Respiratory Threats in the Tropics

WRAIR- GEIS 'Operational Clinical Infectious Disease' Course
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Disclaimer

The views expressed in this presentation are those of the speaker and do not reflect the official policy of the Department of Army, Department of Defense, or U.S. Government.
Outline

• Influenza
  – Introduction
  – ‘Seasonal’ influenza in the tropics
  – Pandemic Influenza
  – Avian Influenza
• Other Respiratory Threats
• Respiratory viruses with high mortality
• Summary
Influenza

I had a little bird,
And its name was Enza.
I opened the window
And in-flew-enza.*

*Children’s skipping rhyme during the 1918 Spanish Influenza pandemic.

www.cdc.gov
Influenza Virus

- Family: Orthomyxoviridae

- First isolated 1933

- 8 single stranded, negative sense RNA molecules

- Encodes for 10 proteins
  - Nucleoprotein (NP), Matrix (M) protein
  - Important surface glycoproteins
    - Hemagglutinin (HA)
    - Neuraminidase (NA)

Figure 1 | Schematic diagram of an influenza A virus virion. Two surface glycoproteins, haemagglutinin (HA) and neuraminidase (NA), and the M2 ion-channel protein are embedded in the viral envelope, which is derived from the host plasma membrane. The ribonucleoprotein complex comprises a viral RNA segment associated with the nucleoprotein (NP) and three polymerase proteins (PA, PB1 and PB2). The matrix (M1) protein is associated with both ribonucleoprotein and the viral envelope. A small amount of non-structural protein 2 is also present, but its location within the virion is unknown.
HA and NA

• Hemagglutinin initiates infection by binding to sialic acid residue on respiratory epithelial cells

• Neuraminidase liberates new virions after viral replication and help virions stay separated
Antigenic Drift

• Occurs in Influenza A and B

• Point mutations in the viral RNA genes

• Leads to production of new hemagglutinin or neuraminidase

• **Annual occurrence** to avoid host immune system

• Less severe ‘seasonal’ epidemics

• Occurs as virus spreads through a susceptible population
Each year’s flu vaccine contains three flu strains – two A strains and one B strain – that can change from year to year.

After vaccination, your body produces infection-fighting antibodies against the three flu strains in the vaccine.

If you are exposed to any of the three flu strains during the flu season, the antibodies will latch onto the virus’s HA antigens, preventing the flu virus from attaching to healthy cells and infecting them.

Influenza virus genes, made of RNA, are more prone to mutations than genes made of DNA.

If the HA gene changes, so can the antigen that it encodes, causing it to change shape.

If the HA antigen changes shape, antibodies that normally would match up to it no longer can, allowing the newly mutated virus to infect the body’s cells.

This type of genetic mutation is called “ANTIGENIC DRIFT.”

Case

• You are deployed to the Philippines. You see a 24 yo male pig farmer with no medical history, previously in excellent health. The patient appears very ill, complaining of fevers, diffuse myalgias, cough, and shortness of breath. The patient requires intubation, but dies a week later. You hear of several other locals with similar symptoms, some young adults with severe disease.

• Pulmonary aspirates sent on your patient return from the lab in AFRIMS (Bangkok). Samples sent on 3 different days were negative on 2 of the days, and positive for Influenza A on a single sample. Confirmatory testing has not been able to determine the viral subtype.

• WTF?! (i.e. What the Flu?)
Antigenic Shift

• Major changes in HA and NA

• Influenza A viruses only

• Reassortment of viral genetic material between viruses co-infecting the same cell

• **Pandemic strains** result from exchange of genetic material between animal and human viruses

• No protective immunity in host

• Usually more rapidly spreading and severe infection

VIDEO OF INTEREST (1918 Spanish Flu):
http://www.youtube.com/watch?v=48Klc3DPdtk
• All HA and NA in birds
• Crossing of species is limited
  - Humans
    • H1, H2, H3
    • N1, N2
  - Horses
    • H7, N7
    • H3, N8
  - Pigs
    • H1, H3
    • N1, N2
Influenza Typing

• Classified based on antigenic differences in NP and M

• Influenza A viruses have various types of HA and NA

• Influenza B viruses **DO NOT** have shifts and major changes in HA and NA

• Example Nomenclature

  Type /Host / Place / Strain #/Year (Influenza subtype)

  A / Duck / Vietnam/ 11 / 04 (H5N1)
Influenza in the Tropics

• Less distinct ‘seasonal’ pattern vs. temperate regions

• **Year round infections**

• ‘Seasonal’ patterns vary by location
  – Peaks related to rainy seasons
  – Biannual peaks (rainy season and winter months)
  – Year round infection without clear peaks
Environmental Predictors of Seasonal Influenza Epidemics across Temperate and Tropical Climates

• Study conducted at 78 study sites globally

• Influenza infections peaked during low specific humidity and temperatures in areas where these values fell below threshold

• In areas with constant high humidity and temperature, influenza infections peaked in month of high precipitation


Editor: Steven Riley, Imperial College London, United Kingdom

Received August 28, 2012; Accepted December 26, 2012; Published March 7, 2013
Influenza in the tropics

Cold-Dry Peaks  
Humid-Rainy Peaks
Rainy season = influenza peak

Tamerius et al.  
*Environ Health Perspect* 2011
Multiple Factors Impact Influenza Epidemics

Figure 2. Putative relationship and causal connections among key seasonal stimuli, mediating mechanisms, and influenza epidemics. The notation adjacent to each seasonal stimulus indicates whether it potentially explains influenza seasonality in the tropics (Tr), temperate regions (T), or both (T/Tr). The diagram also includes a component depicting the effects of intrinsic dynamics.

Tamerius et al. Environ Health Perspect 2011
Seasonal Influenza Vaccine

- Surveillance at 130 influenza centers in 101 countries
- WHO centers (Atlanta, London, Melbourne, Tokyo, Beijing)
- Meetings and decision for inclusion:
  - September for Southern hemisphere’s vaccine
  - February for Northern hemisphere’s vaccine

- WHO recommended 2014-2015 vaccine:
  - A/California/7/2009 (H1N1) pdm09-like virus
  - A/Texas/50/2012 (H3N2)-like virus
  - B/Massachusetts/2/2012-like virus
  - B/Brisbane/60/2008-like virus

- Identify strain to be used, growing virus strain, quality control, production, sale, distribution, administration
  - TAKES TIME (at least 6 months) and MISMATCHES OCCUR
# Vaccine Efficacy

<table>
<thead>
<tr>
<th>Population (dates)</th>
<th>Patients randomly allocated to receive TIV and placebo</th>
<th>Vaccine efficacy (95% CI)</th>
<th>Reported antigenic match</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (18–64 years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ohmit et al (2006)(^4)</td>
<td>Healthy adults aged 18–46 years (2004–05)</td>
<td>728</td>
<td>75% (42 to 90)</td>
</tr>
<tr>
<td>Ohmit et al (2008)(^5)</td>
<td>Healthy adults aged 18–48 years (2005–06)</td>
<td>1205</td>
<td>16% (–171 to 70)</td>
</tr>
<tr>
<td>Beran et al (2009)(^6)</td>
<td>Healthy adults aged 18–64 years (2005–06)</td>
<td>6203</td>
<td>22% (–49 to 59)</td>
</tr>
<tr>
<td>Beran et al (2009)(^7)</td>
<td>Healthy adults aged 18–64 years (2006–07)</td>
<td>7652</td>
<td>62% (46 to 73)</td>
</tr>
<tr>
<td>Monto et al (2009)(^8)</td>
<td>Healthy adults aged 18–49 years (2007–08)</td>
<td>1139</td>
<td>68% (46 to 81)</td>
</tr>
<tr>
<td>Jackson et al (2010)(^9)</td>
<td>Healthy adults aged 18–49 years (2005–06)</td>
<td>3514</td>
<td>50% (14 to 71)</td>
</tr>
<tr>
<td>Jackson et al (2010)(^10)</td>
<td>Healthy adults aged 18–49 years (2006–07)</td>
<td>4144</td>
<td>50% (–3 to 75)</td>
</tr>
<tr>
<td>Frey et al (2010)(^11)</td>
<td>Healthy adults aged 18–49 years (2007–08)</td>
<td>7576</td>
<td>63% (one-sided 97.5% lower limit of 47%)</td>
</tr>
<tr>
<td>Madhi et al (2011)(^12)</td>
<td>Adults aged 18–55 years with HIV infection (2008–09)</td>
<td>506</td>
<td>76% (9 to 96)</td>
</tr>
<tr>
<td>Children (6–24 months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hoberman et al (2003)(^13)</td>
<td>Healthy children aged 6–24 months (1999–2000)</td>
<td>411</td>
<td>66% (34 to 82)</td>
</tr>
<tr>
<td>Hoberman et al (2003)(^14)</td>
<td>Healthy children aged 6–24 months (2000–01)</td>
<td>375</td>
<td>–7% (–247 to 67)</td>
</tr>
</tbody>
</table>

No studies were available for adults aged 65 years or older or children aged 2–17 years. *One other study by Loeb and colleagues*\(^*\) met inclusion criteria and contained data for all age groups. \(^*\)Our calculation.

Table 2: Randomised controlled trials of trivalent inactivated vaccine (TIV) meeting inclusion criteria.

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**Trivalent Inactivated**

_Lancet Infect Dis_ 2012; 12:36-44
# Vaccine Efficacy

## Live Attenuated

<table>
<thead>
<tr>
<th>Population (dates)</th>
<th>Patients randomly allocated to receive LAIV and placebo</th>
<th>Vaccine efficacy (95% CI)</th>
<th>Reported antigenic match</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adults (≥60 years)</strong></td>
<td>Community-dwelling ambulatory adults aged ≥60 years (2001-02)</td>
<td>3242</td>
<td>Overall 42% (21 to 57); 31% (-3 to 53) for patients aged 60–69 years; 57% (29 to 75) for patients aged ≥70 years</td>
</tr>
<tr>
<td>De Villiers et al (2010) [7]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ohmit et al (2006) [8]</td>
<td>Healthy adults aged 18–46 years (2004-05)</td>
<td>725</td>
<td>48% (-7 to 74)</td>
</tr>
<tr>
<td>Ohmit et al (2008) [9]</td>
<td>Healthy adults aged 18–48 years (2005-06)</td>
<td>1191</td>
<td>8% (-194 to 67)</td>
</tr>
<tr>
<td>Monto et al (2009) [10]</td>
<td>Healthy adults aged 18–49 years (2007-08)</td>
<td>1138</td>
<td>36% (0 to 59)</td>
</tr>
<tr>
<td><strong>Children (6 months–7 years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Belshe et al (1998) [11]</td>
<td>Healthy children aged 15–71 months (1996–97)</td>
<td>1602</td>
<td>93% (88 to 96)</td>
</tr>
<tr>
<td>Belshe et al (2000) [12]</td>
<td>Healthy children aged 26–85 months (1997–98)</td>
<td>1358</td>
<td>87% (78 to 93)</td>
</tr>
<tr>
<td>Vesikari et al (2006) [13]</td>
<td>Healthy children aged 6–36 months attending day care (2000–01)</td>
<td>1784</td>
<td>84% (74 to 90)</td>
</tr>
<tr>
<td>Vesikari et al (2006) [13]</td>
<td>Healthy children aged 6–36 months attending day care (2001–02)</td>
<td>1119</td>
<td>85% (78 to 90)</td>
</tr>
<tr>
<td>Bracco Neto et al (2009) [14]</td>
<td>Healthy children aged 6–36 months (2000–01)</td>
<td>1886</td>
<td>72% (62 to 80)</td>
</tr>
<tr>
<td>Tam et al (2007) [15]</td>
<td>Healthy children aged 12–36 months (2000–00)</td>
<td>3174</td>
<td>68% (59 to 75)</td>
</tr>
<tr>
<td>Tam et al (2007) [15]</td>
<td>Healthy children aged 12–36 months (2001–02)</td>
<td>2947</td>
<td>57% (30 to 74)</td>
</tr>
<tr>
<td>Lum et al (2010) [16]</td>
<td>Healthy children aged 11–24 months (2002–03)</td>
<td>1233</td>
<td>64% (40 to 79)</td>
</tr>
</tbody>
</table>

No studies were available for adults aged 50–59 years or children aged 8–17 years. * Authors reported culture, RT-PCR, and RT-PCR/culture; we report RT-PCR/culture results.

**Table 3:** Randomised controlled trials of live attenuated influenza vaccine (LAIV) meeting inclusion criteria

*Lancet Infect Dis 2012; 12:36-44*  
*OCID course 2015*
<table>
<thead>
<tr>
<th>Influenza Season</th>
<th>Reference</th>
<th>Study Site(s)</th>
<th>No. of Patients</th>
<th>Adjusted Overall Vaccine Efficacy (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004-2005</td>
<td>Belongia 2009</td>
<td>WI</td>
<td>762</td>
<td>10</td>
<td>-36,40</td>
</tr>
<tr>
<td>2006-2007</td>
<td>Belongia 2009</td>
<td>WI</td>
<td>871</td>
<td>52</td>
<td>22,70</td>
</tr>
<tr>
<td>2007-2008</td>
<td>Belongia 2011</td>
<td>WI</td>
<td>1914</td>
<td>37</td>
<td>22,49</td>
</tr>
<tr>
<td>2009-2010</td>
<td>Griffin 2011</td>
<td>WI, MI, NY, TN</td>
<td>6757</td>
<td>56</td>
<td>23,75</td>
</tr>
<tr>
<td>2010-2011</td>
<td>Treanor 2011</td>
<td>WI, MI, NY, TN</td>
<td>4757</td>
<td>60</td>
<td>53,66</td>
</tr>
<tr>
<td>2011-2012</td>
<td>Ohmit 2014</td>
<td>WI, MI, PA, TX, WA</td>
<td>4771</td>
<td>47</td>
<td>36,56</td>
</tr>
<tr>
<td>2012-2013</td>
<td>McLean 2014</td>
<td>WI, MI, PA, TX, WA</td>
<td>6452</td>
<td>49</td>
<td>43,55</td>
</tr>
<tr>
<td>2013-2014</td>
<td>Unpublished</td>
<td>WI, MI, PA, TX, WA</td>
<td>5990</td>
<td>51</td>
<td>43,58</td>
</tr>
<tr>
<td>2014-2015</td>
<td>ACIP presentation, Flannery</td>
<td>WI, MI, PA, TX, WA</td>
<td>4913</td>
<td>19</td>
<td>7,29</td>
</tr>
</tbody>
</table>
Seasonal Influenza Vaccine

• 20 yo soldier is adamant that he does not want to get his flu vaccine because it “gave him the flu” last year the following day.

• Your response is….?
Seasonal Influenza Vaccine

• You can’t get the flu from the injection (it’s inactivated virus)

• Flumist is a live attenuated virus, but other than causing runny nose and mild congestion for a few days it can’t cause the flu in a healthy individual

• There are other viruses that cause the common cold that are circulating the same time of year

• It takes approximately 14 days to develop an immune response to the vaccine

• If there is a mismatch for that year (ahem...like this year), there is the possibility that you can develop influenza despite vaccination
Pandemic Influenza

- Influenza A virus introduction
  - Novel HA gene
  - No ‘herd’ immunity
  - Ability to spread efficiently among humans

- Pandemics of 20th century
  - All originated from avian influenza viruses
  - Intervals of 11-39 years
  - 1918 (H1N1: Spanish)
  - 1957 (H2N2: Asian)
  - 1968 (H3N2: Hong Kong)
  - 2009 (H1N1: US, Mexico)

- Pseudo- and Abortive pandemics
  - 1947 (H1N1: Japan/Korea/New Jersey)
  - 1976 (H1N1: New Jersey)
  - 1977 (H1N1: Soviet Union)
Pandemic Influenza Phases

- Phases 1-3: Mostly animal infections
- Phase 4: Human-human transmission
- Phase 5-6: Pandemic, widespread human infection
- Post Peak: possibility of recurrence
- Post Pandemic: Seasonal
Pandemic Influenza

• Severe influenza syndrome
  – Fever, cough, fatigue, shortness of breath
  – Abdominal pain, diarrhea, vomiting
  – No conjunctivitis

• Chest X-ray with bilateral infiltration, lobar collapse, focal consolidation

• Complications
  – Acute respiratory distress, renal failure, **bacterial superinfection**
1918 Influenza Pandemic

- 1/3 of the world’s population infected
- Case fatality rates of >2.5%
- 3 waves: spring/summer, summer/fall, winter
- Unclear source of pandemic virus, limited capabilities

Figure 1. Three pandemic waves: weekly combined influenza and pneumonia mortality, United Kingdom, 1918–1919 (21).

Figure 2. “U-” and “W-” shaped combined influenza and pneumonia mortality, by age at death, per 100,000 persons in each age group, United States, 1911–1918. Influenza- and pneumonia-specific death rates are plotted for the interpandemic years 1911–1917 (dashed line) and for the pandemic year 1918 (solid line) (33,34).
2009 H1N1 Pandemic

- ‘Swine flu’ first reported March 2009 in Mexico
- High human to human transmission, WHO pandemic level declared 6 June 2009
- Influenza A virus
  - Reassortment of 2 swine, one human strain, one avian strain
- Incubation: 1-4 days; viral shedding peak: 2-3 day into illness
- Secondary attack rate: 14-19%
- Viral shedding peaks first 2-3 days of illness
2009 H1N1 Pandemic

- Estimated death and impact varies by method
  - Actual deaths vs. laboratory confirmed
  - Average global H1N1 related fatality estimate: 201,200

- Less severe than 1918 H1N1 pandemic

- Immunity: natural infection, immunization, preexisting immunity from remote infection with related strain
2009 H1N1 Pandemic

Global deaths from 2009 H1N1 influenza pandemic, by week of notification

Figure 1: Global deaths from the 2009 H1N1 influenza pandemic, by week (Data Source: ECDC, 2010)
2009 H1N1 Pandemic

Figure 2: Map of cumulative global deaths from the 2009 H1N1 influenza pandemic, as of February 2010 (Data source: ECDC, 2010)
2009 H1N1 Pandemic

Figure 3: Age distribution of influenza mortality: comparing seasonal flu to the 1918 and 2009 pandemics
Figure 4: Early outbreak characteristics of the 2009 H1N1 virus in the U.S.: number of cases per 100,000 people from April to July 2009 (left) and early fatalities by age (right) (Data Source: CDC, 2009).

Figure 5: Age distribution of U.S. hospitalized cases (left) and fatalities (right) from the 2009 H1N1 pandemic from April 2009 through January 30, 2010 (Data Source: CDC, 2010c)
# 2009 H1N1 Pandemic

Table 2: Estimates of fatalities, hospitalizations, and cases for the 2009 H1N1 influenza pandemic, as modeled by RMS and estimated by the CDC as of February 13, 2010 (Data source: CDC, 2010a). Note: The CDC estimates are preliminary and do not represent the entire H1N1 pandemic. These numbers are expected to increase as more data becomes available.

<table>
<thead>
<tr>
<th>Age</th>
<th>RMS Modeled Expected Value</th>
<th>CDC Lower Bound</th>
<th>CDC Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fatalities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-17 yrs</td>
<td>6,000</td>
<td>890</td>
<td>1,840</td>
</tr>
<tr>
<td>18-64 yrs</td>
<td>13,500</td>
<td>6,530</td>
<td>13,500</td>
</tr>
<tr>
<td>over 65 yrs</td>
<td>8,500</td>
<td>1,100</td>
<td>2,280</td>
</tr>
<tr>
<td>Total</td>
<td>28,000</td>
<td>8,520</td>
<td>17,620</td>
</tr>
<tr>
<td><strong>Hospitalizations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-17 yrs</td>
<td>71,660</td>
<td>60,000</td>
<td>125,000</td>
</tr>
<tr>
<td>18-64 yrs</td>
<td>155,646</td>
<td>109,000</td>
<td>226,000</td>
</tr>
<tr>
<td>over 65 yrs</td>
<td>102,280</td>
<td>19,000</td>
<td>38,000</td>
</tr>
<tr>
<td>Total</td>
<td>329,586</td>
<td>188,000</td>
<td>389,000</td>
</tr>
<tr>
<td><strong>Cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-17 yrs</td>
<td>25,000,000</td>
<td>14,000,000</td>
<td>28,000,000</td>
</tr>
<tr>
<td>18-64 yrs</td>
<td>37,000,000</td>
<td>24,000,000</td>
<td>50,000,000</td>
</tr>
<tr>
<td>over 65 yrs</td>
<td>3,000,000</td>
<td>4,000,000</td>
<td>8,000,000</td>
</tr>
<tr>
<td>Total</td>
<td>65,000,000</td>
<td>42,000,000</td>
<td>86,000,000</td>
</tr>
</tbody>
</table>
Pandemic H1N1 vaccine

March 2009: Confirmed H1N1 in Veracruz, Mexico

October 2009: First H1N1 vaccine available for administration in the U.S.
Lessons from 2009 pandemic

• Vigilance and surveillance for novel strains
• Identify at risk populations
• Limitations of laboratories and hospitals
• Educating the public about preventive measures
• Vaccine manufacturing and quality control
• Availability of antiviral drugs
• Each epidemic, pandemic is different (current treatments and technologies are on our side)
Avian Influenza

Outbreaks of Avian Influenza A (H5N2), (H5N8), and (H5N1) Among Birds — United States, December 2014–January 2015

Michael A. Jhung, MD, Deborah I. Nelson, PhD
Avian Influenza

• Reservoir: Aquatic birds
• Transmission between birds
  – Direct
  – Indirect (fecal aerosols, water, feed, etc.)

• Clinically
  – Asymptomatic → Mild respiratory illness → Fatal systemic disease

• Most isolates are avirulent
• Epidemic fowl mortality caused by highly pathogenic variants
  – H5 and H7
  – Decreased egg production, respiratory disease, head edema, diarrhea, death
Asian Bird Migratory Patterns

Figure 2. Migration routes of Asian birds. A) Distribution and migration routes of bar-headed geese (courtesy of P. Leader). B) The Asia-Pacific region contains >240 species of migratory birds. The 3 flyways run primarily in a north-south direction, overlapping and extending from Australia/New Zealand to India, Central Asia, and Siberia. The outbreak of highly pathogenic (HP) H5N1 in migratory waterfowl at Qinghai Lake, China, affected primarily bar-headed geese (Anser indicus); however, other species, including gulls and ducks, were affected (16,17). The outbreak started in early May 2005, and by June >5,000 birds had died. The birds exhibited neurologic signs, inability to stand, diarrhea, and death. Systemic infection was detected in all organs tested. C) Bar-head-
Table 2. Serologic and Clinical Characteristics of Avian Influenza A (H5N1) Infection among Contacts of Patients or Infected Animals.*

<table>
<thead>
<tr>
<th>Group</th>
<th>Location</th>
<th>Year</th>
<th>Assay Method†</th>
<th>No. Tested</th>
<th>No. (%) Positive</th>
<th>Comment</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household contacts</td>
<td>Hong Kong</td>
<td>1997</td>
<td>MN, ELISA, WB</td>
<td>51</td>
<td>6 (12)</td>
<td>Concurrent exposure to poultry in 5 of 6 positive household contacts; 0 of 9 non-household contacts positive</td>
<td>Katz et al.⁸</td>
</tr>
<tr>
<td>Tour group contacts</td>
<td></td>
<td></td>
<td></td>
<td>26</td>
<td>1 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Workplace contacts</td>
<td></td>
<td></td>
<td></td>
<td>47</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poultry cutlers</td>
<td>Hong Kong</td>
<td>1997</td>
<td>MN, WB</td>
<td>293</td>
<td>9 (3)</td>
<td>Seroconversion in 1 with mild acute respiratory illness</td>
<td>Bridges et al.⁷</td>
</tr>
<tr>
<td>Poultry-market workers</td>
<td>Hong Kong</td>
<td>1997</td>
<td>MN, WB</td>
<td>1525</td>
<td>— (estimated 10%)</td>
<td>Most asymptomatic</td>
<td>Bridges et al.⁷</td>
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<tr>
<td>Health care workers with contact</td>
<td>Hong Kong</td>
<td>1997</td>
<td>MN, WB</td>
<td>217</td>
<td>8 (4)‡</td>
<td>Seroconversion in 2; most asymptomatic</td>
<td>Buxton Bridges et al.⁹</td>
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<tr>
<td>Household contacts§</td>
<td>Vietnam</td>
<td>2004</td>
<td>MN</td>
<td>51</td>
<td>0</td>
<td>0 of 83 controls positive</td>
<td>Liem et al.¹⁰</td>
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<tr>
<td>Contacts of sick poultry§</td>
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<td>2 with suspected illness (not confirmed)</td>
<td>Schultsz et al.¹¹</td>
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<td>Health care workers with contact§</td>
<td>Thailand</td>
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<td>Clinical only</td>
<td>35</td>
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<td>No fever or influenza-like illness</td>
<td>Apisarnthanarak et al.¹²</td>
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<tr>
<td>Poultry cutlers§</td>
<td>Indonesia</td>
<td>2005</td>
<td>MN</td>
<td>79</td>
<td>1 (1)</td>
<td>Asymptomatic</td>
<td></td>
</tr>
</tbody>
</table>

* Some serologic surveys of apparent human-to-human transmission may have been confounded by concurrent exposure to ill poultry.
† MN denotes identification of serum antibody against influenza A (H5N1) by microneutralization, ELISA enzyme-linked immunosorbent assay, WB detection of influenza A (H5)–specific bands by Western blotting, and RT-PCR reverse-transcriptase–polymerase-chain-reaction assay for viral RNA.
‡ P=0.01 for the comparison with 2 of 309 health care workers without contact (0.6 percent).
§ Data are from the WHO Meeting on Case Management and Research on Human Influenza A (H5) held in Hanoi, May 10 through 12, 2005.
Avian Influenza Human to Human Transmission

- A few reports of probable transmission among close family or hospital contacts
- WHO: limited non-sustained human to human spread
Avian Influenza A (H7N9)

As of March 2015
- 826 confirmed cases
- 440 deaths (53% CFR)

2 recent imported cases to Canada
Cumulative Numbers of Confirmed Human H5N1 Avian Influenza reported to the WHO (as of March 2015)

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<td>125</td>
<td>33</td>
<td>826</td>
<td>440</td>
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## Avian Influenza

### Table 1. Direct transmission of avian influenza viruses to humans

<table>
<thead>
<tr>
<th>Virus subtype</th>
<th>Year</th>
<th>Location</th>
<th>No. cases (no. deaths)</th>
<th>Clinical features</th>
<th>Notes</th>
<th>Reference(s)</th>
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<tr>
<td>H5N1</td>
<td>1997</td>
<td>Hong Kong</td>
<td>18 (6)</td>
<td></td>
<td></td>
<td>(5, 6)</td>
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<tr>
<td>H9N2</td>
<td>1999</td>
<td>Hong Kong</td>
<td>2 (0)</td>
<td>Mild influenzalike illness</td>
<td></td>
<td>(7)</td>
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<tr>
<td>H9N2</td>
<td>1999</td>
<td>Guangdong Province, China</td>
<td>5 (0)</td>
<td>Mild influenzalike illness</td>
<td></td>
<td>(8)</td>
</tr>
<tr>
<td>H9N2</td>
<td>2003</td>
<td>Hong Kong</td>
<td>1 (0)</td>
<td>Mild influenzalike illness</td>
<td></td>
<td>(9)</td>
</tr>
<tr>
<td>H5N1</td>
<td>2003</td>
<td>Hong Kong</td>
<td>2 (1)</td>
<td>Primary viral pneumonia, lymphopenia, respiratory distress</td>
<td>7-year-old girl died in Fujian Province, China, and H5N1 infection was not confirmed. Her 33-year-old father died from confirmed H5N1 influenza infection in Hong Kong, and her 8-year-old brother recovered from H5N1 infection.</td>
<td>(10)</td>
</tr>
<tr>
<td>H7N7</td>
<td>2003</td>
<td>Netherlands</td>
<td>89 (1)</td>
<td>Conjunctivitis (78 cases), mild influenzalike symptoms (2 cases) or both (5 cases). In fatal case, pneumonia followed by respiratory distress syndrome</td>
<td>Most cases were in persons involved in handling poultry (88), with 3 family members also affected.</td>
<td>(11)</td>
</tr>
<tr>
<td>H10N7</td>
<td>2004</td>
<td>Egypt</td>
<td>2 (0)</td>
<td>Fever and cough</td>
<td>Both cases were in infants, who recovered without complications</td>
<td>(12)</td>
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<tr>
<td>H5N1</td>
<td>2003—present</td>
<td>Asia (Vietnam, Thailand, Cambodia, Indonesia)</td>
<td>116 (60)*</td>
<td>Fever, respiratory symptoms, lymphopenia, elevated liver enzymes. Severe cases progress to respiratory failure, multiple organ dysfunction, and death.</td>
<td>Human cases concomitant with unprecedented outbreaks of highly pathogenic H5N1 AI in poultry</td>
<td>WHO* (13–15)</td>
</tr>
</tbody>
</table>

Typically younger

Short incubation period

High level of poultry exposure

**Common Symptoms:**
- Fever
- Cough
- Runny nose
- Shortness of breath
- Abnormal CXR
- Low lymphocytes
- Low platelets
- Increased AST/ALT
Severe Illness from H5N1

**Figure 1. Chest Radiographs from the Three Patients with Avian Influenza A (H5N1).**

Panel A shows a chest radiograph from the index patient, an 11-year-old girl, on day 6 of her illness. The image shows right-lower-lobe consolidation and patchy left-lower-lobe infiltrates. Panel B shows a radiograph from the girl's 26-year-old mother on day 9 of her illness. There is bilateral lower-lobe consolidation. Panel C shows a radiograph from the girl's 32-year-old aunt on day 7 of her illness; left-lower-lobe consolidation is visible.
# Severe Illness from H5N1

<table>
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<tr>
<th>Outcome or Measure</th>
<th>Hong Kong, 1997 (N=18)</th>
<th>Thailand, 2004 (N=17)</th>
<th>Vietnam, 2004 (N=10)</th>
<th>Ho Chi Minh City, 2005 (N=10)</th>
<th>Cambodia, 2005 (N=4)</th>
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<td><strong>Hospital course — no. (%)</strong></td>
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<tr>
<td>Respiratory failure</td>
<td>8 (44)</td>
<td>13 (76)</td>
<td>9 (90)</td>
<td>7 (70)</td>
<td>4 (100)</td>
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<tr>
<td>Cardiac failure</td>
<td>NS</td>
<td>7 (41)</td>
<td>NS</td>
<td>0</td>
<td>NS</td>
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<tr>
<td>Renal dysfunction</td>
<td>4 (22)</td>
<td>5 (29)</td>
<td>1 (10)</td>
<td>2 (20)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Antiviral therapy</strong></td>
<td></td>
<td></td>
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<tr>
<td>Amantadine</td>
<td>10 (56)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NS</td>
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<tr>
<td>Ribavirin</td>
<td>1 (6)</td>
<td>0</td>
<td>2 (20)</td>
<td>0</td>
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</tr>
<tr>
<td>Oseltamivir</td>
<td>0</td>
<td>10 (59)</td>
<td>5 (50)</td>
<td>10 (100)</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids**</td>
<td>5 (28)</td>
<td>8 (47)</td>
<td>7 (70)</td>
<td>5 (50)</td>
<td>NS</td>
</tr>
<tr>
<td>Inotropic agents</td>
<td>NS</td>
<td>8 (47)</td>
<td>2 (20)</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td><strong>Time from onset of illness to death — days</strong></td>
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<td>Median</td>
<td>23</td>
<td>12</td>
<td>9</td>
<td>12.8†</td>
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<td>Range</td>
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<td>6–10</td>
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<td>Deaths — no. (%)</td>
<td>6 (33)</td>
<td>12 (71)</td>
<td>8 (80)</td>
<td>8 (80)</td>
<td>4 (100)</td>
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Avoid These

Table 4. Exposures That May Put a Person at Risk for Infection with Influenza A (H5N1).*

Countries and territories where influenza A (H5) viruses have been identified as a cause of illness in human or animal populations since October 1, 2003

During the 7 to 14 days before the onset of symptoms, one or more of the following:

- Contact (within 1 m) with live or dead domestic fowl or wild birds or domestic ducks
- Exposure to settings in which domestic fowl were confined or had been confined in the previous 6 weeks
- Unprotected contact (within touching or speaking distance) with a person for whom the diagnosis of influenza A (H5N1) is confirmed or being considered
- Unprotected contact (within touching or speaking distance, 1 m) with a person with an unexplained acute respiratory illness that later resulted in severe pneumonia or death
- Occupational exposure†

Countries and territories where influenza A (H5) viruses have not been identified as a cause of illness in human or animal populations since October 1, 2003

During the 7 to 14 days before the onset of symptoms, close contact with an ill traveler from one of the areas with known influenza A (H5) activity, history of travel to a country or territory with reported avian influenza activity due to influenza A (H5N1) in the animal populations, or living in an area in which there are rumors of the death of domestic fowl, and one or more of the following:

- Contact (within 1 m) with live or dead domestic fowl or wild birds in any setting or with domestic ducks
- Exposure to settings in which domestic fowl were confined or had been confined in the previous 6 weeks
- Contact (within touching or speaking distance) with a patient with a confirmed case of influenza A (H5)
- Contact (within touching or speaking distance) with a person with an unexplained acute respiratory illness that later resulted in severe pneumonia or death
- Occupational exposure†

* These summaries do not present formal WHO guidelines, although they contain content from WHO documents.†

† At-risk occupations include domestic-fowl worker, worker in a domestic-fowl processing plant, domestic-fowl culler (catching, bagging, or transporting birds or disposing of dead birds), worker in a live-animal market, chef working with live or recently killed domestic fowl, dealer or trader in pet birds, health care worker, and a worker in a laboratory processing samples possibly containing influenza A (H5N1) virus.
Pandemic & Avian Influenza: Management

• Early suspicion and recognition
• Isolation and testing
• Symptom management
• Neuraminidase inhibitors
  – Oseltamivir (oral), zanamivir (inhaled), and peramivir (IV)
  – Effective for both influenza A and B (unlike amantadine)
  – Give within 48 hr of symptom onset
  – Prevention of H5N1 but resistance develops rapidly
• Vaccine if available
  – Pandemic H1N1 influenza vaccine in 2009-2010
  – H5N1 avian influenza vaccine manufactured by Sanofi Pasteur approved by FDA in 2007
  – Testing H7N9 avian influenza vaccine (NIH sponsored)

Good Rule of Thumb:
Severe Respiratory Disease → isolate patient until you know you’re dealing with
Oseltamivir Treatment

• Shortens symptoms and may reduce risk of complications, especially **started within 48 hrs**.

• Highest benefit:
  – Hospitalized, children < 2, adults > 65, chronic illness, immunocompromised, pregnant, those < 19 and receiving aspirin therapy, American Indians/Alaska Natives, morbidly obese, nursing home residents

• Do not wait for laboratory confirmation

• **Standard dose is 75 mg twice daily for 5 days**
  – Dose adjust but approved for 2 weeks and older

• Side effects: mostly nausea, vomiting, neuropsychiatric in Japan.
Oseltamivir Prophylaxis

- CDC dose NOT recommend widespread prophylaxis use.
- Vaccination and close monitoring as alternative
- 70-90% effective
- **75 mg once daily, exposure time + 7 days**
  - Likely not helpful to start > 48 hrs since exposure.
  - 2 weeks after last case in long-term care facilities
Other Common Respiratory Viruses

• Adenovirus
  – 51 serotypes, types 1-7 responsible for most infections.
  – Oral adenovirus type 4 & 7 vaccine for military recruits

• Respiratory syncytial virus (RSV)
  – Annual epidemics, bronchiolitis in infants

• Coronaviruses
  – Common Cold virus

• Human metapneumovirus (HMPV) = Similar to RSV

• Parainfluenza virus = Four types, type 3 in spring and early summer

• Rhinoviruses
  – Common cold virus, 100 + serotypes, year-round in tropics
All photos from CDC website
Measles

• Incubation period typically 7-14 days
• **Highly contagious** (AIRBORNE transmission)---- **154 cases** in 2015
  – Can spread to others up to 4 days prior to rash
  – Adults can be affected

• Typical presentation (high fever, cough, runny nose, conjunctivitis, and rash erupting a few days later)
  – Rash spreads from face and head downward (fever spikes)

• Complications (This kills kids: 1 to 2 kids/1000 die)
  – ~25% require hospitalization
  – Ear infections in 10% (can result in hearing loss)
  – Diarrhea (10%)
  – Pneumonia (5%) – **most common cause of death**
  – Encephalitis (0.1%) – can result in major neurologic sequelae
  – Subacute Sclerosing Panencephalitis (SSPE)
    • Rare, but fatal occurring ~10 years after full recovery from infection
Measles Cases and Outbreaks
January 1 to February 20, 2015*

154 Cases
reported in 17 states and Washington DC: Arizona, California, Colorado, Delaware, Georgia, Illinois, Michigan, Minnesota, Nebraska, New Jersey, New York, Nevada, Pennsylvania, South Dakota, Texas, Utah, Washington

3 Outbreaks
representing 90% of reported cases this year

U.S. Measles Cases by Year

*Provisional data reported to CDC’s National Center for Immunization and Respiratory Diseases
Koplik Spots
Measles

• Vaccination with MMR
  – Single dose is 93% protective (97% with 2 doses)
    • First dose just after first birthday (can get it as early as 6 mo*)
    • Second dose generally ages 4 to 6 years**
  – Not available in many developed nations
    • 20 million cases worldwide with 146,000 deaths

• Treatment
  – Supportive care
  – Monitor for bacterial superinfections
  – Vitamin A once daily x 2 days (50k to 200k IU/dose)
  – Ribavirin?

*If traveling overseas, but would need 2 additional doses after first birthday
**Can get second dose as early as 28 days after first dose
Impact of Adenovirus type 4 & 7 Vaccination Among Recruits at Eight Training Centers

Adeno vaccine initiated
Case

• You are deployed to Kuwait and you admit a young male SM, smoker with flulike illness, with fevers, shortness of breath and intermittent diarrhea. The SM develops ARDS and is intubated in critical condition. Within 4 days of admission, 2 of your staff are developing similar symptoms.

• What might this be?
Coronavirus

- Meaning ‘crown or halo’
- Large, positive sense RNA virus
- Family Coronaviridae
- Infects humans, mammals, birds

**Severe acute respiratory syndrome coronavirus**
- (SARS-CoV)
- Rapid human to human spread worldwide
- 774 probable deaths, 10% fatality rate
- Started in Hong Kong Feb. 2003
  - Civet cats and other small mammals to humans?
  - Delayed peak transmission period
    - Rare within first 5 days of symptom onset
    - Easier recognition, isolation, and interruption
- **No cases since 2004**
Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

- Severe, contagious, respiratory illness
  - 376 deaths in 1026 lab confirmed cases (37% case fatality rate) as of 23 FEB 2015

- First cluster in Jordan, April 2012
- First Saudi Arabia case, June 2012
- Cluster among family contacts, returning travelers in Europe
- Nosocomial transmission (24% of cases)
- Reservoir (bats? camels ← EID 2014 Dec; 20: 1999)
- Geographically diverse animal reservoir, initial emergence in July 2011, sporadic introduction into humans and human-to-human transmission
MERS-CoV

Countries in or near the Arabian Peninsula with Cases
- Saudi Arabia
- United Arab Emirates (UAE)
- Qatar
- Oman
- Jordan
- Kuwait
- Yemen
- Lebanon
- Iran

Countries with Travel-associated Cases
- United Kingdom (UK)
- France
- Tunisia
- Italy
- Malaysia
- Philippines
- Greece
- Egypt
- United States of America (USA)
- Netherlands
- Algeria
- Austria
- Turkey

CDC, updated Jul 31, 2014
OCID course 2015
Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study


<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients (n=47)</th>
<th>Deaths (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>46 (98%)</td>
<td></td>
</tr>
<tr>
<td>Fever with chills or rigors</td>
<td>41 (87%)</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>39 (83%)</td>
<td></td>
</tr>
<tr>
<td>Dry</td>
<td>22 (47%)</td>
<td></td>
</tr>
<tr>
<td>Productive (sputum)</td>
<td>17 (36%)</td>
<td></td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>8 (17%)</td>
<td></td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>34 (72%)</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>7 (15%)</td>
<td></td>
</tr>
<tr>
<td>Sore throat</td>
<td>10 (21%)</td>
<td></td>
</tr>
<tr>
<td>Runny nose</td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>8 (17%)</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>10 (21%)</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (21%)</td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>12 (26%)</td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>15 (32%)</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>6 (13%)</td>
<td></td>
</tr>
</tbody>
</table>

*Proportion of patients who died according to comorbidity.

Table 3: Symptoms of Middle East respiratory syndrome in 47 Saudi cases at presentation

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Patients (n=47)</th>
<th>Deaths (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any comorbidity</td>
<td>45 (96%)</td>
<td>28 (60%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>32 (68%)</td>
<td>21 (66%)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>23 (49%)</td>
<td>17 (74%)</td>
</tr>
<tr>
<td>Chronic heart disease</td>
<td>13 (28%)</td>
<td>10 (77%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (34%)</td>
<td>13 (81%)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>12 (26%)</td>
<td>10 (83%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>8 (17%)</td>
<td>5 (63%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>11 (23%)</td>
<td>7 (64%)</td>
</tr>
<tr>
<td>Malignant disease</td>
<td>1 (2%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Steroid use</td>
<td>3 (6%)</td>
<td>3 (100%)</td>
</tr>
</tbody>
</table>

Table 4: Comorbidities in 47 Saudi cases of Middle East respiratory syndrome

Overall CFR = 36%
Any comorbidity = 60%
Figure 1: Imaging findings at presentation in Saudi patients with Middle East respiratory syndrome

(A) Chest radiograph of a 61-year-old man, showing bilateral fine reticulonodular air-space opacities, increased vascular markings, and cardiomegaly. (B) Chest radiograph of an 83-year-old man, showing right lung consolidation, right basal pleural thickening, and reticulonodular air-space opacities. Rib fractures on the right are old. (C) Chest radiograph of a 56-year-old man, showing extensive bilateral extensive diffuse and focal alveolar space opacities, with opacification of the left lower lobe. (D) Chest radiograph of a 67-year-old man, showing extensive bilateral disease, with diffuse alveolar space densities, opacification, reticulonodular opacities, and bronchial wall thickening. (E) Chest radiograph of a 49-year-old man, showing extensive bilateral mid and lower zone disease, with diffuse reticulonodular alveolar space opacities. A thoracic CT scan in the same patient (F) shows extensive bilateral opacities and ground-glass reticulonodular shadowing and bronchiolar wall thickening.

Lancet Infect Dis 2013; 13: 752–61
• 89% cases traced to 3 hospital-linked ‘super-spreading’ events
• Pattern resembles Middle East cases
  – Spread is slow beyond hospital-linked cases
• Incubation times longer in tertiary infected compared to those secondarily infected
• Better patient contact tracing could have prevented spread
### MERS Co-V vs. SARS

<table>
<thead>
<tr>
<th>Demographic factors</th>
<th>MERS-CoV</th>
<th>SARS, global(^{27, 34})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of first case report (place)</td>
<td>April, 2012 (Jordan); June, 2012 (first Saudi case)</td>
<td>November, 2002 (China)</td>
</tr>
<tr>
<td>Mean (95% CI) incubation period (days)</td>
<td>5.2 (1.9–14.7); range 2–13</td>
<td>4.6 (3.8–5.8); range 2–14</td>
</tr>
<tr>
<td>Serial interval (days)</td>
<td>7.6</td>
<td>8.4</td>
</tr>
<tr>
<td>Age distribution</td>
<td>98% adults, 2% children</td>
<td>93% adults, 5–7% children</td>
</tr>
<tr>
<td>Mean (range) age (years)</td>
<td>56 (14–94)</td>
<td>39.9 (1–91)</td>
</tr>
<tr>
<td>Sex distribution</td>
<td>77% male, 23% female</td>
<td>43% male, 57% female</td>
</tr>
<tr>
<td>Sex ratio (male:female)</td>
<td>3:3:1</td>
<td>1:1.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>MERS-CoV</th>
<th>SARS, global(^{27, 34})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>55%</td>
<td>0–40%</td>
</tr>
<tr>
<td>Case-fatality rate (overall)</td>
<td>Undefined</td>
<td>9.6%</td>
</tr>
<tr>
<td>In patients with comorbidities</td>
<td>60%</td>
<td>1–2%</td>
</tr>
<tr>
<td>Mean time from onset to death (days)</td>
<td>16.5</td>
<td>23.7</td>
</tr>
</tbody>
</table>

OCID course 2015*
Current Guidance – MERS-CoV

- All cases linked to travel or residence in affected areas
- Assess risk, suspect disease
- Lower respiratory tract specimen for rRT-PCR preferred
  - Nasopharyngeal wash or swabs
  - Serum for PCR and serologic testing
  - Stool for PCR
- Follow up serology testing
- Isolation Precautions
  - Airborne for suspected cases
    - For SARS, CDC: ‘airborne precaution preferred’
  - Other standard AND contact precautions
Current Guidance – MERS-CoV: Case Definition

• PATIENT UNDER INVESTIGATION (PUI) PER CDC WEBSITE:
  – FEVER AND PNEUMONIA OR ARDS **AND**:
    • A HISTORY OF TRAVEL FROM COUNTRIES IN OR NEAR THE ARABIAN PENINSULA WITHIN 14 DAYS BEFORE SYMPTOM ONSET, **OR**
    • CLOSE CONTACT WITH A SYMPTOMATIC TRAVELER WHO DEVELOPED FEVER AND ACUTE RESPIRATORY ILLNESS (NOT NECESSARILY PNEUMONIA) WITHIN 14 DAYS AFTER TRAVELING FROM COUNTRIES IN OR NEAR THE ARABIAN PENINSULA **OR**
    • A MEMBER OF A CLUSTER OF PATIENTS WITH SEVERE ACUTE RESPIRATORY ILLNESS (E.G., FEVER AND PNEUMONIA REQUIRING HOSPITALIZATION) OF UNKNOWN ETIOLOGY IN WHICH MERS-COV IS BEING EVALUATED, IN CONSULTATION WITH STATE AND LOCAL HEALTH DEPARTMENTS.
  OR
  – FEVER AND SYMPTOMS OF RESPIRATORY ILLNESS AND BEING IN A HEALTHCARE FACILITY WITHIN 14 DAYS BEFORE SYMPTOM ONSET IN A COUNTRY OR TERRITORY IN OR NEAR THE ARABIAN PENINSULA IN WHICH RECENT HEALTHCARE-ASSOCIATED CASES OF MERS HAVE BEEN IDENTIFIED.
Hantavirus Pulmonary Syndrome

- Bunyavirus, enveloped, neg. SS RNA
- New World Hantavirus
  - ~300 cases per year, mortality up to 50%
  - Sporadic cases in the Americas: US, Canada, Argentina, Bolivia, Brazil, Chile, Panama, Paraguay, Uruguay
- Mice and rats are reservoirs
  - Urine, dropping, nesting materials are aerosolized and inhaled by humans
  - Bites and ingestion of contaminated food
  - Barns, outbuildings, and shed are exposure sites
- Incubation 1-4 weeks, initially non-specific myalgia, HA, chills, nausea, vomiting, GI symptoms
- Shortness of breath and cough develops later
  - Rapidly progressive cardiopulmonary phase
  - Bilateral infiltrates, pulmonary edema
- Conjunctival injection, renal involvement, and hemorrhage reported
Nipah Virus

- RNA virus, paramyxoviruses, henipavirus
- Recent outbreaks in Malaysia and Bangladesh
- Reservoir are bats in China, SE Asia, India, Madagascar, and Ghana
- Pigs are hosts
- Humans, cats, dogs develop infection through direct contact with pig respiratory secretions and urine
- Malaysia outbreak: ? Person to person transmission
- Viral encephalitis with progression to coma, + respiratory symptoms, high mortality
Nipah Virus

Geographic distribution of Henipavirus outbreaks and fruit bats of Pteropodidae Family

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Alert and Response Department
World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

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Hendra Virus

• RNA virus, paramyxoviruses, henipavirus
• Bats are the natural reservoir
• Outbreak in horses in Australia
• Four identified human cases in after close contact with horses
  – Two died
• Acute influenza-like illness, meningoencephalitis, seizures, coma
Hendra Virus

Geographic distribution of Hendra virus outbreaks in Australia from 1994 to July 2008

- Clifton Beach (2007)
- Townsville (2004)
- Proserpine (2008)
- Mackay (1994)
- Peachester (2006, 2007)
- Brisbane (1994, 2008)
- Murwillumbah (2006)

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Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

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Summary

• Virus are constantly evolving and novel highly virulent respiratory viruses WILL circulate in the future

• An influenza strain that is highly transmissible (e.g. H1N1) AND highly virulent (e.g. H5N1) will likely result in high mortality

• Get vaccinated, some protection even when mismatches occur

• Maximize good hand hygiene, distance from others, and personal protective measures

• Consider isolation of patients and assume worst case initially

• Use common sense and avoid contact with animals, local markets, and areas with known outbreaks of respiratory infections
Thank You
Questions?

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