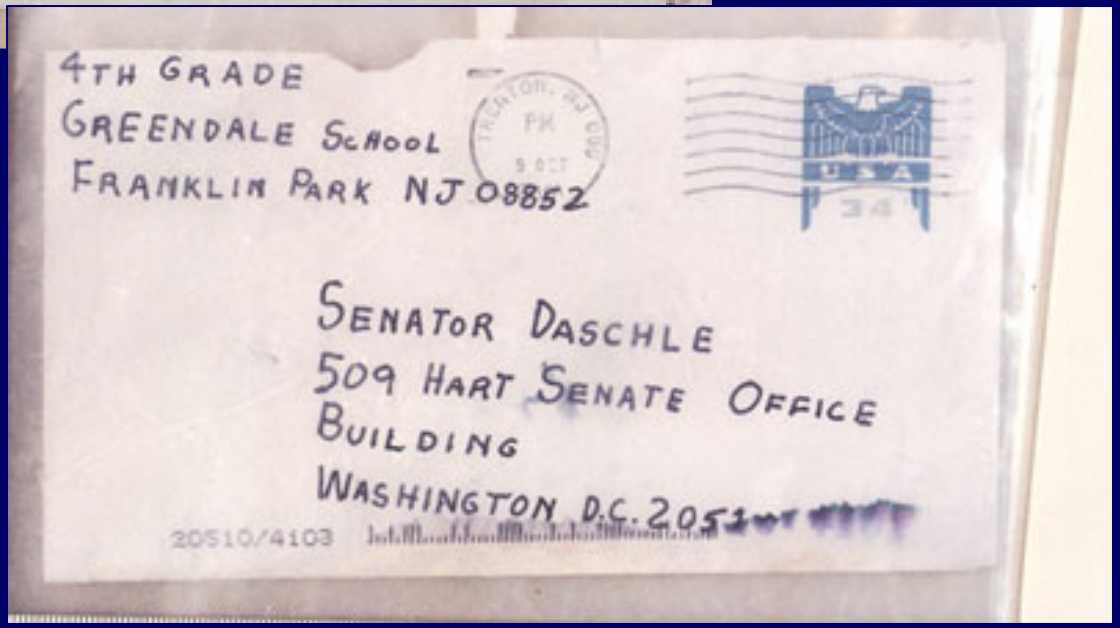
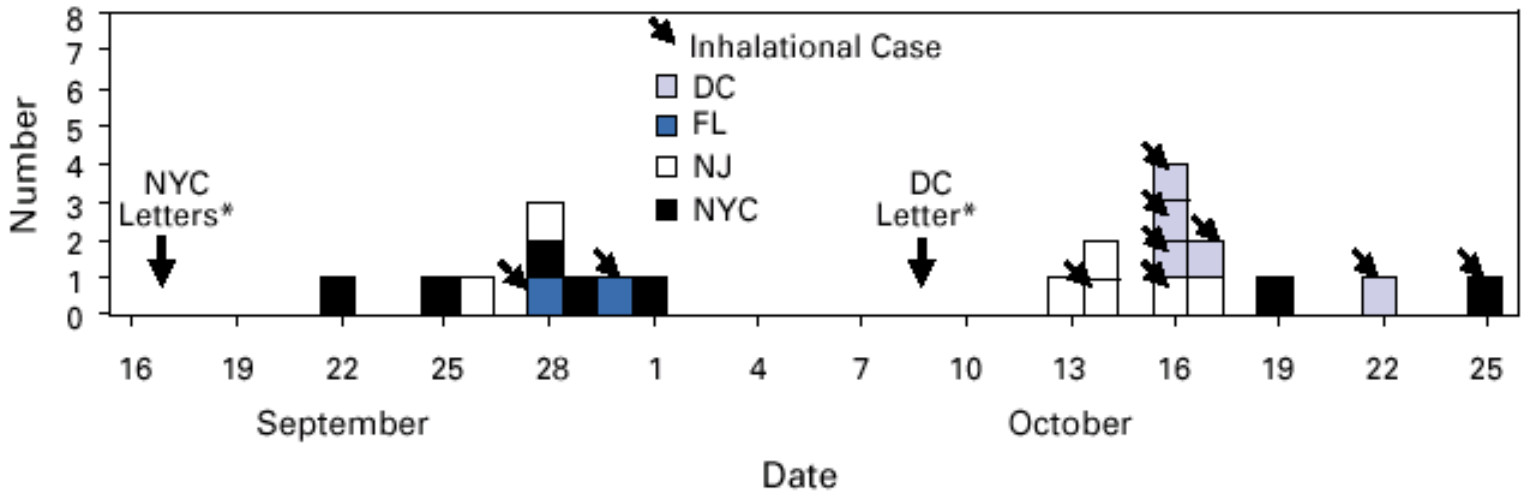

4TH GRADE
GREENDALE SCHOOL
FRANKLIN PARK NJ 08852
SENATOR DASCHLE
509 HART SENATE OFFICE
BUILDING
WASHINGTON D.C. 20510
20510/4103

Anthrax Cases (Sept.-Oct. 2001)

FIGURE 1. Number of bioterrorism-related anthrax cases, by date of onset and work location — District of Columbia (DC), Florida (FL), New Jersey (NJ), and New York City (NYC), September 16–October 25, 2001



* Postmarked date of known contaminated letters.

Source: CDC. MMWR November 2, 2001

Anthrax 2001: How Were the Cases Identified?

- Florida: Inhalation anthrax suspected by infectious disease clinician
- NYC: Cutaneous case identified by clinician

... and reported to Health Dept.

Infectious Etiologies of Chronic Diseases

Examples: WELL-RECOGNIZED ASSOCIATIONS

"Classics"	
Polio	Polio virus
Trachoma	*Chlamydia trachomatis*
Chagas cardiomyopathy	*Trypanosoma cruzi*
Chronic Infection or Disease Process	
Cervical cancer	Human papillomavirus
CLD, Liver cancer	Hepatitis B and C viruses
Lyme arthritis	*Borrelia burgdorferi*
Peptic ulcer disease	*Helicobacter pylori*
Whipple's disease	*Tropheryma whippelii*
Bladder cancer	*Schistosoma haematobium*

Infectious Causes of Chronic Diseases

- **For more information:**
  - *The Infectious Etiology of Chronic Diseases: Defining the Relationship, Enhancing the Research, and Mitigating the Effects* (IOM, 2004)

Available at:
http://www.nap.edu/catalog.php?record_id=11026

  - O'Connor SM, Taylor CE, Hughes JM (2006). Emerging infectious determinants of chronic diseases. *Emerging Infectious Diseases* **12** (No. 7): 1051-1057.

Summary: Main Themes

- **There are factors responsible for emergence of novel infections**
- **Interspecies transfer is an important source**
- **Humans do things that increase the risk of exposure or transmission**
- **Therefore, we can do things to reduce or manage these risks**
- **What should we do to make the future safer?**

Website Resources

CDC Journal “Emerging Infectious Diseases”:
www.cdc.gov/eid/

WHO outbreak information:
www.who.int/csr/don/en/

NYC Department of Health & Mental Hygiene:
www.nyc.gov/html/doh/

ProMED-mail:
www.promedmail.org