UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

A Virus to Die for: Influenza 2018

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Disclosures

- Related Activities:
  - Member, Technical Advisory Panel on Evaluating the Use of Rapid Influenza Testing in Outpatient Medical Settings, Centers for Disease Control/The Joint Commission
  - Member, Infectious Diseases Society of America (ISDA), Influenza Testing and Antiviral Treatment Guidelines Panel
- Commercial Relationship:
  - Pfizer consultant related to Sickle Cell Disease

What We Will Cover Today:

- Influenza 2018
  - Brief historical and scientific review
  - Discussion of this season's impact
  - Current testing and treatment recommendations
- Respiratory hygiene in the emergency department (ED)


Zombie Apocalypse!!

Why Discuss Influenza?

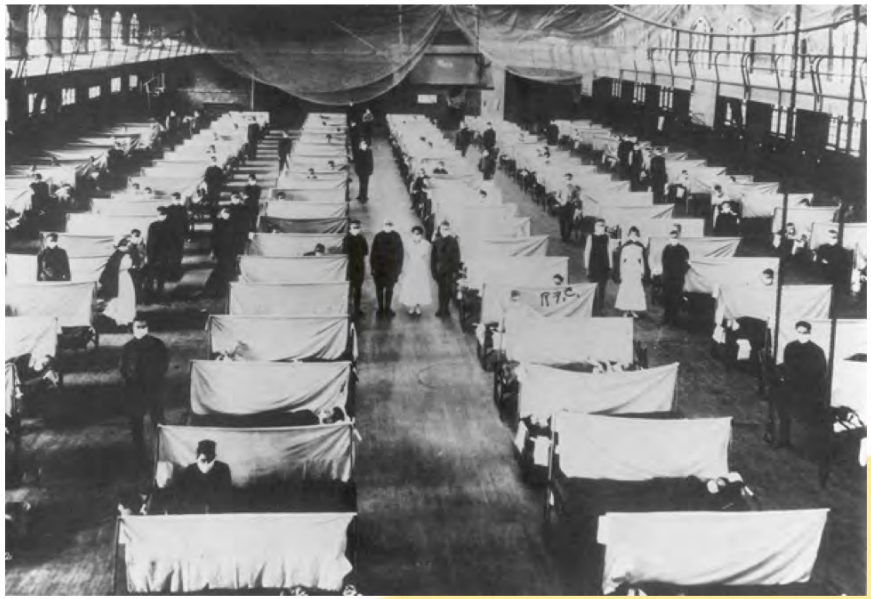
- Common disease that causes significant morbidity and mortality
  - Both seasonal and pandemic influenza
  - Preventable with vaccination
  - Potential treatment to decrease severity of disease

Influenza Quiz: Question #1

- Which killed more people, the 1918 “Spanish” Influenza or World War I?

1918 Influenza Pandemic

- **World War 1 (The Great War):**
  - Killed over 16.5 million individuals
    - 2/3 died in battle, 1/3 from diseases including influenza
    - Of note, approximately 60 million were killed in World War II



*http://wwwnc.cdc.gov/eid/article/12/1/05-0979_article.htm

Influenza Quiz: Question #2

- Which killed more people, the 1918 “Spanish” Influenza or World War I?

- Approximately what percentage of the world’s population was infected with the Spanish Flu?

1918 Influenza Pandemic

- **World War 1 (The Great War):**
  - Killed over 16.5 million individuals
    - 2/3 died in battle, 1/3 from diseases including influenza
    - Of note, approximately 60 million were killed in World War II

- **1918 H1N1 Influenza pandemic infected an estimated 500 million globally***
  - Approximately 20% of the world's population was infected

*http://wwwnc.cdc.gov/eid/article/12/1/05-0979_article.htm

Influenza Quiz: Question #3

- Which killed more people, the 1918 “Spanish” Influenza or World War I?
- Approximately what percentage of the world’s population was infected with the Spanish Flu?
- What percentage of the world died from the Spanish Flu?

1918 Influenza Pandemic

- **World War 1 (The Great War):**
  - Killed over 16.5 million individuals
    - 2/3 died in battle, 1/3 from diseases including influenza
    - Of note, approximately 60 million were killed in World War II

- **1918 H1N1 Influenza pandemic infected an estimated 500 million globally***
  - Approximately 20% of the world's population was infected

- **Killed an estimated 50 million (maybe as high as 100 million)***
  - 2%-3% of the world's population died

*http://wwwnc.cdc.gov/eid/article/12/1/05-0979_article.htm

What is Influenza?

Influenza is…

- A major, acute respiratory illness resulting from infection with an influenza virus

- Highly infectious (depending on strain)
  - Can spread rapidly from person to person
  - Can cause severe illness

- Severity of illnesses also depends on the baseline health of the individual

Influenza Virus

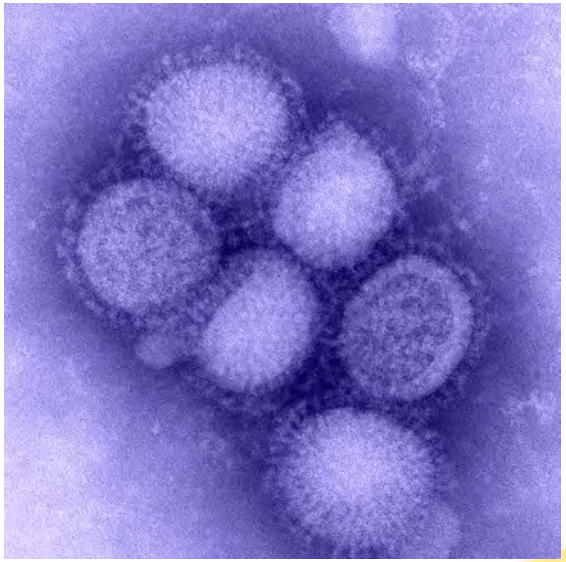
- Orthomyxoviruses
  - RNA virus
    - negative-sense, single-stranded, segmented
  - 6 genera:
    - Influenzavirus A, Influenzavirus B, Influenzavirus C, Isavirus, Thogotovirus, newly discovered 6th genera
- Influenza A- characterized by viral surface proteins
  - hemagglutinin (HA or H)- 16 serotypes
  - neuraminidase (NA or N)- 9 serotypes

Influenza Virus Types

Influenza viruses that infect humans:

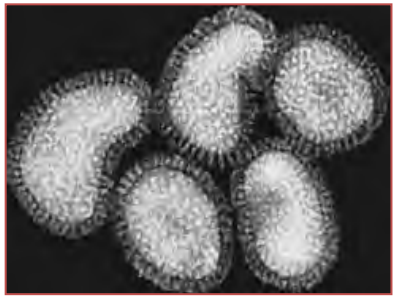
- **A viruses** – infect humans, other mammals and birds; causes pandemics
- **B viruses** – infects humans and seals
- **C viruses** – infects humans and pigs

Swine Flu

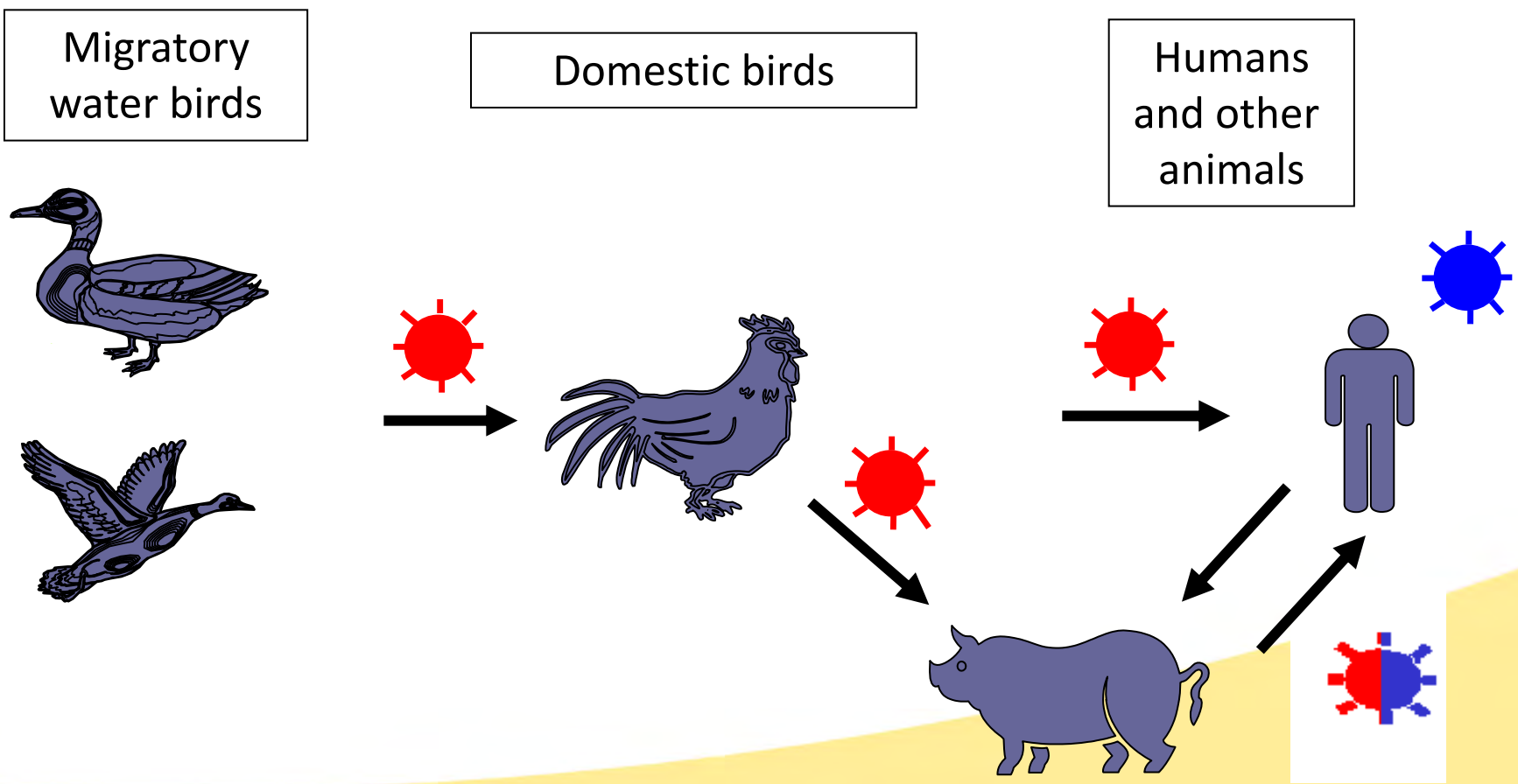


http://www.cdc.gov/flu/podcasts/images/SwineFlu.jpg

Where Does Influenza A Virus Come From?



Human influenza A viruses start as avian (bird) influenza viruses



How Influenza Spreads

- Spreads easily from person to person through coughing and sneezing

- Transmitted by:
  - Inhaling respiratory aerosols containing virus
  - Touching an infected person or an item contaminated with the virus and then touching your eyes, nose, or mouth

Courtesy of CDC

Seasonal Influenza:
Minor Changes – Antigenic Drift

- **Influenza A & B viruses**
  - Results in new variants of prevailing strains every year
    - Result in seasonal influenza each winter
  - Some years are worse than others
    - partly related to degree of 'drift'
  - Primarily Influenza A

- About 3-5 million severe global cases annually
  - Between 290,000 and 650,000 deaths*

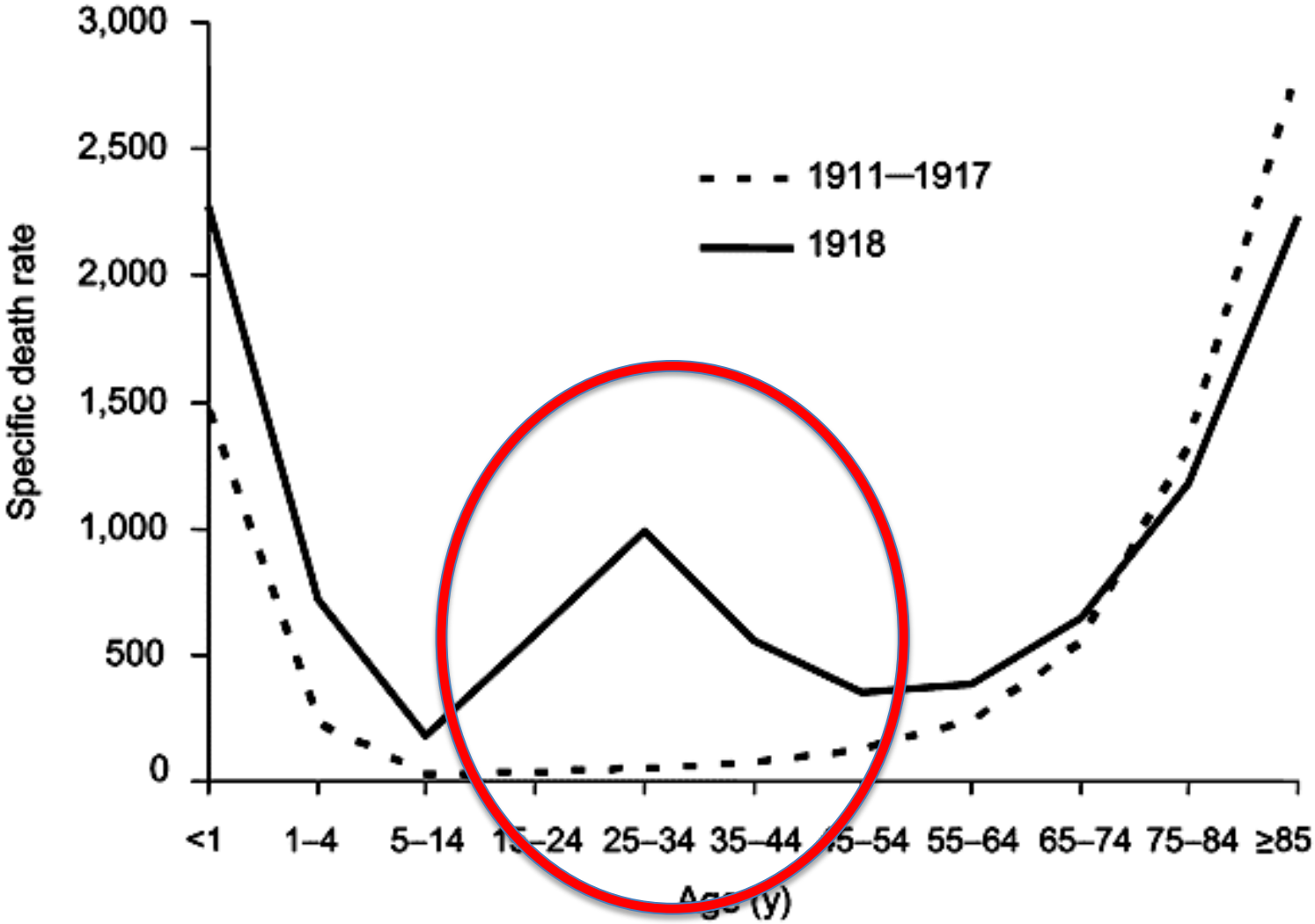
*Iuliano AD, Roguski KM, Chang HH, et al. Lancet **2017**

Pandemic Influenza:
Major Changes – Antigenic Shift

- Major changes occur in the surface antigens of influenza A viruses
  - Caused by mutation or reassortment
- More significant than those associated with antigenic drift
- Lead to the emergence of potentially pandemic strains
  - creates a virus that is markedly different from recently circulating strains
  - people have no pre-existing immunity

Seasonal vs. Pandemic Influenza

- Pandemic influenza is not just a "bad flu,"
  - It is a wholly new threat to humans
- Compared to seasonal influenzas, pandemic influenzas infect
  - More people
  - Cause more severe illness
  - Cause more deaths
- Seasonal influenza viruses
  - Most often cause severe disease in the very young, the very old, and those with chronic illnesses
- Pandemic influenza strains
  - Can infect and kill young, healthy people
  - In the 1918-19 pandemic, very high mortality rate among people aged 20-40 years



Taubenberger JK, Morens DM. 1918 influenza: the mother of all pandemics. Emerg Infect Dis [serial on the Internet]. 2006 Jan [date cited].

Influenza Pandemics and Threats

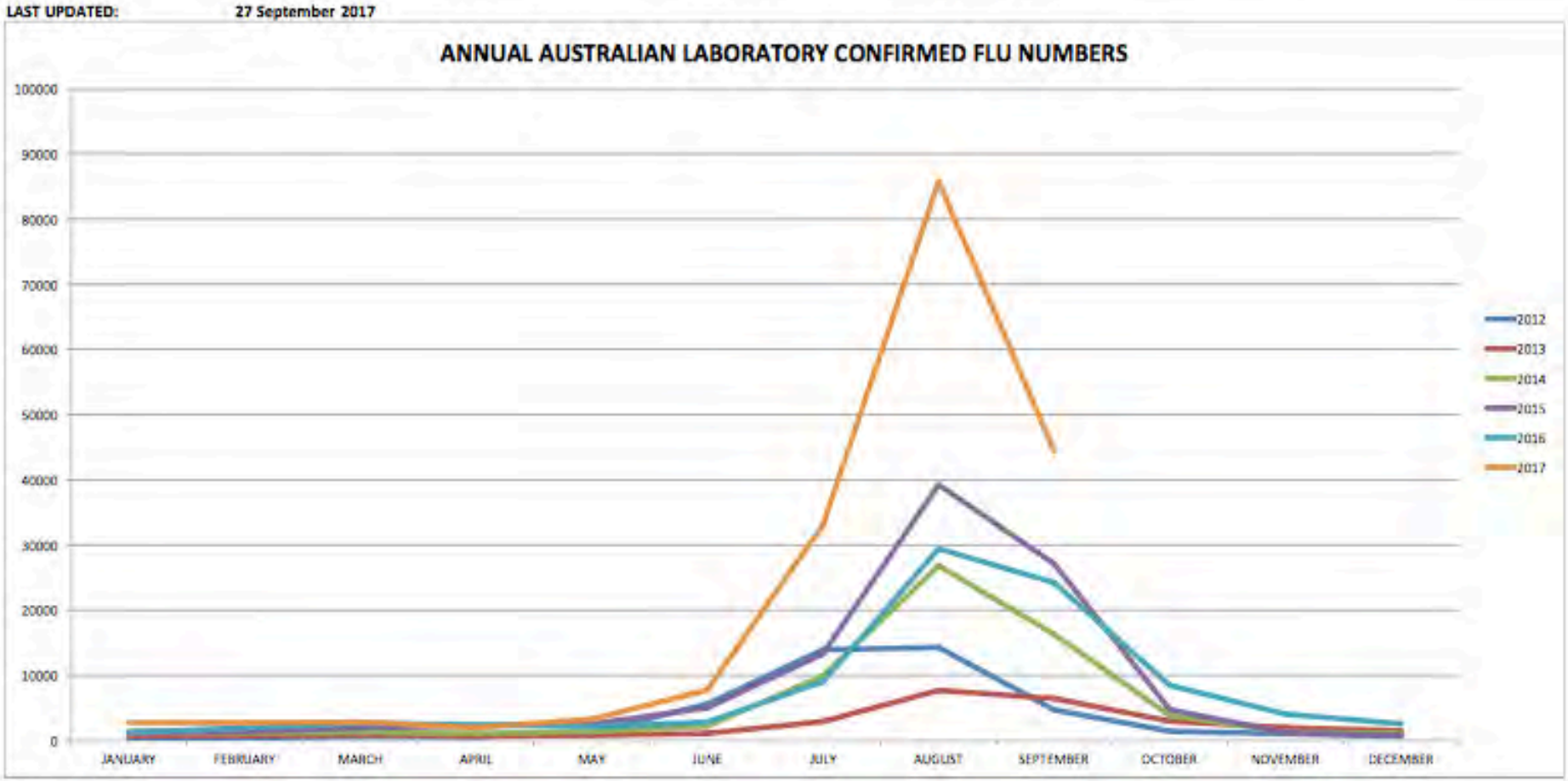
	Years	Case Fatality	Subtype	Pandemic Severity Index
1918 Influenza (Spanish Flu)	1918-1920	2%	H1N1	5
Asian Flu	1957-1958	0.13%	H2N2	2
Hong Kong Flu	1968-1969	<0.1%	H3N2	2
Russian Flu	1977-1978	N/A	H1N1	N/A
2009 Flu Pandemic	2009-2010	0.03%	H1N1/09	N/A

Pandemic Severity Index

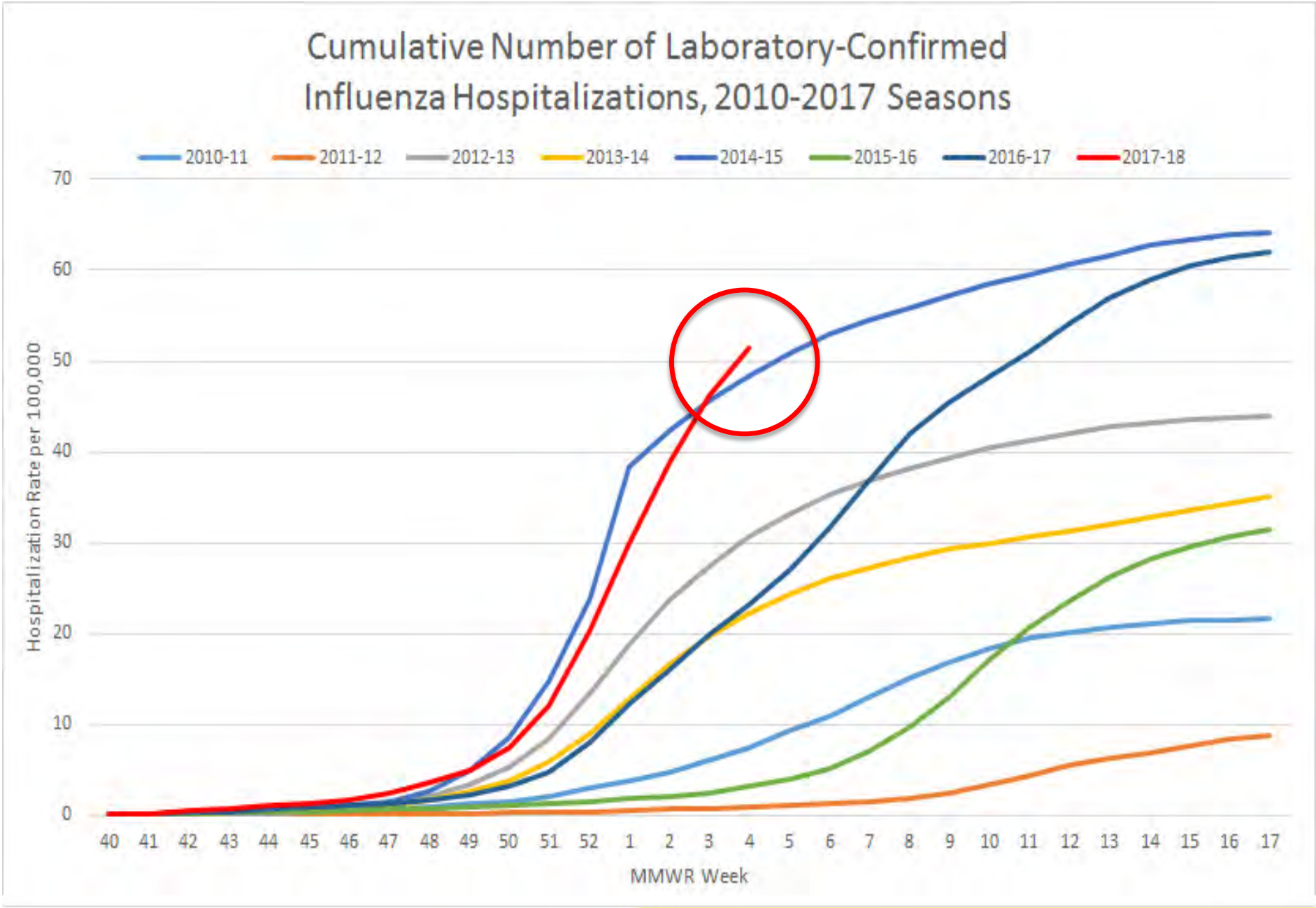
Characteristics	Category 1	Category 2	Category 3	Category 4	Category 5
Case Fatality Ratio (percentage)	<0.1	0.1 - <0.5	0.5 - <1.0	1.0 - <2.0	≥ 2.0
Excess Death Rate (per 100,000)	<30	30 - <150	150 - <300	300 - <600	≥600
Illness Rate (percentage of the population)	20 - 40	20 - 40	20 - 40	20 - 40	20 - 40
Potential Number of Deaths (based on 2006 U.S. population)	<90,000	90,000-<450,000	450,000-<900,000	900,000-<1.8 million	≥1.8 million
20th Century U.S. Experience	Seasonal Influenza (Illness rate	1957, 1968 Pandemic	None	None	1918 Pandemic

Influenza Season: 2018

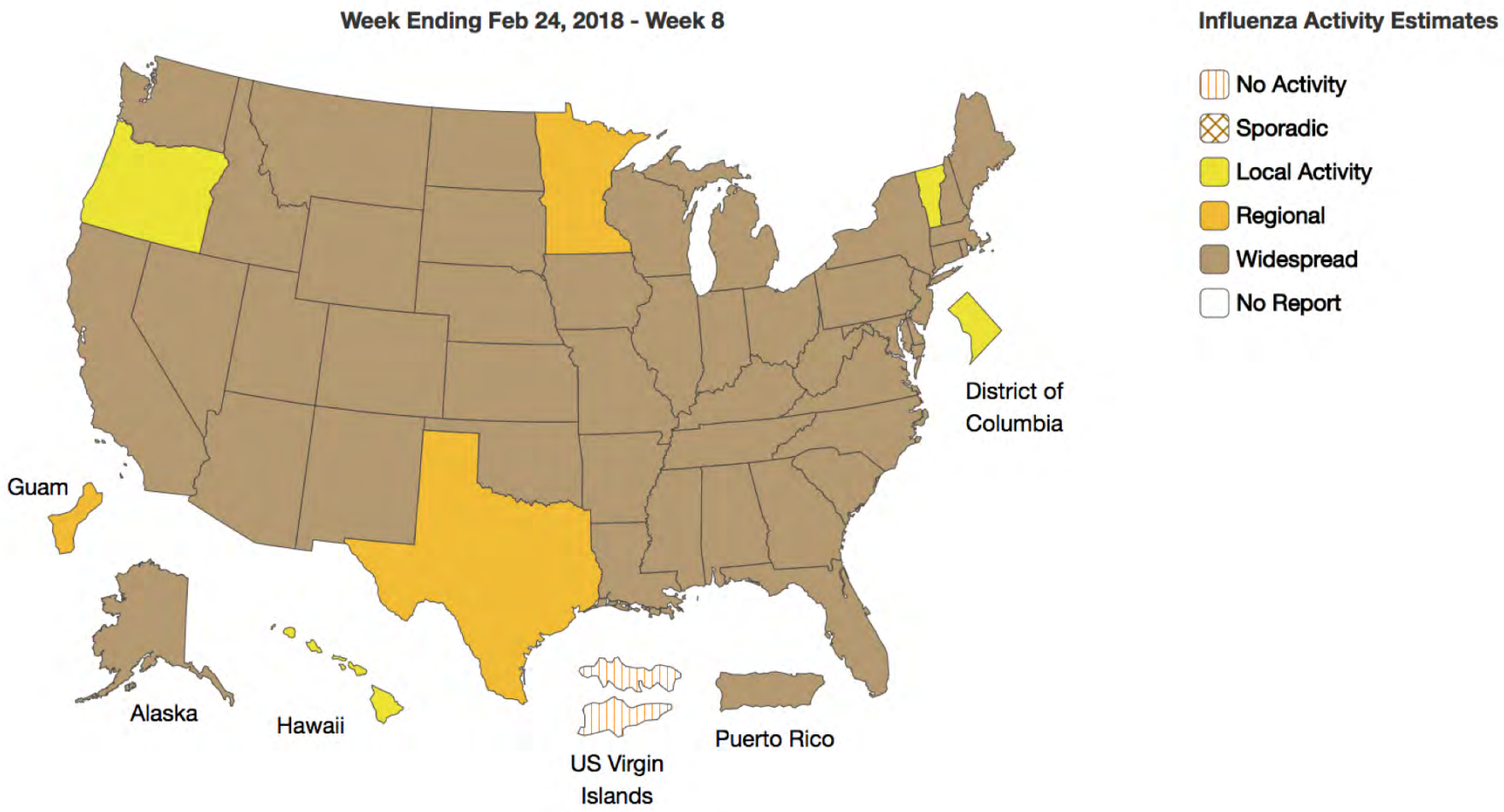
We Knew It Was Coming:



Reference: These statistics are taken from the Aust Government Department of Health, National Notifiable Diseases Surveillance System.


Cumulative Number of Laboratory-Confirmed Influenza Hospitalizations, 2010-2017 Seasons
2010-11
2011-12
2012-13
2013-14
2014-15
2015-16
2016-17
2017-18
Hospitalization Rate per 100,000
0
10
20
30
40
50
60
70
40 41 42 43 44 45 46 47 48 49 50 51 52 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
MMWR Week

Current Influenza Activity: Week 8

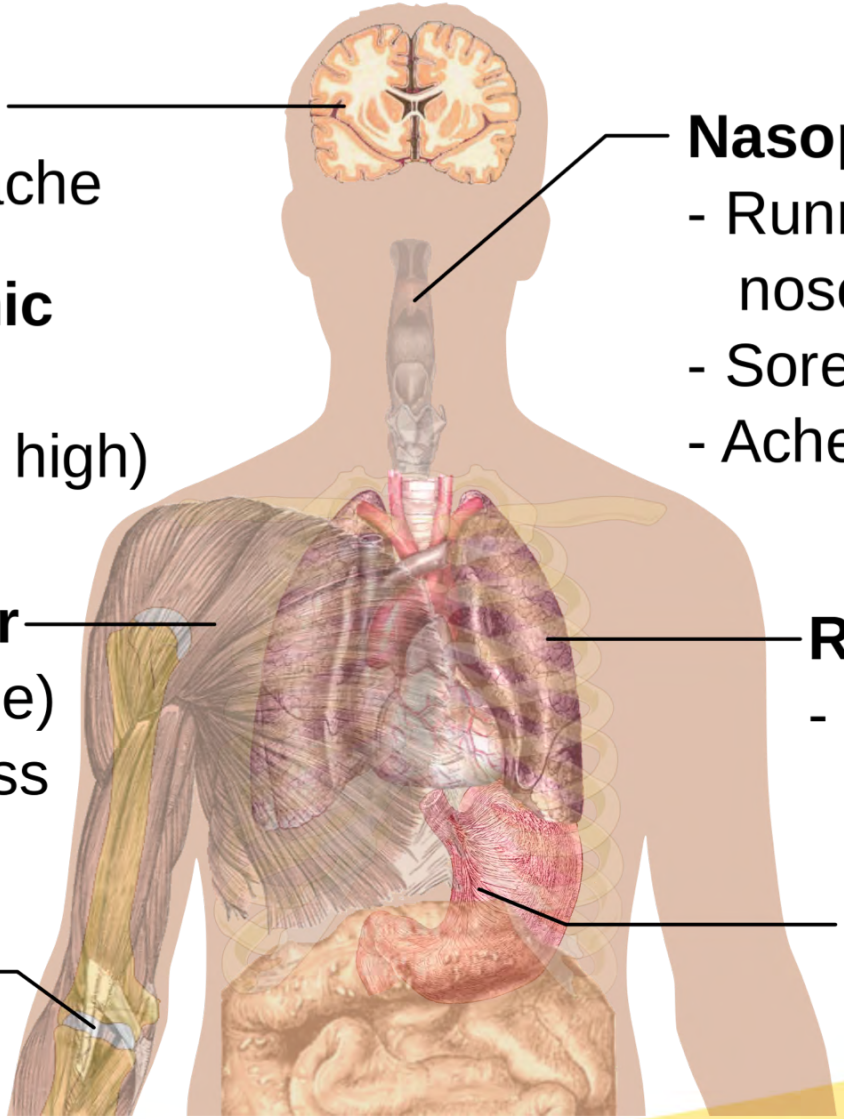


https://www.cdc.gov/flu/weekly/usmap.htm

What Should You Do During the Influenza Season?

Symptoms of

Influenza



Central
- Headache

Systemic
- Fever (usually high)

Nasopharynx
- Runny or stuffy nose
- Sore throat
- Aches

Muscular
- (Extreme) tiredness

Respiratory
- Coughing

Joints
- Aches

Gastric
- Vomiting

Influenza Differential Diagnosis

- Acute Respiratory Distress Syndrome
- Adenoviruses
- Arenaviruses
- Cytomegalovirus
- Dengue Fever
- Echoviruses
- Hantavirus Pulmonary Syndrome
- HIV Disease
- Legionnaires Disease
- Parainfluenza Virus

http://emedicine.medscape.com/article/219557-differential

Which ED Patients Should be Tested?

- **Immune-compromised and high-risk patients**
  - Presenting with influenza-like illness, pneumonia, or nonspecific respiratory illness (e.g., cough without fever)
- **Patients with exacerbation of chronic conditions**
  - E.g., asthma, COPD, heart failure
- **Patients with known complications of influenza**
  - E.g., pneumonia

Patients at Higher Risk of Complications

- Children aged <5 years (especially aged <2 years);
- Adults aged ≥65 years;
- Persons with chronic diseases:
  - Pulmonary (including asthma)
  - Cardiovascular (except hypertension alone)
  - Renal
  - Hepatic
  - Hematologic (including sickle cell disease)
  - Metabolic disorders (including diabetes mellitus)
  - Neurologic, neurodevelopment and muscle conditions, such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or prior spinal cord injury

Patients at Higher Risk (cont.)

- Persons with immunosuppression, including that caused by medications or by HIV infection;
- Women who are pregnant or postpartum (within 2 weeks after delivery);
- American Indians/Alaska Natives;
- Persons who are morbidly obese (i.e., BMI ≥40); and
- Residents of nursing homes and other chronic-care facilities.

Which ED Patients Might be Tested?

- **Consider testing patients, who are not high risk and likely to be discharged**
  - Presenting with influenza-like illness, pneumonia, or nonspecific respiratory illness
- **If the testing will influence**
  - Treatment choice,
  - Further diagnostic testing
  - ED length of stay

What Specimens Should Be Collected?

- **<u>Collect upper respiratory tract specimens</u>** from outpatients for influenza testing as soon after illness onset as possible,
  - Preferably within 4 days of onset
- Nasopharyngeal > Combined nasal and throat swab > Mid-turbinate nasal swab > Throat swab

What Tests Should Be Used?

- Outpatient (ED) setting
  - Rapid molecular assays > Rapid Influenza Diagnostic Tests (RIDTs)
- Hospitalized patients
  - Multiplex RT-PCR assays targeting a panel of respiratory pathogens, including influenza viruses

Comparison of Types of Influenza Diagnostic Tests

Influenza Diagnostic Test	Method	Availability	Typical Processing Time	Sensitivity	Distinguishing Subtype Strains of Influenza A	Cost
Rapid influenza diagnostic tests (RIDTs)	Antigen detection	Wide	<30 minutes	10-80%	No	$
Direct and indirect immunofluorescence assays (DFA and IFA)	Antigen detection	Wide	1-4 h	70-100%	No	$
Viral cell culture	Virus isolation	Limited	3-10 d	100%	Yes	$$
Rapid cell culture (shell vials and cell mixtures)	Virus isolation	Limited	1-3 d	100%	Yes	$$
Nucleic acid amplification tests (including rRT-PCR)	RNA detection	Limited	1-6 h	86-100%	Yes	$$$
Rapid Influenza molecular assays	RNA detection	Wide	<15 minutes	86-100%	No	$$$

Adapted from the Centers for Disease Control and Prevention (CDC) Guidance for clinicians on the use of rapid influenza diagnostic tests. http://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm Accessed June 29, 2015.

Who Should Be Treated?

- **Patients, of any age, with documented or suspected influenza**
  - Hospitalized, regardless of illness duration
  - Outpatients with severe or progressive illness, regardless of illness duration
  - Outpatients at high risk of complications from influenza
  - Pregnant women and those within 2 weeks postpartum

Who Might Be Treated?

- Outpatients with illness onset <2 days
- Symptomatic outpatients who have high risk household contacts
  - Especially if household contacts are severely immune-compromised

What Antivirals Should Be Used?

- A single neuraminidase inhibitor
  - E.g.: oral oseltamivir, inhaled zanamivir, or intravenous peramivir
  - Do not use a combination of neuraminidase inhibitors
- Treatment duration for uncomplicated influenza
  - 5 days

Issues with Oseltamivir

- Expensive:
  - $135 average retail price
- Common side effects
  - Nausea/vomiting
  - Diarrhea
  - Headaches
  - Nose bleeds
- Other side effects include:
  - Dizziness, mood changes, sleep problems, seizures, abdominal pain

When Should Co-Infections Be Considered?

- Severely ill patients
  - Respiratory failure, hypotension and fever
- Patients who deteriorate after initial improvement
- Patients who fail to improve after 3-5 days of treatment

Should adjunctive therapy be administered to patients?

- Clinicians **should not** administer
  - Adjuvant corticosteroid therapy
  - Routinely administer immune-modulation using immune globulin preparations
    - E.g. IVIg
- Remember symptomatic treatment
  - Rest, fluids, antipyretics (acetaminophen)

2017-2018 Flu Season

Language: English (US)

https://www.cdc.gov/flu/about/season/current.htm

More >

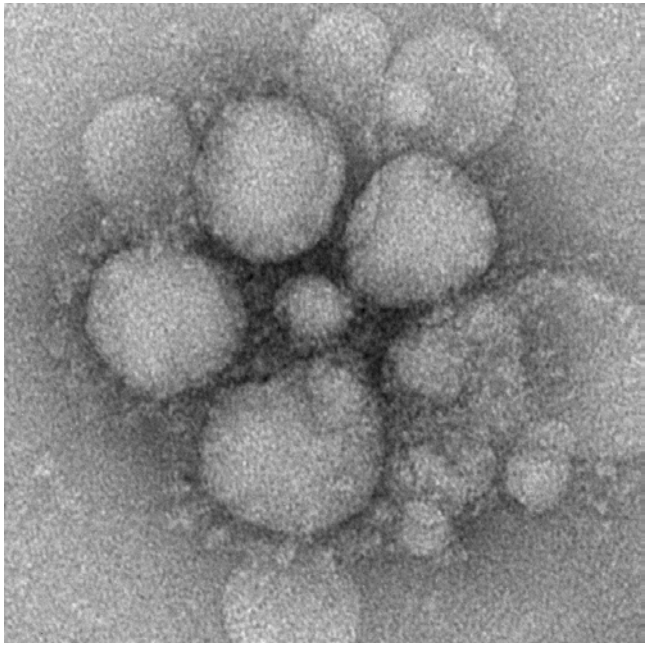
More >

More >

Resources

- Transcript for CDC Update on Widespread Flu Activity
- Transcript for CDC Update on Flu Activity
- CDC Grand Rounds: Public Health Response to Severe Influenza
- Transcript for CDC Telebriefing Update on Widespread Flu Activity
- Health Advisory: Seasonal Influenza A(H3N2) Activity and Antiviral Treatment of Patients with Influenza
- Update: Influenza Activity — United States, October 1–November 25, 2017

Protecting Yourself and Your Patients from Killer Respiratory Viruses



Disease Containment Measures

- **Isolation:** restriction of movement/separation of ill infected persons with a contagious disease
- **Quarantine:** restriction of movement/separation of well persons presumed exposed to a contagious disease
- **Self-shielding:** self-imposed exclusion from infected persons or those who may be infected
- **Social distancing/cohorting:** reducing interactions between people to reduce the risk of disease transmission
- **Snow days:** days on which offices, schools, transportation systems are closed or cancelled, as if there were a major snowstorm

Containing Pandemic Influenza

- Surveillance and diagnostic services
- Information sharing and dissemination
- Community support
- Hospital and physician capacity
- Supply and delivery of vaccines and drugs

  – Note: There are significant concerns lack of surge capacity within the US health system to deal with significant influenza events

Special Report: Tracking the new killer viruses - MERS & H7N9 Bird Flu

Personal Transmission Reduction Methods

- Hand hygiene (cleaning hands with soap and water or an alcohol-based hand rub)
- Respiratory hygiene, e.g., “Cover your cough”
- Cleaning and disinfection of contaminated objects, surfaces
- Physical barriers (e.g., glass or plastic “windows” to protect front desk workers)
- Use of personal protective equipment (PPE) in some settings (e.g., healthcare) such as gowns, gloves, eye, and respiratory protection

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