Pandemic Influenza: Threat, Preparedness and Response

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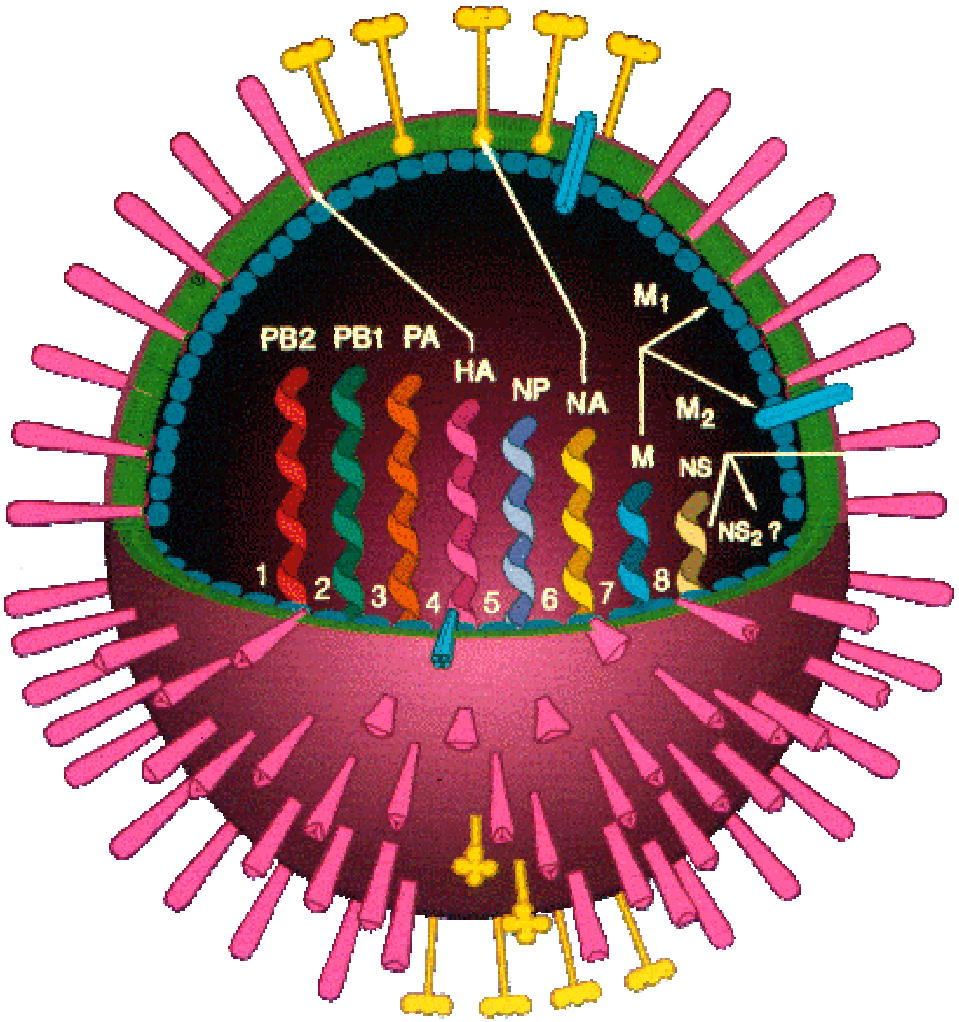
Outline

- Background on Influenza
- H5N1 Influenza in Asia
- Pandemic Influenza Preparedness

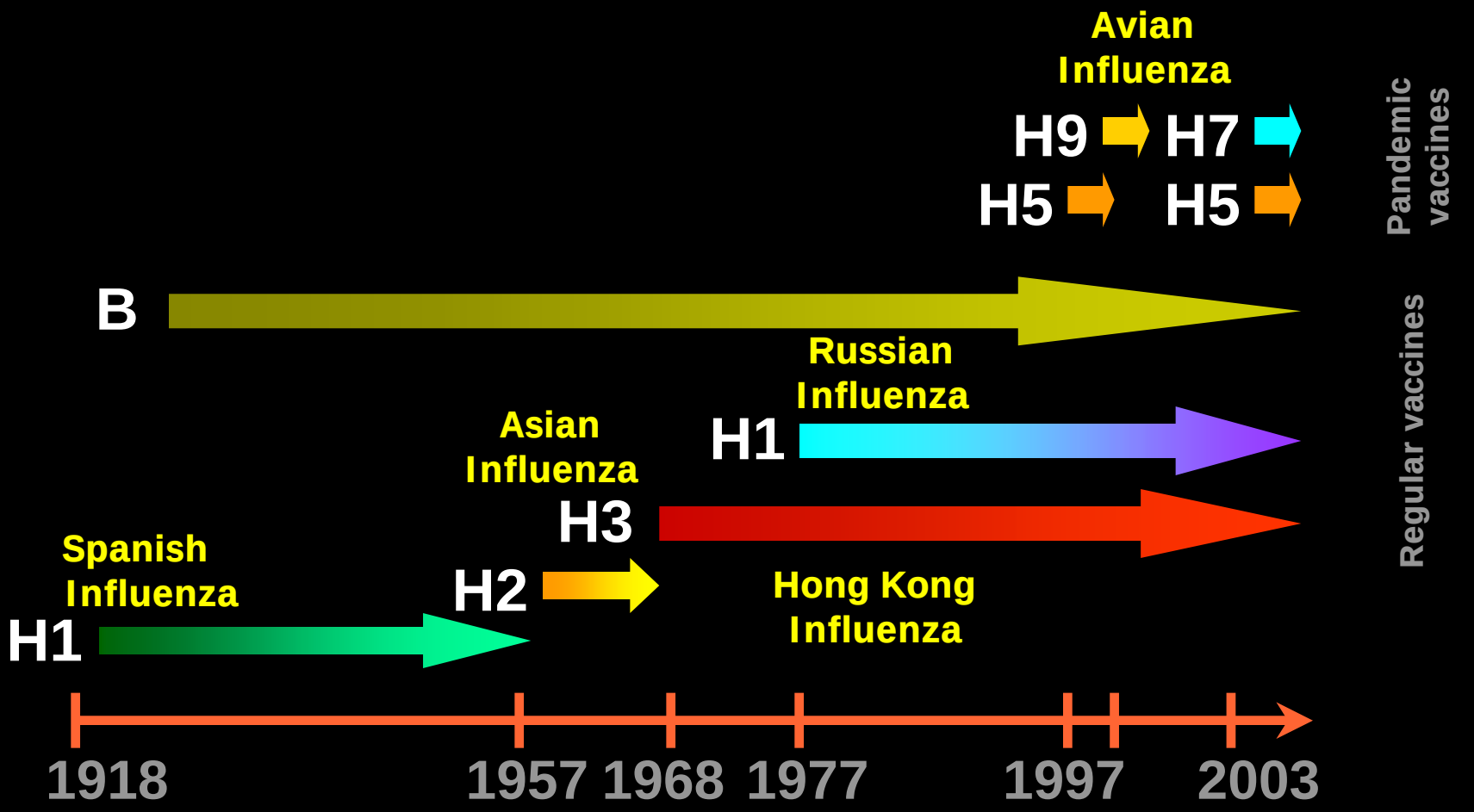
Influenza Virus



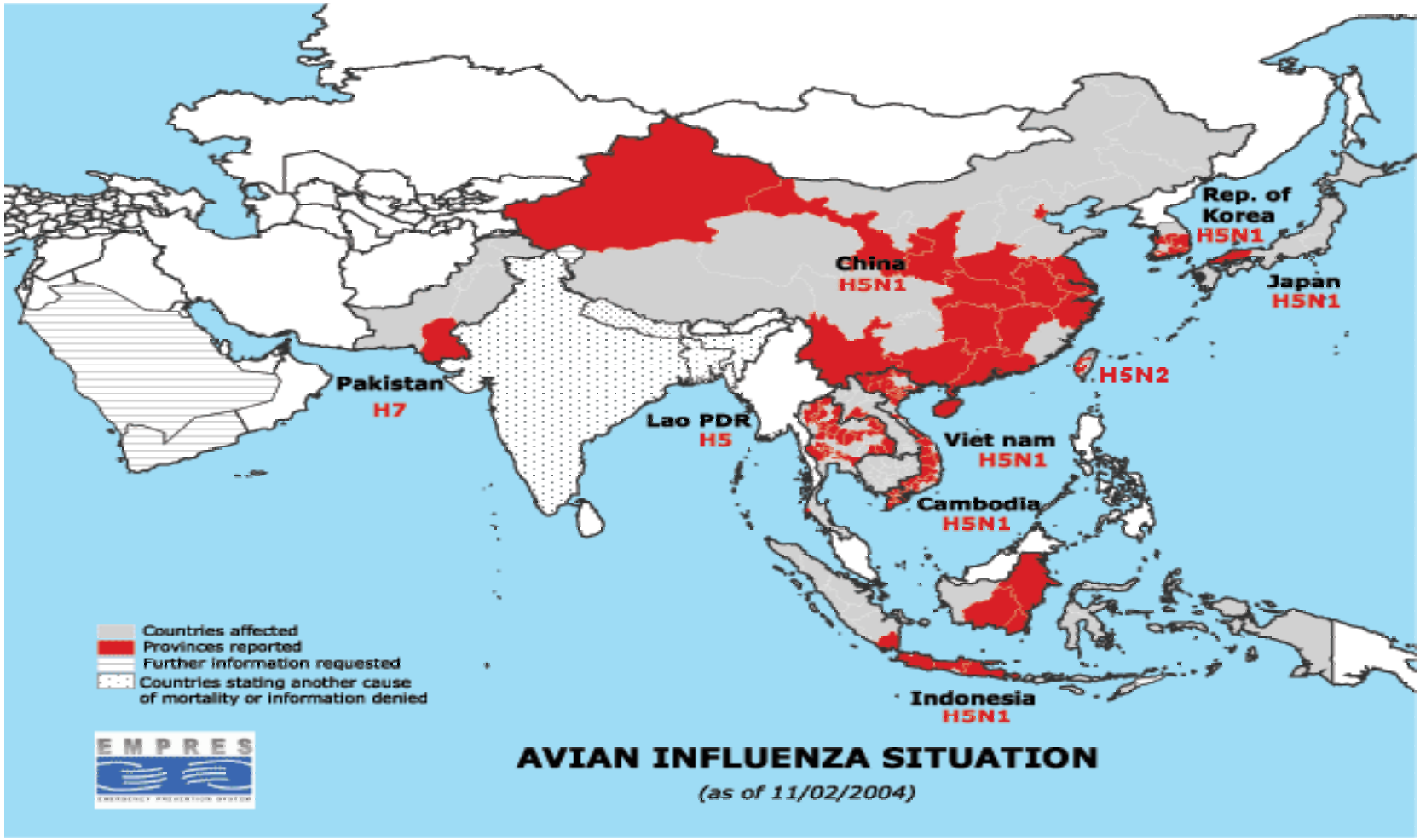
Antigenic Change: Evolving Threat of Influenza

- Antigenic “drift” occurs in HA and NA
  - Associated with seasonal epidemics
  - Continual development of new strains secondary to genetic mutations
  - Antigenic drift occurs at a faster rate in A than B viruses
- Antigenic “shift” occurs in HA and NA
  - Associated with pandemics
  - Appearance of novel influenza A viruses bearing new HA or HA & NA

Timeline of Emergence of Influenza Viruses in Humans



Avian Influenza Poultry Outbreaks, Asia, 2003-04



ASIA FIGHTS AN EPIDEMIC

SHAKIL ADIL / Associated Press

Alarm over the bird flu has risen at poultry farms such as this one near Karachi, Pakistan, as the country became the eighth to report a variant of the disease. A 6-year-old boy in Thailand marked the seventh recent fatality from bird flu.

Killer bird flu rampant

By M.A.J. McKENNA
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The massive Asian epidemic of avian influenza chalked up its seventh human fatality Monday, making the outbreak the most serious on record.

At the same time, a variant of the disease that has swept through Southeast Asia appeared in an eighth country, Pakistan.

The international medical community began to express alarm over the expanding epidemic. The influential journal The Lancet called the prospect of the disease spreading widely among humans "massively frightening."

Simultaneously, scientists with the U.S. Centers for Disease Control and Prevention said many human cases of influenza A/H5N1, also known as bird flu, have almost certainly gone unrecognized. And the World Health Organization made a global appeal for money, equipment and personnel to help block the flu's further spread.

In Thailand, where health officials from flu-affected nations are expected to gather Wednesday for an emergency summit, the Ministry of Public Health confirmed that a 6-year-old boy died of H5N1 infection. Thailand has confirmed two other cases both in children,

➤ Please see **BIRD FLU, A10**

Impact of Avian Influenza (1)

- Hundreds of millions of affected poultry
  - > 100 million birds died or destroyed
  - Inadequate compensation to farmers
    - Discourages reporting
    - Encourages hiding/smuggling of valuable birds
  - Poultry and poultry products have become a food staple, may provide 30% of total protein intake

Impact of Avian Influenza (2)

- Elimination of H5N1 in short terms unlikely
  - Large size of epizootic unprecedented in geographical scope, international spread, and economic consequences for the agricultural sector
  - Capacity to control varies significantly by country
  - Backyard flocks pose particular difficulties
    - China has 13 billion birds
    - 80% of “farms” have < 100 birds
  - Infections in wild birds documented
  - Many factors underlying spread not understood

Avian Influenza: Implications for Human Health

- Human influenza surveillance poor or nonexistent in countries affected by poultry outbreaks
- Small number of human cases suggests virus not (currently) easily transmitted from birds to humans.
- No evidence to date of efficient human-to-human transmission
- Circulation of avian H5N1 and human H3N2 viruses increases possibility for reassortment or adaptation through mutation
- Limited therapeutic options
  - Human isolates resistant to adamantanes, sensitive only to oseltamivir (Tamiflu)

Human H5N1 Cases

(as of March 22, 2004)

Country	H5N1 Cases	Deaths
Thailand	11	7
Vietnam	23	15
Total	34	22

H5N1 Vaccine

- 2003 H5N1 virus (from human case) not optimal antigenic match to 2004 H5N1 viruses
- Reference strain prepared with reverse genetics
  - Genetically modified organism?
  - Intellectual property constraints?
- Investigational ("Pilot") lots pending
  - Clinical trials summer→ early fall '04

U.S. Pandemic Influenza Preparedness and Response Plan

"The pandemic influenza clock is ticking. We just don't know what time it is."

"This is the one health threat we're preparing for that we know will happen"

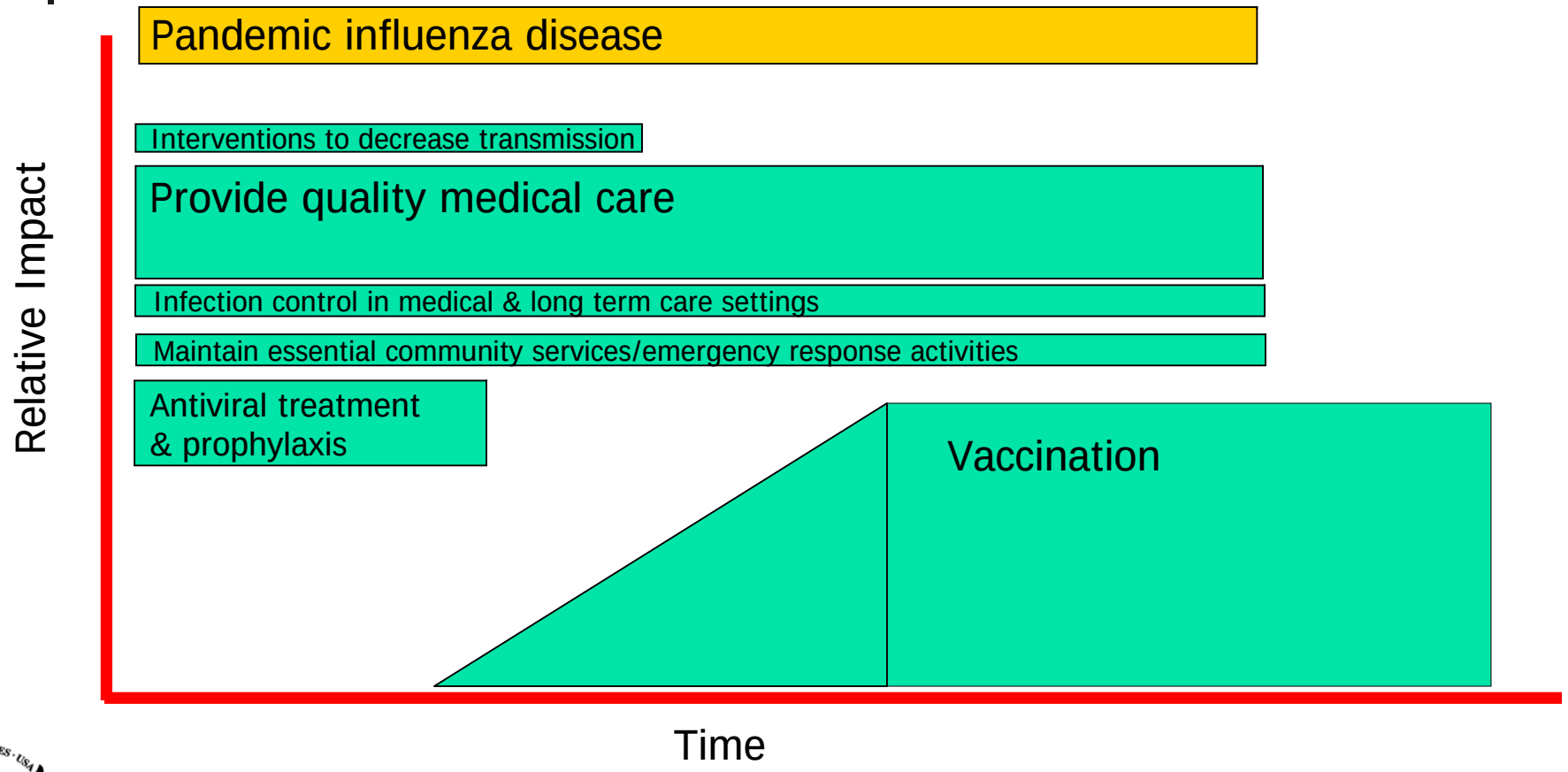
Goals of Pandemic Influenza Response

- Decrease the burden of disease
- Minimize social disruption
- Reduce economic impacts

Purposes of the Pandemic Influenza Preparedness and Response Plan

- Define and recommend preparedness activities
- Describe roles, responsibilities and actions of federal coordination of response
  - International
  - State and local levels
- Guide health departments and health care system in developing state and local preparedness and response plans
- Provide technical information on which preparedness and response are based

Pandemic Response Components



The U.S. Pandemic Influenza Preparedness and Response Plan

- **Core Plan**
  - Describes National coordination and decision-making
  - Provides an overview of key preparedness issues
  - Outlines response actions at national, state, & local levels
- **Guides** (2)
  - Guidance for State/local Health Departments planning
  - Guidance for health care system planning
- **Annexes** (10)
  - More detailed and technical information on key preparedness and response issues
    - (e.g., surveillance, vaccine development and production, vaccine and antiviral drug use strategies, strategies to decrease influenza transmission, communications, research, lessons learned from 1976 swine influenza program, comparisons between influenza and SARS)

Pandemic Phases
(WHO, 1999)

Phase	Level	Definition
0 ***Inter-pandemic Phase***	*0*	Epidemic influenza viruses circulate in human populations causing yearly outbreaks; no evidence that a novel influenza virus has infected humans
	1	*Novel Virus Alert*: Identification of a novel influenza virus in a person
	2	Confirmation that the novel influenza virus has infected two or more people, but the ability of the virus to spread rapidly person-to-person and cause multiple outbreaks of disease leading to epidemics remains questionable.
	3	*Pandemic Alert:* Confirmation of person-to-person spread in the general population with at least one outbreak lasting for more than 2 weeks in one country
1		Confirmation that the novel influenza virus is causing several outbreaks in one country and has spread to other countries, with consistent disease patterns indicating serious morbidity and mortality is likely in at least one segment of the population
2		Outbreaks and epidemics are occurring in multiple countries and spreading across the world
3		End of the first wave of the pandemic
4		Confirmation of a second or later wave caused by the same novel virus strain
5		Confirmation that the pandemic has ended

Vaccine and Vaccination Preparedness Goals

- Enhance surge production capacity
- Shorten timelines to availability
- Ensure effective distribution & administration to achieve pandemic response goals

Improving Vaccine Preparedness

- Enhance annual influenza vaccine use
- Ensure year-round egg supply
- Increase and diversity U.S. manufacturing capacity
- Develop and test vaccine investigational lots of pandemic-like vaccine strains
- Conduct research to improve ability to rapidly develop reference strains that grow well in production systems

Improving Vaccine Preparedness

- $50 million FY 2004 funding to...
  - Assure year-round egg supply
  - Promote U.S. licensure and manufacture of influenza vaccine produced in cell culture
- NIAID currently is negotiating with manufacturers for production of pilot lots of H5N1 vaccine

Influenza Antivirals (1)

- Chemoprophylaxis and therapy can have major health impacts
- Drug availability & manufacturing capacity limited
- Initial oseltamivir stockpile in SNS

Influenza Antivirals (2)

- Modeling of antiviral drug use strategies, health impacts, and cost effectiveness
  - Substantial impact on deaths: Rx >> chemoprophylaxis
  - Likely strategies all cost saving to society
- Key preparedness issues
  - Assess availability and consider stockpile options
  - Work with health departments to develop strategies for effective distribution and use

Priority Groups for Antiviral Prophylaxis

- “Front-line” healthcare workers
- Persons involved in development/manufacture of influenza vaccine
- Public health personnel who are critical for pandemic response activities
- Persons who provide essential community safety services (e.g., police and fire department personnel and others whose functions are defined as critical to public safety)
- Persons culling infected animal populations if disease in people is derived from an animal focus and culling activities occur

Additional Priority Groups for Antiviral Prophylaxis

- Persons at high risk for severe disease or mortality from influenza or its complications based on age and underlying disease
- Persons in institutional settings (e.g., long-term care facilities for the elderly)
- Persons who provide important community services (e.g., maintaining utility service and essential transportation)

Interventions to Decrease Disease Spread in an Influenza Pandemic

- Health care system interventions
  - Infection control and isolation of patients in hospitals
  - Antiviral prophylaxis/vaccination/of HCWs and in LCTF
- Community interventions
  - Travel advisories and precautions and protocols
  - Screening travelers from areas with disease
  - Quarantine of exposed persons

...based on the epidemiology & transmission of infection

Interventions to Decrease Influenza Spread

- Objectives
  - Contain clusters of human disease caused by strains not well transmitted between people
  - Slow spread of strains that are more effectively transmitted buying time for specific preventive measures (e.g., vaccine)
- Control strategies in avian influenza outbreaks
  - Cull infected flocks
  - Prevent reassortment with human strains by protecting exposed persons with vaccine and antiviral chemoprophylaxis

State & Local Preparedness

- State and local health departments
  - Synergy with BT/other preparedness planning
  - CDC support for surveillance and public health laboratories
  - Tabletop and field exercises
- Health care system
  - Need for planning and education and coordination with state/local health departments
  - HRSA grants to coordinate medical care and enhance capacity

Thanks

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