A REVIEW ON COVID-19 AND MEDICATION TARGETS

M. SOLDUZIAN

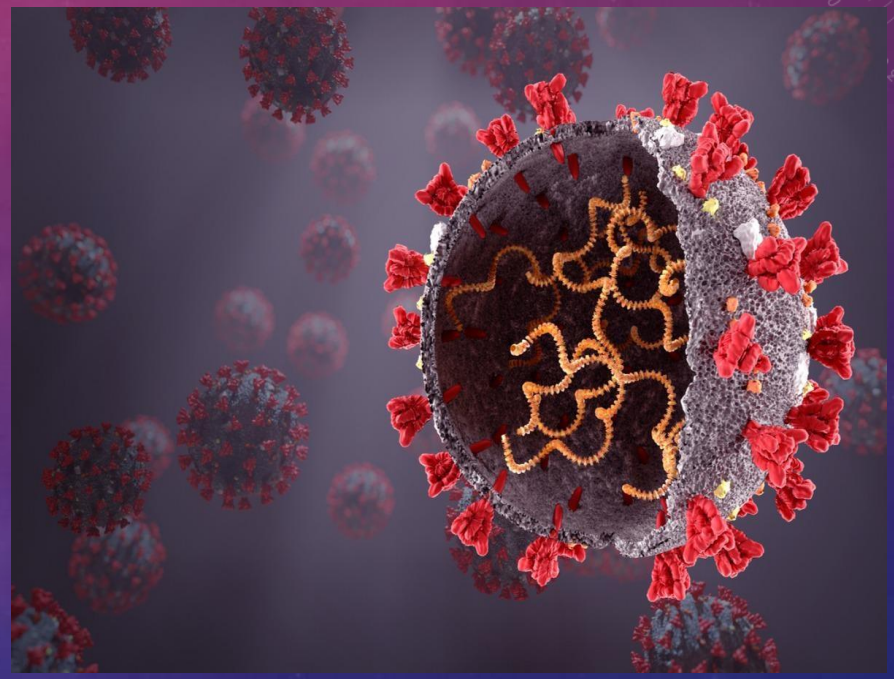
PHARM. D BCPS

ASSISTANT PROFESSOR OF PHARMACOTHERAPY

TABRIZ UNIVERSITY OF MEDICAL SCIENCES

INTRODUCTION

- Coronaviruses are important human and animal pathogens.
- The virus that causes COVID-19 is designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).



VIROLOGY

- Coronaviruses are enveloped positive-stranded RNA viruses
- Coronavirus that causes COVID-19 is a betacoronavirus in the same subgenus as the severe acute respiratory syndrome (SARS) virus (as well as several bat coronaviruses), but in a different clade.
- The host receptor for SARS-CoV-2 cell entry is the same as for SARS-CoV, the angiotensin-converting enzyme 2 (ACE2).
- SARS-CoV-2 binds to ACE2 through the receptor-binding domain of its spike protein
- The cellular protease TMPRSS2 also appears important for SARS-CoV-2 cell entry

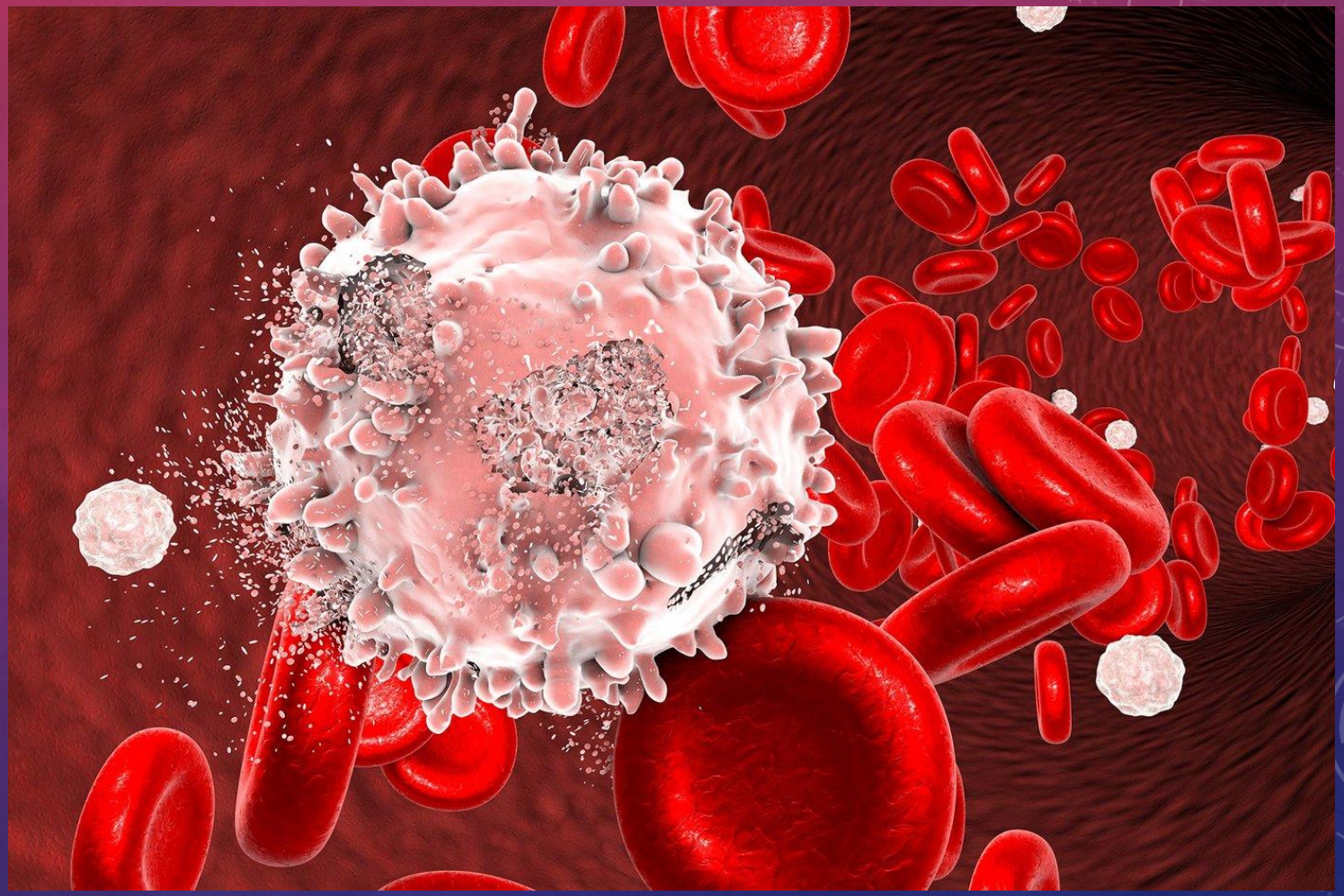
MECHANISM OF SARS-COV-2 INVASION INTO HOST CELLS

- The life cycle of the virus with the host consists of the following 5 steps: attachment, penetration, biosynthesis, maturation and release
- Once viral contents are released inside the host cells, viral RNA enters the nucleus for replication.
- Coronaviruses consist of four structural proteins; Spike (S), membrane (M), envelop (E) and nucleocapsid(N)
- Spike comprises two functional subunits; S1 subunit is responsible for binding to the host cell receptor and S2 subunit is for the fusion of the viral and cellular membranes.

MECHANISM OF SARS-COV-2 INVASION INTO HOST CELLS (CONT.)

- Structural and functional analysis showed that the spike for SARS-CoV-2 also bound to ACE2.
- ACE2 expression was high in lung, heart, ileum, kidney and bladder. In lung, ACE2 was highly expressed on lung epithelial cells.

DISEASE PATHOPHYSIOLOGY



ASYMPTOMATIC PHASE

- The SARS-CoV-2 which is received via respiratory aerosols binds to the nasal epithelial cells in the upper respiratory tract.
- The main host receptor for viral entry into cells is the ACE-2, which is seen to be highly expressed in adult nasal epithelial cells
- The virus undergoes local replication and propagation, along with the infection of ciliated cells in the conducting airways.
- This stage lasts a couple of days and the immune response generated during this phase is a limited one.
- In spite of having a low viral load at this time, the individuals are highly infectious, and the virus can be detected via nasal swab testing

INVASION AND INFECTION OF THE UPPER RESPIRATORY TRACT

- In this stage, there is migration of the virus from the nasal epithelium to the upper respiratory tract via the conducting airways.
- Due to the involvement of the upper airways, the disease manifests with symptoms of fever, malaise and dry cough.
- There is a greater immune response during this phase involving the release of C-X-C motif chemokine ligand 10 (CXCL-10) and interferons (IFN-β and IFN-λ) from the virus-infected cells
- The majority of patients do not progress beyond this phase as the mounted immune response is sufficient to contain the spread of infection

INVOLVEMENT OF THE LOWER RESPIRATORY TRACT AND PROGRESSION TO ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

- About one-fifth of all infected patients progress to this stage of disease and develop severe symptoms. The virus invades and enters the type 2 alveolar epithelial cells via the host receptor ACE-2 and starts to undergo replication to produce more viral Nucleocapsids.
- The virus-laden pneumocytes now release many different cytokines and inflammatory markers such as interleukins (IL-1, IL-6, IL-8, IL-120 and IL-12), tumour necrosis factor-α (TNF-α), IFN-λ and IFN-β, CXCL-10, monocyte chemoattractant protein-1 (MCP-1) and macrophage inflammatory protein-1α (MIP-1α).

INVOLVEMENT OF THE LOWER RESPIRATORY TRACT AND PROGRESSION TO ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) (CONT.)

- This ‘cytokine storm’ acts as a chemoattractant for neutrophils, CD4 helper T cells and CD8 cytotoxic T cells, which then begin to get sequestered in the lung tissue. These cells are responsible for fighting off the virus, but in doing so are responsible for the subsequent inflammation and lung injury
- The host cell undergoes apoptosis with the release of new viral particles, whichthen infect the adjacent type 2 alveolar epithelial cells in the same manner.
- Due to the persistent injury caused by the sequestered inflammatory cells and viral replication leading to loss of both type 1 and type 2 pneumocytes, there is diffuse alveolar damage eventually culminating in an acute respiratory distress syndrome

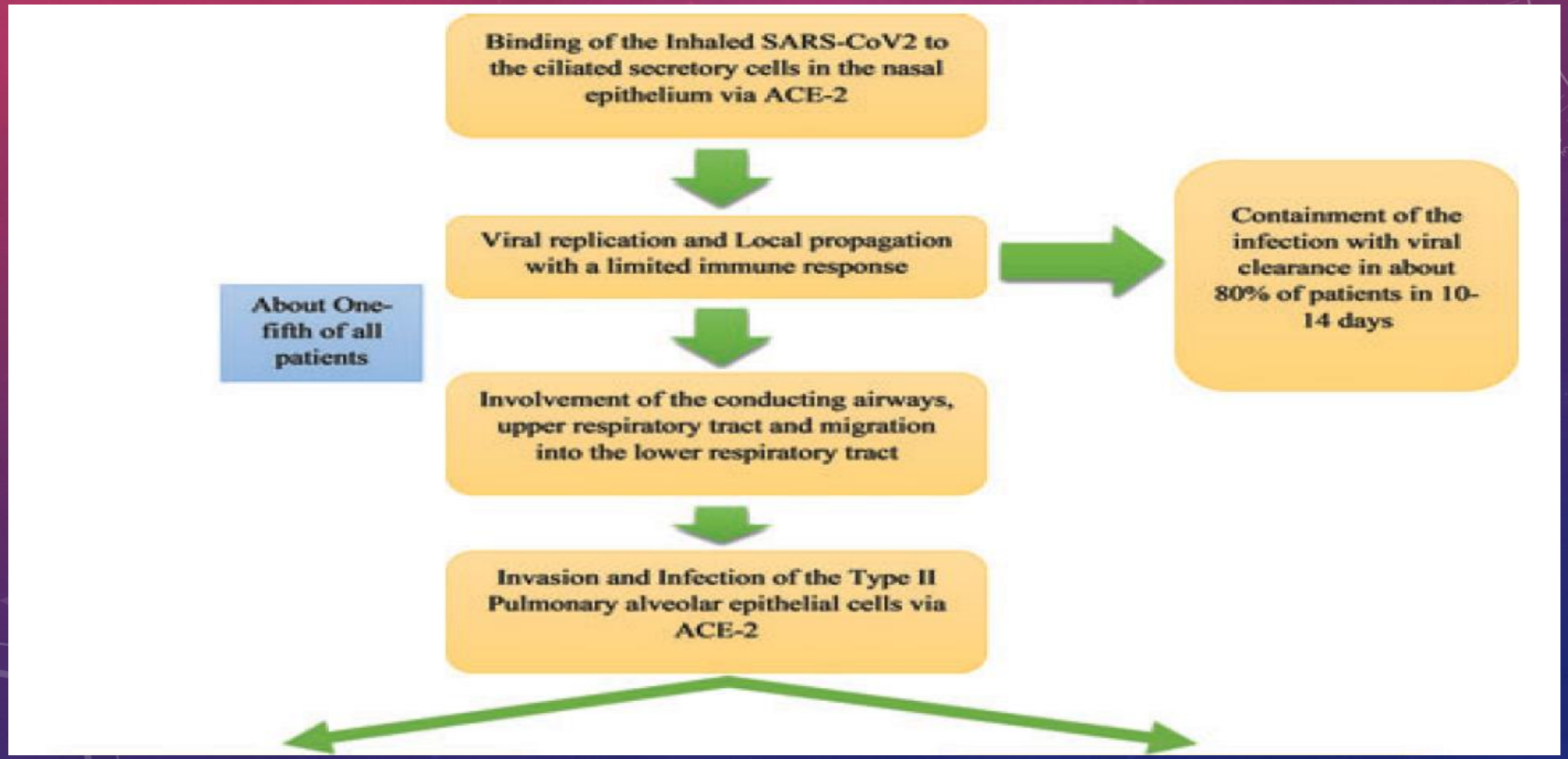
CLINICAL SPECTRUM OF COVID-19 DISEASE

Severity of disease	Presentation
Asymptomatic	► No clinical symptoms ► Positive nasal swab test ► Normal chest X-ray
Mild illness	► Fever, sore throat, dry cough, malaise and body aches or ► Nausea, vomiting, abdominal pain, loose stools
Moderate illness	► Symptoms of pneumonia (persistent fever and cough) without hypoxemia ► Significant lesions on high-resolution CT chest
Severe illness	► Pneumonia with hypoxemia ($SpO_2 < 92\%$)
Critical state	► Acute respiratory distress syndrome, along with shock, coagulation defects, encephalopathy, heart failure and acute kidney injury

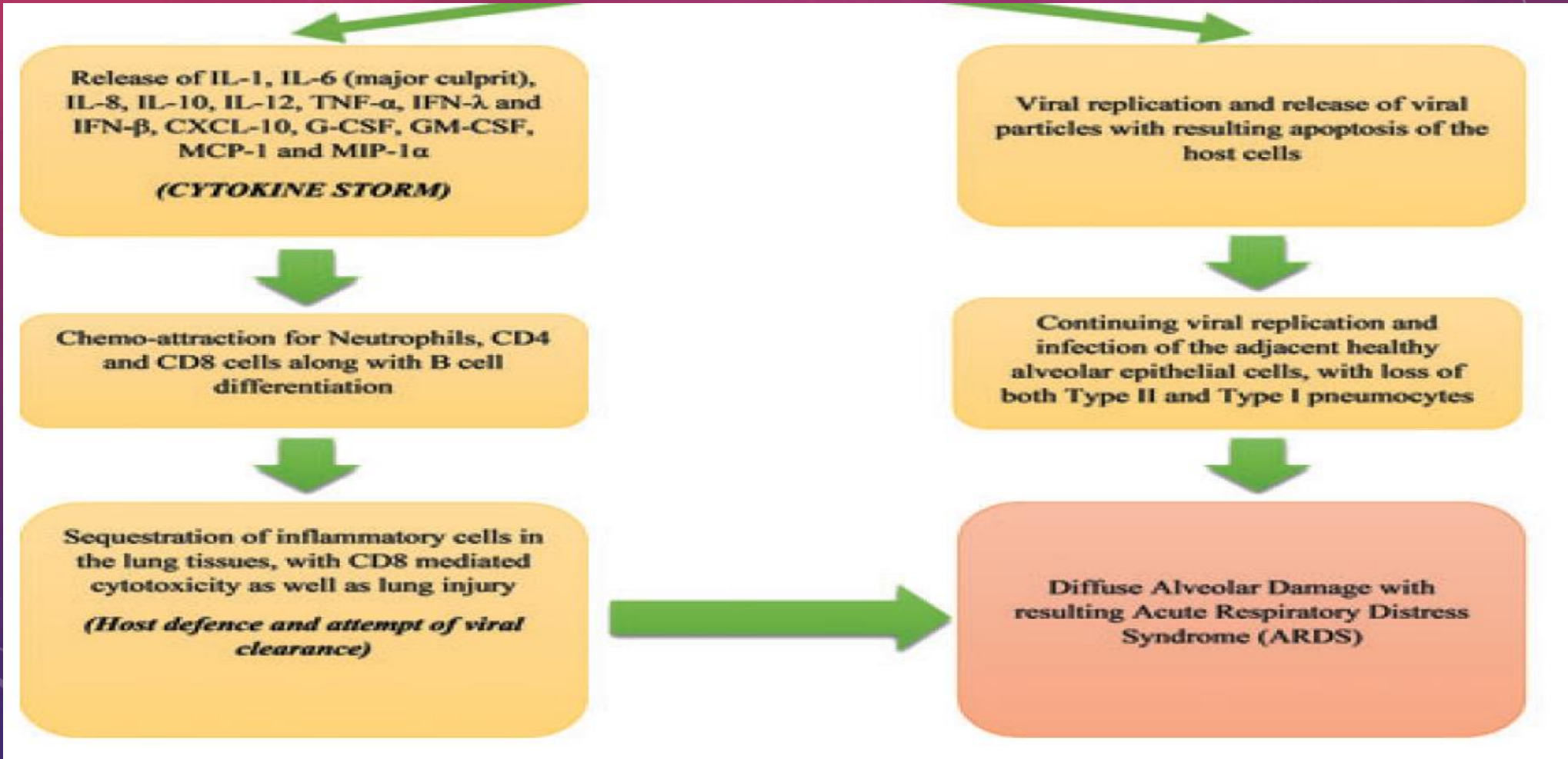
COMPLICATIONS SEEN IN PATIENTS WITH COVID-19

Frequency	Complication
Commonly seen	► Acute respiratory distress syndrome ► Acute respiratory failure ► Sepsis ► Disseminated intravascular coagulation ► Acute liver and kidney injury ► Pulmonary embolism
Rare	► Rhabdomyolysis ► Multisystem inflammatory syndrome ► Aspergillosis ► Pancreatitis ► Autoimmune haemolytic anaemia ► Neurological complications

PATHOPHYSIOLOGY OF COVID-19



PATHOPHYSIOLOGY OF COVID-19 (CONT.)



VARIANTS OF CONCERN

- Like other viruses, SARS-CoV-2 evolves over time. Most mutations in the SARS-CoV-2 genome have no impact on viral function.
- Certain variants have garnered widespread attention because of their rapid emergence within populations and evidence for transmission or clinical implications
- The World Health Organization (WHO) has also designated labels for notable variants based on the Greek alphabet
- Alpha, Beta and Gamma variants are no longer widely circulating.
- B.1.617.2 does not contain mutations associated with reduced susceptibility to bamlanivimab-etesevimab, casirivimab-imdevimab, or sotrovimab.

VARIANTS OF CONCERN (CONT.)

WHO label[1]	Name (Pango lineage*)	Name (Nextstrain*)	Spike protein substitutions (receptor-binding domain substitutions in bold)	First detected	Known attributes
Alpha¶	**B.1.1.7**	20I/501Y.V1	Δ69/70 Δ144Y **(E484K◇)** **(S494P◇)** **N501Y** A570D D614G P681H	United Kingdom	▪ ~50% increased transmission[2] ▪ Potential increased severity based on hospitalizations and case fatality rates[3] ▪ Minimal impact on neutralization by monoclonal antibody therapies§ • Bamlanivimab-etesevimab: No change in susceptibility[4] • Casirivimab-imdevimab: No change in susceptibility[5] • Sotrovimab: No change in susceptibility[6] ▪ Minimal impact on neutralization by convalescent and post-vaccination sera[7-13]
Beta¶	**B.1.351**	20H/501.V2	**K417N** **E484K** **N501Y** D614G	South Africa	▪ ~50% increased transmission[14] ▪ Significant impact on neutralization by some monoclonal antibody therapies§ • Bamlanivimab-etesevimab: Unlikely to be active (>45-fold decrease in susceptibility)[4] • Casirivimab-imdevimab: No change in susceptibility[5] • Sotrovimab: No change in susceptibility[6] ▪ Moderate reduction in neutralization by convalescent and post-vaccination sera

VARIANTS OF CONCERN (CONT.)

Gamma[¶]	**P.1**	20J/501Y.V3	**K417N/T** **E484K** **N501Y** D614G	Japan/Brazil	▪ Significant impact on neutralization by some monoclonal antibody therapies[§] • Bamlanivimab-etesevimab: Unlikely to be active (>511-fold decrease in susceptibility)[4] • Casirivimab-imdevimab: No change in susceptibility[5] • Sotrovimab: No change in susceptibility[6] ▪ Reduced neutralization by convalescent and post-vaccination sera[15]
Delta	**B.1.617.2**	20A	T19R (G142D[◇]) Δ156 Δ157 R158G **L452R** **T478K** D614G P681R D950N	India	▪ Increased transmissibility compared with B.1.1.7 (Alpha)[16] ▪ Potential increased severity based on associated hospitalization rate[16,17] ▪ Potential minimal reduction in neutralization by monoclonal antibody therapies[¥] ▪ Potential modest/moderate reduction in vaccine effectiveness against symptomatic COVID-19 without significant impact on vaccine effectiveness against severe disease[17-20]

VARIANTS OF CONCERN (CONT.)

Omicron	**B.1.1.529**	21K	A67V Δ69-70 T95I G142D Δ143-145 Δ211 L212I ins214EPE **G339D** **S371L** **S373P** **S375F** **K417N** **N440K** **G446S** **S477N** **T478K**	**E484A** **Q493K** **G496S** **Q498R** **N501Y** **Y505H** **T547K** D614G H655Y N679K P681H N764K D796Y N856K Q954H N969K L981F	Botswana/South Africa	Clinical implications are not yet known.[21]

OMICRON (B.1.1.529 LINEAGE)

- This variant was first reported from southern Africa in November 2021. In South Africa, it was associated with an increase in regional infections, and it was promptly identified in multiple other countries.
- The variant contains over 30 mutations in the spike protein, including mutations that have been found in other variants of concern and that have been associated with increased transmissibility and decreased susceptibility to neutralizing antibodies (including therapeutic monoclonal antibodies)
- Emerging data on whether the variant is more transmissible, escapes from infection- or vaccine-induced immunity, or results in more or less severe disease are preliminary and limited.

OMICRON (B.1.1.529 LINEAGE) (CONT.)

- In an unpublished study evaluating national surveillance data from South Africa, the ratio of reinfections (repeat positive test at least 90 days after an earlier positive test) to primary infections was higher during the beginning of the case surge associated with the Omicron variant compared with the surges associated with the Beta and Delta variants (0.25 versus 0.12 and 0.09)
- Although these data suggest that the risk of reinfection may be higher with Omicron, they do not account for the possibility that changes in testing patterns or variable risks of exposure could contribute to the differences observed.
- Other data have been interpreted to suggest that the risk of severe disease with Omicron infection may be less than with other variants. An informal report from a South African hospital at the center of the surge indicated that only 33 percent of the 42 patients in their COVID-19 ward required supplemental oxygen, which was a lower proportion than observed in the beginning of earlier surges, and 8 of the 9 individuals with COVID-19 pneumonia were unvaccinated

OMICRON (B.1.1.529 LINEAGE) (CONT.)

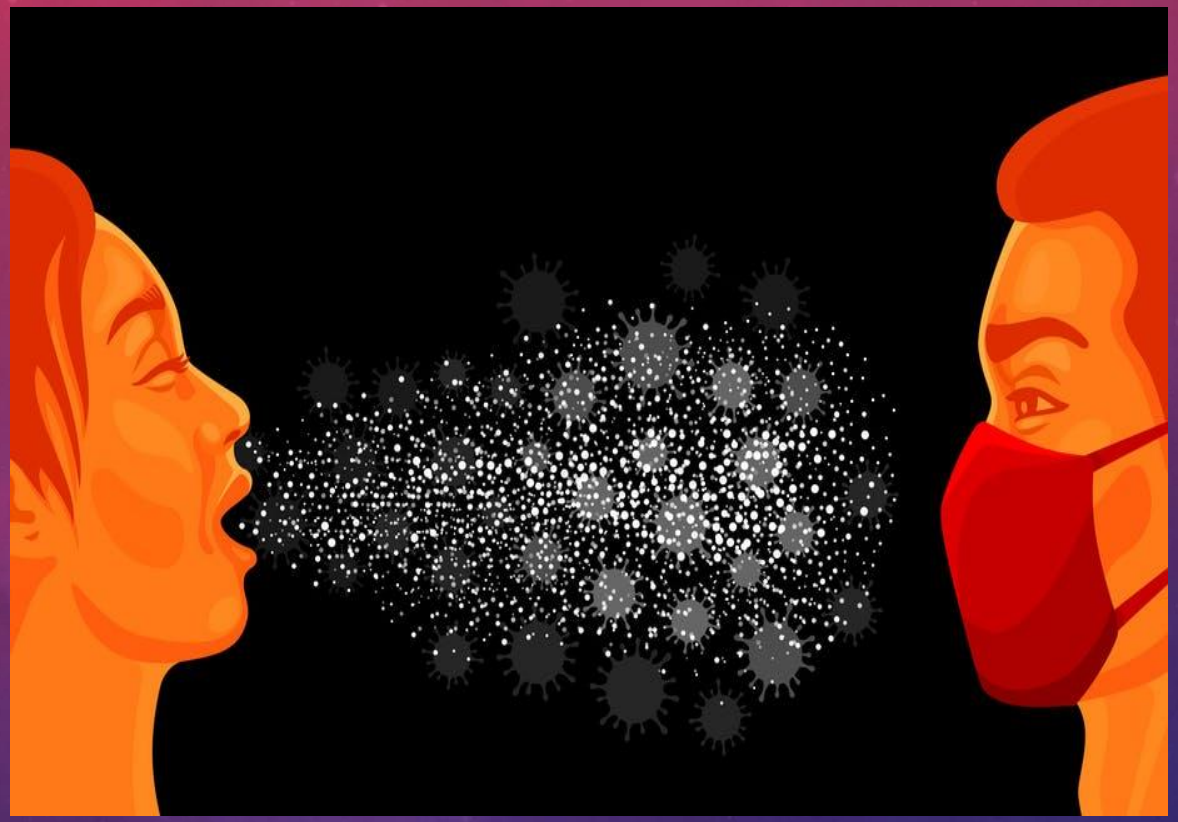
- However, making conclusions based on these small, early reports is premature. The relative mildness of disease may reflect the younger age of individuals impacted at this stage of the surge, and since there is often a delay between symptom onset and respiratory complications, the scope of clinical severity may not be evident for several weeks.
- One of the mutations in the Omicron variant is a deletion in the spike protein that results in the inability of some SARS-CoV-2 molecular tests to detect the S gene (which encodes the spike protein).
- These tests would still be able to detect viral RNA since they employ more than one gene target and thus would not result in false-negative results. Nevertheless, S gene target failure can be used as a marker to detect the Omicron variant with those tests, with the caveat that S gene target failure can also occur with other variants, such as Alpha. Antigen testing, which relies mainly on the nucleocapsid protein, is thought to be unaffected.

EPIDEMIOLOGY

GEOGRAPHIC DISTRIBUTION AND CASE COUNTS

- Globally, over 250 million confirmed cases of COVID-19 have been reported.
- Seroprevalence surveys in the United States and Europe have suggested that after accounting for potential false positives or negatives, the rate of prior exposure to SARS-CoV-2, as reflected by seropositivity, exceedsthe incidence of reported cases by approximately 10-fold or more

TRANSMISSION



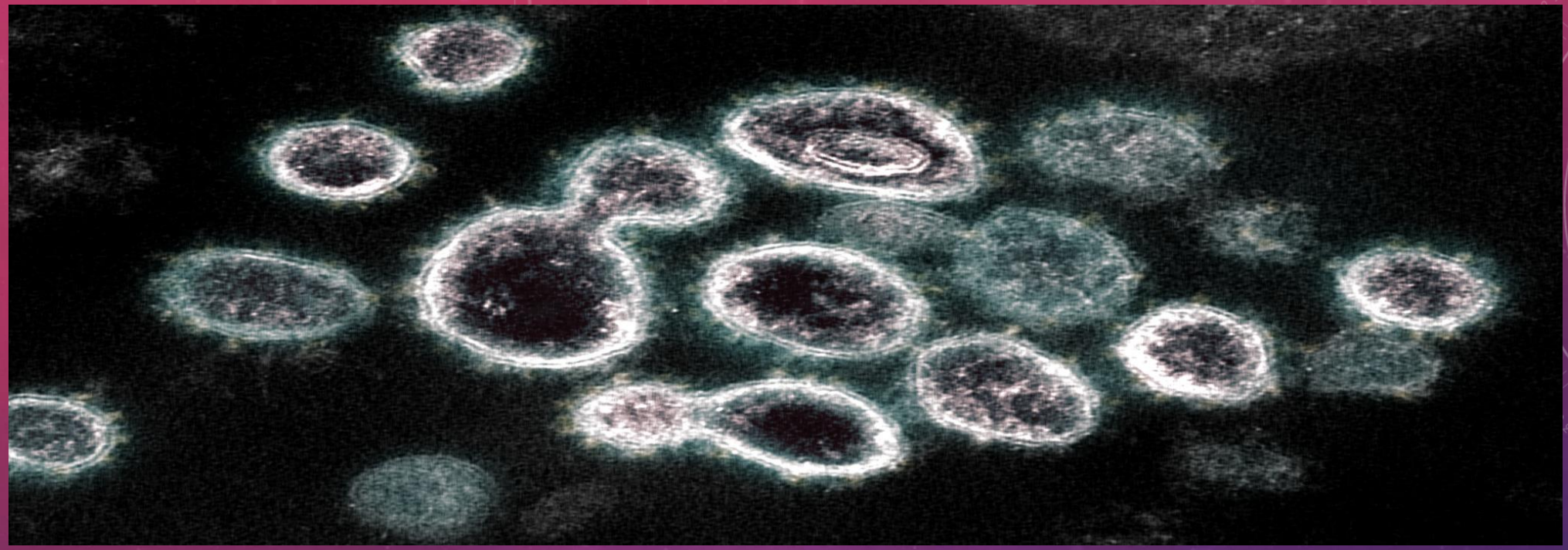
PERSON-TO-PERSON SPREAD IS THE MAIN MODE OF SARS-COV-2 TRANSMISSION.

PERSON-TO-PERSON

- Direct person-to-person respiratory transmission is the primary means of transmission
- It is thought to occur mainly through close-range contact (ie, within approximately six feet or two meters) via respiratory particles; virus released in the respiratory secretions when a person with infection coughs, sneezes, or talks can infect another person if it is inhaled or makes direct contact with the mucous membranes.
- Infection might also occur if a person's hands are contaminated by these secretions or by touching contaminated surfaces and then they touch their eyes, nose, or mouth, although contaminated surfaces are not thought to be a major route of transmission.
- SARS-CoV-2 can also be transmitted longer distances through the airborne route (through inhalation of particles that remain in the air over time and distance), but the extent to which this mode of transmission has contributed to the pandemic is uncertain

PERSON-TO-PERSON (CONT.)

- The overall transmission and secondary attack rates of SARS-CoV-2 suggest that long-range airborne transmission is not a primary mode
- Airborne precautions are universally recommended when aerosol-generating procedures are performed
- According to a joint WHO-China report, transmission through the fecal-oral route did not appear to be a significant factor in the spread of infection
- The likelihood of bloodborne transmission (eg, through blood products or needlesticks) appears low; respiratory viruses are generally not transmitted through the bloodborne route, and transfusion-transmitted infection has not been reported for SARS-CoV-2 or for the related Middle East respiratory syndrome coronavirus (MERS-CoV) or SARS-CoV



VIRAL SHEDDING AND PERIOD OF INFECTIOUSNESS

THE PRECISE INTERVAL DURING WHICH AN INDIVIDUAL WITH SARS-COV-2 INFECTION CAN TRANSMIT INFECTION TO OTHERS IS UNCERTAIN.

PERIOD OF GREATEST INFECTIOUSNESS

- The potential to transmit SARS-CoV-2 begins prior to the development of symptoms and is highest early in the course of illness; the risk of transmission decreases thereafter.
- Transmission after 7 to 10 days of illness is unlikely, particularly for otherwise immunocompetent patients with nonsevere infection.
- Infected individuals are more likely to be contagious in the earlier stages of illness when viral RNA levels from upper respiratory specimens are the highest
- One modeling study, in which the mean serial interval between the onset of symptoms among 77 transmission pairs in China was 5.8 days, estimated that infectiousness peaked between two days before and one day after symptom onset and declined within seven days

PROLONGED VIRAL RNA DETECTION DOES NOT INDICATE PROLONGED INFECTIOUSNESS

- The duration of viral RNA shedding is variable and may increase with age and the severity of illness .
- In a review of 28 studies, the pooled median duration of viral RNA detection in respiratory specimens was 18 days following the onset of symptoms; in some individuals, viral RNA was detected from the respiratory tract several months after the initial infection. Detectable viral RNA, however, does not necessarily indicate the presence of infectious virus, and there appears to be a threshold of viral RNA level below which infectiousness is unlikely.
- As an example, in a study of nine patients with mild COVID-19, infectious virus was not detected from respiratory specimens when the viral RNA level was <106 copies/mL.

PROLONGED VIRAL RNA DETECTION DOES NOT INDICATE PROLONGED INFECTIOUSNESS (CONT.)

- In other studies, infectious virus has only been detected in respiratory specimens with high concentrations of viral RNA. Such high viral RNA concentrations are reflected by lower numbers of reverse transcriptase polymerase chain reaction (RT-PCR) amplification cycles necessary for detection.
- Depending on the study, the cycle threshold (Ct) for specimen culture positivity may vary from <24 to ≤32
- According to information from the United States Centers for Disease Control and Prevention (CDC), by three days after clinical recovery, if viral RNA is still detectable in upper respiratory specimens, the RNA concentrations are generally at or below the levels at which replication-competent virus can be reliably isolated; additionally, isolation of infectious virus from upper respiratory specimens more than 10 days after illness onset has only rarely been documented in patients who had nonsevere infection and whose symptoms have resolved

PROLONGED VIRAL RNA DETECTION DOES NOT INDICATE PROLONGED INFECTIOUSNESS (CONT.)

- Infectious virus has not been isolated from respiratory specimens of immunocompetent patients who have a repeat positive RNA test soon after clinical improvement and initial viral RNA clearance, and in studies evaluating such patients, secondary infections in their close contacts have not been documented despite opportunities for transmission
- Occasional reports have described isolation of infectious virus from respiratory specimens for several months following symptom onset in immunocompromised patients.
- Prolonged shedding of virus in fecal specimens has also been described.
- Further data are needed to understand the frequency and clinical significance of these findings.

RISK OF TRANSMISSION DEPENDS ON EXPOSURE TYPE

- Many individuals do not transmit SARS-CoV-2 to anyone else, and epidemiologic data suggest that the minority of index cases result in the majority of secondary infections
- The risk of transmission after contact with an individual with COVID-19 increases with the closeness and duration of contact and appears highest with prolonged contact in indoor settings
- Most secondary infections have been described in the following settings:
  - Among household contacts: Within households, spouses or significant others have the highest secondary infection rates
  - In health care settings when personal protective equipment was not used (including hospitals and long-term care facilities
  - In other congregate settings where individuals are residing or working in close quarters

RISK OF TRANSMISSION DEPENDS ON EXPOSURE TYPE (CONT.)

- Although transmission rates are highest in household and congregate settings, frequently reported clusters of cases after social or work gatherings also highlight the risk of transmission through close, non-household social contact
- Higher respiratory tract RNA levels (taken at a median of four days after symptom onset) were independently associated with higher secondary attack rates.
- Traveling with an individual with COVID-19 is also a high-risk exposure, as it generally results in close contact for a prolonged period.

ASYMPTOMATIC OR PRESYMPTOMATIC TRANSMISSION

- Transmission of SARS-CoV-2 from individuals with infection but no symptoms (including those who later developed symptoms and thus were considered presymptomatic) has been well documented
- The biologic basis for this is supported by a study of a SARS-CoV-2 outbreak in a long-term care facility, in which infectious virus was cultured from RT-PCR-positive upper respiratory tract specimens in presymptomatic and asymptomatic patients as early as six days prior to the development of typical symptoms .
- The levels and duration of viral RNA in the upper respiratory tract of asymptomatic patients are also similar to those of symptomatic patients
- The risk of transmission from an individual who is asymptomatic appears less than that from one who is symptomatic

ASYMPTOMATIC OR PRESYMPTOMATIC TRANSMISSION (CONT.)

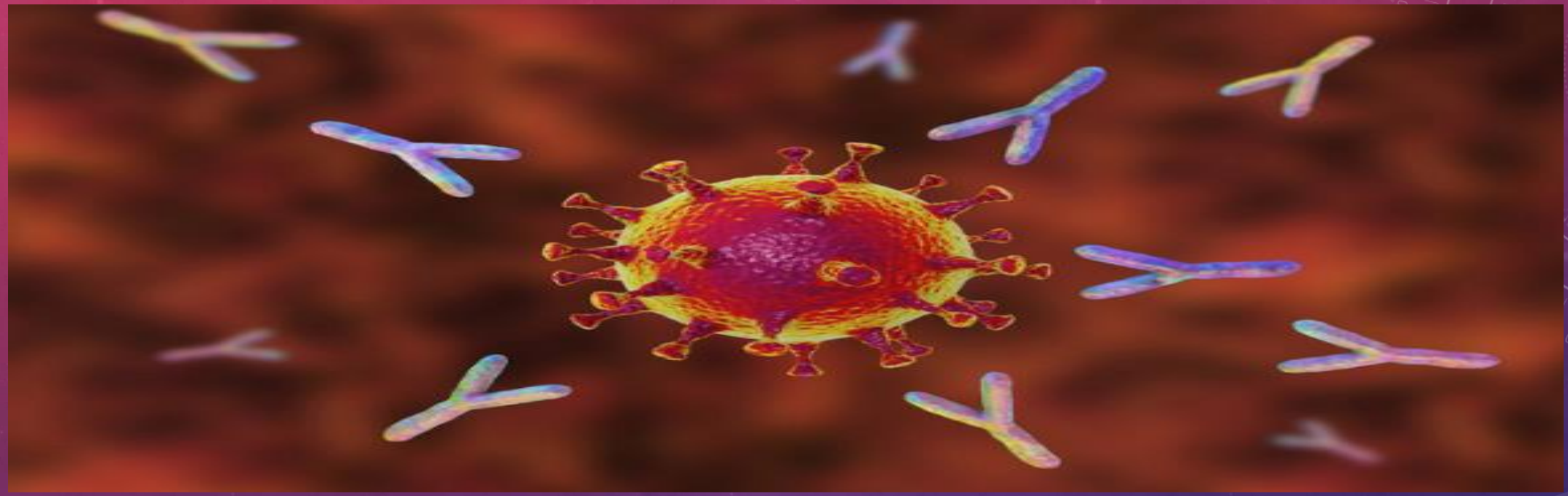
- Nevertheless, asymptomatic or presymptomatic individuals are less likely to isolate themselves from other people, and the extent to which transmission from such individuals contributes to the pandemic is uncertain.
- A CDC modeling study estimated that 59 percent of transmission could be attributed to individuals without symptoms: 35 percent from presymptomatic individuals, and 24 percent from those who remained asymptomatic

ENVIRONMENTAL CONTAMINATION

- Virus present on contaminated surfaces may be another source of infection if susceptible individuals touch these surfaces and then transfer infectious virus to mucous membranes in the mouth, eyes, or nose.
- The frequency and relative importance of this type of transmission are uncertain, although contaminated surfaces are not thought to be a major source of transmission.
- It may be more likely a potential source of infection in settings where there is heavy viral contamination (eg, in an infected individual's household or in health care settings).
- It is unknown how long SARS-CoV-2 can persist on surfaces [162-164]; other coronaviruses have been tested and may survive on inanimate surfaces for up to six to nine days without disinfection.

RISK OF ANIMAL CONTACT

- SARS-CoV-2 infection is thought to have originally been transmitted to humans from an animal host, but the ongoing risk of transmission through animal contact is uncertain.
- There is no evidence suggesting animals (including domesticated animals) are a major source of infection in humans.
- Given the uncertainty regarding the transmission risk and the apparent susceptibility of some animals to SARS-CoV-2 infection, the United States CDC recommends that pets be kept away from other animals or people outside of the household and that people with confirmed or suspected COVID-19 try to avoid close contact with household pets, as they should with human household members, for the duration of their self-isolation period.
- There have been no reports of domesticated animals (other than mink) transmitting SARS-CoV-2 infection to humans.



IMMUNE RESPONSES FOLLOWING INFECTION

PROTECTIVE SARS-COV-2-SPECIFIC ANTIBODIES AND CELL-MEDIATED RESPONSES ARE INDUCED FOLLOWING INFECTION. EVIDENCE SUGGESTS THAT SOME OF THESE RESPONSES CAN BE DETECTED FOR AT LEAST A YEAR FOLLOWING INFECTION.

HUMORAL IMMUNITY

- Following infection with SARS-CoV-2, the majority of patients develop detectable serum antibodies to the receptor-binding domain of the viral spike protein and associated neutralizing activity.
- However, the magnitude of antibody response may be associated with severity of disease, and patients with mild infection may not mount detectable neutralizing antibodies
- When neutralizing antibodies are elicited, they generally decline over several months after infection, although studies have reported detectable neutralizing activity up to 12 months

CELL-MEDIATED IMMUNITY

- Studies have also identified SARS-CoV-2-specific CD4 and CD8 T cell responses in patients who had recovered from COVID-19 and in individuals who had received COVID-19 vaccination, which suggest the potential for a durable T cell immune response

RISK OF REINFECTION

- The short-term risk of reinfection (eg, within the first several months after initial infection) is low. Prior infection reduces the risk of infection in the subsequent six to nine months by at least 80 to 85 percent.
- Several studies have estimated the risk of reinfection as less than 1 percent over that time frame
- Some studies suggest that reinfections are milder than initial infections

PREVENTION

PERSONAL PREVENTIVE MEASURES

- If community transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is present, residents are generally encouraged to practice social distancing by avoiding crowds and maintaining a distance of six feet (two meters) from others when in public
- Individuals are also encouraged to wear masks when out in public.
- The American Academy of Ophthalmology suggests that people not wear contact lenses, because they make people touch their eyes more frequently

WHEN TO WEAR A MASK

- The World Health Organization (WHO) recommends mask-wearing as part of a comprehensive approach to reducing SARS-CoV-2 transmission in either indoor or outdoor settings where there is widespread transmission and social distancing is difficult as well as indoor settings with poor ventilation (regardless of ability to distance)
- Individuals who are caring for individuals with suspected or documented COVID-19 at home should also wear a mask when in the same room as that person.
- In the United States, cloth masks and disposable masks (eg, commercially available surgical masks) are recommended for community use

OTHER FACE PROTECTION

- Although eye protection is recommended in health care settings, the role of face shields or goggles in addition to masks to further reduce the risk of infection in the community is uncertain.
- Although one study suggested that the proportion of hospitalized patients with COVID-19 who used eyeglasses daily was lower than that estimated for the general population, eyeglasses are generally considered insufficient for eye protection

MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)

MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)

- Coronavirus disease 2019 (COVID-19) in children is usually mild. However, in rare cases, children can be severely affected, and clinical manifestations may differ from adults.
- Multisystem inflammatory syndrome in children (MIS-C) is an uncommon complication of COVID-19 that has a presentation similar to Kawasaki disease (KD) or toxic shock syndrome.
- it appears to be a relatively rare complication of COVID-19 in children. MIS-C can occur at any age from infancy through late adolescence. Most cases have occurred in previously healthy children between the ages of 6 to 12 years.

MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) (CONT.)

- It is thought to result from an abnormal immune response to the virus, with some clinical similarities to KD, macrophage activation syndrome (MAS), and cytokine release syndrome.
- Most affected children have positive serology for SARS-CoV-2 with negative polymerase chain reaction (PCR), a finding that further supports the hypothesis that MIS-C is related to immune dysregulation occurring after acute infection has passed. However, some children do have positive PCR testing
- Preliminary studies suggest that patients with severe MIS-C have persistent immunoglobulin G (IgG) antibodies with enhanced ability to activate monocytes, persistent cytopenias (particularly T cell lymphopenia), and greater activation of CD8+ T cells that differ from findings in acute COVID-19 infection. The certainty of these findings is limited due to the small number of patients in these studies.

MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) (CONT.)

- The clinical presentation of MIS-C may include persistent fevers, gastrointestinal symptoms (abdominal pain, vomiting, diarrhea), rash, and conjunctivitis. Patients typically present with three to five days of fever, followed by development of shock and/or multisystem involvement. Laboratory findings include lymphocytopenia, elevated inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], D-dimer), and elevated cardiac markers (troponin, brain natriuretic peptide [BNP]).

GOOD LUCK