Overview of Viral Infections

- A virus is composed of nucleic acid, either DNA or RNA, surrounded by a protein coat.
- It requires a living cell in which to multiply.
- A viral infection can lead to a spectrum of symptoms from asymptomatic (no overt symptoms) to severe disease.
- People may get viruses by swallowing or inhaling them, by being bitten by insects, or through sexual contact.
- Most commonly, viral infections involve the nose, throat, and upper airways, or systems such as the nervous, gastrointestinal, and reproductive systems.
- Doctors may base the diagnosis on symptoms, blood tests and cultures, or examination of infected tissues.
- Antiviral drugs may interfere with the reproduction of viruses or strengthen the immune response to the viral infection.

- A virus is a small infectious organism—much smaller than a fungus or bacterium—that must invade a living cell to reproduce (replicate).

- The virus attaches to a cell (called the host cell), enters the cell, and releases its DNA or RNA inside the cell.

- The virus's DNA or RNA is the genetic material containing the information needed to make copies of (replicate) the virus.

- The virus's genetic material takes control of the cell and forces it to replicate the virus.

- The infected cell usually dies because the virus keeps it from performing its normal functions.

- When it dies, the cell releases new viruses, which go on to infect other cells.

- Viruses are classified as DNA viruses or RNA viruses, depending on whether they use DNA or RNA to replicate.

- DNA viruses include herpesviruses.
- RNA viruses include retroviruses, such as HIV (human immunodeficiency virus), and coronaviruses, such as SARS-CoV2 that causes COVID-19.

- RNA viruses, particularly retroviruses, are prone to mutate, meaning the set of genetic instructions that contain all the information that the virus needs to function can change as the virus spreads.

- Some viruses do not kill the cells they infect but instead alter the cell's functions.

- Sometimes the infected cell loses control over normal cell division and becomes cancerous.

- Some viruses, such as hepatitis B virus and hepatitis C virus, can cause chronic infections. Chronic hepatitis can last for years, even decades. In many people, chronic hepatitis is quite mild and causes little liver damage. However, in some people, it eventually results in cirrhosis (severe scarring of the liver), liver failure, and sometimes liver cancer.

Types of viral infections

Probably the most common viral infections are

- Respiratory infections: Infections of the nose, throat, upper airways, and lungs

→The most common respiratory infections are upper respiratory infections, which include sore throat, sinusitis, and the common cold.

→Other viral respiratory infections include influenza, pneumonia, and coronaviruses.

→In small children, viruses also commonly cause croup (which is inflammation of the upper and lower airways, called laryngotracheobronchitis) or lower airways (bronchiolitis).

→Respiratory infections are more likely to cause severe symptoms in infants, older people, and people with a lung or heart disorder.

Other viruses infect other specific parts of the body:

Gastrointestinal tract: Infections of the gastrointestinal tract, such as gastroenteritis, are commonly caused by viruses, such as noroviruses and rotaviruses.

Liver: These infections result in hepatitis.

Nervous system: Some viruses, such as the rabies virus and the West Nile virus, infect the brain, causing encephalitis. Others infect the layers of tissue that cover the brain and spinal cord (meninges), causing meningitis or polio.

Skin: Viral infections that affect only the skin sometimes result in warts or other blemishes. Many viruses that affect other parts of the body, such as chickenpox, also cause a rash.

Placenta and fetus: Some viruses, such as the Zika virus, the rubella virus, and cytomegalovirus, can infect the placenta and fetus in pregnant women.

- Some viruses typically affect many body systems. Such viruses include enteroviruses (such as coxsackieviruses and echoviruses) and cytomegaloviruses.

Spread of viruses

Viruses are spread (transmitted) in various ways.

They may be:

- ✓ Swallowed
- ✓ Inhaled
- ✓ Spread by the bites of insects, such as mosquitoes, certain biting flies, or ticks
- ✓ Spread sexually (in sexually transmitted infections)
- ✓ Spread during transfusion of contaminated blood

- ❖ New human viruses sometimes develop from viruses that usually affect animals (for example, SARS-CoV and SARS-CoV2).

- ❖ This happens when the infected animal host comes into close contact with susceptible humans.

Viruses and cancer

- Some viruses alter the DNA of their host cells in a way that helps cancer develop. Some viruses, such as herpesviruses and HIV, leave their genetic material in the host cell, where the material remains dormant for an extended time (called latent infection). When the cell is disturbed, the virus may begin replicating again and cause disease.

- Only a few viruses are known to cause cancer, but there may be others.

Viruses and Cancer: A Link

Virus	Cancer
Epstein-Barr virus	Burkitt lymphoma Certain nose and throat cancers Hodgkin lymphoma B-cell lymphomas in people with a weakened immune system (such as those with AIDS)
Hepatitis B virus and hepatitis C virus	Liver cancer
Herpesvirus 8	In people with AIDS, Kaposi sarcoma and non-Hodgkin lymphoma
Human immunodeficiency virus (HIV)	Kaposi sarcoma, aggressive B-cell non-Hodgkin lymphoma, and cervical cancer
Human papillomavirus (HPV)	Cervical cancer, cancer of the penis, vaginal cancer, anal cancer, mouth and throat cancer, and esophageal cancer

MSD

Diagnosis of Viral Infections

- Clinical evaluation.
- For infections that occur in epidemics, the presence of other similar cases.
- For some infections, blood tests and cultures
- For infections that occur in epidemics (such as influenza), the presence of other similar cases may help doctors identify a particular infection.
- Laboratory diagnosis is important for distinguishing between different viruses that cause similar symptoms, such as COVID-19 (SARS-CoV2) and influenza.
- For other infections, blood tests and cultures (growing microorganisms in the laboratory from samples of blood, body fluid, or other material taken from an infected area) may be done.

➢ **Polymerase chain reaction (PCR)** techniques may be used to make many copies of the viral genetic material. PCR techniques make it easier for doctors to rapidly and accurately identify the virus.

➢ Blood may also be tested for **antigens**, which are proteins on or in viruses that trigger the body's defense. Blood may also be tested for **antibodies** to viruses.

- A sample of blood or other tissues is sometimes examined with an electron microscope, which provides high magnification with clear resolution….special immunostaining .

Prevention of Viral Infections

- ❑General preventive measures…public health
- ❑Vaccines
- ❑Immune globulins

Viral vaccines in general use include the following:

- ✓ COVID-19
- ✓ Hepatitis A
- ✓ Hepatitis B
- ✓ Human papillomavirus (HPV)
- ✓ Influenza
- ✓ Japanese encephalitis (inflammation of the brain)
- ✓ Measles, mumps, and rubella
- ✓ Polio
- ✓ Rabies
- ✓ Rotavirus
- ✓ Varicella
- ✓ Shingles (herpes zoster)
- ✓ Yellow fever

Immune globulins

- Immune globulins are a sterilized solution of antibodies (also called immunoglobulins) collected from the blood of a group of people. Immune globulins are given directly to a person (called passive immunization).

- Immunoglobulins can be collected from the blood of the following:

- People who are generally healthy (these immunoglobulins are called pooled human immunoglobulin)

- People who have many antibodies that defend against a specific infectious organism, often because they have been infected with that organism (these immunoglobulins are called hyperimmune globulin)

- Hyperimmune globulin is available for only a few infectious diseases, such as hepatitis B, rabies, tetanus, and chickenpox. It is usually given after people have been exposed to a microorganism but before they get sick. For example, people who have been bitten by an animal that might have rabies are immediately given rabies hyperimmune globulin.

Immune globulins are given by injection into a muscle or into a vein.
→The immunity provided by immune globulins lasts for only a few days or weeks, until the body eliminates the injected antibodies.

*Sometimes, such as when people are exposed to rabies or hepatitis B, they are given both immune globulin and a vaccine to help prevent infection from developing or reduce the severity of infection.

Immune globulins may also help treat some infections. For example, they may be given to people whose immune system does not respond adequately to an infection.

Treatment of Viral Infections

- ❑ Treatment of symptoms
- ❑ Sometimes antiviral drugs
- ❑ Antibodies

Treatment of symptoms

- There are no specific treatments for many viruses. However, many things can help relieve certain symptoms, such as the following:

- **Dehydration**: Plenty of fluids, sometimes given by vein (intravenously)
- **Diarrhea**: Sometimes an antidiarrheal drug, such as loperamide
- **Fever and aches**: Acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs)
- **Nausea and vomiting**: A clear-liquid diet and sometimes an antiemetic (antinausea) drug, such as ondansetron
- **Some rashes:** Soothing or moisturizing creams and sometimes an antihistamine taken by mouth for itching
- **A runny nose**: Sometimes nasal decongestants, such as phenylephrine or phenylpropanolamine
- **A sore throat**: Sometimes throat-numbing lozenges containing benzocaine or dyclonine
- Not everyone who has these symptoms needs treatment.
- If symptoms are mild, it may be better to wait for them to go away on their own.

Antiviral drugs:

Drugs that combat viral infections are called antiviral drugs.
There are no effective antiviral drugs for many viral infections.
However, there are several drugs for influenza, many drugs for infection by one or more herpesviruses , and many new antiviral drugs for treatment of HIV , hepatitis C, hepatitis B, and Ebola.

→Many antiviral drugs work by interfering with replication of viruses.

Most drugs used to treat HIV infection work this way. Because viruses are tiny and replicate inside cells using the cells' own metabolic functions, there are only a limited number of metabolic functions that antiviral drugs can target.

In contrast, bacteria are relatively large organisms, commonly reproduce by themselves outside of cells, and have many metabolic functions that antibacterial drugs (antibiotics) can target.

Therefore, antiviral drugs are much more difficult to develop than antibiotics.

Also, unlike antibiotics, which are usually effective against many different species of bacteria, most antiviral drugs are usually effective against only one (or a very few) viruses.

Antibodies:

from the blood of a person who has recovered from the viral infection (convalescent serum) and antibodies that are produced in a laboratory from living cells that have been altered to produce the desired antibodies (monoclonal antibodies) are used to treat some viral infections including:

- ✓ COVID-19
- ✓ Ebola

Chickenpox and Herpes Zoster (Varicella-Zoster Virus)

DEFINITION

• Varicella-zoster virus (VZV) is an alpha herpesvirus that causes chickenpox and herpes zoster.

EPIDEMIOLOGY

• Chickenpox is the primary infection occurring primarily in childhood.

• Chickenpox is usually a benign infection but can cause life-threatening disease in the immunocompromised host.

• Disease is more likely to occur in late winter and early spring.

• Herpes zoster is the consequence of reactivation of latent virus, occurring mainly in the elderly.

• Herpes zoster causes significant pain in many individuals.

• There is no seasonal predilection for occurrence of herpes zoster.

MICROBIOLOGY

• Varicella-zoster virus is a double-stranded DNA virus. Following primary infection, latency is established in sensory ganglia.

DIAGNOSIS

• The diagnosis of chickenpox and herpes zoster is usually clinical.

• Chickenpox is characterized by a maculopapular, vesicular, and papular rash in all stages of evolution.

• Herpes zoster is usually a unilateral vesicular rash. Dissemination can occur in immunocompromised patients.

• Tzanck smears of lesion scrapings may demonstrate intranuclear inclusions; however, the sensitivity is low.

• Polymerase chain reaction (PCR) can be applied to lesion scraping in order to detect VZV DNA and is the diagnostic procedure of choice.

• Viral culture can be used to make a diagnosis, but it is less sensitive than PCR.

THERAPY

- Three drugs are licensed for the treatment of VZV infections.

• Chickenpox in children 2 to 16 years of age can be treated with acyclovir at a dosage of 20 mg/kg 4 times per day for 5 days. For older patients, the dosage of acyclovir is 800 mg 5 times a day.

• By class effect, the prodrugs valacyclovir and famciclovir are used by some experts to treat chickenpox.

• Herpes zoster can be treated with acyclovir at 800 mg five times daily for 7 to 10 days.
• Herpes zoster can be treated with valacyclovir at 1 g three times daily for 7 to 10 days.
• Herpes zoster can be treated with famciclovir at 500 mg three times daily for 7 to 10 days.
• Herpes zoster will likely require control of pain with analgesics and medications such as pregabalin.

PREVENTION

• High-titered varicella-zoster immune globulin (VariZIG) can be administered to high-risk patients to attempt to prevent infection.

• A VZV vaccine is available to prevent chickenpox.

- It is a two-dose series with the first administered at 12 to 15 months of age and the second between 4 and 6 years.

- This two-dose series has dramatically decreased the incidence of chickenpox and its associated complications.

• A high-titered VZV vaccine is available for adults older than 50 years of age that will reduce the incidence of herpes zoster, the burden of illness, and postherpetic neuralgia.

Epstein-Barr Virus (Infectious Mononucleosis, Epstein-Barr Virus–Associated Malignant Diseases, and Other Diseases)

DEFINITION

• Infectious mononucleosis is a clinical syndrome characterized by pharyngitis, fever, lymphadenopathy, and the presence of atypical lymphocytes on a peripheral blood smear.

Primary Epstein-Barr virus (EBV) infection is the most common cause of this syndrome.

VIROLOGY AND EPIDEMIOLOGY

• EBV is a ***herpesvirus*** that establishes lifelong latent infection in B lymphocytes.

• Replication occurs in oral epithelium, and infectious EBV is frequently present in the saliva of asymptomatic seropositive individuals.

• EBV is transmitted predominantly through exposure to infected saliva, frequently as a result of kissing.

• Seroprevalence approaches 95% in adults, and EBV is distributed throughout the world.

• In childhood, primary EBV infection is usually asymptomatic or a nonspecific illness.

• Frequency of presentation as infectious mononucleosis increases with age to about 50% of primary infections by adolescence.

• EBV is tightly linked with several malignancies, including endemic Burkitt's lymphoma, nasopharyngeal carcinoma, and lymphoproliferative disease.

MICROBIOLOGY:

- EBV is a gamma-1 herpesvirus, genus Lymphocryptoviral.
- EBV is a double-stranded DNA virus that is enveloped.
- EBV is also known as human herpesvirus 4.

CLINICAL MANIFESTATIONS:

- Infectious mononucleosis is generally a self-limited, spontaneously remitting syndrome.

- Complications may occur, including splenic rupture, neurologic manifestations such as encephalitis, autoimmune hemolytic anemia, and mild hepatocellular enzyme elevations.

DIAGNOSIS:

• The appearance of nonspecific, heterophile antibodies (IgM reacting with sheep or horse red blood cells) can distinguish primary EBV infection from other causes of infectious mononucleosis.

• The presence of IgM viral capsid antigen (VCA) antibodies is closely correlated with acute EBV infection.

• Heterophile antibodies in a person with clinical infectious mononucleosis is sufficient to establish the diagnosis.

• EBV serology may be helpful in atypical cases and in children (who are frequently heterophile negative).
• Primary human immunodeficiency virus infection is the most important differential diagnostic consideration.
• Serial measurement of EBV viral loads may be useful in the detection of EBV-associated malignancies in immunosuppressed individuals, especially for lymphoproliferative disease.

THERAPY

- Treatment of mononucleosis is primarily supportive.

- Corticosteroids may be helpful in managing mononucleosis complications such as airway impingement from tonsillar enlargement.

- Antiviral therapy is of no proven benefit in infectious mononucleosis.

PREVENTION

- There is currently no EBV vaccine.

Coronaviruses, Including Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS)

DEFINITION

- The coronaviruses (CoVs) commonly cause mild but occasionally more severe community acquired acute respiratory infections in humans.
- CoVs also infect a wide variety of animals, and several CoVs (e.g., severe acute respiratory syndrome [SARS], Middle East respiratory syndrome [MERS]) have crossed the species barrier, producing outbreaks of severe respiratory disease. As of January 23, 2015, 956 cases of laboratory-confirmed MERS were reported to the World Health Organization, with 351 deaths.

EPIDEMIOLOGY

- Community-acquired CoV infections cause about 15% of common colds.
- They are typically epidemic in the winter months.
- MERS has occurred in patients in the Arabian Peninsula and those who recently traveled from this locale.

MICROBIOLOGY

• CoVs are members of the Nidovirales order, single-stranded, positive-sense RNA viruses with a large genome.

- They mutate and also recombine frequently.

DIAGNOSIS

• Laboratory diagnosis is best accomplished by finding viral RNA through polymerase chain reaction

THERAPY

• There are no accepted effective antiviral drugs for CoVs.

PREVENTION

• Prevention is through epidemiologic methods. The SARS epidemic was halted through careful case finding, quarantine, and use of barrier precautions.

Coronavirus COVID-19 (SARS-CoV-2)

MICROBIOLOGY

Coronaviruses , Positive sense, single-stranded enveloped RNA virus belongs to the family Coronaviridae.

Coronavirus name is derived from the Latin corona, meaning crown.

The viral envelope under electron microscopy appears crown-like due to small bulbar projections formed by the viral spike (S) peplomers.

Neutralizing antibodies against the S-protein are believed to play an important role in protective immunity.

CLINICAL

COVID-19 (novel COronaVirus Disease-2019) is the disease, SARS-CoV-2 is the virus.

Epidemiology

COVID-19 cases

Ongoing pandemic, declared by the WHO. It is unlikely this virus will disappear and likely become part of the repertoire of respiratory viruses that infect humans regularly.

World	Coronavirus Cases: 649,523,351	Deaths: 6,645,542
Jordan	Coronavirus Cases: 1,746,997	Deaths: 14,122

Despite global vaccination efforts and mitigation strategies, including facial masks and social distancing, vaccination, and therapies, millions of cases may be occurring worldwide, many now not documented, including among immunized populations, which allows for continued opportunities for the emergence of variants with immune evasiveness features.

Omicron appears at least more transmissible than Delta and the Delta variant and is 50-70% more transmissible than earlier variants, including Alpha.BA.5 sub lineage variant of Omicron is predominant in the US, estimated to have a R^o 18.6, which approaches measles contagiousness and appears to have the most evasion of preexisting immunity.

BA.4.6 represent a smaller but growing proportion of variants detected in the U.S. Severe infections remain more prevalent in the unimmunized with risk factors and people with poor vaccine responses.

Risks (per CDC):
Comorbidities (alphabetical order): age ≥ 50 years, cancer, chronic kidney disease, COPD, chronic lung disease, dementia or other neurological conditions, diabetes (types 1 and 2), Down syndrome, HIV, immunocompromised people, mental health conditions (depression, schizophrenia), BMI ≥ 25 (so overweight or obesity), pregnancy, sickle cell or thalassemia, smoking (current or former), solid organ or blood stem cell transplant, stroke/CVA, substance use disorders, active TB.

Multiple comorbidities are additive in risk.

Children/Teens: generally at less risk for severe illness; however, underlying medical problems, if present, elevate risk.

Younger adults are also hospitalized in the U.S., reflecting increasing percentages in many states.
These cases in the later phases of the pandemic account for an increasing percentage of cases.
Children < 1 yr at high risk for severe illness
Children 1–10 yrs: low risk of disease and transmission
Children 10–18 yrs: higher risk of disease compared to 1–10 yr group; however, some studies show a higher risk of transmission than adults.
People in congregate settings with disabilities or chronic health problems have worse outcomes and face barriers to care.

Transmission

- Through respiratory droplets, aerosolization is possible (especially indoors/prolonged exposure, areas with poor ventilation).
- Acquisition from fomites is likely uncommon.
- Virus are found in respiratory secretions and saliva.
- Spread from a fomite, the risk is considered very low.
- Viral shedding by asymptomatic people may represent a subset of total infections, though some uncertainty remains regarding how much they contribute to totals.
- Viral shedding may antedate symptoms, usually two days.
- Viral titers are highest in the earliest phases of infection, 1-2 days before the onset of symptoms, and then in the first 4-6 days of illness in patients without immunosuppression.

Incubation period and viral shedding, isolation, quarantine or airborne isolation

- Mean incubation with Omicron is 4.3 days, median 3-4d, range 2–14d.

- Quarantine and Isolation: some local health departments and institutions may vary from CDC guidance.

- Isolation: a term used if SARS-CoV-2 is infected with or without symptoms.
- If tested positive (antigen or PCR) regardless of vaccine status: isolate at home and from others x 5d.
- End isolation after 5 full days if fever-free and not using antipyretics and symptoms improve.
- If severely ill or immunocompromised: isolate x 10d and consult your clinician before ending isolation.
- Wear a mask for 10 days inside your home and in public.
- Note by author: growing evidence that with the latest Omicron sublineage variants (BA.5), some people with immunity may yield infectious virus through days 10-14, longer if severely immunosuppressed.
- Avoid being around people who are at high risk.

Quarantine: a term if potentially exposed.

Quarantine is no longer advised by CDC (Aug 2022) if entirely up to date on immunization.

If exposed (close contact defined as < 6ft from infected person x 15 minutes cumulatively over 24 h) and either unimmunized or not up-to-date (including recommended boosters):
stay home x 5d [the quarantine], wear a well-fitted mask if you cannot be away from others, do not travel, and get tested at least 5d after close contact.
Watch for symptoms x 10d and avoid travel
If you develop symptoms, isolate and get tested
Wear a mask for a full 10 days.
Avoid being around people at high risk
No travel, regardless of immunized status, is recommended x 10 days.
Watch for COVID-19 symptoms x 10 days.

Viral shedding as an infectious risk Occurs following recovery but does not appear to play a role in transmission in relatively healthy people >10d following the onset of infection (though some variants may be infectious longer, viral RNA may be detected long after for many weeks; hence, why repeated routine testing for negative SARS-CoV-2 RT-PCR not recommended).

It may not be so short for ill hospitalized patients or those with health problems, but 20-28d is a conservative stance used by some hospitals to remove airborne precautions rather than the two negative nucleic acid amplification tests (NAAT) rule.

Rare reports of cultivatable virus > 60 days, especially in severely immunocompromised patients:
A **low cycle threshold (CT),** e.g., < 30 and usually < 25 may indicate an infectious virus is present.
However, difficult to compare results when different testing platforms are used.
Some accumulating data suggest that high viral inoculum may lead to an increased risk for disease severity.

Symptoms (in the unimmunized): note symptoms of Omicron infection may be milder, resembling a URTI, in both immunized and unimmunized but still capable of producing a severe infection.

Most common

- Fever
- Cough (dry)
- Fatigue

Less common

- Myalgia
- Pharyngitis (or other respiratory symptoms)
- Headache
- GI including diarrhea
- Conjunctivitis
- Loss of taste or smell
- Rash (chilblains, discoloring on fingers/toes)
- Serious/warning symptoms
- Shortness of breath
- Chest pain/pressure
- Confusion
- Lethargy
- Cyanosis

Laboratory and imaging findings

In COVID-19 pneumonia

- Leukopenia is common among hospitalized patients.
- LDH may be modestly elevated.
- LFTs are elevated more commonly than in typical community-acquired pneumonia cases.

Note: detecting other respiratory viruses in COVID-19 may be as high as 20% (e.g., influenza in spring 2020; however, near-zero for the 2020-2021 respiratory season).

Lab detection of viruses such as RSV, influenza, etc. should not conclude that SARS-2-CoV is not present→ coinfx

- Chest CT may show ground-glass opacities that may evolve into consolidation or ARDS.
- Findings appear to peak at 10d of illness; resolution begins after day 14 for those who are hospitalized.
- Among hospitalized patients, about one-third need to be in the ICU/intubated with an ARDS picture.
- Elevations in IL-6 (> 40–100), CRP (> 10x normal), and ferritin (> 1000) suggested correlating with a hyperinflammatory state and may portend the development of ARDS.

Differential diagnosis

- COVID-19 cannot be easily distinguished from other causes of a viral respiratory infection such as influenza, RSV, other respiratory viruses or community-acquired pneumonia based only on clinical grounds.
- Consider multiplex testing, including influenza and RSV, especially with severe illness/hospitalized patients.
- Anosmia and dysgeusia occur much more frequently than other respiratory viruses, though less so with Omicron and immunization; studies have cited ranges from 15-48%.
- Influenza may be more abrupt onset; COVID-19 often with more perturbations of taste, and viral multiplex testing incorporating SARS-CoV-increasingly 2 is available; however, influenza and RSV rates were very low in the 2020-2021 winter respiratory season.
- Influenza again circulating during the U.S. winter respiratory season 2022-2023.

➢ Also, consider pulmonary embolus, acute myocardial infection, chest crisis (sickle cell disease), etc.

❖ Thromboses complicate critical COVID-19 patients with significant frequency, up to 40% in some series, especially in the critically ill.

COVID-19 testing

Molecular testing remains the gold standard (PCR, multiplex panels), but outpatient settings often have a longer turnaround time of 48-72h.

Sensitivity for molecular testing is excellent but does depend on sample collection. Depending on the technique and timing of illness, a small percentage may be missed, perhaps more so with immunized/boosted people with Omicron in the earliest phases of infection.

A repeat swab is needed if high suspicion exists.

Lower respiratory tract samples have higher yields with Delta and earlier variants.

Detection of viral RNA infectious virus necessarily, but is valid for the first 8-10d of symptoms in patients who are not severely ill or immunosuppressed.

Cycle threshold values are not standardized, vary among platforms, and are not reported as clinical data. However, if values are available, if in the 30s-40+, then a low likelihood that the viral shedding correlates with an active, replicating virus.

TREATMENT

Those with minor symptoms stay home and do not seek care in health clinics or hospitals but monitor symptoms and consider if antiviral treatment should be used.

Medical care is focused on those who are short of breath, have severe symptoms, or require oxygen and supportive care that is only available in a hospital.

In-hospital supportive care

Consider influenza or RSV co-infection in severe/hospitalized patients, as severity appears greater than infection with only SARS-CoV-2.

If also infected with influenza, use neuraminidase inhibitors for severe infection (or baloxivir for outpatient use in high-risk patients). There are no drug-drug interactions of concern between influenza and SARS-CoV-2 antivirals.

Oxygen, mechanical ventilation if needed:

Oxygen saturation ≤ 94% used as a threshold for consideration of antiviral or immunomodulatory therapy.

Secondary infections, especially in severe/critically ill patients:

Evaluate and treat bacterial or fungal superinfection (especially Aspergillus)
Sputum culture, and serum or BAL galactomannan are helpful in decision-making.

Often “nosocomial” pathogens (ESBL, P. aeruginosa, A. baumannii, Aspergillus spp.)

Antivirals

Studies for EUA or FDA approval were primarily carried out in the early part of the pandemic in unimmunized individuals. Efficacy is likely less in the population that is now either immunized or previously infected +/- lessening of virulence of recent variants (Omicron).

Remdesivir (RDV) first anti viral drug /Doses in hospital / hepatotoxicity

outpatient and Inpatient Use:
Nirmatrelvir/ritonavir (Paxlovid)
Received EUA December 2021.
Nirmatrelvir is a SARS-CoV-2 3CLpro protease inhibitor boosted by ritonavir.
EPIC-HR RCT enrolled unvaccinated adults with mild COVID-19 as outpatients using five days of PAXLOVID vs. placebo.
The primary endpoint was death or hospitalization within 28d.

Interim analysis of 2,085 participants showed that 8 (0.8%) in the nirmatrelvir arm vs. 66 (6.3%) in the placebo arm reached the primary endpoint for an impressive relative risk reduction of 88% (p=0.001).
No significant safety signals.

→ delyed viral clear

Imunomodulators (Dexamethasone)

Results from the RECOVERY trial showed dexamethasone 6 mg PO or IV daily for up to 10 days reduced 28-day mortality in certain groups of hospitalized COVID-19 patients: recommended for patients with severe COVID-19 (requiring oxygen), including those on mechanical ventilation by the National Institutes of Health (NIH) and IDSA.

high blood p / hyperten / PU

Vaccines

Multiple vaccines worldwide. Three used in the U.S. have modules in this guide.

The initial high efficacy of 94-95% for the mRNA vaccines is now lower due to the Delta and Omicron variants; however, they remain effective in reducing hospitalization or death from COVID-19.

Booster doses are recommended for ages ≥ 12 years, which improves vaccine efficacy against the Omicron variant.

Efficacy improved preliminary reports by 80-88% for infection prevention and hospitalization.

FDA has fully approved Pfizer/BioNTech for two doses and Moderna COVID-19 for two doses. Booster doses are also approved for Pfizer ages ≥ 12 yrs.

See vaccine modules for details, including third-dose information (immunocompromised patients) and booster recommendations.

FDA has authorized a second booster mRNA vaccine (dose #4) for ages ≥ 50 years, solid organ transplant recipients or those with similar immune risk.

Pfizer now has a EUA for children ≥ 6 months of age.

Children 5 years and older are now eligible for a booster dose (one).

Influenza (Including Avian Influenza and Swine Influenza)

DEFINITION

• Influenza viruses are enveloped, negative-sense, single-stranded RNA viruses whose genome is segmented. They cause epidemic acute respiratory disease characterized by fever, cough, and systemic symptoms. Three types (A, B, and C) are recognized, as well as many subtypes within the type A viruses.

EPIDEMIOLOGY

• Influenza viruses are transmitted by the respiratory route and cause large epidemics, which generally occur during the winter in temperate climates. In addition to infecting humans, influenza A viruses infect a wide variety of animals, particularly migratory waterfowl. New influenza A virus subtypes sporadically emerge in humans to cause widespread disease, or pandemics.

MICROBIOLOGY

• Influenza viruses are readily isolated in eggs or mammalian cell culture at 33° C. They undergo constant antigenic evolution, referred to as antigenic drift or shift that allows them to reinfect individuals who have had previous infections.

DIAGNOSIS

• In the context of recognized epidemics, influenza is usually diagnosed clinically on the basis of characteristic symptoms of fever and urt sx.

-viral panel can be done

THERAPY

• Antiviral therapy with oseltamivir, zanamivir, or peramivir is available and may shorten the duration of illness and reduce the rate of complications. Therapy is most effective when used early in the course of illness.

PREVENTION

• Influenza vaccines are effective in the prevention of influenza illness, although improved vaccines are needed.

• Inactivated and live-attenuated vaccines are available in trivalent and quadrivalent formulations.

• The objectives of vaccination include protection of the individual, as well as protection of the population through herd immunity. Antiviral drugs can also be used prophylactically in selected circumstances.

TABLE 102-1 Antiviral Chemotherapy and Chemoprophylaxis for Influenza

INFECTION	DRUG	ROUTE	DOSAGE
Influenza A and B: treatment	Oseltamivir	Oral	Adults: 75 mg bid × 5 days Children aged 1-12 years: 30-75 mg bid, depending on weight†, × 5 days
	Zanamivir	Inhaled orally	Adults and children aged ≥7 yr: 10 mg bid × 5 days
Influenza A: treatment	Amantadine*	Oral	Adults: 100 mg qd or bid × 5-7 days Children aged 1-9 yr: 5 mg/kg/day (maximum, 150 mg/day) × 5-7 days
	Rimantadine*	Oral	100 mg qd or bid × 5-7 days in adults
Influenza A and B: prophylaxis	Oseltamivir	Oral	Adults: 75 mg/day Children aged ≥1 yr: 30-75 mg/day, depending on weight†
	Zanamivir	Inhaled orally	Adults and children aged ≥5 yr: 10 mg/day
Influenza A: prophylaxis	Amantadine* or rimantadine*	Oral	Adults: 200 mg/day Children aged 1-9 yr: 5 mg/kg/day (maximum, 150 mg/day)

*Amantadine and rimantadine are not considered for use because of widespread resistance in influenza A/H3N2 and A/H1N1 viruses currently circulating (2012-2013). They may be considered if sensitivities become reestablished.

†For detailed dosage recommendations in children aged <1 yr, see www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.