

Recombinant DNA Research with Pathogenic Viruses: Meeting the Public Health Challenges

Elias A. Zerhouni, M.D.

Director, National Institutes of Health



**NIH Recombinant DNA Advisory
Committee Safety Symposium
September 21-22, 2004**



Public Health Challenges



Acute to Chronic Conditions



Aging Population



Health Disparities



Emerging Diseases



Biodefense

New Research on Emerging Infections: Challenges for Biosafety Review

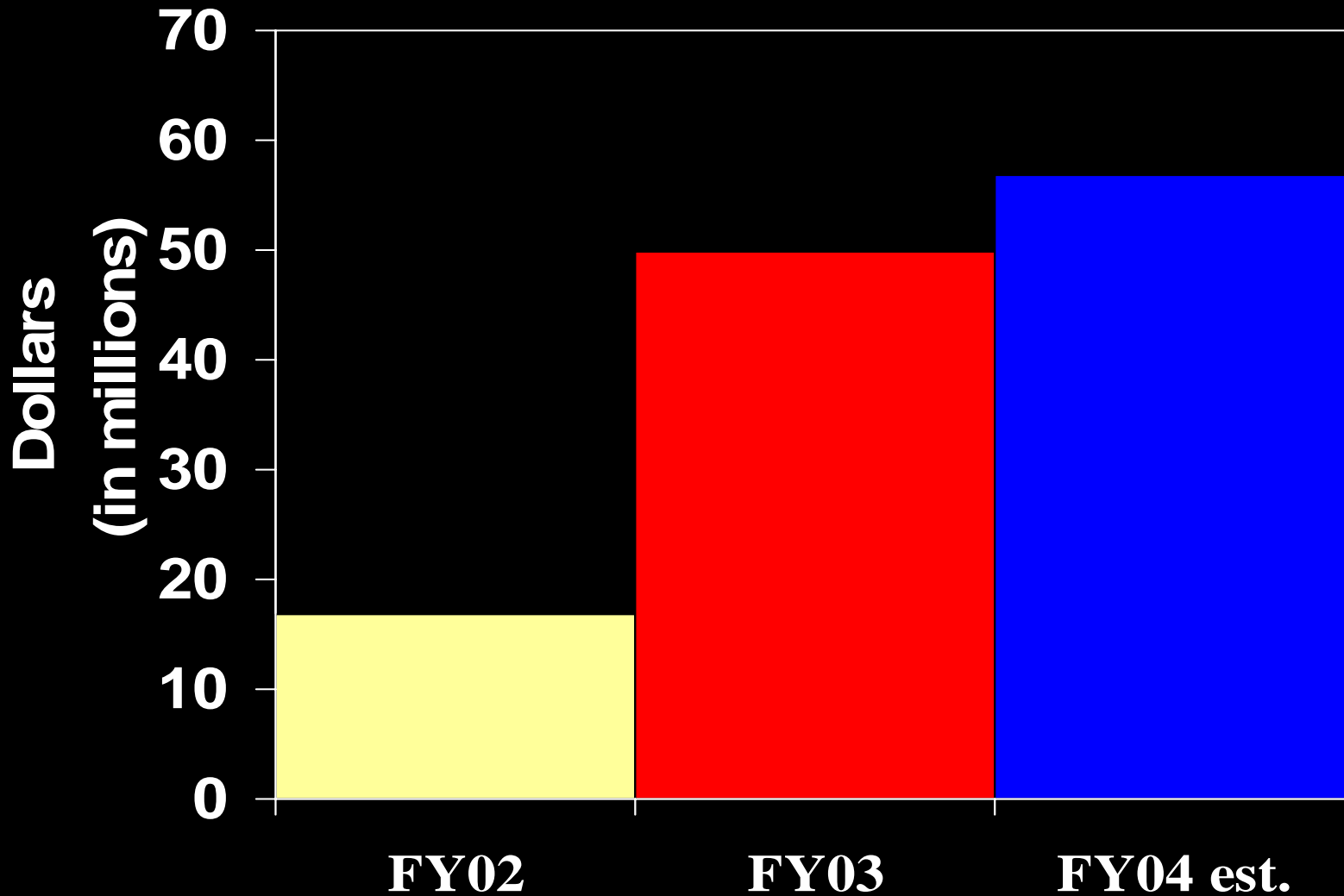
Increased research with pathogenic viruses

- Improved methods for generation of recombinant viruses from plasmids
- Public health concerns
- Biodefense

Examples of areas of research

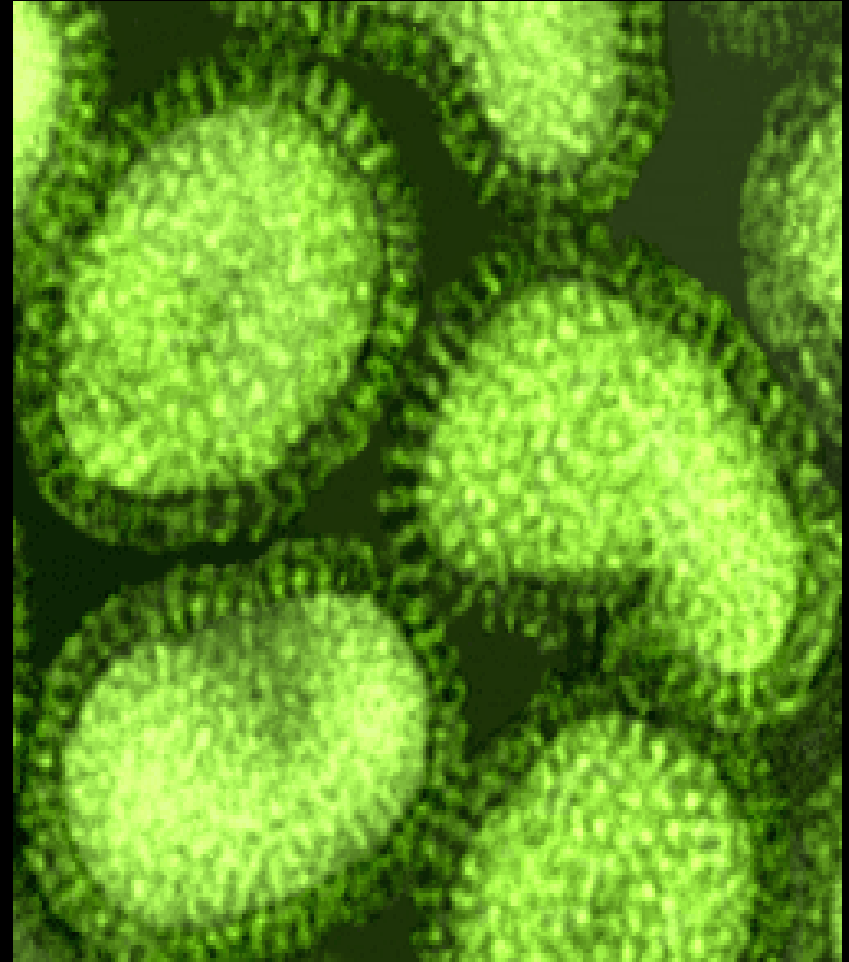
- 1918 “Spanish” Influenza Virus
- Highly Pathogenic Avian Influenza Viruses
- Severe Acute Respiratory Syndrome
Coronavirus

Increasing NIAID Funding of Extramural Influenza Research



Public Health Impact of Influenza Virus

- Novel viruses created each year by the high mutation rate and reassortment of genes among different viral strains
 - Virus escapes neutralization by antibodies to previous strains
 - No immunity from one year to the next



Public Health Impact of Influenza Virus

Yearly epidemics

- ~ 20,000 deaths/yr in U.S.

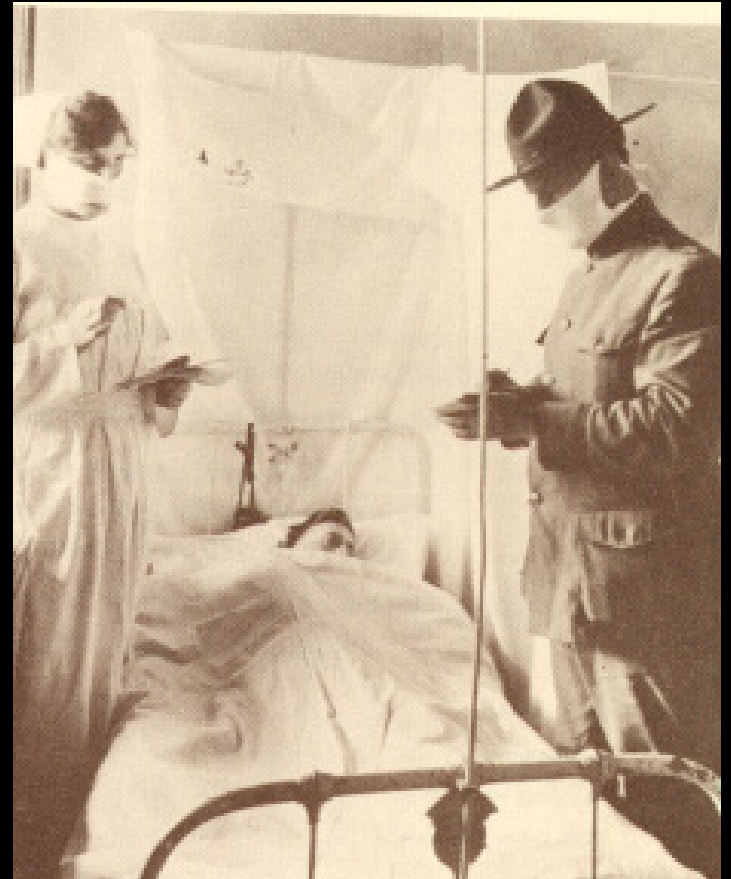
Pandemics in the last century

- **1918 H1N1**
 - ~ 675,000 deaths in U.S
 - 20 - 40 million world wide
- **1957 H2N2**
 - ~ 66,000 excess deaths in US
- **1968 H3N2**
 - ~ 34,000 excess deaths in US



1918 Influenza Virus Research

- **1918 influenza virus RNA recovered from:**
 - US soldiers who died of the Spanish flu during World War I
 - British patients
 - An Aleut woman who was buried in permafrost.
- **Sequence determined for 5 of 8 viral genes and ongoing for remaining virus.**



Goals of Research on 1918 Influenza Virus

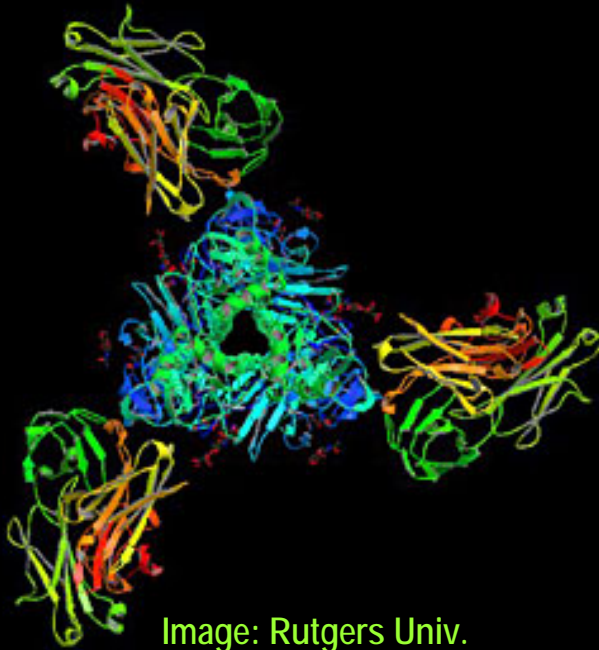
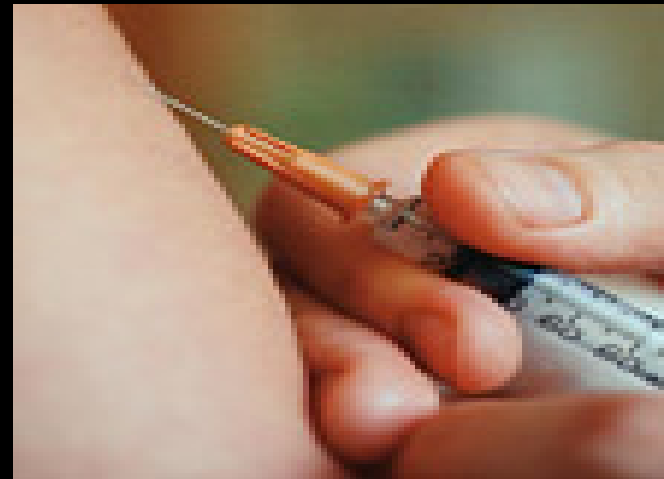


Image: Rutgers Univ.

- Determine virulence factors and molecular mechanisms for the high pathogenicity
- Evaluate efficacy of vaccine candidates and antiviral drugs



Highly Pathogenic Avian Influenza Viruses

- **H5N1**

- 1997 Hong Kong
 - 18 cases, 6 deaths
- 2003 Hong Kong
 - 3 cases, 2 deaths
- 2004 Vietnam and Thailand
 - 37 cases, 26 deaths

- **H9N2**

- 1999 Hong Kong and China
 - 7 cases
- 2003 Hong Kong
- 2 cases

- **H7N7**

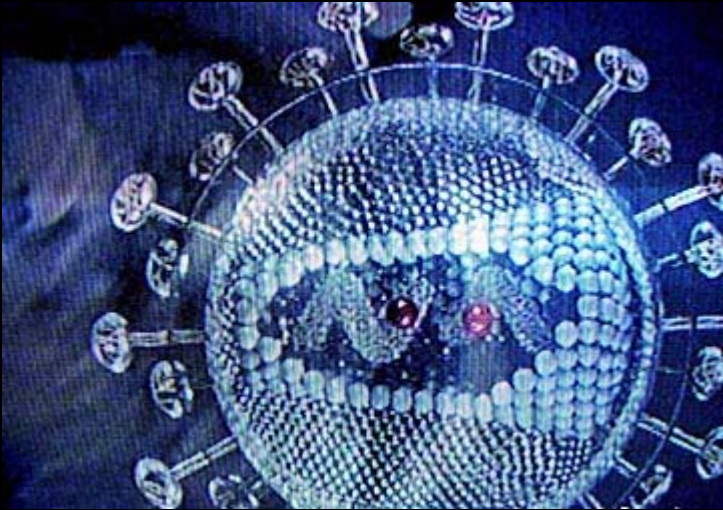
- 2003 Netherlands
 - 79 conjunctivitis
 - 13 influenza-like illnesses
 - 1 death
 - 3 person-to-person transmissions

Highly Pathogenic Avian Influenza Viruses

- Source of next pandemic?
- Reassortment with a human influenza virus or direct infection from birds (H5N1) and adaptation to transmit efficiently from person to person?



SARS Coronavirus



- Novel coronavirus was the causative agent of the SARS outbreak in 2002-2003 in which ~ 8000 individuals were infected and ~ 800 deaths occurred.

- The sequence of the ~ 30,000 nt RNA genome was determined within two months of viral isolation.



Public Health Goals of Research on SARS Coronavirus

- Determine functions of viral protein's role in virulence
- Develop rapid diagnostic assays for clinical SARS
- Develop live attenuated virus vaccine candidates
- Identify targets for antiviral drugs



Biosafety and Public Health

- **Research into viral virulence mechanisms and the development of vaccines and antiviral drugs are public health priorities.**
- **While this research is of critical importance, it is equally important that the research be performed responsibly to protect the health of laboratory researchers and the public.**

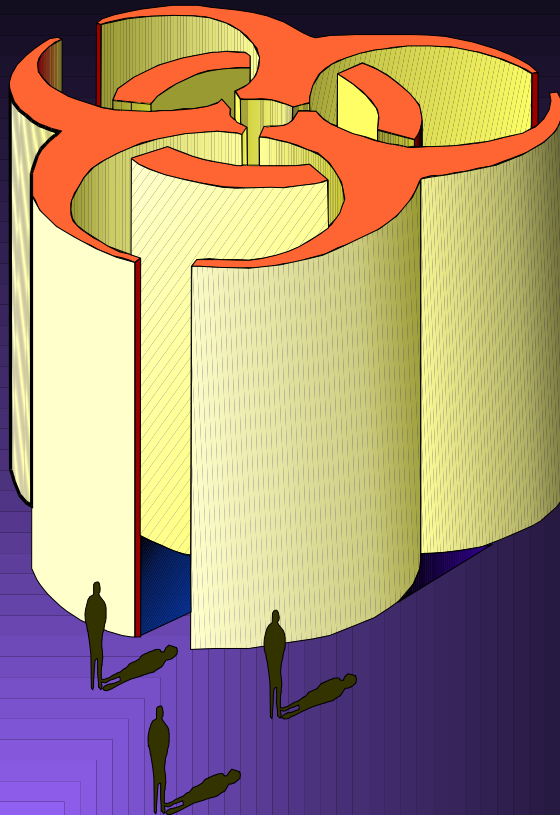
Standards of Biosafety Practice

- **Established:**

- *NIH Guidelines for Research Involving Recombinant DNA Molecules*
- *Biosafety in Microbiological and Biomedical Laboratories*

- **Needed:**

- Interpretation and application of biosafety principles to new rDNA research areas



Goals

- **Enhance awareness of the critical safety issues**
- **Promote a “culture of responsibility”**
- **In light of new methodologies, develop guidance for rigorous biosafety review and appropriate biologic and physical containment.**