Bird Flu Arrives to US Trailer Park in Florida October 2011
Interaction of Host, Organism, & Environment

HOST

- Immunity
- Antimicrobials
- Mode of Transmission
- Vector control
- Isolation

ORGANISM

- Virulence Factors
- Contamination
- Sanitation, Sterilization
- (Strain)

ENVIRONMENT

- (Reservoir)
Chapter XII  

Influenza  
synonym: la grippe

- Influenza is an infectious, communicable disease, which is now generally admitted to be due to the bacillus described by Pfeiffer in 1892.

- Treatment.....The fumigation of apartments after attacks should be regularly practiced, preferably with formalin gas; this with isolation will do much to control house epidemics...The cough which persists after influenza is best controlled by cod-liver oil and creosote, used as after acute bronchitis.
Influenza Virus

- **15th Century Italians**
  - “to influence”; illness influenced by the stars and planets

- **Family Orthomyxoviridae**
  - “myxo” mucus
  - Segmented, single-stranded RNA

- **Influenza A** first isolated 1933; **Influenza B** 1940

- **15 hemagglutinin (HA) and 9 neuraminidase (NA) subtypes**
  - Only H1N1, H2N2, H3N2 subtypes associated with widespread epidemics in humans
Clinically Relevant Influenza Viruses

- **Type A**
  - Potentially severe illness
  - Epidemics and pandemics
  - Rapidly changing
  - Birds, swine, horses, seals, humans

- **Type B**
  - Usually less severe illness
  - Epidemics
  - More uniform
  - Humans

- **Type C**
  - Usually mild or asymptomatic illness
  - Minimal public health impact
  - Humans, swine

Naming Influenza Viruses

- **Type**
- **Origin**
- **Strain**
- **Sequence No.**
- **Yr Isolated**
- **Neuraminidase**
- **Hemagglutinin**

**Examples:**
- **A/Sydney/5/93(H1N1)**
- **B/Beijing/184/93**
Influenza: A Continuously Changing Virus

Polymerase Proteins (PP)
Hemagglutinin (HA) *cell entry
Neuraminidase (NA) *cell escape
M1, M2
Nucleoprotein (NP)

Pathology of Influenza Infection

A. Binding to Sialic Acid

B. Entering Cell

C. Replication

D. Release From Cell
Antigenic Drift (A & B)

RNA

Hemagglutinin

Neuraminidase

Antibodies

Sialic acid
Antigenic Shift (A only)
Transmission of Influenza

- Person to person
- Droplet spread-
  - small particle aerosols
- Fomite contamination
  - Steel and plastic 24-48 hrs
  - Cloth, paper, tissues 8-12 hrs
  - Hands 5 min (high viral titer)

- Principal site of replication - columnar epithelium
- Incubation period - 18 hrs to 5 or more days (avg 2-3 days)
- Virus shedding 3-7 days
- Viral titers are generally higher in young children with shedding lasting 10 days or longer
Influenza Terms

**Seasonal flu**
- respiratory illness transmitted person to person
- most people with some immunity, vaccine available

**Avian (bird) flu (AI)**
- influenza viruses occurring naturally among wild birds
- low pathogenic AI (LPAI)
- H5N1 = highly pathogenic (HPAI)

**Pandemic flu**
- human flu causing a global outbreak of serious illness
- little natural immunity so spread easily from person to person
Epidemiology of Influenza

- Epidemics of influenza back to 12th century
  - Russian catarrh
  - Chinese flu
  - Scottish rant

- Influenza is restricted to the winter seasons in the northern (Sept/Oct) and southern hemispheres (Mar/Apr)

- Occurs year round in South-east Asia
  - Lifestyle of farmers- frequent contacts between man, pigs, and aquatic birds
Children are a “Vector”

- Influenza uniquely allows children to spread its virus
  - children less sick than adults
  - Higher viral titer
  - longer viral excretion

- School-age children have the highest attack rates of influenza
  - disease rates peak first in children during an outbreak

- Schools facilitate the infection
  - 1918 and 1957 first cases appeared in the spring but real outbreaks began in fall after school began
  - 1968 pandemic mild- “interrupted” by school holiday break
## Recognizing Pediatric Influenza

<table>
<thead>
<tr>
<th>Neonates</th>
<th>Infants/ Toddlers</th>
<th>Children/ Teens</th>
</tr>
</thead>
<tbody>
<tr>
<td>High fever</td>
<td>GI symptoms</td>
<td>Rapid onset</td>
</tr>
<tr>
<td>Lethargy</td>
<td>Fever &gt;103°F (&gt;39.5°C)</td>
<td>High fever</td>
</tr>
<tr>
<td>Decreased eating</td>
<td>Anorexia</td>
<td>Cough</td>
</tr>
<tr>
<td>Mottling</td>
<td>Respiratory syndromes</td>
<td>Chills</td>
</tr>
<tr>
<td>Apnea</td>
<td>Malaise</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sore throat</td>
<td></td>
</tr>
</tbody>
</table>

Influenza Virus Infection Complications

Common Complications
- Acute otitis media (children)
- Sinusitis
- Pneumonia
- Exacerbation of underlying illness
- Dehydration (infants)

Uncommon Complications
- Encephalopathy
- Reye syndrome (children)
- Myositis
- Myocarditis
- Febrile seizures
Influenza Disease Burden in the US in an Average Year

- Infections and illnesses: 50-60 million
- Physician visits: ~25 million
- Hospitalizations: 117,000 – 816,000
- Deaths*: 25,000-72,000

*All-cause hospitalization and mortality associated with influenza virus infection

### Estimated Rates of Influenza-Associated Hospitalization (per 100,000 people)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age Group</th>
<th>High Risk</th>
<th>Not High Risk</th>
<th>All</th>
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</thead>
<tbody>
<tr>
<td>Neuzil KM NEJ M 2000; 342:225.</td>
<td>0-11 mths</td>
<td>1,900</td>
<td>496-1,038*</td>
<td></td>
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<tr>
<td>Neuzil KM J Peds 2000; 137:856.</td>
<td>1-2 yrs</td>
<td>800</td>
<td>186</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3-4 yrs</td>
<td>320</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-14 yrs</td>
<td>92</td>
<td>41</td>
<td></td>
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<tr>
<td>Izurieta HS NEJ M 2000; 342:232.</td>
<td>0-23 mths</td>
<td></td>
<td>144-187</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2-4 yrs</td>
<td></td>
<td>0-25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-17 yrs</td>
<td></td>
<td>8-12</td>
<td></td>
</tr>
<tr>
<td>Barker WH Am J Epi 1980; 112:789.</td>
<td>45-64 yrs</td>
<td>392-635</td>
<td>13-23</td>
<td>399-518</td>
</tr>
<tr>
<td></td>
<td>≥ 65 yrs</td>
<td>399-518</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simonsen L J Infect Dis 2000; 181:831.</td>
<td>≥ 65 yrs</td>
<td>125-228</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 0-5 mths=1,038 and 6-11 mths=496
Pneumonia and Influenza Mortality Rates by Age

MAKE WAY FOR DA FLU BUG!!
Pneumonia and Influenza Mortality for 122 U.S. Cities
Week Ending 03/6/04

Weeks

% of All Deaths Due to P&I

Epidemic Threshold
Seasonal Baseline
Impact of Influenza 2003-4 Colorado

- 12 Pediatric deaths
  - 6 previously healthy
  - 5 < 23 months old
  - 5 with history of influenza vaccination this season
  - 5/7 cases with autopsy specimens confirmed by immunohistochemical staining at CDC

Colorado’s fever has broken

The especially nasty flu outbreak that struck Colorado is believed to have caused the deaths of 11 children. Altogether, 11,785 Coloradans have been hit with the flu this season. And those are just the confirmed cases reported to the state. Health officials suspect thousands more have been sick during the worst flu season in recent years.
'Kids have been hit hard and hit early. Adults will be coming along soon.'

Chris Nyquist, medical director for infection control, Children's Hospital

Shots urged as flu surges

Nearly 4,000 cases in state; clinics swamped

By David Olinger and Diedtra Henderson
Denver Post Staff Writers

With four children dead and nearly 4,000 flu cases confirmed, Colorado's chief medical officer is recommending vaccinations for everyone in the state.

"If you want to avoid getting the flu, a flu shot is the best defense," Dr. Ned Calonge said.

Colorado health officials warned that the outbreak now concentrated in young people will soon spread to adults.

While Colorado, Texas and New Mexico have had the most cases, officials say flu is spreading to other parts of the country.
Flu hits 30-year high

More than 400 cases reported in Jeffco this year

Flu hitting state early, often

Cases confirmed since Nov. outnumber combined total of '01 '02

Doubling of flu deaths predicted

FLU FROM PAGE 1A

over 60. The virulent strain of flu that's

identifying to get a vaccine with the Fujian

strain into production," Fisher said.

Eckhoff disagreed, saying enough

was done even though the FDA com-

mittee wasn't happy about the deci-

sion to approve the vaccine. "They

should have told the public some-

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something. No one is served by mak-
3 more Colo. kids die from flu

Cases already surpass total for all of last year

By Karen Auga
Denver Post Medical Writer

Three more children have died from complications of the flu in Colorado, bringing the state's death toll to at least four in a season that has hit early and hard.

Josephine Williams, 4, of Wellington, died Monday. On Tuesday, Children's Hospital reported the death of a 1-year-old and a 2-month-old. A 15-year-old girl died at Children's last week.

The 15-year-old and the 3-year-old had medical conditions that made them especially vulnerable to the disease. According to health officials, Josephine and the other child had been healthy.

Pueblo County health officials reported nearly 3,000 flu cases in Colorado. The total for all of last year's flu season was 5,497.

Colorado had 11 flu-related and two pneumonia-related deaths last year among people of all ages, according to health officials. Pneumonia is a recurrent complication of the flu.

The state's chief medical officer said this flu season is earlier and worse than usual.

"Young physicians in emergency departments are saying they never saw a flu season this bad. Others are saying they have not seen it this bad in 20 years," said Dr. Neil Colgrove of the state health department.

Adding to the problem is the fact that this year's vaccine does not protect against the so-called Fujian strain from Australia, which is causing some of the most severe illness elsewhere and is believed to be in Colorado.

Colgrove said he did not know whether the children who died had been vaccinated.

Diego Huckabay leans against his mother, Janelle Portillis, Friday, as she holds a photo of Diego's twin, Desmond, who died from influenza on Wednesday. Diego is recovering from the flu.
Influenza Mortality in Children 2003-2004: Healthy Children Also Affected

152 children <18-years-old reportedly died of influenza-related causes
36 were vaccinated (≥1 dose)

<table>
<thead>
<tr>
<th>By age</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 months-old</td>
<td>11%</td>
</tr>
<tr>
<td>6-23 months-old</td>
<td>30%</td>
</tr>
<tr>
<td>2-5 years-old</td>
<td>22%</td>
</tr>
<tr>
<td>≥5 years-old</td>
<td>37%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>By medical condition</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ACIP high-risk condition</td>
<td>27%</td>
</tr>
<tr>
<td>Other underlying medical condition</td>
<td>31%</td>
</tr>
<tr>
<td>Previously healthy</td>
<td>40%</td>
</tr>
<tr>
<td>Unknown</td>
<td>2%</td>
</tr>
</tbody>
</table>
Stunning predictions of...

EDGAR CAYCE AND DEAD SEA SCROLLS

THOUSANDS WILL DIE IN NEW FLU EPIDEMIC - HOW YOU CAN SURVIVE!

Sun's Good Doctor and Mayo Clinic:

December 30, 2003
FLU PANDEMIC
A Once and Future Menace
BY ROBIN MARANTZ HENIG
“When the plague came, on those chilly days of autumn, some said it was a terrible new weapon of war. The plague germs were inserted into aspirin made by the German drug company Bayer. Take an aspirin for a headache and the germs will creep through your body. Then your fate is sealed.”
“Spanish Flu” “la Grippe” 1918-19

• Attack rate: 20-30% in adults, 30-45% in children
• Case-fatality rate 2.5% (prior epidemics 0.1%)

• More people died of influenza in a single year than in four years of the Black Death Bubonic Plague from 1347 to 1351
• An estimated 675,000 Americans died of influenza during the pandemic
  - Killed over 10,000 people per week in US at the height of the pandemic
• The average life span in the US was depressed by 10 years

Close genetic relationship between 1918 virus and A/Swine/Iowa/30 (H1N1)
Phylogenetic analysis- mammalian-like, avian like
Committee of American Public Health Association

- Disease extremely communicable
- Advocated legislation that would prevent the use of common cups and utensils and ban public coughing and sneezing
- Good handwashing
- Nervous and physical exhaustion should be avoided
- Encouraged exposure to fresh air
- Gargling with elixirs (chlorinated soda, mixture of sodium bicarb and boric acid)
I had a little bird,
Its name was Enza.
I opened the window,
And in-flu-enza.
Obey the laws
And wear the gauze
Protect your jaws
From Septic Paws.
United States 1918

• First wave appeared in Spring of 1918 in Kansas and military camps throughout US

• September 1918 second more deadly wave of the epidemic

• Early 1919 President Woodrow Wilson suffered from the flu while negotiating the Treaty of Versailles to end World War I
Figure 5. Deaths from pneumonia and influenza in the U.S.A. by age during the pandemic years 1892 (Massachusetts only), 1918, and 1957. Adapted from Dauer and Serfling.\textsuperscript{29} (---)1892; (—) 1918; (.....) 1957.
Lessons from 1918 Pandemic
• Killed over 10,000 people per week in US at the height of the pandemic
• Mortality very high in developing countries
  ▪ 10 million deaths in India
• Close genetic relationship between 1918 virus and A/Swine/Iowa/30 (H1N1)
  ▪ Phylogenetic analysis- mammalian-like, avian like
NOTICE

Effective, Wednesday, December 11, 1968, to safeguard our patients during the present flu epidemic, this hospital has restricted all visitors until further notice.
Timeline of Emergence of Influenza Viruses in Humans


H1 B H2 H3 H1 H1 H9 → H7 H5 → H5 Avian Influenza

Seasonal vaccines Pandemic vaccines

Spanish Influenza Russian Influenza Hong Kong Influenza
Deaths Associated with Influenza
## 20th Century Influenza Pandemics

<table>
<thead>
<tr>
<th>Year</th>
<th>Name</th>
<th>Strain</th>
<th>Worldwide Deaths</th>
<th>US Deaths</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918 - 1919</td>
<td>Spanish flu</td>
<td>H1N1</td>
<td>25-50 million</td>
<td>&gt;500,000</td>
<td>Human-adapted avian virus</td>
</tr>
<tr>
<td>1957</td>
<td>Asian flu</td>
<td>H2N2</td>
<td>&gt; 1 million</td>
<td>70,000</td>
<td>Reassortment with avian virus</td>
</tr>
<tr>
<td>1968</td>
<td>Hong Kong flu</td>
<td>H3N2</td>
<td>&gt; 1 million</td>
<td>34,000</td>
<td>Reassortment with avian virus</td>
</tr>
<tr>
<td>1977</td>
<td>Russian flu</td>
<td>H1N1</td>
<td>low</td>
<td>low</td>
<td>1950’s H1N1 (frozen stock?)</td>
</tr>
</tbody>
</table>

All spread around the world within 1 year of being detected
The turkeys have bird flu. The cows have mad cow disease. I'm telling you, boys... unless we want to see more ham served on Thanksgiving, we're going to have to get our own disease!
REACTION: 50 cases confirmed in U.S., some as close as Kansas

From 1A

On Monday, there were no confirmed cases of swine flu in Colorado, though a few suspected cases were pending lab results, according to the state health department. The sickness is suspected of killing 149 in Mexico, and 50 cases have been confirmed in the U.S., including in nearby Kansas and Texas.

"It's literally a plane flight away," said Chief Medical Officer Ned Conlon of the Colorado Department of Public Health and Environment. "It's hard for me to predict which flight that will be."

Getting ready for a storm

Colorado health officials urged people not to panic but at the same time said they are bracing for a hurricane, so to speak.

"We're putting the plywood on the windows, and we are getting ready for the storm, because once the storm"
Flu kills 4 children in 5 weeks
For kids in Colorado, worst season in 5 years

By Jennifer Brown The Denver Post

Four children have died of the flu in Colorado since mid-January, alarming health officials who said that at least some of the deaths could have been prevented if the children were vaccinated.
World braces for flu siege
Flu cuts China’s pork buys

By Whitney McFerron Bloomberg News

One in every five people in China still believe pork puts a consumer at risk for swine flu. U.S. pork exports to China and Hong Kong have plunged 73 percent.

Agence France-Presse file photo

consumers may still associate the virus with pork and hogs,” Joel Haggard, the federal fun director, the Miami Herald
Feliz Cinco de Mayo
Novel H1N1 aka “Swine Flu”

• H1N1 declared pandemic by WHO 06/11/09
• Current H1N1 involves a new strain that appears to be a result of reassortment of human influenza, avian and swine influenza viruses

Theories About the Emergence of Pandemic Viruses

1. Genetic reassortment occurring in man or between human and animal viruses
2. Direct transfer of viruses between animals and humans
3. Re-emergence of viruses from unrecognized or unsuspected reservoirs
Definition of a Pandemic

Global outbreak occurring when:

(1) A new influenza A virus appears/emerges in the global immunologically naïve human population
   - New subtype
   - Subtype that has never circulated among humans
   - Or has not circulated for a long time

(2) Infection results in serious illness and high mortality

AND

*** (3) Effective person-to-person transmission
Occurrence of Influenza Pandemics and Epidemics

Introduction of hypothetical A HxNx virus

Disease Incidence

- Incidence of clinically manifest influenza
- Mean level of population antibody vs A HxNx
- Mean level of population antibody vs A HyNy

Mean Population Antibody Level

Interpandemic Period

1. Introduction of hypothetical A HxNx virus
2. Introduction of hypothetical A HyNy major (new subtype) variant A HxNx disappears
## Predicted impact of Influenza Pandemic in US

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Moderate (1958/68-like)</th>
<th>Severe (1918-like)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness</td>
<td>90 million (30%)</td>
<td>90 million (30%)</td>
</tr>
<tr>
<td>Outpatient medical care</td>
<td>45 million (50%)</td>
<td>45 million (50%)</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>865,000</td>
<td>9,900,000</td>
</tr>
<tr>
<td>ICU care</td>
<td>128,750</td>
<td>1,485,000</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>64,875</td>
<td>745,500</td>
</tr>
<tr>
<td>Deaths</td>
<td>209,000</td>
<td>1,903,000</td>
</tr>
</tbody>
</table>

**Perspective:** Seasonal influenza 36,000 deaths annually
CDC Influenza Surveillance Components

• WHO Collaborating Laboratories
  ▪ 70 in United States

• State and Territorial Epidemiologists
  ▪ No activity, Sporadic, Regional, Widespread

• Sentinel Physician Surveillance Network
  ▪ 250 volunteer FPs

• Pneumonia and Influenza Deaths from 122 Cities
Influenza Type A (H5N1)

- Fatal epidemic among Hong Kong poultry in 1997
- Two months later appeared in humans in Hong Kong, 1997
- Primarily associated with avian species
- 18 total confirmed cases, with 6 deaths
  - Each human case caused by independent transmission from birds in poultry markets

Avian Influenza = “Bird Flu”

- **Extensive reservoir**
- **Worldwide distribution**

Low Pathogenicity Avian Influenza (LPAI)
- Milder form of influenza
- Definition = Death in 0-5/8 inoculated chickens
- Coughing, sneezing, rales, lacrimation, sinusitis, depression, decreased egg production and quality
- H5, H7, H9, H10

Highly Pathogenic Avian Influenza (HPAI)
“Fowl Plague”, “Fowl Ebola”
- Severe form of influenza
- 1st documented in Italy 1878
- Definition = Death in ≥ 6/8 inoculated chickens
- Onset sudden, course short, mortality near 100%
- Respiratory, enteric, or nervous system signs
- All Avian HPAI outbreaks have been H5 or H7
Avian Influenza: Sick Chickens

Blue Comb

Vesicles on comb

Swollen Wattle

Congestion and Blood Spots on Hocks and Shanks
Transporting chickens to market in Vietnam

Live poultry market in Cambodia
Examining Sick Thai Chickens

Decontamination and Culling in Thailand

Ban on Thai Chicken in Japan

Decontamination and Culling in Thailand
Prevention and Control Measures
Why H5N1 is of Particular Concern

- Rapidly reassorts and mutates (2004 strain different from 1997)
- Acquires genes from viruses infecting other animal species
- Severe disease in humans (50% case fatality rate)
- Surviving birds excrete virus for >10 days (oral and fecal) facilitating spread in poultry markets and migratory birds
- Spread of infection in birds increases opportunity for direct infection of humans
- Person-to-person spread documented in 1997, 2003 outbreaks (but only in limited number of cases)
- Further adaptation to humans: The start of a pandemic
Genesis of a Pandemic Avian Influenza Strain

1. Genetic reassortment
   - Human directly co-infected with human and avian strains (e.g. poultry workers)
     - Reassortment leading to human-adapted virus with newly acquired avian-derived HA
   OR
   - Pig co-infected with human and avian strains
     - Reassortment in pig (intermediate)
     - Subsequent passage to human

2. Mutation of Avian Influenza genome
   - Change in host receptor binding specificity
   - Improved viral replication efficiency
Phases of a Pandemic

- **Interpandemic period**
  - Phase 1: No new flu virus subtypes in humans
  - Phase 2: Circulating animal subtype poses substantial risk to humans

- **Pandemic alert period**
  - Phase 3: Human infection with new subtype, but no human to human spread or rare spread to close contacts
  - Phase 4: Small clusters with limited human to human transmission but spread highly localized
  - Phase 5: Larger cluster of localized human to human spread
    - increasingly better adapted to humans but not yet easily transmissible
  - Pandemic Period
    Phase 6: Increased sustained transmission in general population
The first time one of them sneezes, cut the rope....
Methods of Influenza Prevention

- CDC-recommended infection control practices
  - Standard precautions, especially hand hygiene
  - Droplet precautions
  - Add contact precautions for infants
  - Respiratory hygiene/cough etiquette
- Vaccines
  - Trivalent Influenza Vaccine (TIV)
  - Live-attenuated Influenza Vaccine (LAIV)
- Chemoprophylaxis for those at high risk who have not received an influenza vaccine or in conjunction with late receipt of TIV

To Vaccinate or Not To Vaccinate?

"C'mon, c'mon—it's either one or the other."
Influenza Vaccines Approved in the United States

- **Trivalent Inactivated Vaccine (TIV)**
  - Delivered by intramuscular injection
  - Available for ages > 6 mths

- **Live-attenuated Influenza Vaccine (LAIV)**
  - Delivered by intranasal administration
  - Healthy people age 2-49 yrs
Influenza Vaccine (TIV) Manufacturing Schedule

- 1 year before production- order chickens
- 3 mths before production- hens moved into laying houses
- Early spring- inoculate eggs
- Strain selection
  - First strain- late Jan
  - Second strain- Mar
  - Third strain- early April
- Purification is by centrifugation
- Neutralized by chemical
- Inactive vaccine preparation only
- Production cycle = 70 weeks
Reassortants for each of 3 vaccine strains derived by coinfection
At least 5 point mutations for both A and B master donor viruses

Master donor virus

New wild-type strain

Coinfect cells

6 genes from MDV confer attenuation

HA and NA genes from wild-type confer immunity

### Comparing TIV and LAIV-T

<table>
<thead>
<tr>
<th>Category</th>
<th>TIV</th>
<th>LAIV-T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration</td>
<td>Intramuscular</td>
<td>Intranasal</td>
</tr>
<tr>
<td>Immune response</td>
<td>Serum antibodies</td>
<td>Serum antibodies, Mucosal immunity, ? Cellular immunity</td>
</tr>
<tr>
<td>Efficacy children</td>
<td>~30-70%</td>
<td>70-90%</td>
</tr>
<tr>
<td>Efficacy adults &lt;65 y</td>
<td>70-90%</td>
<td>70-90%</td>
</tr>
<tr>
<td>Virus</td>
<td>Split-virus or subunit inactivated virus</td>
<td>Cold-adapted, temperature-sensitive, live attenuated virus</td>
</tr>
<tr>
<td>Growth medium</td>
<td>Chick embryos</td>
<td>Chick embryos</td>
</tr>
<tr>
<td>Indication</td>
<td>Any person ≥ 6 mo</td>
<td>Healthy persons ≥ 5-49 yrs</td>
</tr>
</tbody>
</table>
“Don’t think of it as getting a flu shot. Think of it as installing virus protection software.”
Influenza Antivirals

- **Adamantanes**
  - Amantidine & rimantidine
  - M2 ion channel inhibitors
  - Effective against type A viruses only (Rx & prophylaxis)

- **Neuraminidase inhibitors**
  - Oseltamivir (Tamiflu) & zanamivir (Relenza)
  - Effective against type A & B viruses (Rx & prophylaxis)

- **Issues**
  - Resistance among seasonal influenza viruses
  - Resistance among some H5N1 viruses
  - None approved for Rx or prophylaxis for children < 1yr
  - Unproven effectiveness for Rx of H5N1 infection
Pandemic Flu Response Planning

- Surveillance
- Laboratory testing
- Healthcare planning
- Infection control
- Clinical guidelines
- Vaccine distribution and use
- Antiviral drug distribution and use
- Community disease control & prevention
- Communications
- Psychosocial workforce support services
Patient presenting to ED outpatient clinic

Patients presenting with symptoms **consistent with Influenza**

1. Place immediately in and rigorously enforce DROPLET PRECAUTIONS
2. Give information sheet that recommends notification of high-risk contacts

Patient requiring hospitalization

Rapid Flu IA* with backup PCR

Treat presumptively (even if symptoms >48 hrs) until both tests are influenza negative. Use Oseltamivir or Zanamivir while prevalence of seasonal influenza is low. (See tables)

Patient NOT requiring hospitalization

High-Risk Childα

Respiratory Flu IA* with backup PCR

Low-Risk Child

No Test Recommended

No treatment recommended
Pandemic Planning: Unique Challenges

- Pandemics last longer than other emergency events
- Waves of activity
  - Historically, 2\textsuperscript{nd} wave 3-12 months after first
- Numbers of health care workers/first responders reduced
- Resources limited simultaneously in many locations
Pandemic Response Challenges

- Healthcare system capacity - overwhelmed
- Antiviral supplies - insufficient
- Vaccine - none for at least 5 months
- Critical infrastructure - disruption
- Economy - disruption
## Predicted impact of Influenza Pandemic in US

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Moderate (1958/68-like)</th>
<th>Severe (1918-like)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness</td>
<td>90 million (30%)</td>
<td>90 million (30%)</td>
</tr>
<tr>
<td>Outpatient medical care</td>
<td>45 million (50%)</td>
<td>45 million (50%)</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>865,000</td>
<td>9,900,000</td>
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<tr>
<td>ICU care</td>
<td>128,750</td>
<td>1,485,000</td>
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<tr>
<td>Mechanical ventilation</td>
<td>64,875</td>
<td>745,500</td>
</tr>
<tr>
<td>Deaths</td>
<td>209,000</td>
<td>1,903,000</td>
</tr>
</tbody>
</table>

*Perspective: Seasonal influenza 36,000 deaths annually*
Collective Leadership

- Government
  - Maintain public trust through honest and direct communication and by taking definitive action

- Business
  - “if you don’t take care of yourself, you can’t take care of others”
  - Well-thought-out contingency plans to ensure access to health care, food, and supplies for employees and their families
  - Mass telecommuting → extra traffic could render internet unusable within 2-4 days of an outbreak

- Government + business
  - Identify essential industries and services
    - Defense, public safety, media, food, transportation and logistics, communications, all enterprises in the medical/pharmaceutical chain

- NGOs
  - Export information from affected regions to the rest of the global community

Penfield S, Larkin J. Strategy+business issue 43
Collective Leadership (2)

- Media and Communications Organizations
  - Communicate critical information, accurately and honestly, to the general public and employees

- Individuals and localities

  “No single institution has the capacity to do [everything needed].”

  Dr. Pierre Formenty, WHO to the New York Times

  “All industries need to think of themselves as part of a larger system; each organization must play its role while supporting the others as well.”