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#### Risk factors for infection in older adults include:

- comorbid illness,
- polypharmacy,
- functional status (physical, cognitive, sensory),
- place of residence,
- and individual variations in physiologic changes that accompany age
   (e.g., declining glomerular filtration rate, reduced gag/cough reflexes).

#### **Comorbid Illness**

- The most important cofactor for infection in older adult.
- chronic comorbid conditions (e.g., diabetes mellitus, renal failure, chronic pulmonary disease, edema, immobility).
- These comorbidities most often result in reduced local innate immunity.
- For example, COPD is associated with impaired mucociliary clearance, alveolar macrophage dysfunction, and suppressed cough mechanism, substantially increasing the risk for lower respiratory tract infection in older adults with COPD.

#### **Comorbid Illness**

- comorbid diseases in older adults with infection can also be important predictors for worse outcomes—more important than age itself.
- declining immunity with advancing age (immune senescence)
- there is an underlying waning of immune responses that accompany old age even in the absence of comorbidity; this is called immune senescence.
- both innate and adaptive responses are significantly dysregulated.
- right and physiologic changes that accompany age (e.g., reduced stomach acid, gag/cough reflexes).

The decline in basal temperature and blunted response to pyrogens make it
more likely that an older adult will have a body temperature within the "normal"
range despite infection, and a normal temperature with significant infection
often leads to delayed diagnosis and treatment.

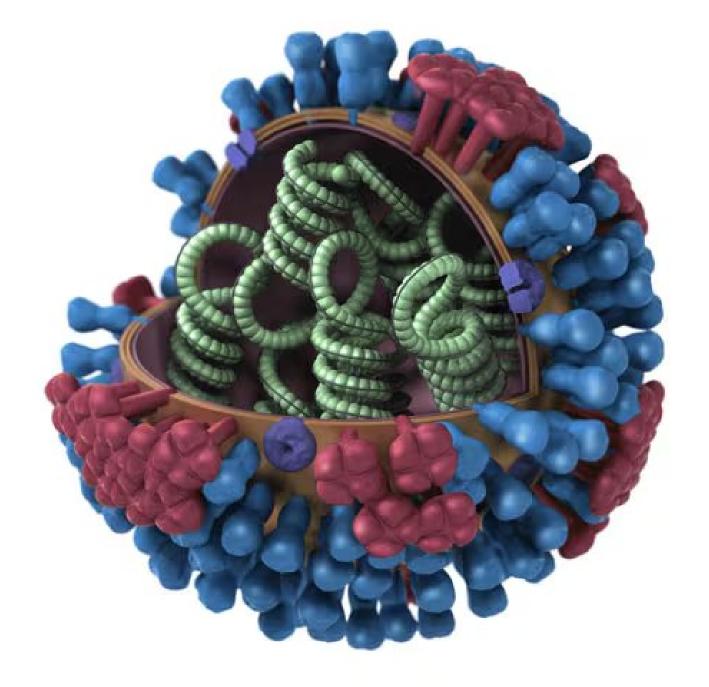
• Cognitive impairment may also contribute to the difficulty of diagnosing infection in older adults, with patients unable to communicate symptoms. This can lead to overdiagnosis, as well when colonization (e.g., asymptomatic bacteriuria) is often assumed to be the cause of nonspecific symptoms.

- Infection, even serious life-threatening infection, frequently presents with atypical features in older adults.
- Serious infections may be signaled by seemingly trivial, nonspecific declines in function or mentation and underlying illness (e.g., congestive heart failure or diabetes mellitus) may be exacerbated by infection, leading older adult patients to seek medical attention for symptoms related to comorbidity rather than infection.

• The most fundamental sign of infection, fever, is absent in up to one-third of older adults with serious infection. Several studies show that frail older adults have lower mean baseline body temperatures than the currently accepted normal of 98.6°F (37°C). Further, temperature increases in response to pyrogens are diminished with advanced age.

- Flu can be serious for everyone—but for adults age 65 years and older, the risk of flu-related complications (including pneumonia) and hospitalization is higher.
- Flu increases the risk of heart attack by 3-5 times and stroke by 2-3 times in the first 2 weeks of infection for those 65+. The risk remains elevated for several months.
- This all adds up to a 6-times higher risk of dying from flu and related complications in age 65 years or older.
- Getting an annual flu vaccine lowers your risk of heart attack and stroke.

- There are four types of influenza viruses: A, B, C, and D. Influenza A and B viruses cause seasonal epidemics of disease in people (known as flu season) almost every winter.
- Influenza A viruses are the only influenza viruses known to cause flu pandemics (i.e., global epidemics of flu disease). A pandemic can occur when a new and different influenza A virus emerges that infects people, has the ability to spread efficiently among people, and against which people have little or no immunity.
- Influenza C virus infections generally cause mild illness and are not thought to cause human epidemics.
- Influenza D viruses primarily affect cattle with spillover to other animals but are not known to infect people to cause illness

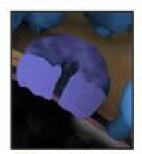




Hemagglutinin



Neuraminidase



M2 Ion Channel

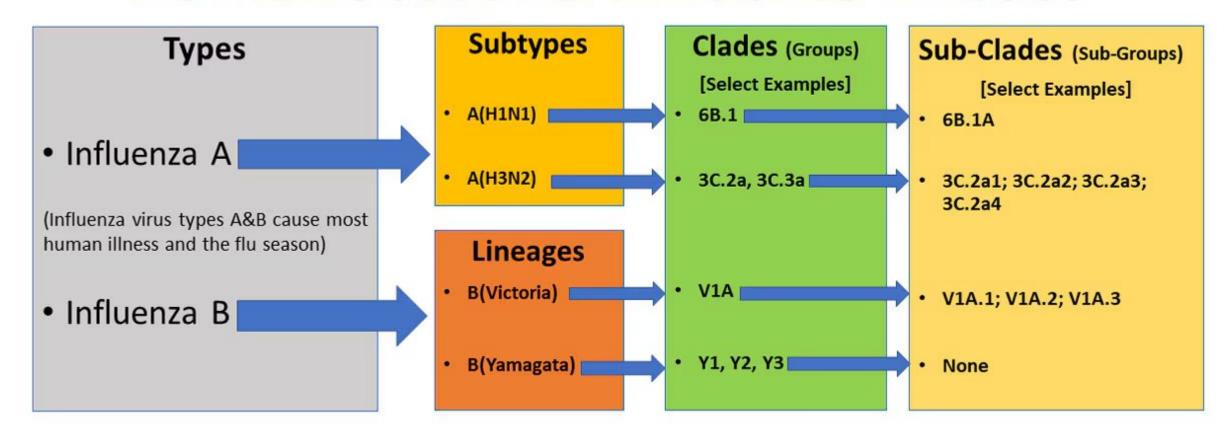


RNP

• Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus: hemagglutinin (H) and neuraminidase (N). There are 18 different hemagglutinin subtypes and 11 different neuraminidase subtypes (H1 through H18 and N1 through N11, respectively). While more than 130 influenza A subtype combinations have been identified in nature, primarily from wild birds, there are potentially many more influenza A subtype combinations given the propensity for virus "reassortment." Reassortment is a process by which influenza viruses swap gene segments. Reassortment can occur when two influenza viruses infect a host at the same time and swap genetic information

• Current subtypes of influenza A viruses that routinely circulate in people include A(H1N1) and A(H3N2). Influenza A virus subtypes and Influenza B virus lineages can be further broken down into different HA genetic "clades" and "sub-clades." See the "Influenza Viruses" graphic below for a visual depiction of these classifications.

# Human Seasonal Influenza Viruses



#### **Symptoms**

- Flu can cause mild to severe illness, and at times can lead to death. Flu symptoms usually come on suddenly. People who have flu often feel some or all of these signs and symptoms:
- fever\* or feeling feverish/chills
- cough
- sore throat
- runny or stuffy nose
- muscle or body aches
- headaches
- fatigue (tiredness)
- some people may have vomiting and diarrhea, though this is more common in children than adults.

#### **Period of Contagiousness**

- You may be able to spread flu to someone else before you know you are sick, as well as when you are sick with symptoms.
- People with flu are most contagious during the first three days of their illness.
- Some otherwise healthy adults may be able to infect others beginning one day before symptoms develop and up to five to seven days after becoming sick.
- Some people, including young children and people with weakened immune systems, may be contagious for longer periods of time.

#### **Onset of Symptoms**

• The time from when a person is exposed and infected with influenza virus to when symptoms begin is about two days but can range from about one to four days.

#### People at risk

 Anyone can get flu (including healthy people), and serious problems related to flu can happen at any age, but some people are at higher risk of developing serious flu-related complications if they get sick. This includes people 65 years and older, people of any age with certain chronic medical conditions (such as asthma, diabetes, or heart disease), people with a body mass index (BMI) of 40 kg/m<sup>2</sup> or higher, pregnant people, and children younger than five years. https://www.cdc.gov/flu/about/index.html

#### **Treatment of Flu**

- If you get sick with flu, flu antiviral drugs may be a treatment option.
- Antiviral drugs can make illness milder and shorten the time you are sick. They might also prevent some flu complications, like pneumonia.
- Flu antiviral drugs work best when started early, ideally within two days after your flu symptoms begin.

 CDC recommends prompt treatment for people who have flu or suspected flu and who are at increased risk of serious flu complications, such as pregnant people, people with asthma and chronic lung disease, diabetes (including gestational diabetes), or heart disease.

#### Who should take antiviral drugs

- It's very important that flu antiviral drugs are started as soon as possible to treat patients who are:
- hospitalized with flu,
- people who are <u>very sick with flu</u> but who do not need to be hospitalized

#### When to seek medical care

- Fever over 102°F for more than 3 days
- Symptoms that last over 10 days and get worse instead of better
- Shortness of breath
- Confusion or disorientation
- Severe or persistent vomiting
- Pain/pressure in your chest

#### Who should take antiviral drugs

- people who are at increased risk of serious flu complications based on their age or underling health conditions, if they develop flu symptoms. For example, people with asthma and chronic lung disease, diabetes, or heart disease are at higher risk, as well as pregnant people.
- Although patients with mild illness who are not at higher risk for flu complications may also be treated with antiviral drugs, most do not need to be.

- Recommended antiviral drugs for this flu season
- There are four FDA-approved antiviral drugs recommended by CDC to treat flu this season.
- oseltamivir phosphate (available as a generic version or under the trade name Tamiflu<sup>®</sup>),
- zanamivir (trade name Relenza<sup>®</sup>),
- peramivir (trade name Rapivab<sup>®</sup>), and
- baloxavir marboxil (trade name Xofluza<sup>®</sup>).

#### **Oseltamivir**

• Generic oseltamivir and Tamiflu® are available as a pill or liquid suspension(6mg/ml 1) and are FDA approved for early treatment of flu in people 14 days and older.



Creatinine Clearance	Treatment Dose	Chemoprophylaxis Dose
>60 ml/min	75 mg bid	75 mg daily
31-60 ml/min	30 mg bid	30 mg daily
11-30 ml/min	30 mg daily	30 mg every other day
≤10 ml/min, not on dialysis	Tamiflu not recommended.	Tamiflu not recommended.
ESRD on hemodialysis (CrCl 10 ml/min or less)	30 mg after every hemodialysis cycle Treatment duration not to exceed 5 days.	30 mg after alternate hemodialysis cycles



#### **XOFLUZA (BALOXAVIR)**

- Only indicated for treatment of uncomplicated influenza A or B virus infection.
- Not recommended by the CDC for outpatients with complicated or progressive illness or hospitalized patients because of the lack of information on use of this antiviral for these groups to date.





- There are no available data on the use of baloxavir for treatment of influenza more than 2 days after illness onset.
- Adults weighing 80 kg or more: 80 mg by mouth as a single dose given within 48 hours of symptom onset.
- Adults weighing 40-79 kg: 40 mg by mouth as a single dose given within 48 hours of symptom onset.

Treatment of acute, uncomplicated influenza caused by influenza A
 or B viruses in adults and adolescents ≥12 years of age who have
 been symptomatic for ≤48 hours, including those who are otherwise
 healthy and those who are at high risk for influenza-related
 complications.



#### RAPIVAB (PERAMIVIR) 200 mg per 20 mL (10 mg/mL)

- IV antiviral indicated for treatment only.
- Can be used as a treatment option for patients who cannot absorb orally or enterally administered oseltamivir.
- For uncomplicated influenza infection: 600 mg IV as a single dose.

- Renally dosed:
  - CrCl 30 to 49 mL/minute: 200 mg IV as single dose.
- Rapivab
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- CrCl 10 to 29 mL/minute: 100 mg IV as single dose.
- Limitation: efficacy based on clinical trials in which the main virus was influenza A. A limited number of patients infected with influenza B were enrolled. Efficacy not established in those with serious infection requiring hospitalization.

**RELENZA (ZANAMIVIR): INHALED ANTIVIRAL** 

Not recommended in those with underlying respiratory disease (i.e. asthma, COPD, etc.). Use with caution in any patient with high-risk underlying medical conditions (e.g., geriatric patients, severe metabolic disease, lung or cardiac disease); safety and efficacy have not been established in these patients.

Usual Adult Dose for Influenza 10 mg via oral inhalation twice a day for 5 days





#### **Antiviral Drug Options**

- For hospitalized patients with suspected or confirmed influenza, initiation of antiviral treatment with oral or enterically administered oseltamivir is recommended as soon as possible.
- For outpatients with complications or progressive disease and suspected or confirmed influenza (e.g., pneumonia, or exacerbation of underlying chronic medical conditions), initiation of antiviral treatment with oral oseltamivir is recommended as soon as possible.

 For outpatients with suspected or confirmed uncomplicated influenza, <u>oral oseltamivir</u>, <u>inhaled zanamivir</u>, <u>intravenous peramivir</u>, <u>or oral baloxavir</u> may be used for treatment, depending upon approved age groups and contraindications.

#### **Self-care measures**

- Rest as much as possible.
- Drink plenty of non-alcoholic fluids.
- Use saline nose drops to loosen mucus.
- Use Ibuprofen (Advil®) or Acetaminophen (Tylenol®) to reduce fever/discomfort according to package instructions. Do NOT take aspirin.

#### **Self-care measures**

- Use nasal decongestant (Oxymetazoline) for short-term relief of nasal congestion (do not use for more than 3 days).
- Gargle with warm salt water and use throat sprays/lozenges (containing Benzocaine) for throat pain.

#### **Preventing spread to others**

- Getting the flu vaccine annually is the best prevention.
- If already sick, stay home and away from others (no classes, sports, group meetings, etc.).
- Wait for temperature to become less than 100°F (without medication) for more than 24-hours before resuming classes, etc.
- Wash hands frequently.
- Contain coughs and sneezes using the crook of your elbow.
- Don't share cups or other personal items.

