Influenza: The past, the present, the (future) pandemic

Kristin Butler, MLS (ASCP)^{cm}
Department of Clinical Laboratory Sciences
Louisiana Health Sciences Center - Shreveport
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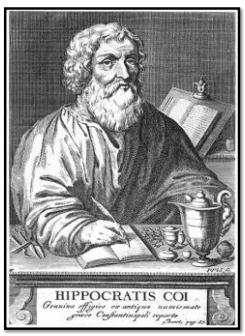
Objectives

1) Detail influenza epidemics of the past.
2) Explain the influenza virus structure, reservoirs, pathogenicity, and vaccination prevention.
3) Discuss future threats of novel influenza virus strains.

A virus as old as time?

- As far back as 400 BC
- Described by Hippocrates, *Of the Epidemics*



Influenza Etymology

- Italian for "*influence*", referring to the cause of the disease
- Later modified to *influenza de freddo*

- First used in English by J. Hugger in 1703

- Other archaic terms:

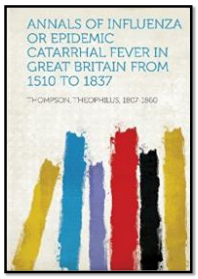
"*epidemic catarrh*" "*la grippe*"
"*sweating sickness*" "*Spanish fever*"

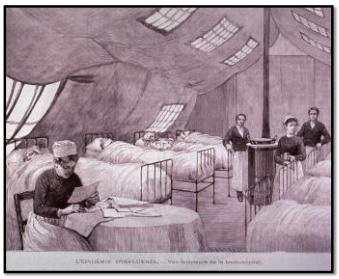
Influenza of the past

- 1510 pandemic in Europe

Influenza of the past

- "Catarrhal fever" epidemics continue through the 1800s





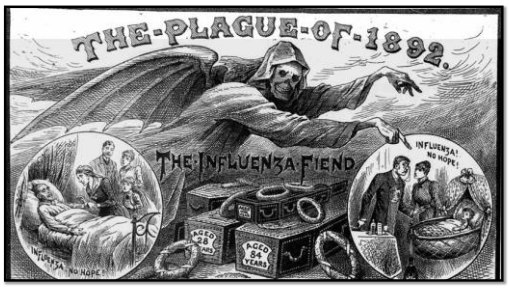
Influenza of the past

- *European Influenza: Or the Greatest Disease Epidemic of the Modern Age*

by Georg Friedrich Most, 1820

Influenza of the past

- 1889 Asiatic (Russian) flu



Pandemics of the past

- 1918 Spanish flu

Pandemics of the past

1957 Asian flu

1968 Hong Kong flu

1977 Russian flu

Pandemics of the past

2009 H1N1 swine flu

- Novel virus strain
- Similar to 1918 virus
- First cases seen in children in Mexico and California
- Some antiviral resistance

Influenza today

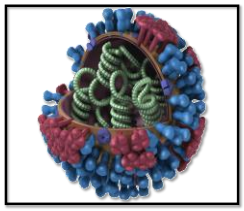
- Endemic virus strains
- Seasonal epidemics

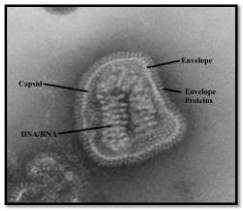
- Evolved healthcare
- Antivirals and antibiotics
- Ongoing threats of future pandemics to novel avian virus strains

Influenza Virus

Three types of flu viruses:

- Influenza A – most common, most pathogenic
- Influenza B – less common, less pathogenic
- Influenza C – least common, least pathogenic

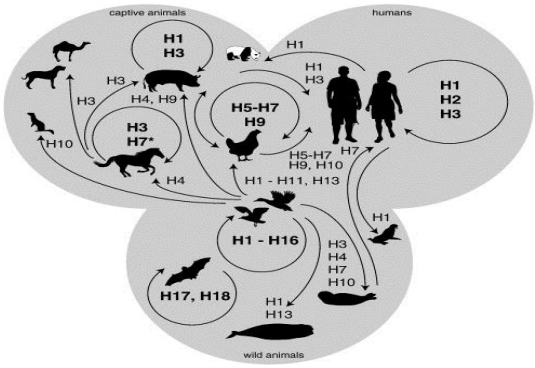




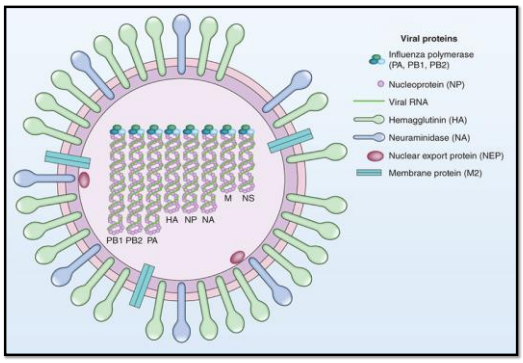
Influenza Season

- A flu epidemic every year
  - "Flu Season" from October to May
  - Peaks in December to March
- Increasing number of virus reservoirs today
  - Avian, swine, equine, canine, other mammals
  - Human viruses similar to animal viruses
  - Unpredictable viral genetics

Influenza Virus Reservoirs



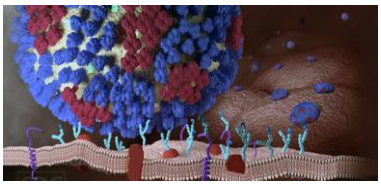
Influenza structure

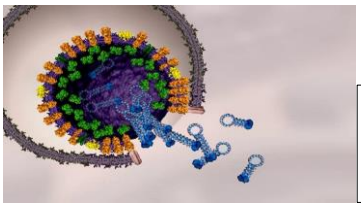


Influenza antigens

- Subtypes are named for surface proteins, ex: H1N1
- Hemagglutinin = binds to epithelial cells
  - All 15 infect birds, only 6 infect humans
  - H1, H2, H3 most common
- Neuraminidase = opens host cells to free new virions
  - All 9 infect birds, only 3 infect humans
  - N1, N2 most common

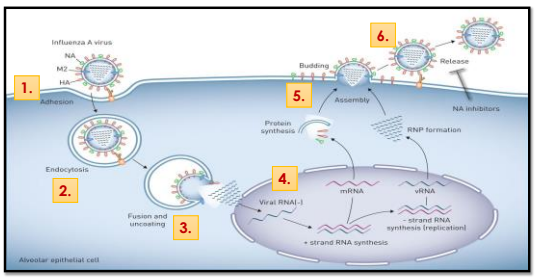
Influenza virus binding to host cell





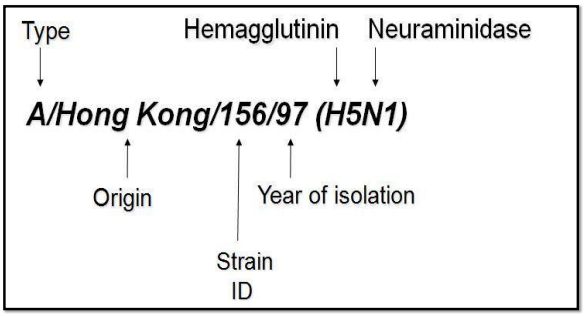
Influenza virus opening host cell to release newly formed virions

Influenza life cycle



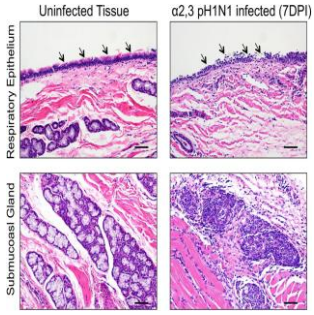
1. HA binds to cell
2. Endocytosis
3. M2 proteins uncoat
4. Viral replication
5. New virus assembled
6. NA buds and releases

Naming influenza strains



Influenza pathology

- Necrosis of epithelial cells
- Severe inflammation in mucosal glands



Influenza pathogenicity

Signs & symptoms

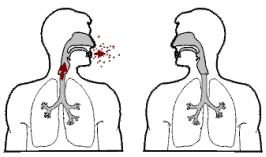
- Fever
- Chills
- Muscle aches
- Cough, congestion
- Runny nose
- Headache
- Fatigue

Complications

- Dehydration
- Pneumonia
- Acute bronchitis
- Sinus infections
- Ear infections
- Worsening of chronic conditions

Transmission

Respiratory droplets

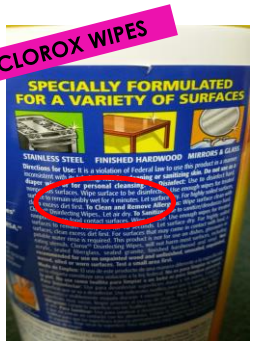


Contaminated surfaces

Why Winter?

- Cold air
- Dry air
- More time indoors
- Crowded conditions
- Decreased immune systems

Disinfecting surfaces



Is it really the flu, or just a cold?

Signs/symptoms	Influenza	Common cold
Onset	Abrupt	Gradual
Fever	Usual, 3-4 days	Rare
Aches, fatigue	Usual, severe	Slight
Chills	Common	Rare
Rhinitis	Common	Common
Sore throat	Sometimes	Common
Cough	Usual, severe	Mild
Headache	Common	Rare

Diagnosis

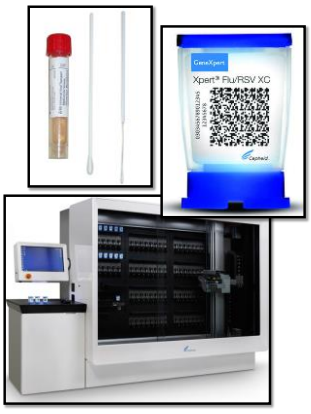
Rapid tests

- Detect viral antigens
- POCT
- Better detection in children than adults
- TAT 10-15 mins

Diagnosis

PCR

- Detect viral RNA
- Best sensitivity and specificity
- Flu/RSV combo
- TAT 30 mins



Prevention

- **Vaccinations are a MUST every year**
  - Unpredictable virus
  - Antibodies form in 2 weeks, remain constant, then gradually decline
  - Immunity from vaccine ~ 1 year
    - All persons 6 months or older should be vaccinated
    - 2nd booster vaccine when necessary
    - High dose shot for elderly

Flu Vaccine

- Available in trivalent and quadrivalent formulations
- 2017-2018 vaccine:
  - A/Michigan/45/2015 (H1N1)pdm09-like virus
  - A/Hong Kong/4801/2014 (H3N2)-like virus
  - B/Brisbane/60/2008-like virus
  - B/Phuket/3073/2013-like virus

trivalent

quadrivalent

Flu Vaccine

2017-2018 Vaccine	**2016-2017 Vaccine**
A/Michigan/45/2015 (H1N1)pdm09-like virus	A/California/7/2009 (H1N1)pdm09-like virus
A/Hong Kong/4801/2014 (H3N2)-like virus	A/Hong Kong/4801/2014 (H3N2)-like virus
B/Brisbane/60/2008-like virus	B/Brisbane/60/2008-like virus
B/Phuket/3073/2013-like virus	B/Phuket/3073/2013-like virus

How Flu Vaccines are made

1) Egg based flu vaccines
   - Grown in chicken eggs
   - 70+ years
2) Cell based flu vaccines
   - Grown in mammalian cells
   - FDA approval August 2016
3) Recombinant flu vaccines
   - Grown in insect eggs
   - Since 2013

How are vaccine viruses selected?

- Year-round surveillance of influenza
- WHO Centers for Reference & Research on Influenza
  - Atlanta, Georgia, USA (Centers for Disease Control and Prevention, CDC)
  - London, United Kingdom (The Francis Crick Institute)
  - Melbourne, Australia (Victoria Infectious Diseases Reference Laboratory)
  - Tokyo, Japan (National Institute for Infectious Diseases)
  - Beijing, China (National Institute for Viral Disease Control and Prevention)

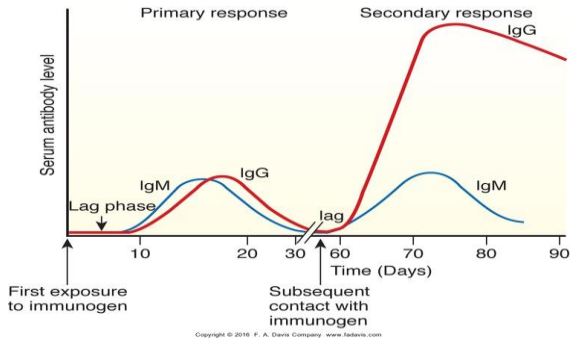
Viral evolution

- Antigenic drift: minor genetic changes to HA/NA antigens
  - Gradual, continuous change over time
  - Lack of proofreading in replication
  - Silent mutations in HA/NA proteins
  - Occurs in A and B virus types
  - Cause of yearly epidemics
  - Cause of infection even after vaccine

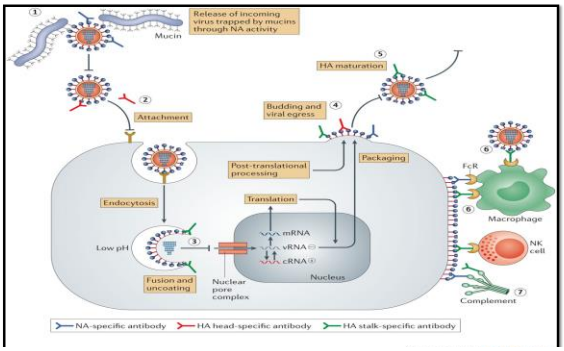
Flu Vaccine options

- Standard-dose shot
- High-dose trivalent shot
- Recombinant trivalent shot
- Trivalent shot w/adjuvant
- Standard-dose quadrivalent shot
- Intradermal quadrivalent shot

Antibody protection



Antibody protection against influenza



CDC recommendations

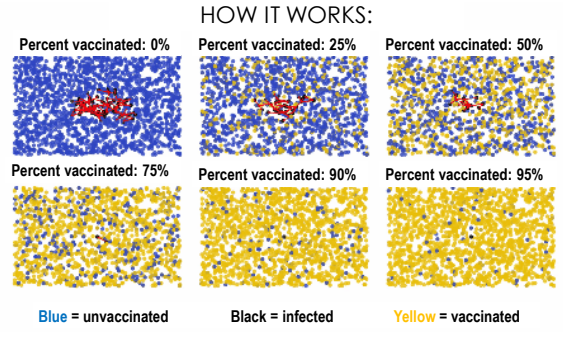
High risk pop.

- Adults over 65
- Children under 2
- Pregnant women
- Nursing home and LTAC residents
- Immuno-compromised persons

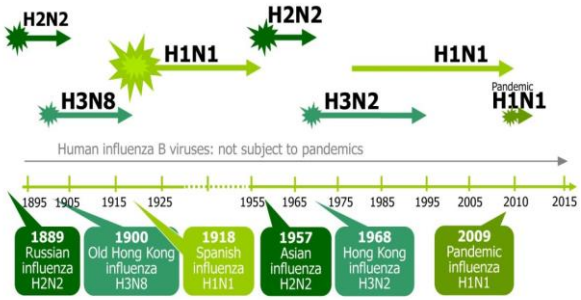
Options

- Only injectable vaccines recommended
- Nasal spray vax is NOT recommended
- Egg-free options
- High dose for elderly
- Generic Tamiflu now available

Herd Immunity



Threat of a future pandemic

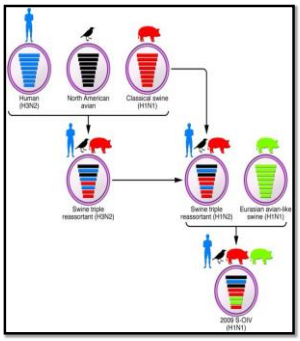


Viral evolution

- Antigenic shift: major change to virus
  - Reassortment of viral genes
  - Sudden change
  - Rapid infection in population
  - Occurs in type A virus only
  - Origin of novel viruses
  - Cause of pandemics
  - Limited to no protection from vaccine

Influenza Virus Reassortment

- How antigenic shift occurs
- Domestic pigs and birds are mixing vessel for new combination of influenza viral genes
- 2009 H1N1 pandemic virus contained avian, swine, and human flu genes



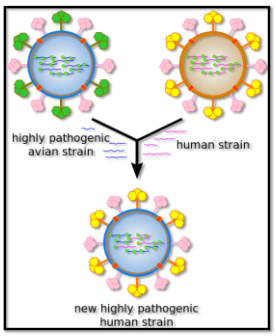
Deadly Avian flu?

H5N1
H7N9

- Highly pathogenic avian influenza (HPAI)
- Wild aquatic waterfowl and domestic poultry are reservoirs for influenza type A
- Genetically different from viruses that cause human infection…for now…

Pandemic potential

- Animal is co-infected with genetically different viruses
- Reassortment occurs
- Novel virus emerges
  - Ability to directly infect humans
  - Human-to-human transmission



Threat of a future pandemic

HPAI Asian H5N1

- Endemic in poultry
- 700 human infections since 2003
- Most cases from direct or close contact with sick or dead poultry
- Person-to-person transmission is rare, limited, and not sustained

- Pandemic potential if genetic reassortment of avian H5N1 and human influenza A

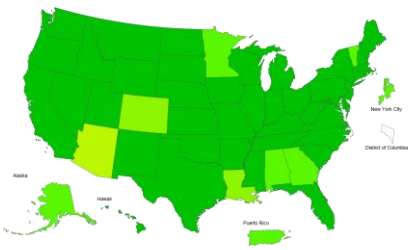
Threat of a future pandemic

HPAI Asian H7N9

- Endemic in poultry in China
- 5th epidemic in China currently
- 1562 human infections since 2013
- Most cases from direct or close contact with sick or dead poultry
- Person-to-person transmission is limited and not sustained

- Greater pandemic potential than H5N1

https://gis.cdc.gov/grasp/fluview/main.html



Additional Info

- WHO Influenza
  http://www.who.int/influenza/en/

- CDC Seasonal Influenza Resource
  https://www.cdc.gov/flu/index.htm

- Louisiana DHH
  http://ldh.louisiana.gov/index.cfm/page/1591

Thank you for listening!

Kristin Butler, MLS (ASCP)^{cm}
Department of Clinical Laboratory Science
School of Allied Health Professions
LSU Health Sciences Center
(318) 813-2919
kbutl1@lsuhsc.edu