Challenges in the Prevention and Control of Influenza: Implications for Pandemic Influenza Preparedness

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OUTLINE

- BACKGROUND ON INFLUENZA
- BACKGROUND ON PANDEMICS
- H5N1 INFLUENZA IN ASIA
- STATE AND FEDERAL PLANNING EFFORTS
- IMPLICATIONS FOR PANDEMIC INFLUENZA PREPAREDNESS

Influenza Pathogenesis

- Typical incubation 2 days (range 1-4 days)
- Viral shedding
  - Can begin 1 day before symptom onset
  - Peak shedding first 3 days of illness
    - Correlates with temperature
  - Subsides usually by 5-7th day in adults
    - Can be 10+ days in children

Clinical Illness

- Characterized by
  - Abrupt onset fever, chills, muscle aches, headache, fatigue
  - Cough, pharyngitis, rhinnitis
  - Gastrointestinal symptoms in children
- Complications
  - Primary viral or secondary bacterial pneumonia
  - Worsening of underlying illnesses
- Symptoms overlap those of many other pathogens

Average Annual Impact Inter-Pamdemic Influenza, USA

- 5-20% infected
- Over 200,000 hospitalized
  - About half in 65+
- 36,000 deaths
  - >90% in 65+

Transmission of Influenza

- Limited studies, varying interpretations
- Contact, droplet and droplet nuclei (airborne) transmission may all occur
  - Relative contribution of each unclear
    - Droplet thought most important
      - Generated via coughing, sneezing, talking
  - Most studies
    - Animals or human experiments under artificial conditions
    - Outbreak investigations
      - Unclear of infection source when community outbreak

Influenza Virus Primer

- Single-stranded RNA virus
- Family Orthomyxoviridae
- 8 separate gene segments
- Characterized by ability to change
- 3 types: A, B, C

  - Influenza A viruses infect humans, pigs, birds, horses, and aquatic mammals
- Influenza A subtypes based on external glycoproteins, hemagglutinin (HA) and neuraminidase (NA)
  - 16 types HA
  - 9 types NA

INFLUENZA VIRUS

Influenza: Epidemics and Pandemics

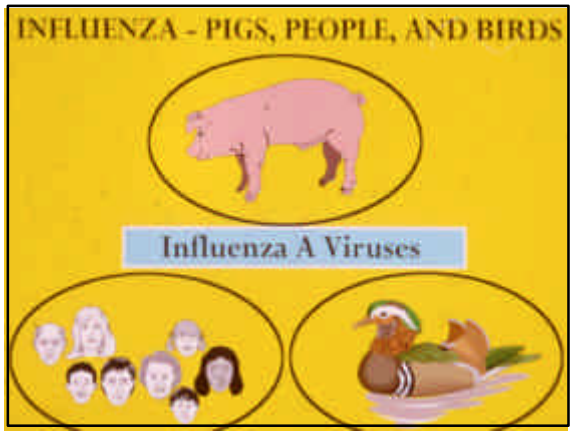
- Influenza annual cause of significant morbidity and mortality: epidemics recognized in temperate areas
- Unpredictably and at irregular intervals, pandemics associated with increased mortality occur
- Attack rates 40-50% in some populations
- Criteria for pandemic influenza virus:
  - Novel influenza A strain
  - Little or no immunity in population
  - Person-to-person transmission with disease

Antigenic Change

- **Antigenic 'drift' occurs in HA and NA**
  - Associated with seasonal epidemics
  - Continual development of new strains secondary to genetic mutations
  - A viruses >> B viruses
- **Antigenic 'shift' occurs in HA and NA**
  - Associated with pandemics
  - Appearance of novel influenza A viruses bearing new HA or HA & NA

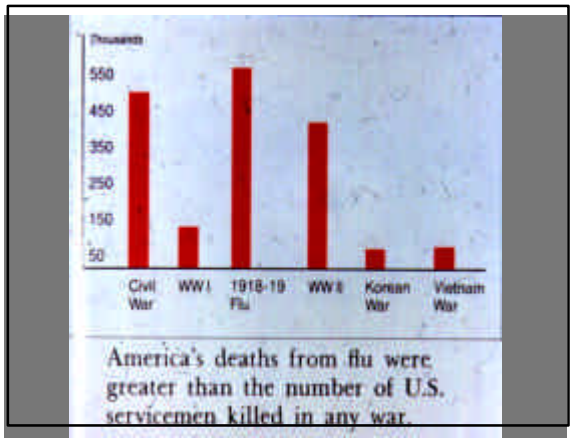
Influenza Viruses Infect Several Animal Species

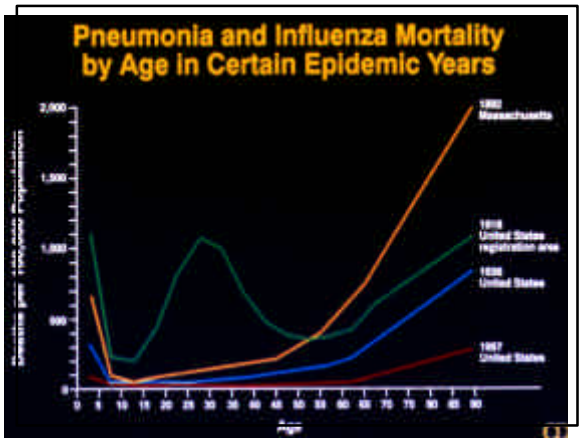
- **All influenza A subtypes recognized to date are found in wild birds**
  - Fecal transmission common among wild birds
  - Usually, infectious occur without illness
- **Other animal species**
  - Domestic poultry (chickens, ducks and quail)
  - Humans, swine, horses, seals, whales
- **Humans usually infected by human influenza viruses**



Influenza Pandemics, 20th Century

YEAR	NAME	SUBTYPE	DEATHS- Worldwide	USA
1918-19	Spanish	H1N1	25-50 million	>500,000
1957	Asian	H2N2	>1 million	70,000
1968	Hong Kong	H3N3	>1 million	34,000





Pandemic Spread and Seasonality

- Spread of a pandemic/"shifted" virus
  - Months before U.S. community outbreaks for prior pandemic strains
    - 1918 – 0; 1957 – 4-5; 1968 – 2-3; 1977 – 3-4
  - Spread of the next pandemic
    - More rapid because of increased international travel
    - More warning because of better surveillance
- Seasonality
  - Fall – Spring seasonality generally preserved
  - Multiple pandemic waves occur – potentially in the same season

Estimated Impact of Future Influenza Pandemic: USA & Maine

- Deaths: 89,000-207,000 (900 Maine)
- Hospitalizations: 314,000-734,000 (4000 Maine)
- Outpatient visits: 18-42 million (165,000 Maine)
- Additional illnesses: 20-47 million (390,000)
- Economic impact: $71.3-165.5 billion

- Model assumes attack rates of 15-35% and is based on the 1968 pandemic; and US population of 290 million persons. (Meltzer et al, CDC)

Swine Influenza Program, 1976

Year	Vaccine status
1976	•4 US-based manufacturers •New strain identified in February •US government guaranteed purchase •150 m vaccine doses produced under federal contract •Vaccine distributed to states for mass vaccination (no defined priority groups) •Vaccination begun in October •45 m doses administered before program halted due to occurrence of GBS (85% in clinics)

THE NEXT INFLUENZA PANDEMIC

?

WHAT WE DON'T KNOW

- When
- Where
- What subtype
- How virulent it will be

CONFIRMED HUMAN INFECTIONS WITH AVIAN INFLUENZA VIRUSES

YEAR	COUNTRY	SUBTYPE	CHARACTERISTICS
997	HONG KONG*	H5N1	18 PEOPLE WERE INFECTED, 6 OF WHOM DIED
999	HONG KONG	H9N2	VIRUS WAS ISOLATED FROM 2 CHILDREN WITH MILD INFLUENZA-LIKE SYMPTOMS; BOTH RECOVERED
003	HONG KONG	H5N1	INFECTION OCCURRED AMONG 2 FAMILY MEMBERS AFTER RETURNING FROM CHINA, 1 OF WHOM DIED; SOURCE OF INFECTION REMAINS UNCERTAIN
003	THE NETHERLANDS*	H7N7	INFECTION OCCURRED IN 83 HUMANS (MOSTLY CONJUNCTIVITIS), 1 OF WHOM DIED
003-2005	SEVERAL ASIAN COUNTRIES*†	H5N1	THIS IS THE LARGEST OUTBREAK OF AVIAN INFLUENZA IN POULTRY EVER REPORTED
004	BRITISH COLUMBIA, CANADA	H7N7	INFECTION (MOSTLY CONJUNCTIVITIS) OCCURRED IN 5 HUMANS

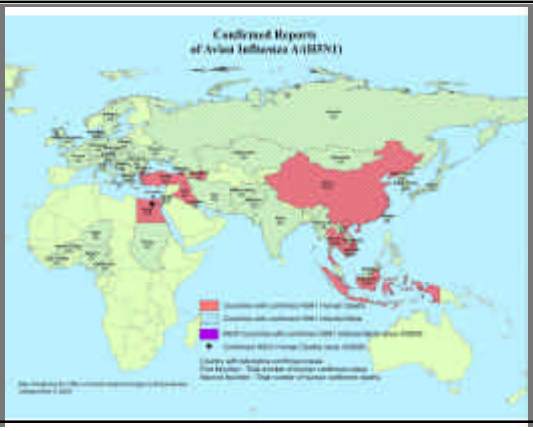
imited person-to-person transmission occurred.
As of March 2005, outbreaks in poultry have been confirmed in 8 countries: Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam. In most of these countries, this is the first outbreak of avian influenza.

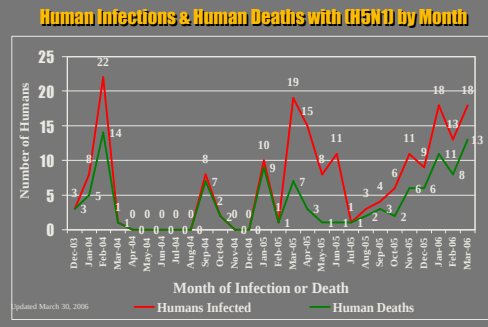
WHAT ABOUT H5N1?

- Will the next pandemic be as server as 1918?
- Given the experience with human H5N1 infection, should we prepare for the 'worst case' scenario?
- Influenza 'extrapolitis'

HUMAN H5N1 CASES (MAY '06)

- Azerbiajan: 8 cases; 5 deaths
- Cambodia: 6 cases; 6 deaths
- China: 18 cases; 12 deaths
- Djibouti: 1 case; 0 deaths
- Egypt: 13 cases: 5 deaths
- Indonesia 33 cases; 25 deaths
- Iraq 2 cases; 2 deaths
- Thailand 22 cases; 14 deaths
- Turkey 12 cases, 4 deaths
- Vietnam 93 cases, 42 deaths
- TOTAL 208 cases; 115 deaths (CFR: 55%)





Clinical Illness with H5N1 Compared with Typical Influenza

- More severe illness in younger persons
- Primary viral pneumonia appears to be more common and with rapid onset
- Incubation period may be longer (up to 14 days?)
- Duration of infectious period likely longer, particularly in adults

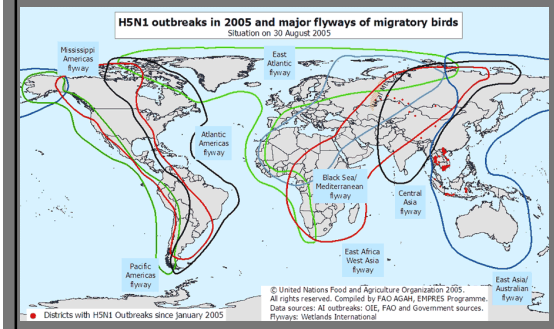
H5N1 MORTALITY BY AGE

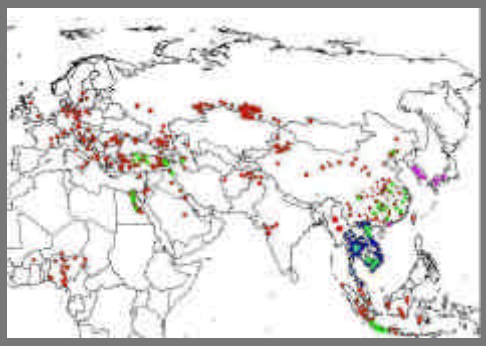
- What does high mortality in persons <40 reflect?
  - Population demographics in affected countries?
  - Behavioral—disproportionate number of children & young adults interacting with sick/dying chickens?
  - Inherent feature of the virus?
  - Role of acute inflammatory response to pathophysiology of H5N1 infection?
  - Is this reflective of dose?
  - Parallels to 1918?

“. . . In the highly interconnected and readily traversed ‘global village’ of our time, one nation’s problem soon becomes every nation’s problem . . .”

“Microbial Threats to Health: Emergence, Detection, and Response”, Institute of Medicine, March 2003.

Bird Flu Hit The 1st Mobile Home Park In Florida





IMPACT OF H5N1 AVIAN INFLUENZA (1)

- HUNDREDS OF MILLIONS AFFECTED POULTRY
  - > 150 MILLION BIRDS DIED/ DESTROYED
  - INADEQUATE COMPENSATION FARMERS
  - DISCOURAGES REPORTING
  - ENCOURAGES HIDING/SMUGGLING VALUABLE BIRDS
  - POULTRY AND POULTRY PRODUCTS A FOOD STAPLE: 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; FEW FAMILY CLUSTERS REPORTED
- CIRCULATION OF AVIAN H5N1 AND HUMAN H3N2 VIRUSES INCREASEES POSSIBILITY FOR REASSORTMENT OR ADAPTATION THROUGH MUTATION
- LIMITED THERAPEUTIC OPTIONS
  - HUMAN ISOLATES RESISTANT TO ADAMANTANES, SENSITIVE ONLY TO OSELTAMIVIR (TAMIFLU)

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."

PURPOSES OF THE PANDEMIC INFLUENZA PREPAREDNESS AND RESPONSE PLAN

- DEFINE AND RECOMMEND PREPAREDNESS ACTIVITIES
- DESCRIBE ROLES, RESPONSIBILITIES AND ACTIONS OF COORDINATION OF RESPONSE
- GUIDE PUBLIC HEALTH AND HEALTH CARE SYSTEM IN DEVELOPING PREPAREDNESS AND RESPONSE PLANS
- PROVIDE TECHNICAL INFORMATION ON WHICH PREPAREDNESS AND RESPONSE ARE BASED

GOALS OF PANDEMIC INFLUENZA RESPONSE

- DECREASE THE BURDEN OF DEATHS AND DISEASE
- MINIMIZE SOCIAL DISRUPTION; MAINTAIN ESSENTIAL INFRASTRUCTURE

Pandemic Influenza Vaccine Issues

1918 "CURES"

- Intravenous hydrogen peroxide
- Injection blister fluid, morphine, strychnine & caffeine
- Typhoid vaccine to promote an immune Rx
- Cupping and bleeding

VACCINE RESEARCH AND DEVELOPMENT CHALLENGES

- Adjuvanted inactivated vaccine (alum, ME59)
- Formulation immunogenic vaccine (15 vs 90 ug HA)
- Number doses: priming/partial
- Alternate vaccination strategies: intradermal; subcutaneous, intranasal, oral
- Life attenuated vaccines

VACCINE RESEARCH (con't)

- Cross protective (universal) vaccines (potential antigens: ectodomain M2; NS antigen
- Cell culture (unlikely)
- Other vaccine production technologies and vaccine production systems: DNA; recombinant HA antigens, insect cell culture
- Alternative delivery technologies
  - Immunostimulant patch; dose sparing needles; syringes; jet injectors

POULTRY VACCINES FOR PEOPLE

- "What is good for the goose is good for Mr. and Mrs. Gander?

Pandemic Influenza Vaccine Production Timelines

- **Development of reference strain**
  - Use of reverse genetics allows HA and NA from pandemic strain to be combined with other genes from a strain well adapted to growth in eggs
- **Vaccine production (monovalent)**
  - Master seed developed from reference strain
  - Growth in eggs and purification
  - Formulation and filling
- **Regulatory process**
- **Optimal timing – 3-4 months (if reference strain and potency testing reagents already developed)**

Pandemic Influenza Vaccine Supply Estimates: Current Status

- Pandemic vaccine supply assumptions
  - Only US produced vaccine will be available (1mfr)
  - 15 ug antigen/dose and 2 doses/person will be needed for protection
  - Monovalent vaccine production capacity will be 3-fold that of annual vaccine (e.g., similar Ag yield/egg)
- Current Sanofi production is sufficient to deliver
  - 250 M monovalent doses/year (~5 million/week)
  - Implication – about 1% of the population can be protected per week

Pandemic Influenza Vaccine Supply: Possible Additional Options

- If 7.5ug/dose is immunogenic, vaccine supply is doubled
- One or two additional new manufacturers may offer additional pandemic supply

Potential Antigen-Sparing Approaches to Influenza Vaccination

- Vaccine delivery strategies
  - Partial doses (1/2 dose or other)
  - Alternate route of injection (e.g., intradermal, subcutaneous, intranasal, oral)
- Immune enhancement strategies
  - Adjuvanted vaccine (e.g., alum, MF59)
- Alternative delivery technologies
  - Immunostimulant patch, dose-sparing needles, syringes, jet injectors

Influenza Vaccine Partial Doses

- Treanor et al, Vaccine 2002, documented small differences in healthy adults 18-49 yrs, between 7.5ug and 15 ug doses:
  - <20% in achieving hemagglutinin inhibition titer of 1:40
  - <1.5 in ratios for GMTs between doses for all 3 antigens
- Authors concluded that vaccinating N healthy adults with half dose will protect more persons than vaccinating ½ N with full dose
- DoD conducting study with 2004 vaccine; data to be available spring 2005

Alternate route of injection for Influenza Vaccine

- Options include intradermal, subcutaneous, intranasal, oral
- Antigens deliverd to nasal, other mucosal surfaces, dermis may increase immunogenicity (more immune receptors)
- Belshe et al, Kenney et al, NEJM, 2004 intradermal studies suggest ID delivery may allow dose sparing, but small studies. Not as immunogenic in adults >59 years
- Need larger studies, proper controls

Immune enhancement strategies: Adjuvanted vaccine

- No licensed U.S. influenza vaccine contains an adjuvant
  - MF59, ISCOMS (immunostimulating reconstitued influenza virosomes) licensed in Europe
- Adding an adjuvant may provide greater immunogenicity with less antigen
- Alum, MF59 may be most likely choices; do increase local reactions
- Studies with U.S. licensed vaccines necessary

Alternative Delivery Technologies

- Immunostimulant patches (e.g., with E. coli heat stable enterotoxin)
- Jet injectors for intradermal vaccination
- Dose-sparing needle/syringe combinations (may add ½ to 1 dose to a 10 dose vial)

Potential Target Groups for Pandemic Vaccine Based on Response Goals

- Decrease pandemic health impacts
  - Public health and pandemic response personnel
  - Health care providers
  - High-risk groups
  - Children
- Decrease social disruption & preserve essential functions
  - Pubic safety personnel (police & fire)
  - Essential community service providers

THE DICTUM “FIRST, DO NO HARM” IS “THE FUNDAMENTAL RATIONALE FOR PROMOTING INFLUENZA IMMUNIZATION OF HEALTH CARE WORKERS AND FOR ALL OF US TO TAKE RESPONSIBILITY TO MAKE SURE THAT HEALTH CARE WORKERS ARE IMMUNIZED.”

- KRISTIN NICHOL, MD, MPH

- 38% HCW’S VACCINATED (2002 NATIONAL HEALTH INTERVIEW SURVEY, CDC)

Pandemic Influenza Planning: The Antiviral Response

Influenza Antiviral Drug Questions

- What drug(s) should be used?
- How should they be used?
- Who should get it?
- How much public sector supply will there be?
- How can it be delivered?

Advantages of Oseltamivir for Antiviral Interventions in a Pandemic

- Documented effectiveness in decreasing influenza complications
- Low rate of antiviral resistance NA’s and less risk of resistance spreading with widespread therapy
- Low incidence of adverse events
- Orally administered, simple dosing, few contraindications (infants < 1 year old)

Critical Factors in Defining Drug Use Strategy: Prophylaxis vs Treatment

- Effectiveness—impact on health outcomes and social & economic function
- Efficiency—optimal use of a limited antiviral supply
- Feasibility—can the recommended approach be implemented?
- Acceptability—is the approach ethical and acceptable to the public?

Prophylaxis vs Therapy in Occupational Settings: Critical Unknows

- Severity of pandemic disease
  - Need for prevention (vs therapy) to avoid absenteeism from fear of infection
  - Ability to cope with some work loss due to illness
- Risk of transmission to co-workers and patients in health care settings
- Implementation factors
  - Ability to implement early therapy
  - Ability to assure availability of therapy

Potential Priority Groups for Antiviral Drug Interventions: Critical Unknowns

- Ability to stratify among HCWs
  - Definition of "front-line"
  - Potential barriers to implementation
- Definition of "essential service personnel"
- Ability to stratify among high-risk outpatients
  - By underlying condition
  - By risk of severe disease
- Ability to implement early therapy
- Need to treat at < 48 hours

Implementation Issues

- Drug likely to be distributed to States *pro rata*
- Treatment delivery site will become the point of care
- Hospitals may be critical delivery node
  - Through occupational health for employees
  - At admission
  - In Emergency Department for high-risk outpatients
- Delivery sites for other occupational groups?
- Monitoring delivery, impact, resistance & safety

U.S. Oseltamivir Availability for a Pandemic

- Strategic National Stockpile
  - 85 million doses
  - 5-year dating with extensions possible
  - 1.5 million courses in private sector before the influenza season
    - Divided between pharmacies, large distributors and manufacturer
  - U.S. supply chain being considered

Surge Capacity Challenges

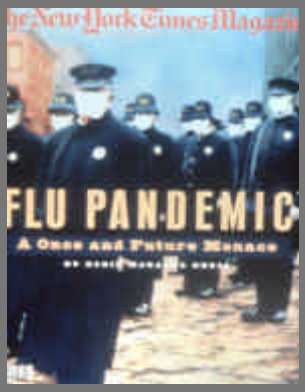
- Staffing
  - Cross training
  - Personnel who may be used to support other hospital services
  - Credentialing additional HCWs during emergency
  - Identify insurance and liability issues related to use of non-facility staff

Surge Capacity Challenges (con't)

- Bed Capacity
  - ICU; Isolation wards
- Consumable and Durable Supplies
  - Respirators; antibiotics
- Mortuary Issues
  - Morgue capacity; body bags; refrigeration

Surge Capacity Challenges (con't)

- Provision of care in non-hospital healthcare facilities
  - Communication; coordination
  - Infection Control
    - Hand hygiene
    - Lavatory/shower capacity
    - Staffing
    - Personal protective equipment
    - Cleaning disinfection supplies
  - Policies/procedures



INTERVENTIONS TO DECREASE INFLUENZA SPREAD

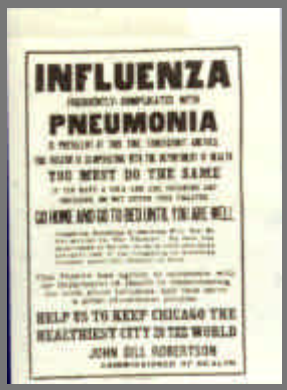
- **OBJECTIVES**
  - CONTAIN CLUSTERS OF HUMAN DISEASE CAUSED BY STRAINS NOT WELL TRANSMITTED BETWEEN PEOPLE
  - SLOW SPREAD OF STRAINS THAT ARE MORE EFFECTIVELY TRANSMITTED BUYING TIME FOR SPECIFIC PREVENTIVE MEASURES (e.g., VACCINE)
- **CONTROL STRATEGIES IN AVIAN INFLUENZA OUTBREAKS**
  - CULL INFECTED FLOCKS
  - PREVENT REASSORTMENT WITH HUMAN STRAINS BY PROTECTING EXPOSED PERSONS WITH VACCINE AND ANTIVIRAL CHEMOPROPHYLAXIS

Public Health Interventions Before and During an Influenza Pandemic

- Objectives: will vary as the epidemiologic situation evolves
  - Prevent further cases by virus that has not yet established efficient human-to-human transmission
  - Slow pandemic spread and gain time for strengthening preparedness measures (I.e. vaccine supply)
  - Reduce impact of first wave of epidemic

Key Measures

- Measures to reduce risk that cases transmit infection
- Measures to reduce risk that contacts transmit infection
- Measures to increase social distance
- Measures for persons entering or exiting an infected area within the country/county/locality
- Public health information, communication
- Disinfection measures



KFC Introduces NEW Bird-Flu Dipping Vaccine

Isolation and Contact Tracing

- Likely difficult to implement with low chance reducing transmission
  - Short incubation period
  - 50% may be infectious but without symptoms
- If incubation period longer, may have more role in decreasing community spread
- May be appropriate with initial introductions of new pandemic virus into USA

Evidence Benefit Community Measures

- School closures
  - No systematic studies
  - Often closed at peak of outbreak when benefit to community spread difficult to demonstrate
    - Often closed due to inadequate staffing
  - Cancellation large gatherings/social distancing not studies as means to limit community spread

Evidence for Use of Masks

- No evidence available on benefits of masks in preventing health care or community influenza transmission
  - Short incubation period
  - Difficult to trace source of outbreak since cases usually occur during community outbreaks
  - Unknown if type mask may make a difference (N-95 versus surgical, etc)
  - Did not appear to be helpful in 1918-19, but quality of masks and adherence use questionable
  - Use prudent at least in health care settings
- SARS studies: clear benefit mask use in health care

How to Avoid All Respiratory Diseases;

Surgeon General of the Army Gives Rules

Washington, Sept 21 – The Surgeon General of the army today issues the following rules to the public to safeguard against the spread of respiratory diseases:

Avoid needless crowding –
influenza is a crowd disease

Smother your coughs and sneezes –
others do not want the germs which you throw away

Your fate may be in your own hands – wash your hands before eating

Remember the three C's –
a clean mouth, clean skin, and clean clothes

Open the windows – always at home at night; at the office when practicable

When the air is pure breathe all of it you can – breathe deeply

Food will win the war if you give it a chance – help by choosing and chewing your food well

Avoid tight clothes, tight shoes, light gloves - seek to make nature your ally not your prisoner

Don't let the waste products of digestion accumulate – drink a glass or two of water on getting up

Assumptions and Guiding Principles

- Measures must be adapted to the epidemiologic context:
  - Opportunities for averting a pandemic or substantially slowing its spread will end once sustained person-to-person transmission has been established
  - As levels of morbidity and mortality increase, measure that made sense early will cease to be effective or feasible

Assumptions (con't)

- Because of the predictable need to change the recommended mix of interventions over time, communications to public, policy makers and health care staff must be well planned
- Legal authority and procedures for introducing unusual public health measures (ie. school closures,) must be established and understood by key personnel before pandemic begins

Implications for Planning:

- Decisions will need to be made in atmosphere of scientific uncertainty; basis for interventions need to be carefully explained to the public and to professionals
- Broad range of agencies/institutions need to be involved in planning and decision-making regarding interventions having potentially broad impact outside of health sector
- Non-medical measures will be principal control measures until adequate supplies of vaccine available
- Necessary legal authority for implementation of potentially extraordinary measures under emergency conditions must be in place before hand

The Influenza Pandemic Of 1918

- As noted in the journal of the AMERICAN medical association final edition of 1918:
  - "The 1918 has gone: a year momentous as the termination of the most cruel war in the annals of the human race; A year which marked, the end at least for a time, of man's destruction of man; Unfortunately a year in which developed a most fatal infectious disease causing the death of hundreds of thousands of human beings. Medical science for four and one-half years devoted itself to putting men on the firing line and keeping them there. Now it must turn with its whole might to combating the greatest enemy of all—infectious disease," JAMA: December 28, 1918

Anthrax and Influenza

"That we have chosen to worry more about anthrax than about the flu is hardly surprising. The novel is always scarier than the familiar, and the flu virus, as far as we know, isn't being sent through the mails by terrorists. But it is a strange kind of public-health policy that concerns itself more with the (origins) of illness than with its consequences; and the consequences of the flu, year in, year out, dwarf everything but the most alarmist bioterror scenarios."

Malcolm Gladwell
The New Yorker
October 29, 2001, pp 33-4

It is no use saying, "We are doing our best. You have got to succeed in what is necessary"
Winston Churchill

- If Public officials fail to do what is necessary to develop an effective planning process and a highly virulent pandemic virus emerges within the next few years, the consequences of that failure will be all too evident, and they will haunt us for years to come.