# COVID-19 and Influenza: A Fall 2022 Update

Spencer H. Durham, Pharm.D., FCCP, BCPS, BCIDP
Associate Clinical Professor of Pharmacy Practice
Director, Alumni & Professional Affairs
Auburn University Harrison College of Pharmacy

*Advancing Pharmacy for a Healthier Alabama*

# Objectives

- Pharmacist:
  - Review relevant background information about the influenza and COVID-19 viruses
  - Evaluate the 2022-2023 influenza treatment guidelines and identify specific vaccine updates for this season
  - Identify current and potential vaccine and treatment options for COVID-19
- Technician:
  - Review relevant background information about the influenza and COVID-19 viruses
  - Identify current and potential vaccine and treatment options for COVID-19

# Disclosures

- I, Spencer H. Durham, served on a one-time advisory board meeting for TheraTechnologies in November 2021. The relationship has since been mitigated.


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https://www.nfid.org/infectious-diseases/influenza-flu/

# Patient Case

C.P. is a 70-year-old male who presents today to his PCP for an annual physical evaluation. The patient has heard this flu season may be particularly bad, but is reluctant to receive the vaccine.

- PMH: Hypertension, diabetes, depression
- Medications: various
- Allergies: NKDA
- PE:
  - BP 152/90 mmHg
  - HR 80 bpm
  - RR 20 bpm
  - Temp 98.9°F

# Patient Case

- Questions for consideration:
  - Is this patient at an increased risk of complications from the flu?
  - Does this patient meet criteria to receive the flu vaccine?
  - If so, which vaccine product should he receive?

# Influenza

- Highly contagious, RNA respiratory virus spread through droplets
  - Sneezing, coughing, talking
  - Fomites (less common)
- Disease severity varies widely
  - Mild, uncomplicated disease
  - Moderate severity requiring hospitalization
  - Severe, life-threatening disease, sometimes resulting in death
- All age groups affected

# Influenza

- Outbreaks occur on a yearly basis
- Worldwide pandemics can occur less frequently
- Influenza season
  - Occurs when influenza viruses are circulating in the community
  - Usually, September through April in the Northern Hemisphere
  - Typically peaks from December to March
  - Types A and B occur in humans

# Influenza A

- Most common and most virulent of the different types
- Mutates more quickly compared to influenza B
- Affects both animals (birds, swine, etc.) in addition to humans
- Typically implicated in pandemics due to antigenic shift
- Responsible for ~75% of influenza infections during most seasons

# Influenza A

- Divided into subtypes based viral surface proteins
- Hemagglutinin (H) – helps with recognizing and binding to target cells
  - Types 1-18
- Neuraminidase (N) – involved with releasing viral particles from the host cell to infect other cells
  - Types 1-11
- Examples: H1N1, H3N2

# Influenza B

- Not divided into different subtypes
  - Can be identified based on geographic origin and year of isolation
- Mutates more slowly compared to influenza A
- Only infects humans
- Not implicated in pandemics
- Responsible for ~25% of infections during most influenza seasons
  - Variable per season – can be as high as ~50%

# Influenza Variations

- Antigenic *drift*
  - Natural, frequent, and minor mutations cause changes to H and N
    - Results in a new strain and loss of immunity
    - Partially explains why the influenza vaccine efficacy is variable year to year
  - Responsible for the variations in influenza strains seen each season
  - Responsible for influenza epidemics
- Antigenic *shift*
  - Abrupt, major mutations in a virus that results in new H and N proteins
  - Often results when 2 different strains combine to form an entirely new strain
    - Can also occur when a strain that typically infects animals gains the ability to infect humans
      - Example: H1N1 in 2009
  - Only occurs in influenza A
  - Responsible for pandemics

# Clinical Presentation

- Signs/Symptoms
  - Fever
    - >100.4°F sustained for 1 hour
    - ≥101°F as a single temperature
  - Chills
  - Fatigue
  - Muscle/body aches
  - Sore throat
  - Runny nose
  - Headache
  - GI symptoms (more common in pediatric patients)

# Influenza Complications

- Complications:
  - Ear/sinus infections
  - Exacerbations of chronic disease states:
    - Heart failure
    - Diabetes mellitus
    - Asthma
    - COPD
  - Secondary bacterial pneumonia
  - Severe dehydration
  - Respiratory failure
  - Death

# Influenza Complications

- Groups at high risk of complications:
  - ≥50 years of age
  - Children aged 6-59 months
  - Any pediatric patients receiving salicylates
  - Patients with chronic diseases
  - Pregnant women
  - Immunocompromised patients
  - Residents of long-term care facilities
  - BMI ≥40
  - American Indians/Alaska Natives

# Influenza Vaccine

- Annual vaccination is recommended for all individuals aged 6 months and older
  - Children receiving their first vaccine should receive two doses given 1 month apart
- Vaccine efficacy varies from year to year and depends on several factors:
  - Age and overall health of the patient
  - The types of circulating influenza strains (some strains are more virulent than others)
  - How well-matched the strains included in the vaccine are to circulating strains
- Vaccination prevents millions of illnesses and thousands of hospitalizations and deaths
- Even if a vaccinated patient acquires influenza infection, the disease tends to be less severe than if the patient had not been vaccinated



Grohskopf LA, Blanton LH, Ferdinands JM, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the advisory committee on immunization practices — United States, 2022–23 Influenza Season. MMWR Recomm Rep 2022;71(No. RR1):1-28.

# Influenza Vaccine

- Different vaccine formulations are available:
  - Inactivated influenza vaccine (IIV)
    - Egg-based vaccines
      - Standard dose (SD-IIV)
      - High-dose (HD-IIV)
      - Adjuvanted (aIIV)
    - Cell-culture (ccIIV)
      - Standard dose
  - Recombinant influenza vaccine (RIV)
    - Does not contain eggs
  - Live attenuated influenza vaccine (LAIV)



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# Influenza Vaccine

- Vaccines may be trivalent or quadrivalent
  - Trivalent vaccines
    - Contain two strains of type A virus (i.e., H1N1 and H3N2) and one strain of type B
  - Quadrivalent vaccines
    - Same composition as the trivalent, with an additional type B
- All available vaccines during the 2022-2023 season are only available as quadrivalent
  - Only quadrivalent has been used for the last several years
  - Trivalent vaccines could be used in future years



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# Inactivated Influenza Vaccine (IIV)

- Manufactured using viruses that have been killed through either physical or chemical means
  - Most products are manufactured with the propagation of the virus in eggs, but some are cell-culture based
- Stimulates a weaker immune response compared to other formulations
- Contains 15µg of each antigen (SD)
  - 60µg total for quadrivalent
- Multiple different brand products exist



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# High-Dose Vaccine

- Contains 60µg of <u>each</u> antigen
  - 4x amount of antigen in standard-dose vaccine
  - 240µg total in a quadrivalent formulation
- Increased amount of antigen stimulates a more potent immunological response
- This higher immune response may be better for older adults who cannot produce a potent response to the standard dose vaccine
- Specifically indicated for adults ≥65 years of age
  - Studies support greater efficacy compared to standard dose



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# Adjuvant Formulation

- Antigen amount is the same as standard dose
- The ingredient MF59, an oil-in-water emulsion of squalene oil, is added to the vaccine to elicit a stronger immune response
- The adjuvant allows for a stronger immune response without additional antigen, which can allow for greater vaccine supply to be produced
- Specifically approved and recommended for adults ≥65 years of age
  - Studies support increased efficacy compared to standard dose
  - Less evidence than with high-dose formulation



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# Recombinant Influenza Vaccine

- Viral components are used to manufacture the vaccine, but not the virus itself
  - Not manufactured through the use of eggs
- Contains 45µg of each antigen
  - 180µg for quadrivalent
- Approved for use in ≥18 years
- Stronger consideration should be given to use in ≥65 years
  - Studies support increased efficacy compared to standard dose
  - Less evidence than with high-dose formulation



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# Live-Attenuated Influenza Vaccine

- A live virus that has been weakened (attenuated) is used for manufacturing the vaccine
  - Stimulates a potent immune response
- Available only as a nasal spray
- Although a live virus is used, it has been severely weakened and has also been cold-adapted, meaning it cannot survive in most parts of the body
  - Can survive in the nasal passage, so these symptoms may be more pronounced
- Recommended for use in ages 2-49 years
- Not recommended for use in several past seasons, but began to be recommended again starting in the 2018-2019 season
  - Available and recommended in the 2022-2023 season



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# Live-Attenuated Influenza Vaccine

- Should not be used in the following populations:
  - Immunocompromised persons
  - Close contacts or caregivers of immunocompromised persons
  - Persons who have received influenza antiviral medications within the preceding 48 hours
  - Pregnant women
  - Children age 2-4 years with asthma



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# Influenza Vaccine Safety

- Adverse effects:
  - Injection site reactions
    - Soreness
    - Redness
    - Swelling
  - Malaise
  - Fever (uncommon)
  - Allergic reactions (uncommon)



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# Influenza Vaccine Safety

- Contraindications:
  - Severe allergic reactions:
    - Previous vaccines
    - Vaccine components
    - Egg protein
- Precautions:
  - History of Guillain-Barré syndrome
  - Acute illness ± fever
  - Egg allergy (hives only)



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# Influenza Vaccines and Egg Allergies

- Hives only
  - Patients may receive any vaccine recommended for their age without the need for medical monitoring
- Reactions other than hives (angioedema, respiratory distress, etc.):
  - Patients may receive any recommended vaccine
  - Must be administered in an inpatient or outpatient setting by a healthcare provider who can manage severe allergic reactions
- Remember, recombinant vaccines and cell culture-based vaccines are truly egg-free and can be safely used in those with egg allergies



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# Influenza Treatment

- Pharmacotherapy can be used for treatment or chemoprophylaxis
- Treatment must be initiated rapidly upon onset of symptoms and diagnosis to achieve maximal efficacy
- Administer treatment as soon as possible if the patient:
  - Requires hospitalization
  - Has severe, complicated, or progressive illness
  - Is at high risk of complications
- Consider treatment if:
  - High risk of complications with persistent symptoms and a positive flu test >48 hours after symptom onset
  - Patients wishing to shorten illness duration who are within 48 hours of symptom onset
  - Patients in contact with high-risk individuals

# Influenza Treatment

- Oseltamivir
  - 75 mg PO BID for 5 days
- Zanamivir (inhalation)
- Baloxavir
  - 40-80 kg: 40 mg orally once
  - >80 kg: 80 mg orally once
- Peramavir
  - One-time intravenous dose

# 2022-2023 Influenza Season

- Predictions for seasonal influenza in the US is based on the preceding season in the Southern Hemisphere (Australia and New Zealand)
  - Season runs ~April-October, but usually peaks in summer
- The recent season in Australia was the worst in 5 years
  - Began ~2 months earlier than average
  - Cases peaked 3x higher than average
  - Population as a whole likely has lower immunity to influenza due to effects from the COVID-19 pandemic
    - Masking, social distancing

# 2022-2023 Influenza Season

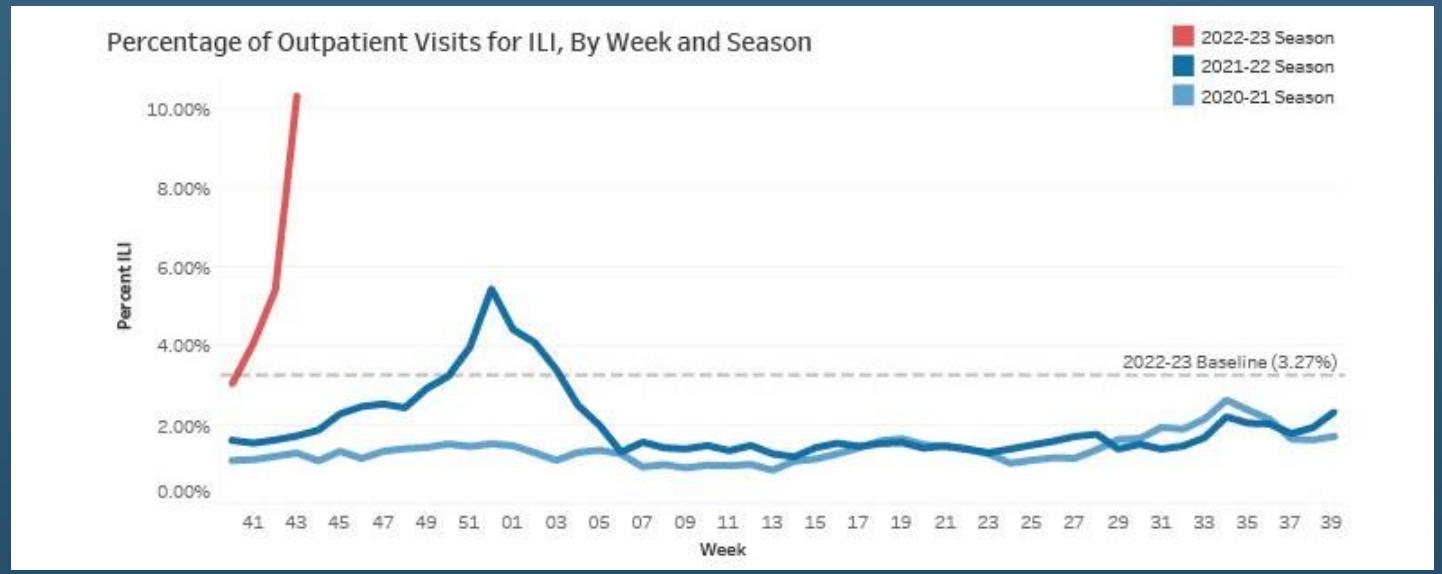
- United States (as of 11/3/22):
  - Influenza activity started earlier than usual and continues to increase
  - First pediatric death due to influenza was reported this week
  - Influenza statistics at this point in the season:
    - At least 880,000 flu illnesses
    - 6,900 hospitalizations
    - 360 deaths
  - Currently, the cumulative hospitalization rate in the FluSurv-NET system is higher than the rate observed in previous seasons since the 2010-2011 season



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

# 2022-2023 Influenza Season

- Alabama (as of 11/3/22):
  - Statewide influenza-like illness (ILI) is 10.34%
    - Increased since last week
    - Highest ILI at this point in the season since the H1N1 pandemic in 2009
  - All districts have had laboratory-confirmed cases during the last 3 weeks



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# 2022-2023 Influenza Guidelines

- Most recommends from previous seasons remain in place and unchanged
- One major new recommendation:
  - Adults ≥65 years of age should preferentially receive one of the following vaccines over the SD-IIV:
    - HD-IIV
    - aIIV
    - RIV
  - Change is based on several studies which show higher benefit in this population for these vaccines compared to SD-IIV
  - HD-IIV has the most evidence of the three recommended formulations



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# COVID-19

# Disclaimer

- This presentation is meant to provide highlights of recent information related to COVID-19
- Information is still changing at a rapid pace
- Several resources are available for the most up-to-date information:
  - CDC website
  - WHO website
  - ACIP
  - NIH guidelines
  - IDSA guidelines

# COVID-19 Statistics 11/03/2022

- World Health Organization:
  - 636,809,258 people diagnosed worldwide
  - 6,601,489 deaths
- Centers for Disease Control and Prevention:
  - 97,604,763 cases in the United States
  - 1,068,667 deaths
  - 20,829 current hospitalizations
- Perspective:
  - MERS: ~2519 cases worldwide since 2012 (~866 deaths)
  - SARS: ~8098 cases in 2003 (~773 deaths)

https://www.worldometers.info/coronavirus/
https://covid.cdc.gov/covid-data-tracker/#datatracker-home
http://www.emro.who.int/health-topics/mers-cov/mers-outbreaks.html
https://www.cdc.gov/sars/about/faq.html

# COVID-19 in Alabama

- Information as of 11/03/2022:
  - 1,534,287 diagnosed cases
  - 20,558 deaths
  - Percent total positivity rate is currently 4.6%
    - Goal is <5% for adequate control of the pandemic



https://www.alabamapublichealth.gov/covid19/

# Introduction

- Anyone can be infected with SARS-CoV-2 and anyone can develop severe COVID-19
  - Certain groups are more likely to experience severe disease:
- In United States – minorities are more likely to experience COVID-19-related hospitalization and death
- Variants continue to emerge – complicates ability to prevent and treat the infection
- Not just a lung disease – leads to complications involving the heart, skin, blood system, liver, CNS, kidneys, and other areas

# COVID-19 disease

- Certain group of individuals are at higher risk of severe disease:
  - Age ≥65 years
  - Obesity
  - Pregnancy
  - Chronic kidney disease
  - Diabetes
  - Immunosuppression
  - Heart disease
  - Chronic lung disease
  - Sickle cell disease
  - Neurodevelopmental disorders (ex: cerebral palsy)
  - Medical device placement (tracheostomy, gastrostomy, etc.)



https://combatcovid.hhs.gov/i-have-covid-19/how-do-i-know-if-im-high-risk

# COVID-19 Complications

- Many potential complications, both short-term and long-term, have been associated with COVID-19 infection
- Short-term complications
  - Extreme exhaustion
  - Confusion/delirium
  - Blood clots
  - Respiratory failure
  - Organ failure



https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html

# COVID-19 Long-term Complications

- Post-COVID conditions occur 4 or more weeks after initial infection
- Symptoms can last weeks or months
- Long-term symptoms can be different than what was experienced in the initial infection
- Patients with very mild symptoms at initial infection can experience long-term complications
- Different terms are used to describe the long-term effects:
  - Long COVID
  - Long-haul COVID
  - Post-acute COVID-19
  - Chronic COVID



https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html#:~:text=Some%20people%20who%20had%20severe,%2C%20skin%2C%20and%20brain%20functions.

# Long COVID Symptoms

- Difficulty breathing/shortness of breath
- Tiredness/fatigue
- Post-exertional malaise
- “Brain Fog” - difficulty thinking or concentrating
- Chronic cough
- Chest or stomach pain
- Headache
- Heart palpitations
- Joint or muscle pain
- Pins-and-needles feeling
- Diarrhea
- Sleep disturbances
- Fever
- Lightheadedness
- Rash
- Mood changes
- Chronic changes in smell or taste
- Changes in menstrual period cycles



https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html#:~:text=Some%20people%20who%20had%20severe,%2C%20skin%2C%20and%20brain%20functions.

# COVID-19 Long-term Complications

- Long COVID treatment & prevention
  - There is no clear reason why some patients experience long-COVID and others do not
    - Nothing specific can be done to prevent long COVID once some is infected with COVID
  - Prevention of COVID itself is key
    - Social distancing, mask, etc.
    - Vaccines!
  - In some patients, symptoms of long COVID seemed to improve after vaccination
    - Currently being studied
    - If not already vaccinated, patients should be encouraged to receive the vaccine after acute infection has resolved



https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html#:~:text=Some%20people%20who%20had%20severe,%2C%20skin%2C%20and%20brain%20functions.

# COVID in 2022

- Has Omicron resulted in COVID becoming endemic?
  - No standard definition of when “endemic” occurs
- What does endemic really mean?
  - Occurs when an infectious disease occurs at a low level at all or most times throughout the year
  - Considered manageable
  - Many other coronaviruses and other respiratory viruses are considered endemic

# COVID Vaccines

- Four different vaccines available in the US:
  - mRNA vaccines
    - Pfizer
    - Moderna
  - Protein subunit vaccine (adjuvanted)
    - Novavax
  - Adenovirus vector
    - Johnson & Johnson
- Monovalent and bivalent vaccines
  - Monovalent contains the original strain of COVID that started the pandemic
  - Bivalent contains both the original strain and Omicron variant



https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

# Vaccine Recommendations

- COVID vaccination is recommended for everyone age 6 months and older
  - No vaccine has been studied in infants <6 months
- Primary series
  - Monovalent vaccine of Pfizer, Moderna, or Novavax
    - All require 2 doses
  - Same vaccine product should be used for both doses of the primary series
- Booster
  - mRNA vaccine recommended
  - 1 bivalent booster dose is recommended after the primary series
    - Novavax monovalent booster may be substituted if mRNA vaccine is contraindicated

# Vaccine Recommendations

- Johnson & Johnson vaccine is not generally recommended for use except in certain situations
  - Increased risk of thrombosis with thrombocytopenia syndrome (TTS)
  - Only use in those patients who cannot or will not receive other COVID vaccine products
- Consult the CDC website or ACIP for the most up-to-date recommendations as they continue to be updated as new information is available

# Treatment Options

- Bebtelovimab
  - Monoclonal antibody that retains activity against omicron variant
  - Consider use in high-risk outpatients with mild/moderate disease COVID-19 within 7 days of symptom onset AND for whom alternative therapies are not accessible or clinically appropriate
  - Not appropriate for those requiring oxygen support
- Tixagevimab/cilgavimab
  - Long-acting monoclonal antibody
  - Pre-exposure prophylaxis in immunocompromised patients unable to develop vaccine immunity

# Treatment Options

- Nirmatrelvir/ritonavir
  - Oral option for high-risk patients with mild/moderate disease not requiring supplemental oxygen and within 5 days of symptom onset
  - Must consider drug-drug interactions and adherence
    - Requires 2 nirmatrelvir tablets plus 1 ritonavir tablet BID
- Molnupiravir
  - Oral option for high-risk adults with mild/moderate disease within 5 days of symptom onset AND where other therapies are not appropriate or accessible
    - Should generally be reserved for last-line use
  - No renal/hepatic adjustments or clinically significant drug-drug interactions
  - Requires 4 capsules BID
  - Concerns for reproductive harm in both males and females
    - Contraception should be used for 4 days after last dose in females but 3 months in males

# QUESTIONS???