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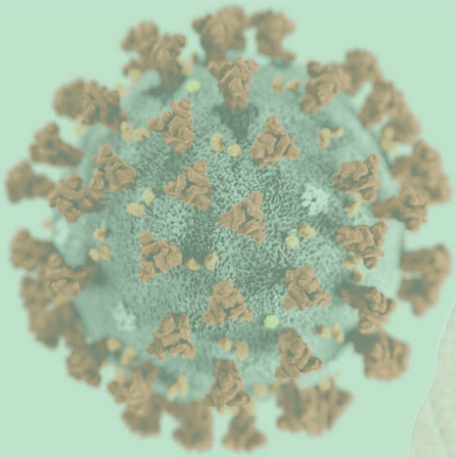
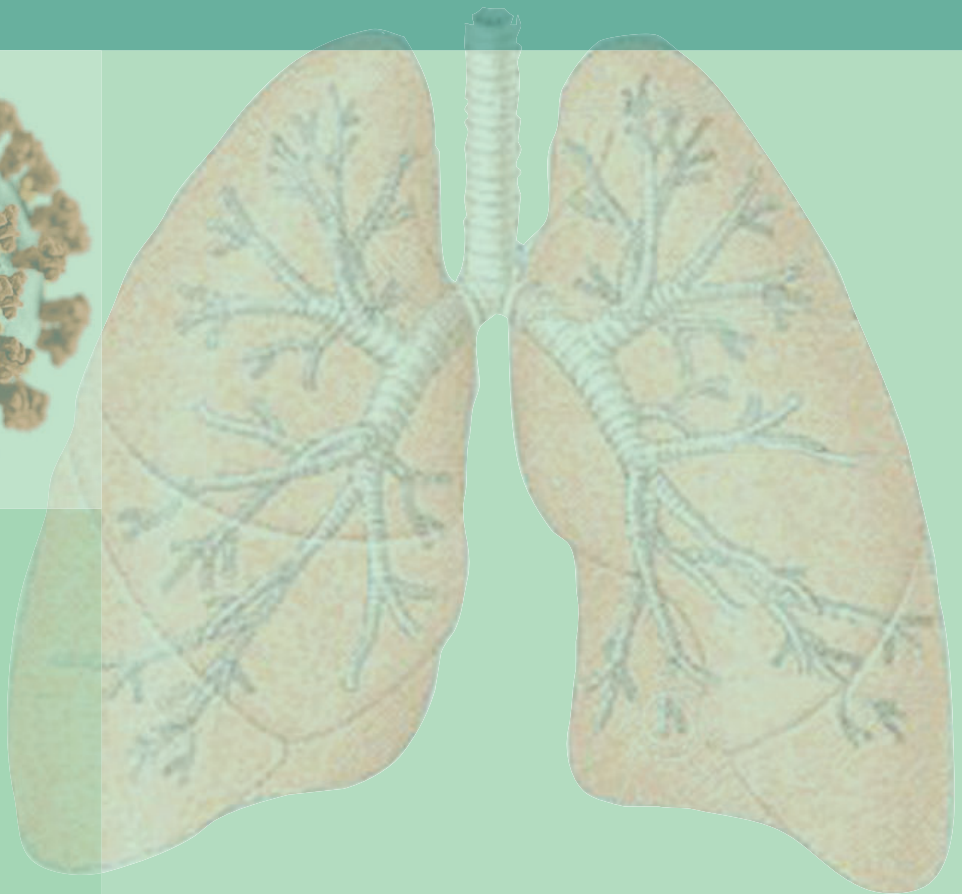
Addressing The Issues Of COVID-19





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Preface

All praises for the Almighty Allah, the most merciful and beneficent, for giving me sufficient opportunity and courage and providing me enough energy and patience to initiate and carry on this Addressing The Issues Of COVID-19.

It is a great pleasure to acknowledge a deep sense of gratitude and indebtedness to the President, Secretary General, Treasurer, Board of Editors, Board of Advisors, Associate Editors, Officials of Asthma Association Bangladesh and Contributing Authors from home and abroad for their valuable suggestions, constructive criticisms and encouragement during the work.

I acknowledge Dr. Romal Chowdhury and Dr. Syed Nesar Ahmed for their wholehearted contribution in this work. Without their sincere and untiring cooperation, it was impossible for me to publish this work. Indeed both Dr. Romal Chowdhury and Dr. Syed Nesar Ahmed have done an excellent effort to make this feasible even in this pandemic situation. So again I am deeply indebted to both of them for their brilliant job.

I appreciate the keen interest taken by my colleagues and students in making useful suggestions, critical revisions and correcting the proofs throughout the work. Although it is not possible to name individually each and everyone associated with the task but it is my bounded duty to acknowledge and remember their contribution always.

Coronavirus Disease-2019 (COVID-19) outbreak, which started in Wuhan, China, in December 2019, have turned into a pandemic. There are lots of dilemma among the physicians about this disease. So We have tried our highest endeavour to solve the issues regarding COVID-19.

We will update the different issues of COVID-19 from time to time to incorporate latest evidences and recommendations by WHO and various established guidelines. We welcome every suggestion and feedback in this work.

May the Almighty bless all of us with His Mercy and Forgiveness.

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Abbreviations

CVST	Cerebral Venous Sinus Thrombosis
EMA	European Medicines Agency
PPE	Personal Protective Equipment
LTVV	Low Tidal Volume Ventilation

Contents

A. Virology And Transmission

1. How Is SARS-CoV-2 Transmitted?

- Person-to-person spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is thought to occur mainly via respiratory droplets, resembling the spread of influenza.
- With droplet transmission, virus released in the respiratory secretions when a person with infection coughs, sneezes, or talks can infect another person if it makes direct contact with the mucous membranes.
- Infection can also occur if a person touches a contaminated surface and then touches his or her eyes, nose, or mouth.
- Droplets typically do not travel more than six feet (about two meters).
- The extent to which SARS-CoV-2 can be transmitted through the airborne route (through particles smaller than droplets that remain in the air over time and distance) under natural conditions and how much this mode of transmission has contributed to the pandemic are controversial.
- While SARS-CoV-2 RNA has been detected in non-respiratory specimens (eg, stool, blood), neither fecal-oral nor bloodborne transmission appear to be significant sources of infection.
- SARS-CoV-2 infection has been described in animals, but there is no evidence to suggest that animals are a major source of transmission.

2. What Is The Incubation Period For COVID-19?

- The incubation period for COVID-19 is thought to be within 14 days following exposure, with most cases occurring approximately four to five days after exposure.

3. What Are Some Of The Important SARS- CoV-2 Variants?

- Multiple SARS-CoV-2 variants are circulating globally.
- Some variants contain mutations in the surface spike protein, which mediates viral attachment to human cells and is a target for natural and vaccine-induced immunity.
- Thus, these variants have the potential to be more transmissible, cause more severe disease, and/or evade natural or vaccine-induced immune responses.
- Although more prevalent in the locations where they were first identified, these variants have subsequently been detected in many other countries, including in the United States:
  - **B.1.1.7 variant** (also known as variant of concern [VOC] 202012/01 or 20I/501Y.V1) was first identified in the United Kingdom in late 2020. This variant is estimated to be more transmissible than wild-type virus. Preliminary data also suggest this variant may cause more severe illness.
  - **B.1.351 variant** (also known as 20H/501Y.V2) was identified in late 2020 in South Africa, where it quickly became the dominant circulating strain. This variant is also believed to be more transmissible than wild-type virus, and there is concern that it evades immune responses; there is no evidence to suggest it impacts disease severity.

- **P.1 variant** (also known as 20J/501Y.V3) was first identified in Japan in travelers from Brazil in late 2020, and subsequently widely detected in specimens from the Amazonas state of Brazil. The variant harbors several mutations, which have the potential to increase transmissibility and impact immunity.

B. Clinical Presentation

4. What Are The Clinical Presentation And Natural History Of COVID-19?

- The spectrum of illness associated with COVID-19 is wide, ranging from asymptomatic infection to life-threatening respiratory failure.
- When symptoms are present, they typically arise approximately four to five days after exposure.
- Symptoms are mild in approximately 80 percent of cases and often include fever, fatigue, and dry cough. Smell and taste disorders have also been reported in patients with COVID-19; whether these symptoms are distinguishing features is unknown.
- Gastrointestinal symptoms are not frequently reported but may be the presenting feature in some patients. Headache, rhinorrhea, and sore throat are less common.
- Dyspnea affects approximately 20 to 30 percent of patients, typically arising five to eight days after symptom onset. Progression from dyspnea to acute respiratory distress syndrome (ARDS) can be rapid; thus, the onset of dyspnea is generally an indication for hospital evaluation and management.
- Pneumonia is the most common manifestation of severe disease.
- ARDS develops in a sizable minority of symptomatic patients and can be associated with a cytokine release syndrome, which is characterized by fever, progressive hypoxia and/or hypotension, and markedly elevated inflammatory markers.
- ARDS is the leading cause of death, followed by sepsis, cardiac complications, and secondary infections.
- The overall case fatality rate is estimated to be between 2 and 3 percent, although it varies widely by age and the true rate is unknown.
- While severe and fatal illness can occur in anyone, the risk rises dramatically with age and the presence of chronic illnesses, including cardiovascular disease, pulmonary disease, diabetes mellitus, kidney disease, and cancer.
- For those who recover, illness is often prolonged, lasting approximately two weeks in those with mild disease and three to six weeks in those with severe disease.

5. What Factors Are Associated With Severe COVID-19?

Severe illness can occur in otherwise healthy individuals of any age, but it predominantly occurs in adults with advanced age and/or certain underlying medical comorbidities. These comorbidities and other less common comorbidities are compiled in a table by the United States Centers for Disease Control and Prevention (CDC); The strength of evidence informing each association varies **(Table I)**.

Table I. Comorbidities The CDC Classifies As Risk Factors For Severe COVID-19 [a] [1,2]

1. Established and probable risk factors (comorbidities that have been associated with severe COVID-19 in at least 1 meta-analysis or systematic review [starred conditions], or in observational studies)
    - Cancer [a]
    - Cerebrovascular disease [a]
    - Children with certain underlying conditions [b]
    - Chronic kidney disease [a]
    - COPD [a] and other lung disease (including interstitial lung disease, pulmonary fibrosis, pulmonary hypertension)
    - Diabetes mellitus, type 1[a] and type 2[a]
    - Down syndrome
    - Heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies) [a]
    - HIV
    - Neurologic conditions, including dementia
    - Obesity [a] (BMI ≥30 kg/m^2) and overweight (BMI 25 to 29 kg/m^2)
    - Pregnancy [a]
    - Smoking [a] (current and former)
    - Solid organ or blood stem cell transplantation
    - Substance use disorders
    - Use of corticosteroids or other immunosuppressive medications
2. Possible risk factors (supported by mostly case series, case reports, or, if other study design, the sample size is small)
    - Cystic fibrosis
    - Thalassemia
3. Possible risk factors but evidence is mixed (comorbidities have been associated with severe COVID-19 in at least 1 meta-analysis or systematic review, but other studies had reached different conclusions)
    - Asthma
    - Hypertension
    - Immune deficiencies
    - Liver disease

COVID-19: Coronavirus disease 2019
CDC: Centers for Disease Control and Prevention
COPD: Chronic obstructive pulmonary disease
BMI: Body mass index

a These comorbidities are associated with severe COVID-19 in adults of all ages. Risk of severe disease also rises steadily with age, with more than 80% of deaths occurring in adults older than age 65. People of color are also at increased risk of severe disease and death, often at a younger age, due to systemic health and social inequities.

b Underlying medical conditions are also associated with severe illness in children, but evidence implicating specific conditions is limited. Children with the following conditions might be at increased risk for severe illness: medical complexity; genetic, neurologic, or metabolic conditions; congenital heart disease; obesity; diabetes; asthma or other chronic lung disease; sickle cell disease; immunosuppression.

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C. Complications And Associated Syndromes

6. What Are The Major Cardiac Complications In Patients With COVID-19? And How Often Do They Occur?

Cardiac manifestations are common in hospitalized patients and occur most frequently in critically ill patients. The most common complications are listed here:

- Cardiac troponin elevation, which is a biomarker of myocardial injury, occurs in approximately 10 to 30 percent of hospitalized patients. In the majority of these patients, cardiac signs and symptoms are not present and the cause of the troponin rise is not acute myocardial infarction (MI). However, patients with a clinical presentation (including history or electrocardiogram) suggestive of acute MI require prompt evaluation and treatment.
- Usually, troponin elevation in COVID-19 patients is due to other causes of myocardial injury including stress cardiomyopathy, hypoxic injury, myocarditis, right heart strain, microvascular dysfunction, and systemic inflammatory response syndrome. For those without suspected acute MI, further evaluation is focused on testing expected to impact management.

The following complications may occur with or without troponin elevation:

- **Arrhythmias** have been reported in approximately 5 to 20 percent of hospitalized cases, and most are asymptomatic. Causes may include hypoxia, electrolyte abnormalities, myocardial injury, and drug effects (such as QT-prolonging agents).

- **Heart failure** is the most common symptomatic cardiac complication. Data on its incidence are limited; however, its presence is associated with increased mortality. Heart failure in patients with COVID-19 may be precipitated by acute illness in patients with pre-existing known or undiagnosed heart disease (eg, coronary artery disease or hypertensive heart disease) or incident acute myocardial injury (eg, stress cardiomyopathy or acute MI).

7. What Are The Major Thrombotic Complications In Patients With COVID-19?

- COVID-19 is a hypercoagulable state associated with an increased risk of venous thromboembolism (VTE; including deep vein thrombosis and pulmonary embolism) and arterial thrombosis, including stroke, myocardial infarction, and possibly limb ischemia.
- The risk is highest in individuals in the intensive care unit (ICU), often despite prophylactic anticoagulation. Bleeding is not common but has been seen, especially in the setting of trauma and/or anticoagulation.

8. What Are The Most Common Dermatologic Syndromes Associated With COVID-19?

- The most common cutaneous findings reported in patients with COVID-19 include an exanthematous (morbilliform) rash, pernio-like acral lesions, livedo-like lesions, retiform purpura, necrotic vascular lesions, urticaria, vesicular (varicella-like) eruptions, and erythema multiforme-like lesions.
- An erythematous, polymorphic rash has also been associated with a related multisystem inflammatory syndrome in children. The frequency of cutaneous findings is estimated to range from less than 1 percent to 20 percent of patients with COVID-19.
- Uncertainty remains about the strength and mechanisms of associations between reported skin findings and COVID-19.
- The timing of the appearance of cutaneous findings in relation to the course of COVID-19 has varied, with reports describing skin changes occurring prior to, concomitantly, or following symptoms of COVID-19.

9. What Is Multisystem Inflammatory Syndrome Associated With COVID-19?

- Multisystem inflammatory syndrome in children (MIS-C) is a rare but serious condition that has been reported in patients with current or recent COVID-19 infection or exposure. It shares clinical features with Kawasaki disease (KD), KD shock, and toxic shock syndrome.
- Clinical features include persistent fever, severe illness with involvement of multiple organ systems, and elevated inflammatory markers (Table IIA and IIB). Most children with MIS-C have survived, although some have required intensive care. Pending additional information, children with clinical features of MIS-C should be promptly referred to a specialist in pediatric infectious diseases, rheumatology, cardiology, and/or critical care, as necessary.
- A very similar syndrome has also been reported in adults in association with COVID-19 infection or exposure and is termed multisystem inflammatory syndrome in adults (MIS-A).

Table IIA. CDC Case Definition

All 4 Criteria Must Be Met:

1. Age <21 years
2. Clinical Presentation Consistent With MIS-C, Including All Of The Following:
   - **Fever:**
     - Documented fever >38.0°C (100.4°F) for ≥24 hours

     or
     - Report of subjective fever lasting ≥24 hours
   - **Laboratory Evidence Of Inflammation**
     - Including, but not limited to, **any** of the following:
       - Elevated CRP
       - Elevated ESR
       - Elevated fibrinogen
       - Elevated procalcitonin
       - Elevated D-dimer
       - Elevated ferritin
       - Elevated LDH
       - Elevated IL-6 level
       - Neutrophilia
       - Lymphocytopenia
       - Hypoalbuminemia
   - **Multisystem Involvement**
     - **2 or more** organ systems involved:
       - Cardiovascular (eg, shock, elevated troponin, elevated BNP,
       - abnormal echocardiogram, arrhythmia)
       - Respiratory (eg, pneumonia, ARDS, pulmonary embolism)
       - Renal (eg, AKI, renal failure)
       - Neurologic (eg, seizure, stroke, aseptic meningitis)
       - Hematologic (eg, coagulopathy)
       - Gastrointestinal (eg, abdominal pain, vomiting, diarrhea, elevated
       - liver enzymes, ileus, gastrointestinal bleeding)
       - Dermatologic (eg, erythroderma, mucositis, other rash)
   - **Severe illness requiring hospitalization**
3. **No Alternative Plausible Diagnoses**
4. **Recent Or Current SARS-CoV-2 Infection Or Exposure**
   - **Any** of the following:
     - Positive SARS-CoV-2 RT-PCR
     - Positive serology
     - Positive antigen test
     - COVID-19 exposure within the 4 weeks prior to the onset of symptoms

Table IIB. WHO Case Definition

All 6 Criteria Must Be Met:
1. Age 0 to 19 years
2. Fever for ≥3 days
3. Clinical Signs Of Multisystem Involvement (at least 2 of the following): ▪ Rash, bilateral nonpurulent conjunctivitis, or mucocutaneous inflammation signs (oral, hands, or feet) ▪ Hypotension or shock ▪ Cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or elevated troponin/BNP) ▪ Evidence of coagulopathy (prolonged PT or PTT; elevated D-dimer) ▪ Acute gastrointestinal symptoms (diarrhea, vomiting, or abdominal pain)
4. Elevated Markers Of Inflammation (eg, ESR, CRP, or procalcitonin)
5. No Other Obvious Microbial Cause Of Inflammation, Including Bacterial Sepsis And Staphylococcal/Streptococcal Toxic Shock Syndromes
6. Evidence Of SARS-CoV-2 Infection ▪ Any of the following: • Positive SARS-CoV-2 RT-PCR • Positive serology • Positive antigen test • Contact with an individual with COVID-19

The Tables IIA and IIB outlines the CDC's and WHO's case definitions of MIS-C.

Patients who meet these criteria and who also fulfill full or partial criteria for Kawasaki disease should be considered to have MIS-C and should be reported. In addition, MIS-C should be considered in any pediatric death with evidence of SARS-CoV-2 infection.

CDC: Centers for Disease Control and Prevention
WHO: World Health Organization
MIS-C: Multisystem inflammatory syndrome in children
CRP: C-reactive protein
ESR: Erythrocyte sedimentation rate
LDH: Lactate dehydrogenase
IL-6: Interleukin-6
BNP: Brain natriuretic peptide
ARDS: Acute respiratory distress syndrome
AKI: Acute kidney injury
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2
RT-PCR: Real-time polymerase chain reaction
COVID-19: Coronavirus disease 2019
PT: Prothrombin time
PTT: Partial thromboplastin time

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10. What Is "Long-COVID"?

- "Long-COVID," also referred to as post-acute COVID-19, chronic COVID-19, post-COVID syndrome, or post-acute sequelae of SARS-CoV-2 infection (PASC), generally refers to symptoms that develop during or after acute COVID-19 illness, continue for ≥12 weeks, and are not explained by an alternative diagnosis.
- It is not yet known whether "long-COVID" represents a new syndrome unique to COVID-19 or overlaps with recovery from similar illnesses.
- Persistent physical symptoms following acute COVID-19 are common and typically include fatigue, dyspnea, chest pain, and cough.
- Headache, joint pain, insomnia, anxiety, cognitive dysfunction, myalgias, and diarrhea have also been reported.
- The time to symptom resolution depends primarily on premorbid risk factors, the severity of the acute illness, and the spectrum of initial symptoms.
- However, prolonged symptoms are common even in patients with less severe disease who were never hospitalized.

D. Clinical Evaluation

11. Is There A Way To Distinguish Covid-19 Clinically From Other Respiratory Illness, Particularly Influenza?

- No, the clinical features of COVID-19 overlap substantially with influenza and other respiratory viral illnesses. There is no way to distinguish among them without testing.

12. When Should Patients With Confirmed Or Suspected Covid-19 Be Advised To Stay At Home? Have An In-Person Clinical Evaluation?

- Home management is appropriate for most patients with mild symptoms (eg, fever, cough, and/or myalgias without dyspnea), provided they can be adequately isolated, monitored, and supported in the outpatient setting.
- However, there should be a low threshold to clinically evaluate patients who have any risk factors for more severe illness, even if they have only mild symptoms. As an example, some outpatients with mild to moderate symptoms, but who have certain risk factors for severe disease, may be candidates for treatment with monoclonal antibody therapy.
- Patients being managed at home should be educated about the potential for worsening disease and advised to closely monitor for symptoms of more serious disease, including dyspnea or persistent chest pain. The development of these symptoms should prompt clinical evaluation and possible hospitalization.

E. Laboratory Evaluation

13. What Laboratory Abnormalitis Are Commonly Seen In Patients With COVID-19?

- Common laboratory abnormalities among hospitalized patients with COVID-19 include:
  - Lymphopenia (reported in up to 90 percent)
  - Elevated aminotransaminase levels
  - Elevated lactate dehydrogenase levels
  - Elevated inflammatory markers (eg, ferritin, C-reactive protein, and erythrocyte sedimentation rate)
- Abnormalities in coagulation testing, elevated procalcitonin levels, and elevated troponin levels have also been reported. The degree of these abnormalities tends to correlate with disease severity.

14. What Are The Major Coagulation Abnormalities In Patients With COVID-19?

- A number of laboratory abnormalities have been reported, including high fibrinogen and D-dimer and mild prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT).
- Abnormal coagulation studies are mainly used to monitor clinical status and to help determine level of care. Very high D-dimer is associated with a high mortality rate. Atypical findings (eg, severe thrombocytopenia) should be further evaluated.

F. Diagnostic Testing

15. What Are The Different Types Of Tests For COVID-19?

- There are three major types of tests for COVID-19 (Table III):
  - **Nucleic Acid Amplifications Tests** (NAATs; eg, reverse transcription polymerase chain reaction [RT-PCR]) – RT-PCR for SARS-CoV-2 is the primary test used to diagnose active COVID-19. The test is performed primarily on upper respiratory specimens (including nasopharyngeal swabs, nasal swabs, and saliva) but can also be performed on lower respiratory tract samples. Sensitivity and specificity are generally high, although performance varies based on the specific assay used, specimen quality, and duration of illness.
  - **Serology** – Serologic tests measure antibodies to SARS-CoV-2 and are primarily used to identify patients who have had COVID-19 in the past as well as patients with current infection who have had symptoms for three to four weeks. Sensitivity and specificity are highly variable, and cross-reactivity with other coronaviruses has been reported.
  - **Antigen Tests** – Antigen tests can also be used to diagnosis active infection, although they are less sensitive than NAATs. These tests are typically performed on nasopharyngeal or nasal swabs.
- Both NAATs and antigen tests can be used to screen patients in congregate settings, such as long-term care facilities.

Table III. Diagnostic Tests For COVID-19 [1,2]

Test category	Primary clinical use	Specimen type	Performance characteristics	Comments
NAATs (including RT-PCR)	Diagnosis of current infection	Respiratory tract specimens [a]	High analytic sensitivity and specificity in ideal settings. Clinical performance depends on the type and quality of the specimen and the duration of illness at the time of testing. Reported false-negative rate ranges from <5 to 40%, depending on the test used. [b]	Time to perform the test ranges from 15 minutes to 8 hours. [c] Turnaround time is influenced by the test used and laboratory workflow. Some assays allow home collection of specimens that are mailed in.
Serology (antibody detection)	Diagnosis of prior infection (or infection of at least 3 to 4 weeks' duration)	Blood	Sensitivity and specificity are highly variable. Detectable antibodies generally take several days to weeks to develop; IgG usually develops by 14 days after onset of symptoms. Cross-reactivity with other coronaviruses has been reported. Individual results should be interpreted with caution in settings of low seroprevalence; serologic tests that have high specificity still have a low positive predictive value.	Time to perform the test ranges from 15 minutes to 2 hours. Turnaround time is influenced by the test used and laboratory workflow. It remains uncertain whether a positive antibody test indicates immunity against future infection.
Antigen tests	Diagnosis of current infection	Nasopharyngeal or nasal swabs	Antigen tests are generally less sensitive than nucleic acid tests. Sensitivity is highest in symptomatic individuals within 5 to 7 days of symptom onset.	Time to perform the test is <1 hour.

COVID-19: Coronavirus disease 2019

NAAT: Nucleic acid amplification test

RT-PCR: Real-time polymerase chain reaction

IgG: Immunoglobulin G

CDC: United States Centers for Disease Control and Prevention

a Nasopharyngeal swabs, nasal swabs (from the mid-turbinate area or from both anterior nares), nasal or nasopharyngeal washes, oropharyngeal swabs, and saliva are recommended by the CDC. The Infectious Diseases Society of America suggests a nasopharyngeal swab, a mid-turbinate swab, an anterior nasal swab, saliva, or a combined anterior nasal/oropharyngeal swab rather than an oropharyngeal swab. Nasal swabs can be self-collected by the patient on-site or at home. Mid-turbinate swabs and saliva can be collected by the patient while supervised. Lower respiratory tract specimens can be collected in hospitalized patients with suspected lower respiratory tract infection if an upper respiratory tract specimen tests negative.

b A single positive test generally confirms the diagnosis. If initial testing is negative and clinical suspicion remains, performing a second test can enhance diagnostic yield.

c Low-complexity rapid tests can be performed at the point of care and provide results in less than 1 hour. Most moderate- to high-complexity laboratory-based tests result in several hours. However, the time for a clinician or patient to receive a result depends on how frequently the test is run and other processing factors.

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16. How Accurate Is RT-PCR For SARS-CoV-2? Should Two Tests Be Performed Or One?

- A positive RT-PCR for SARS-CoV-2 generally confirms the diagnosis of COVID-19.
- However, false-negative tests from upper respiratory specimens have been well documented.
- If initial testing is negative, but the suspicion for COVID-19 remains, and determining the presence of infection is important for management or infection control, we suggest repeating the test.
- For hospitalized patients with evidence of lower respiratory tract involvement, the repeat test can be performed on expectorated sputum or a tracheal aspirate, if available.
- In many cases, because of the limited availability of testing and concern for false-negative results, the diagnosis of COVID-19 is made presumptively based on a compatible clinical presentation in the setting of an exposure risk (residence in or travel to an area with widespread community transmission or known contact).

17. What Are The Indications For Testing Asymptomatic Individuals?

- Indications for testing asymptomatic individuals include close contact with an individual with COVID-19, screening in congregate settings (eg, long-term care facilities, correctional and detention facilities, homeless shelters), and screening hospitalized patients in high-prevalence regions.
- Screening may also be indicated prior to time-sensitive surgical procedures or aerosol-generating procedures and prior to receiving immunosuppression.

18. When Is The Best Time To Test For COVID-19 Following An Exposure?

- The optimal time to test for COVID-19 following exposure is uncertain.
- The United States Centers for Disease Control and Prevention (CDC) recommends testing immediately after the exposure is identified to quickly identify infection and, if the test is negative, retesting five to seven days after the last exposure.
- In some cases, testing can be used to help determine the length of quarantine (eg, reduce the quarantine period to seven days if an individual remains asymptomatic and has a negative viral test within 48 hours of the planned end of quarantine).

19. Can SARS-CoV-2 Variants Be Reliably Detected By Available Diagnostic Assays?

- Thus far, yes. Most circulating SARS-CoV-2 variants have mutations in the viral spike protein.

- While many nucleic acid amplification tests target the gene that encodes the spike protein, they also target other genes. Thus, if a mutation alters one gene target, the other gene targets still function and the test will detect the virus.
- Most antigen tests target nucleocapsid protein, so mutations in the spike protein would not impact the accuracy of such antigen tests.

G. Home Care

20. Are There Any COVID-19-Specific Therapies Available For Non-Hospitalized Patients?

- Antibody-based treatments may reduce the risk of severe disease in high-risk outpatients.
- However, they require intravenous administration, necessitate the use of valuable ancillary services, and must be given early in the course of illness. These factors make administration operationally complicated.
- **Monoclonal Antibody Therapy** – In the United States, two combination monoclonal antibody therapies targeting SARS-CoV-2.
- Bamlanivimab-etesevimab and casirivimab-imdevimab are available for the treatment of non-hospitalized adults (≥18 years) with mild to moderate COVID-19 and any of the following risk factors for severe disease:
  - Body mass index (BMI) ≥35 kg/m^2
  - Chronic kidney disease
  - Diabetes mellitus
  - Immunosuppression (immunosuppressive disease or treatment)
  - ≥65 years of age
  - ≥55 years of age **and** who have cardiovascular disease, **and/or** hypertension, **and/or** chronic obstructive pulmonary disease (or other chronic respiratory disease)
- Given the limited data and intensive resources needed for administration, it is suggested **not** to routinely treating patients with monoclonal antibodies. Nevertheless, if supporting infrastructure is in place, it is reasonable to offer bamlanivimab-etesevimab, which is recommended by the National Institutes of Health based on preliminary evidence of a mortality reduction.
- SARS-CoV-2 variants may impact the clinical efficacy of monoclonal antibody therapies.
- In the United States, due to the increasing prevalence of variants that are resistant to bamlanivimab, this agent is no longer available as for use as monotherapy and should only be administered in combination with etesevimab.
- Clinicians should be aware of the prevalence of variants in their local area and the potential resistance to available monoclonal antibody therapies.
- If monoclonal antibody therapy is used, it should be given **as soon as possible** after illness onset and positive SARS-CoV-2 test has been obtained; ideally within three days, but no longer than 10 days after symptom onset.
- **High-titer Convalescent Plasma** – Limited high-quality data suggest that early administration of high-titer convalescent plasma may lower the risk of progression to severe disease in high-risk older adults (age ≥75 years or ≥65 years with specific comorbidities) with mild illness.
  - Convalescent plasma appears to have the greatest efficacy when given within 72 hours of symptom onset. As with monoclonal antibody therapy, high-titer convalescent plasma therapy remains investigational and should be administered through a clinical trial if available.

- ❖ It is not routinely treated COVID-19 in non-hospitalized patients with glucocorticoids, antibiotics, anticoagulation, or antiplatelet therapy.

21. What Advice Should Be Given To Patients With Known Or Presumed COVID-19 Managed At Home?

- ➢ For most patients with COVID-19 who are managed at home, the following advise are given to patients :
  - ❖ Supportive care with antipyretics/analgesics (eg, acetaminophen) and hydration
  - ❖ Communication with their health care provider
  - ❖ Monitoring for clinical worsening, particularly the development of new or worsening dyspnea, which should prompt clinical evaluation and possible hospitalization
  - ❖ Separation from other household members, including pets (eg, staying in a separate room when possible and wearing a mask when in the same room)
  - ❖ Frequent hand washing for all family members
  - ❖ Frequent disinfection of commonly touched surfaces

22. How Long Should Patients Cared For At Home Stay Isolated?

- ➢ The United States Centers for Disease Control and Prevention (CDC) has issued recommendations on discontinuation of home isolation. A non-test-based strategy is preferred for most patients.
- ➢ For most symptomatic immunocompetent patients cared for at home, isolation can usually be discontinued when the following criteria are met:
  - ❖ At least 10 days have passed since symptoms first appeared **AND**
  - ❖ At least one day (24 hours) has passed since resolution of fever without the use of fever-reducing medications **AND**
  - ❖ There is improvement in symptoms (eg, cough, shortness of breath)
- ➢ In some cases, patients may have had laboratory-confirmed COVID-19 but did not have any symptoms when they were tested.
- ➢ In such patients, home isolation can usually be discontinued using a time-based strategy (when at least 10 days have passed since the date of their first positive COVID-19 test) as long as there was no evidence of subsequent illness.

23. What Is The Significance Of A Persistently Positive RT-PCR For Weeks After Illness?

- ➢ Patients diagnosed with COVID-19 can have detectable SARS-CoV-2 RNA in upper respiratory tract specimens for weeks after the onset of symptoms.
- ➢ However, prolonged viral RNA detection does not necessarily indicate prolonged infectiousness.
- ➢ According to the CDC, isolation of infectious virus more than 10 days after illness onset is rare in patients whose symptoms have resolved.
- ➢ There is no standardized approach to management of patients with persistently positive reverse transcription polymerase chain reaction (RT-PCR) 10 days or more after resolution of symptoms.

- However, such patients are generally felt to have low infectiousness, particularly after mild to moderate disease and in the absence of immunocompromise. This is why symptom- and time-based approaches for discontinuation of precautions are recommended for most patients.

H. Hospital Care

24. What Is The Preferred Approach To Oxygenation?

- As a general approach, target range of peripheral oxygen saturation is maintained between 90 and 96 percent using the lowest possible fraction of inspired oxygen. It is also necessary to encourage patients to self-prone, when possible, based on data that suggest improved oxygenation and minimal downside to proning.
- For most patients, it is better to use low-flow oxygen (eg, low-flow nasal cannula, simple face mask), which minimizes risk of viral aerosolization. Because exertional desaturation is common and can be profound, providing additional support with activity (eg, going to the bathroom) may be needed.
- For those with acute hypoxemic respiratory failure and higher oxygen needs than low-flow oxygen can provide, it is suggested for selective use of noninvasive measures rather than routinely proceeding directly to intubation. Among the noninvasive modalities,it is preferred for high-flow nasal cannula (HFNC) is over non-invasive ventilation (NIV), unless there is separate indication for NIV (eg, acute exacerbation of chronic obstructive pulmonary disease, heart failure).
- In patients who have any of the following, have a low threshold for intubation: rapid progression over a few hours; failure to improve despite HFNC >50 L/min and FiO_2 >0.6; development of hypercapnia; and/or hemodynamic instability or multiorgan failure.
- When mechanical ventilation is required, it is preferred to use low tidal volume ventilation (LTVV) targeting ≤6 mL/kg predicted body weight (PBW; range 4 to 8 mL/kg PBW) that targets a plateau pressure ≤30 cm H_2O and applies positive end-expiratory pressure (PEEP).
- For patients with COVID-19 who fail LTVV, prone ventilation is the preferred next step .
- For those who fail LTVV and prone ventilation, alveolar recruitment maneuvers, inhaled pulmonary vasodilators, and, rarely, extracorporeal membrane oxygenation are considerations.

25. When Are Antiviral Treatment, Glucocorticoids, And Other COVID-19 Specific Therapies Indicated? And Which Agents Are Preferred?

- Indications for antiviral treatment or other COVID-19-specific therapies have not been formally defined.
- Trial data suggest a mortality benefit with dexamethasone.
- Remdesivir may hasten time to recovery but has not clearly been demonstrated to reduce mortality.
- No other therapies have proven effective in hospitalized patients.
- Approach to COVID-19-specific therapy in hospitalized patients depends on the severity of disease. Severe disease is characterized by hypoxia (O_2 saturation ≤94 percent on room air) or need for oxygenation or ventilatory support.
- For patients with nonsevere disease, care is primarily supportive, with close monitoring for disease progression. When clinical trials for treatment of nonsevere disease are available, those are prioritized who have laboratory features associated with disease progression **(Table IV).**
- For hospitalized patients with hypoxia who are not yet on oxygen, it is suggested for remdesivir, if available. It is suggested not using dexamethasone in such patients.

- For hospitalized patients who are receiving low-flow supplemental oxygen, it is suggested low-dose dexamethasone and, if available, remdesivir. For those who have significantly elevated inflammatory markers (eg, C-reactive protein [CRP] level ≥75 mg/L) and continuously increasing oxygen requirements despite dexamethasone, it is suggested to add tocilizumab.
- For hospitalized patients who are receiving high-flow supplemental oxygen or non-invasive ventilation, it is suggested for low-dose dexamethasone. For those who are within 24 to 48 hours of admission to an intensive care unit (ICU) or receipt of ICU-level care, it is suggested to add tocilizumab.
- It is also suggested to add remdesivir; however, if supplies are limited, remdesivir is preferred for patients who are on low-flow oxygen supplementation at baseline.
- For hospitalized patients with severe disease who require mechanical ventilation or extracorporeal membrane oxygenation, it is recommended for low-dose dexamethasone. For those who are within 24 to 48 hours of admission to an ICU, it is suggested to add tocilizumab. It is suggested for not routinely using remdesivir in this population.
- Although it is reasonable to add remdesivir to dexamethasone in individuals who have only been intubated for a short time (eg, 24 to 48 hours), the clinical benefit of this is uncertain.
- If dexamethasone is not available, other glucocorticoids at equivalent doses are reasonable alternatives.

Table IV. Laboratory Features Associated With Severe COVID-19 [1-6]

Abnormality	Possible Threshold
Elevations In:	
▪ D-dimer	>1000 ng/mL (normal range: <500 ng/mL)
▪ CRP	>100 mg/L (normal range: <8.0 mg/L)
▪ LDH	>245 units/L (normal range: 110 to 210 units/L)
▪ Troponin	>2× the upper limit of normal (normal range for troponin T high sensitivity: females 0 to 9 ng/L; males 0 to 14 ng/L)
▪ Ferritin	>500 mcg/L (normal range: females 10 to 200 mcg/L; males 30 to 300 mcg/L)
▪ CPK	>2× the upper limit of normal (normal range: 40 to 150 units/L)
Decrease In:	
▪ Absolute lymphocyte count	<800/microL (normal range for age ≥21 years: 1800 to 7700/microL)

COVID-19: Coronavirus disease 2019
CRP: C-reactive protein
LDH: Lactate dehydrogenase
CPK: Creatine phosphokinase

- Although these laboratory features are associated with severe disease in patients with COVID-19, they have not been clearly demonstrated to have prognostic value.
- Using the thresholds listed above to identify patients who may be at risk for severe disease; they are extrapolated from published cohort data and individualized to the reference values used at respective laboratory.
- However, the specific thresholds are not well established and may not be applicable if laboratories use other reference values.

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26. Is Anticoagulation Indicated In All Hospitalized Patients? And If So, How Much?

- **Yes,** all hospitalized patients with COVID-19 should receive at least prophylactic-dose anticoagulation unless contraindicated.
- For thromboprophylaxis, low-molecular-weight (LMW) heparin is preferred, but prophylactic-dose unfractionated heparin can be used if LMW heparin is unavailable or if kidney function is severely impaired. Prophylactic anticoagulation is continued after discharge in selected patients.
- Some institutional protocols and experts include more aggressive anticoagulation with intermediate-dose or even therapeutic-dose anticoagulation for thromboprophylaxis, especially in critically ill patients.
- If VTE is documented (or, in some cases, strongly suspected) full (therapeutic)-dose anticoagulation is used for at least three months.
- Evaluation and management of COVID-19 hypercoagulability is presented in the table V.

Table V. Evaluation And Management Of COVID-19-Associated Hypercoagulability

Evaluations And Monitoring	
Inpatients	• Daily PT, aPTT, fibrinogen, D-dimer; frequency may be reduced depending on acuity and trend in values • Diagnostic imaging studies if feasible for clinically suspected DVT or PE; consult PERT team • Alternative evaluations if standard imaging studies are not feasible
Outpatients	• Routine coagulation testing is not required
Management	
Abnormal Coagulation Studies	• Use for prognostic information and level of care • Do not intervene solely based on coagulation abnormalities
VTE Prophylaxis	• Prophylactic-dose anticoagulation for all inpatients • Intermediate- or therapeutic-dose anticoagulation for selected critically ill individuals (eg, in the ICU) • Possible continued thromboprophylaxis following discharge • Possible thromboprophylaxis in selected outpatients
VTE Treatment	• Therapeutic (full-dose) anticoagulation for documented or presumptive diagnosis of VTE • Initiate in hospital per standard protocols • Consider extended thromboprophylaxis following discharge • Reserve fibrinolytic agents (eg, tPA) for limb-threatening DVT, massive PE, acute stroke, or acute MI; consult PERT or stroke team
Clotting In Vascular Catheters Or Extracorporeal Circuits [a]	• Therapeutic (full-dose) anticoagulation • Standard protocols for continuous renal replacement therapy or ECMO
Bleeding	• Similar to individuals without COVID-19 • Transfusions for anemia or thrombocytopenia • Anticoagulant reversal and/or discontinuation for anticoagulant-associated bleeding • Specific treatments (eg, factor replacement) for underlying bleeding disorders • Avoid antifibrinolytic agents in individuals with acute decompensated DIC [b]

COVID-19: Coronavirus disease 2019
PT: Prothrombin time
aPTT: Activated partial thromboplastin time
DVT: Deep vein thrombosis
PE: Pulmonary embolism
PERT: Pulmonary embolism response team
VTE: Venous thromboembolism
ICU: Intensive care unit
tPA: Tissue plasminogen activator
MI: Myocardial infarction
ECMO: extracorporeal membrane oxygenation
DIC: disseminated intravascular coagulation

[a] Includes continuous renal replacement therapy (CRRT; eg, hemodialysis), ECMO, or other extracorporeal circuits.

[b] Acute decompensated DIC is associated with clinical bleeding (and/or thrombosis) and laboratory findings including prolonged PT and aPTT, thrombocytopenia, and hypofibrinogenemia. Antifibrinolytic agents (tranexamic acid and epsilon aminocaproic acid) are avoided because they may tip the balance towards thrombosis.

I. Other Medication Considerations

27. Should I Use Acetaminophen Or NSAIDS When Providing Supportive Care?

- Nonsteroidal anti-inflammatory drugs (NSAIDs) have been theorized to cause harm in patients with COVID-19, but clinical data are limited.
- Given the uncertainty, acetaminophen is used as the preferred antipyretic agent for most patients rather than NSAIDs.
- If NSAIDs are needed, we use the lowest effective dose. NSAIDs is not routinely discontinued in patients using them for the management of chronic illnesses.
- The US Food and Drug Administration (FDA), the European Medicine Agency (EMA), and the World Health Organization (WHO) do not recommend that NSAIDs be avoided when clinically indicated.

28. Do ACE Inhibitors And ARBs Increase The Likelihood Of Severe COVID-19?

- Patients receiving angiotensin-converting-enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) should continue treatment with these agents.
- The membrane-bound ACE_2 functions as a receptor for SARS-CoV-2, and because ACE inhibitors and ARBs may increase the expression of ACE_2, there is speculation that patients with COVID-19 who are receiving these agents may be at increased risk for severe disease.
- However, there is no evidence to support an association of ACE inhibitors and ARBs with more severe disease, and it is also possible that these drugs may attenuate the severity of disease.
- In addition, stopping these agents in some patients can exacerbate comorbid cardiovascular or kidney disease and increase mortality.

J. Special Populations

ASTHMA/COPD

29. Should Patients Using Inhaled Glucocorticoids For Asthma Or COPD Be Advised To Stop These Medications To Prevent COVID-19?

- No, patients with asthma or chronic obstructive pulmonary disease (COPD) who need inhaled glucocorticoids to maintain control of their asthma or COPD should continue them at their usual dose.
- When indicated, inhaled steroids help to minimize risk of an asthma or COPD exacerbation and the associated need for interaction with the health care system.
- There is no good evidence that inhaled glucocorticoids increase susceptibility to COVID-19 or have an adverse effect on the course of infection. Stopping them may worsen asthma or COPD control and thereby increase the risk for complications of COVID-19, if acquired.

30. Should Patients With Covid-19 And An Acute Exacerbation Of Asthma Or COPD Be Treated With Systemic Glucocorticoids?

- Yes, patients with COVID-19 infection and a concomitant acute exacerbation of asthma or COPD should receive prompt treatment with systemic glucocorticoids as indicated by usual guidelines.
- Delaying therapy can increase the risk of a life-threatening exacerbation. While the World Health Organization (WHO) and United States Centers for Disease Control and Prevention (CDC) recommend glucocorticoids not be routinely used in the treatment of COVID-19 infection, exacerbations of asthma and COPD are considered appropriate indications for use.
- Overall, the known benefits of systemic glucocorticoids for exacerbations of asthma and COPD outweigh the potential harm in COVID-19 infection.

K. Prevention And Infection Control

31. Have Any Medications Been Shown To Prevent COVID-19?

- No agent is known to be effective for preventing COVID-19. While hydroxychloroquine is being studied as a prophylactic agent, randomized trials found that it was not effective for prevention.
- It is recommended that neither this medication nor any other be used for prophylaxis outside of clinical trials.

32. What PPE Is Recommended For Health Care Workers Taking Care Of Patients With Suspected Or Confirmed COVID-19?

- Any personnel entering the room of a patient with suspected or confirmed COVID-19, regardless of COVID-19 vaccination status, should wear the appropriate personal protective equipment (PPE): gown, gloves, eye protection (full face shield preferred rather than goggles or a surgical mask with an attached eye shield), and a respirator (eg, an N95 respirator).
- If the supply of respirators is limited, medical masks are an acceptable alternative, except during aerosol-generating procedures (eg, tracheal intubation and extubation, tracheotomy, bronchoscopy, noninvasive ventilation, cardiopulmonary resuscitation).

- Health care workers should be aware of the appropriate sequence of putting on and taking off PPE to avoid contamination.

33. What Type Of Room Should Patients With Known Or Suspected COVID-19 Be Placed In?

- Most hospitalized patients should be placed in a well-ventilated, single-occupancy room with a closed door and dedicated bathroom. When this is not possible, patients with confirmed COVID-19 can be housed together.
- Patients undergoing aerosol-generating procedures (eg, tracheal intubation and extubation, tracheostomy, bronchoscopy, noninvasive ventilation) should be placed in an airborne isolation room (ie, a single-patient, negative-pressure room), except when these procedures are performed in the operating room or when such rooms are unavailable.
- Special considerations for patients undergoing aerosol-generating procedures in the operating room are discussed elsewhere.
- Outside of the operating room, patients with suspected or known COVID-19 should not be placed in positive-pressure rooms.

34. Should Patients Be Advised To Wear Masks In Public?

- Yes, patients should be advised to wear masks when in public spaces (indoors or outdoors) or when around individuals outside of their household.
- This is consistent with recommendations from the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention (CDC).
- The CDC also advises that individuals who have been fully vaccinated should still wear masks in public but can forgo mask use when visiting with other vaccinated individuals or with unvaccinated members of a single household who are at low risk for severe COVID-19.
- The rationale for individuals (regardless of symptoms) to wear a mask in the community is to contain secretions of and prevent transmission from individuals with infection, including those who have asymptomatic or presymptomatic infection.
- Masks also reduce exposure to SARS-CoV-2 for the wearer.

L. Vaccination And Immunity

35. Does Protective Immunity Develop After SARS-CoV-2 Infection? Can Reinfection Occur?

- SARS-CoV-2-specific antibodies and cell-mediated responses are induced following infection.
- Evidence suggests that some of these responses are protective and generally last at least several months.
- However, it is unknown whether all infected patients mount a protective immune response and how long protective effects last beyond the first few months after infection.
- The short-term risk of reinfection (eg, within the first few months after initial infection) appears low, though reinfection does occur sporadically.

36. How Efficacious Is Vaccination At Preventing Symptomatic COVID-19?

Vaccine efficacy varies by type. Based on phase III trial data:

- BNT162b2 (Pfizer-BioNTech COVID-19 vaccine) had 95 percent efficacy in preventing symptomatic COVID-19 at or after day 7 following completion of a two-dose series.

- mRNA-1273 (Moderna COVID-19 vaccine) had 95 percent efficacy in preventing symptomatic COVID-19 at or after day 7 following completion of a two-dose series.
- Ad26.COV2.S (Janssen) had 66 percent efficacy against moderate to severe COVID-19 and 85 percent efficacy against severe COVID-19 at or after 28 days following administration of a single dose.
- ChAdOx1 nCoV-19/AZD1222 (AstraZeneca COVID-19 vaccine) had 70 percent efficacy in preventing symptomatic COVID-19 at or after two weeks following completion of a two-dose series.
- Ongoing evaluation is needed to answer outstanding questions about efficacy, safety, the durability of vaccine-induced immunity, and impact on community transmission.

37. Does Vaccination Prevent Asymptomatic Transmission?

- Limited data suggest that certain vaccines can reduce the risk of asymptomatic infection, although the overall impact is uncertain.
- Because asymptomatic infection contributes to SARS-CoV-2 transmission, continued personal and public health preventive measures are recommended for vaccinated individuals.

38. How Effective Is Vaccination Against SARS-CoV-2 Variants?

- Many circulating SARS-CoV-2 variants contain mutations in the surface spike protein, which is the most common vaccine target. The impact of these mutations on vaccine efficacy is not well studied and undoubtedly varies by variant and by vaccine type.
- Preliminary evidence suggests that both BNT162b2 (Pfizer-BioNTech COVID-19 vaccine) and mRNA-1273 (Moderna COVID-19 vaccine) retain neutralizing activity against B.1.1.7, the dominant viral variant in the United Kingdom and other countries. Both vaccines have reduced neutralizing activity against B.1.351, the dominant variant in South Africa, though the clinical significance of this reduction is not known.
- The efficacy of Ad26.COV2.S (Janssen) varied by region: 74 percent in the United States, 66 percent in Brazil, where the P.2 variant was prevalent, and 52 percent in South Africa, where most infections were caused by the variant B.1.351. Nevertheless, vaccine efficacy against severe/critical disease was similar across regions.
- The efficacy of ChAdOx1 nCoV-19/AZD1222 (AstraZeneca COVID-19 vaccine) against B.1.1.7 appears to be similar to wild-type virus despite reduced neutralizing activity.
- As mutations continue to accumulate, there is potential for vaccine efficacy to further decline.

39. What Are The Indications And Contraindications To Vaccination?

- For patients in the United States, it is recommended vaccination with either BNT162b2 (Pfizer-BioNTech COVID-19 vaccine), mRNA-1273 (Moderna COVID-19 vaccine), or Ad26.COV2.S (Janssen COVID-19 vaccine).
- Individuals ≥16 years old are eligible for BNT162b2 (Pfizer-BioNTech COVID-19 vaccine).
- Individuals ≥18 years old are eligible for mRNA-1273 (Moderna COVID-19 vaccine) and Ad26.COV2.S (Janssen COVID-19 vaccine).

- **Contraindications to these vaccines are**:
  - For the mRNA COVID-19 vaccines:
    - A history of a severe allergic reaction, such as anaphylaxis, after a previous dose of an mRNA COVID-19 vaccine or to any of its components (including polyethylene glycol).
    - An immediate allergic reaction of any severity (including hives) to a previous dose of an mRNA COVID-19 vaccine, to any of its components, or to polysorbate (with which there can be cross-reactive hypersensitivity to polyethylene glycol). Such individuals should not receive an mRNA COVID-19 vaccine unless they have been evaluated by an allergy expert who determines that it can be given safely.
    - The United States Advisory Committee on Immunization Practices lists history of severe allergic reaction to any other vaccine or injectable therapy (that does not share the same components as the mRNA COVID-19 vaccines) as a precaution, but not contraindication, to mRNA COVID-19 vaccination.
  - For Ad26.COV2.S (Janssen COVID-19 vaccine) – A history of a severe allergic reaction, such as anaphylaxis, to any of its components.
- Individuals with a precaution to vaccination, as well as any individual with a history of anaphylaxis that does not result in a contraindication to vaccination, should be monitored for 30 minutes after vaccination. All other recipients should be monitored for 15 minutes.

40. What Adverse Effects Are Associated With Vaccination?

- The more common adverse effects for all vaccine types include local injection site reactions, fever, headache, fatigue, chills, myalgias, and arthralgias These reactions are more common in younger individuals and after the second dose.
- Anaphylaxis is a rare adverse event reported following receipt of mRNA vaccines. In the United States, 21 episodes of anaphylaxis were reported to the CDC after 1,893,360 doses had been administered (11.1 events per one million doses). Anaphylaxis is more common in individuals with a history of allergies.

41. Is There An Increased Risk Of Thromboembolism Associated With The ChAdOx1 nCoV-19/AZD1222 (Astrazeneca) Vaccine? Should This Vaccine Be Avoided?

- In March 2021, rare thromboembolic events following vaccination with ChAdOx1 nCoV-19/AZD1222 were investigated by the European Medicines Agency (EMA).
- The EMA found that the overall rate of thromboembolic disorders was lower than expected for the general population, but that two specific types of events, blood clots in multiple vessels (suggestive of disseminated intravascular coagulation [DIC]) and cerebral venous sinus thrombosis (CVST), occurred more frequently than expected.
- The EMA concluded that the benefit of ChAdOx1 nCoV-19/AZD1222 outweighs the extremely small possibility of DIC or CVST.
- Vaccine recipients should be aware of the possible association and seek immediate care for symptoms suggestive of thrombocytopenia and/or thrombotic complications.

42. Can Analgesics Or Antipyretics Be Taken For Side Effects Following Vaccination?

- Analgesics or antipyretics (eg, nonsteroidal anti-inflammatory drugs [NSAIDs] or acetaminophen) can be taken for local or systemic side effects following vaccination.
- However, pre-emptive use of these agents prior to vaccination is not recommended because of the uncertain impact on immune response to the vaccine.

43. Can Other Vaccines Be Given With COVID-19 Vaccine?

- No, other vaccines should generally not be administered within 14 days of COVID-19 vaccine administration because there are no data regarding the safety and efficacy of coadministration.
- However, when the benefits of vaccination are deemed to outweigh the uncertain risk of coadministration (eg, tetanus toxoid-containing vaccination as part of wound management, measles vaccination in an outbreak, repeat mRNA COVID-19 (Moderna COVID-19 vaccine) vaccination when availability is limited), vaccination within a shorter time frame is reasonable.

44. What If The Second Dose Of An mRNA Vaccine Cannot Be Given Because Of A Prior Reaction?

- For individuals who received a first dose of an mRNA vaccine but cannot receive either mRNA vaccine for the second dose (eg, because of contraindications), Ad26.COV2.S (Janssen COVID-19 vaccine)can be given as long as there is not also a contraindication to Ad26.COV2.S (Janssen COVID-19 vaccine).
- The CDC suggests giving Ad26.COV2.S(Janssen COVID-19 vaccine) at least 28 days after the mRNA vaccine(Moderna COVID-19 vaccine) dose. Such individuals should be considered to have received a complete AD26.COV2.S(Janssen COVID-19 vaccine) vaccine regimen.

45. Should People Who Have Had SARS-CoV-2 Infection Be Vaccinated? If So, When? What If A Patient Acquires COVID-19 After The First Dose?

- Yes, individuals with a history of SARS-CoV-2 infection should be vaccinated.
- Vaccination can be given as soon as the individual has recovered from acute infection (if symptomatic) and meets criteria for discontinuation of isolation precautions.
- Pre-vaccination serologic screening is not recommended.
- If infection is diagnosed after receipt of the first vaccine of a two-dose series (eg, with the mRNA COVID-19 vaccines), the second dose should still be given.
- Delaying vaccination for 90 days from the time of infection is also reasonable; the risk of reinfection during this time period is low, and delaying vaccination allows other people to receive the vaccination sooner.

- Delaying vaccination for 90 days is also suggested for individuals who were treated with monoclonal antibodies or convalescent plasma.

M. Blood Donation

46. What Should I Tell Patients About Donating Blood Or Plasma During The Pandemic?

- Blood donation is particularly important during the pandemic due to concerns that the supply could become critically low. Having a history of COVID-19 is not an exclusion to donation as long as the illness resolved at least 14 days prior to donation.
- Vaccination for COVID-19 is also not a contraindication to blood donation.
- Individuals who have received an mRNA vaccine or other non-infectious vaccine (nonreplicating, inactivated) can donate immediately; those who have received a live-attenuated viral vaccine (and those who are unsure which vaccine they received) should refrain from donating blood for a short waiting period (eg, 14 days) after receiving the vaccine.
- Persons who have recovered from COVID-19 are encouraged to donate plasma, because convalescent plasma is an investigational treatment for COVID-19.
- COVID-19 vaccine recipients are not eligible for convalescent plasma donation.

N. Antifibrotics

47. When Will We Start Antifibrotic Therapy In A COVID-19 Patient?

- The study is going on. Not specified yet.
- Currently there is a clinical trial by NIH (USA) on Phase-4 study which will be ended on 21 December, 2021 (24 wks clinical trial). They included the patients by maintaining following criteria:
    1. Age above 18 years.
    2. Diagnosed to have COVID-19 by means of a real-time reverse transcription polymerase chain reaction (rRT-PCR) test performed on a respiratory (upper or lower respiratory) sample or positive IgM antibody test or a rapid antigen test with consistent clinicoradiologic findings within the previous 4 months.
    3. Persistent respiratory symptoms.
    4. Having post-COVID parenchymal involvement >10% of the lung parenchyma on visual inspection of the scans with the presence of radiologic signs of fibrosis (traction bronchiectasis/traction bronchiolectasis or honeycombing or reduced lung volumes), or having persistent reticulation or persistent consolidation despite a trial of glucocorticoids (minimum prednisolone dose of 10 mg/day, or equivalent) for a minimum period of 4 weeks after discharge for the acute COVID-19 illness.
- Pirfenidone will be started at a dose of 600 mg/day. The dose will be escalated by 600 mg/day every 3-7 days up to a targeted dose of 2400 mg/day. The subjects will be administered the maximum tolerated dose for a total period of 24 weeks from randomization. Or
- Nintedanib at a dose of 150 mg twice daily. The liver function tests will be monitored. The dose will be reduced to 100 mg twice daily, if there is intolerance to 300 mg/day dose.

O. Fungal Disease And COVID-19 [1]

48. What Are The Fungal Disease Associated With COVID-19?

- COVID-19 associated Pulmonary Aspergillosis
- COVID-19 associated Mucormycosis (Not Black Fungus)
- Invasive Candidiasis
- Fungal Pneumonia

49. Who Are At Risk Of Developing Fungal Disease?

- Patients with severe COVID-19 (e.g. patients on ventilators in ICUs)
- Diabetes, especially with diabetic ketoacidosis
- Cancer
- Organ transplant
- Stem cell transplant
- Neutropenia
- Long-term corticosteroid use
- Injection drug use
- Too much iron in the body (iron overload or hemochromatosis)
- Skin injury due to surgery, burns, or wounds
- Prematurity and low birthweight (for neonatal gastrointestinal mucormycosis)

50. How Is Mucormycosis Treated?

- Mucormycosis is a serious infection and needs to be treated with antifungal medicine, usually amphotericin B, posaconazole, or isavuconazole.
- These medicines are given through a vein (amphotericin B, posaconazole, isavuconazole) or by mouth (posaconazole, isavuconazole).
- Other medicines, including fluconazole, voriconazole, and echinocandins, do not work against fungi that cause mucormycosis.
- Often, mucormycosis requires surgery to cut away the infected tissue.

References:

1. Centers for disease control and prevention. National center for emerging and zoonotic infectious disease. 2021.https://www.cdc.gov/fungal/diseases/mucormycosis/treatment. html