



## Covid- 19 Diagnosis, Treatment and Control Measure

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### ABSTRACT

Severe acute respiratory syndrome coronavirus (SARS-CoV) 2, a novel coronavirus from the same family as SARS-CoV and Middle East respiratory syndrome coronavirus, has spread worldwide leading the World Health Organization to declare a pandemic. The disease caused by SARS-CoV2, coronavirus disease 2019 (COVID-19), presents flu-like symptoms which can become serious in high-risk individuals. Here, we provide an overview of the covid-19 diagnosis its treatments including pharmacological treatment, Ayurvedic, homeopathic, siddha, Unani treatment of covid-19 and control measure of covid-19. We found that infection is transmitted from human to human and through contact with contaminated environmental surfaces. Hand hygiene is fundamental to prevent contamination. Wearing personal protective equipment is recommended in specific environments. The main symptoms of COVID-19 are fever, cough, fatigue, slight dyspnea, sore throat, headache, conjunctivitis and gastrointestinal issues. Molecular testing Real time PCR is used as a diagnostic tool using nasal swab, tracheal aspirate or bronchoalveolar lavage samples. Serology testing is performed by taking the blood, plasma, or serum of the patient and testing it for IgM and IgG antibodies. Imaging chest x-ray and Computed tomography findings are important for both diagnosis and follow-up. Specific High-sensitivity Enzymatic Reporter unlocking (SHERLOCK) is a rapid test. First, a sample is taken from the upper airway of a suspected COVID patient. To date, there is no evidence of any effective treatment for COVID-19. The main therapies being used to treat the disease are antiviral drugs, chloroquine / hydroxychloroquine and respiratory therapy. In conclusion, although many therapies have been proposed, quarantine is the only intervention that appears to be effective in decreasing the contagion rate. Specifically designed randomized clinical trials are needed to determine the most appropriate evidence-based treatment modality.

**Keywords:** COVID-19 diagnosis, COVID-19 Pharmacological, Ayurvedic, homeopathic, siddha, Unani treatment, control measure of covid-19.

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### INTRODUCTION

Coronavirus disease 2019 also known as (COVID-19) is a highly contagious and infectious disease caused by the novel coronavirus, severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2).<sup>1,2</sup> It is well documented that the initial cases of COVID-19 related infection were first reported in Wuhan, Hubei Province of China in December 2019, and were linked to the Huanan Seafood Market.<sup>3</sup> Since then, the infection has spread to over 216 countries and territories. The World Health Organization (WHO) announced that COVID-19 reached pandemic status on 30 January 2020<sup>4,5</sup> and subsequently, declared a global pandemic in March 2020.<sup>6</sup> It has since been referred to be 'the most crucial global health calamity of the century and the greatest challenge that humankind faced since the 2nd World War'.<sup>7</sup> As of 26 December 2020, there were approximately 80,500,000 confirmed COVID-19 cases worldwide, including 1,700,000 related deaths,<sup>8</sup>

with a case fatality rate of 2.2%. The case fatality rate varies among countries, estimated from 0 to more than 20%.<sup>9</sup> A second wave of COVID-19 infection has already been recorded in many countries, which may be due to premature relaxation of government-enforced lockdown rules in many parts of the world.<sup>10,11</sup> Several countries have reported a new rise in daily cases higher than the first wave in March 2020.<sup>12,13</sup> Although there is no shortage of information on this pandemic virus presented in everyday practice, this paper presents a comprehensive review of the latest information on SARS-CoV-2 highlighting the origin of sars-cov-2, genome variation, structure, transmission, pathogenesis, symptoms, diagnosis and treatments of sars-cov-2.

### ORIGIN OF SARS-COV-2

It has been hypothesized that human coronaviruses are derived from bats.<sup>14</sup> The sequencing of SARS-CoV-2 revealed more than 80% similarity to SARS-CoV and more than 50% similarity to MERS-CoV.<sup>15</sup> Also, this virus shows 96.2% similarity to the bat SARS-related coronavirus, even though the intermediate animal that forms the route of transmission from bats to humans is not known yet. The spike protein of SARS-CoV-2 has been known to be identical to that of a virus found in pangolins. The first COVID-19 case was reported on December 2019 in Wuhan, a city in Hubei province in China. The genomic sequences



of SARS-CoV-2 isolated from many patients were shown to share a sequence identity higher than 99.9%, suggesting a very recent host shift from nature into humans. The phylogenetic tree constructed in research indicated that SARS-CoV-2 was closest to RaTG13 (bat coronavirus), followed by GD Pangolin SARSr-CoV, and then human SARS-CoV.

### Genomic Variations of SARS-COV-2

SARS-CoV-2 is categorized into two major lineages: L, a common strain with a higher number of mutations that is more severe and aggressive than S, the lesser common strain. These strains

were created due to SNPs at positions 8782 and 28 144 in the viral RNA, which are required for replication and are thought to be necessary for pathogenesis.<sup>16</sup>

### Structure of SARS-COV-2

Coronaviruses are known to have a large genome, with sizes ranging from 26 to 32 kilobases.<sup>17</sup> Corona, a Latin word for crown, depicts the spike-like protrusions on its surface. They consist of the following structural proteins:

**(1) Trimeric spike (S) protein:** The S1 protein recognizes ACE2 receptors found in the lungs, heart, kidneys, intestines, esophagus, liver, and blood vessels, and is attached to the host cell

membrane. The host cell proteases (serine 2, cathepsins, trypsin, and furin) cause cleavage of the spike protein, resulting in the fusion of the virus inside the host cell, and this is mediated by S2 protein of the virus.<sup>18</sup>

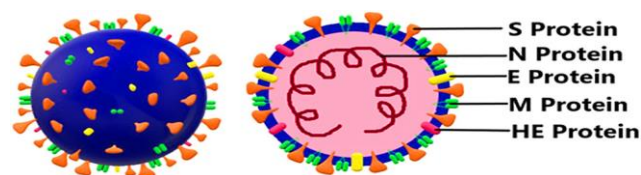
**(2) Envelope (E) protein:** The envelope proteins are the smallest and they are mainly present in the ER and the Golgi Apparatus, where they are responsible for the assembly and release of virus from the host cell. Hence, they are well expressed during viral replication.

**(3) Membrane (M) protein:** The membrane glycoproteins are surface proteins and they are the most abundant proteins of the virus. Their structure is comprised of the N-terminal domain on the outside of the virus, three transmembrane domains, and the C-terminal domain found inside the viral membrane.<sup>19</sup> It helps in the formation and gives shape to the virus envelope, and it also controls the assembly of various components of the virus.<sup>20</sup>

**(4) Nucleocapsid (N) protein:** The nucleocapsid protein is bound to the ssRNA of the virus. Its function is to breakdown the defense mechanism and deregulate the cell cycle of the host cell and to assist in the assembly of the virus by interacting with other structural proteins. It packages the viral genome into capsids to protect it.<sup>21</sup>

**(5) Hemagglutinin-esterase (HE) protein:** Hemagglutinin-esterase, a glycoprotein, helps in the attachment and destruction of sialic acid receptors to the host cell surface. The viral envelope is present underneath the surface proteins. It consists of a fatty bilayer that breaks down on

contact with soap and water. Below the viral envelope is a capsid that surrounds the genetic material of the virus. Hence, it is recommended to wash the hands for at least 20 s with soap and water to break down the lipid bilayer if the virus is present on the hands.



**Figure 1:** Structure of SARS-CoV-2-Detailed 3D model of SARS-CoV-2 virus along with its cross-section showing all the different proteins present in it, namely the spike (S) protein, membrane (M) protein, envelope (E) protein, nucleocapsid (N) protein, and Hemagglutinin-esterase (HE) protein

### TRANSMISSION OF SARS-COV-2

SARS-CoV-2 is highly contagious and can be directly transmitted when an individual comes in contact with the respiratory droplets of an infected person or it can be indirectly transmitted by coming in contact with objects used or touched by an infected person.<sup>22</sup>

### PATHOGENESIS OF COVID-19

The symptoms of the disease can be divided into three stages. First, the Asymptomatic stage, which lasts for 1 to 2 days after being infected. During this stage, the virus attaches to the ACE2 receptors and replicates. The virus can be detected by the swab test, nasal swabs being more effective than throat swabs. There is a limited innate immunity response.<sup>23</sup> Second, the Upper Airway Infection stage, where the virus migrates down the respiratory tract. An innate immune response is triggered. For most infected patients, this infection is restricted to the upper respiratory tract.<sup>23</sup> Third and final, the Acute Respiratory Distress Syndrome (ARDS) and Hypoxia stage, in which the virus reaches, infects, and damages the alveoli in the lungs, which release interferons that signal the nearby healthy cells to release antiviral peptides.<sup>24</sup> The antiviral peptides cause the breakdown of the virus. The damaged cells release danger molecules (called damage-associated molecular patterns, protein-associated molecular patterns, and cytokines) that activate the innate immune system for phagocytosis.<sup>25</sup> These signals are answered by macrophages that release more inflammatory signals, resulting in the filling of fluid between the capillary and alveolus (the area responsible for gas exchange). Neutrophils also reach the site of infection during the killing of viruses and damage the healthy pneumocytes. This leads to a decrease in the surfactant present in the alveolus. These phagocytic cells also release inflammatory mediators, like IL-2, IL-6, IL-10, TNF- $\alpha$ , G-CSF, and MCP-1, all of which cause inflammation.<sup>26,27</sup> This hyperactive immune response of the body is called a cytokine storm. This affects the gas exchange in the alveoli, leading to hypoxemia and ARDS. In the case of a very severe

infection, the protein-rich fluid may enter the bloodstream, causing systemic inflammatory response syndrome (SIRS), which can further lead to multi-organ failure.<sup>28</sup> The cytokines also lead to an increase in levels of pro coagulants, leading to pulmonary embolism.<sup>29</sup> In addition, the infection activates receptors on the cranial nerve and the CNS generates a cough response. Finally, the inflammatory mediators can also act in the hypothalamus, leading to fever.<sup>30</sup>

## SYMPTOMS

According to WHO, on average, it takes 5–6 days after being infected for symptoms to become visible.<sup>31</sup> The major organs affected are lungs, heart, kidneys, liver, intestines, and the brain.<sup>32</sup> The most severe effect of COVID-19 is ARDS due to improper blood circulation and the weakening of blood vessels all over the body. Also, the widespread distribution of ACE2 receptors can cause organ injury and lead to multisystem organ failure. Hence, people with unhealthy blood vessels, such as smokers and people with conditions like high blood pressure, diabetes, cholesterol, and cardiovascular diseases, are more at risk for COVID-19.<sup>33</sup> CDC has listed the following conditions that make up the high risk category for COVID-19.<sup>34</sup>

- (1) Asthma
- (2) Chronic kidney disease that has been treated with dialysis
- (3) Chronic lung disease
- (4) Diabetes
- (5) Hemoglobin disorders
- (6) Immunocompromised
- (7) Liver disease
- (8) People aged 65 years and older
- (9) People in nursing homes or long-term care facilities
- (10) Serious heart conditions
- (11) Severe obesity

## CLINICAL DIAGNOSIS OF COVID-19

The major categories of diagnostic methods available today for COVID-19 include:

### 1. Molecular test

Direct detection of the virus can be achieved by identifying the viral genome or the antigen. A throat swab is preferred over stool and blood samples because it is non-invasive and contains a high concentration of the virus. RT-qPCR is the most common and reliable test with relatively high specificity.<sup>35</sup> The test involves purifying the viral genome from the throat swab and amplifying it using primers specific to the SARS-CoV-2 virus. Usually, the RdRp, N, and E genes are used for the identification of the virus.<sup>36</sup> The only disadvantage to this method is the long turnaround time.

### 2. Serology testing

It is performed by taking the blood, plasma, or serum of the patient and testing it for IgM and IgG antibodies (the proteins made due to the immune response of our body to the viral antigens). The IgM antibodies appear and become detectable at around the 7th day of infection and are present in the blood until the 3rd week of infection. The IgG antibodies, on the other hand, appear during the 2nd week of infection and remain in the blood to provide long-term immunity.<sup>37</sup> Hence, diagnosis using this technique can be done when the patient is in the recovery phase. This is not advantageous, as the patient might have transmitted the virus to others during that time. The major disadvantage of this test is that it could give a false-positive result after the patient recovers by detecting long-term antibodies in the blood. Home Rapid Antibody tests for COVID-19 are being developed on a lateral flow assay device to detect IgM and IgG antibodies.<sup>38,39</sup>

### 3. Imaging

Chest X-Rays and CT scans are supplementary tests used with RT-PCR tests to see the progression and damage due to COVID-19, although they do not always indicate COVID-19. CT scans have been reported to show similar patterns of ground glass opacity, indicating damaged lungs, inflammation, and pneumonia.<sup>40</sup> However, not all patients with COVID-19 develop symptoms like pneumonia and, as a result, a CT scan would fail in diagnosis of the disease. Artificial intelligence can be used to interpret CT scan images for suspected COVID-19 cases.<sup>41</sup> In addition, a technique called a CT angiogram can be performed to help us identify clots in the pulmonary circulatory system.<sup>42</sup>

### 4. Specific High-sensitivity Enzymatic Reporter unlocking (SHERLOCK)

Specific High-sensitivity Enzymatic Reporter unlocking (SHERLOCK) is a rapid test. First, a sample is taken from the upper airway of a suspected COVID patient. The RNAs in the sample are amplified and reporter genes are added. CRISPR-Cas13 is then added along with a guide RNA, which is designed to target the viral RNA (unlike Cas9, which targets the DNA). When the viral RNA is found, Cas13 activates its cleaving mechanism and starts cleaving nearby RNAs and reporter genes randomly. Each end of the reporter carries a different fluorescent label, and hence, their cleavage generates a signal if the virus RNA is present. The sample is then applied on a lateral flow assay device. Two bands are obtained if viral RNA is present, while only one is obtained if the reporter gene is not cleaved (that is, when viral RNA is absent). This technique can successfully detect very low concentrations of pathogens.<sup>43,44</sup>

## TREATMENTS

Currently, there are no approved therapeutics to cure SARS-CoV-2 infection. Most existing treatments aim for relieving the symptoms or interfering with the immune response. Repurposing existing drugs that were known to



be effective against SARS-CoV, ebola, and HIV infections is also being explored, but their use is being restricted to patients with severe infection. Asymptomatic cases and patients with mild symptoms are primarily being managed by self-isolation.

## PHARMACOLOGICAL TREATMENTS OF COVID-19

### 1. Broad-spectrum antiviral drugs

#### a) Hydroxychloroquine and Chloroquine:

These are antimalarial drugs that have been derived from the compound 4 aminoquinolines and have been proven to be antiviral agents. They can inhibit actions of the SARS-CoV virus by interfering with glycosylation ACE2 receptors and preventing the fusion of the virus with the host cell. They have also been shown to inhibit SARS-CoV-2 in vitro.<sup>45</sup> Their use has been limited by the US FDA due to the risk of heart rhythm problems in clinical phase trials.<sup>46</sup> Chloroquine is thought to have serious side effects, while hydroxychloroquine (HCQ) is relatively safer and can suppress the cytokine storm by repressing the activation of T cells.<sup>47</sup>

#### b) Remdesivir:

This drug has been approved by the US FDA against SARSCoV-2 and has been previously used against the Ebola, SARS-CoV, and MERS-CoV viruses.<sup>48-50</sup> Remdesivir blocks the enzyme RNA-dependent RNA polymerase, which is needed by the virus for replication.<sup>51</sup> The mortality rate for the remdesivir group was 8%, compared to 11.6% for the placebo group; that mortality difference was not statistically significant. Unfortunately, this drug is known to have severe side effects, including liver damage in a few patients.<sup>52</sup>

#### c) Combination of drugs Ribavirin, Lopinavir/Ritonavir, and Interferon:

Ribavirin is known to have antiviral activity against SARSCoV-2 in vitro. It functions by mimicking guanosine, interfering in the replication process and RNA capping, and inhibiting the pathway that generates guanine.<sup>53</sup> Lopinavir and ritonavir are used as treatment and preventive medications against HIV, respectively. Lopinavir, a protease inhibitor, is thought to inhibit the enzyme 3-chymotrypsin-like protease, which is used in viral replication and release from the host cell. Also, lopinavir has shown to have antiviral activity against SARS-CoV-2 in vitro. Ritonavir acts to increase the half-life of lopinavir by inhibiting cytochrome P450 3A. Some studies say that ritonavir helps to reduce the risk of severe hypoxia. These drugs, however, have side effects like diarrhea and liver and pancreatic disorders. Also, their effectiveness against COVID-19 is yet to be conclusively established in clinical trials.<sup>54</sup> Interferons are cytokines secreted by the immune system that turn on the genes to boost up the immune response to control and kill the virus. Interferon- $\alpha$  provides innate, antiviral protection. A study on SARS-CoV and MERS-CoV has shown that these two coronaviruses have the mechanism to delay interferon production.<sup>55</sup> The only

problem with type-1 interferons is that they could generate a cytokine storm or increase inflammation, causing flu-like symptoms to worsen. A newer type of Interferon- $\beta$  has only been tried on mice and is believed to not cause any inflammation or tissue damages as it activates only neutrophils (unlike interferon- $\alpha$ , which activates macrophages and lymphocytes in addition to neutrophils). However, further research is required to study its antiviral effects.<sup>56</sup>

#### d) Nelfinavir, Tenofovir, and Emtricitabine

Nelfinavir is a protease inhibitor and an antiviral drug used in the treatment of AIDS. According to a study, Nelfinavir was able to reduce the cytopathic effect of the SARS-CoV virus and also inhibit its replication. Since SARS-CoV-2 is quite similar to SARS-CoV, it could be a possible form of treatment.<sup>57</sup> Tenofovir and emtricitabine are reverse transcription inhibitors. They inhibit viral RNA synthesis[58]

#### e) Favipiravir

It is a broad-spectrum antiviral that inhibits RNA-dependent RNA polymerase of RNA viruses. It is commonly used in Japan against the influenza virus.<sup>59</sup> It is being explored for its efficacy against SARS-CoV-2.<sup>60</sup>

### 2. Mesenchymal stem cells

These are multipotent stem cells that can be isolated from various tissues, like bone marrow, dental pulp, adipose tissue, and fetal liver tissues.<sup>61</sup> They have been successfully used to treat

autoimmune diseases, like multiple sclerosis and arthritis, and also to prevent rejection of organs after transplant in the past.<sup>62</sup> The main reason why COVID-19 is considered life-threatening is due to the cytokine storm that further leads to ARDS and multisystem organ failure. Stem cell therapy is thought to prevent the cytokine storm and promote repair of the damaged tissues by reducing the amount of pro-inflammatory proteins and by increasing the number of anti-inflammatory proteins.

### 3. Anti-SARS-CoV-2 Neutralizing Antibody Products

Individuals recovering from COVID-19 develop neutralizing antibodies against SARS-CoV-2, and the duration of how long this immunity lasts is unclear. Nevertheless, their role as therapeutic agents in the management of COVID-19 is extensively being pursued in ongoing clinical trials.

a) **Convalescent Plasma** : therapy was evaluated during the SARS, MERS, and Ebola epidemics; however, it lacked randomized control trials to back its actual efficacy. The FDA approved convalescent plasma therapy under a EUA for patients with severe life-threatening COVID-19. Although it appeared promising, data from multiple studies evaluating the use of convalescent plasma in life-threatening COVID-19 has generated mixed results. One retrospective study based on a U.S. national registry reported that among patients hospitalized with COVID-19, not on mechanical ventilation, there was a lower risk of death





in patients who received a transfusion of convalescent plasma with higher anti-SARS-CoV-2 IgG antibody than patients who received a transfusion of convalescent plasma with low antibody levels. Data from three small randomized control trials showed no significant differences in clinical improvement or overall mortality in patients treated with convalescent plasma versus standard therapy. An *in vitro* analysis of convalescent plasma obtained from individuals previously infected with the ancestral SARS-CoV-2 strains demonstrated significantly reduced neutralization against SARS-CoV-2 variant B.1.351/501Y.V2. Another *in vitro* study reported B.1.351 variant exhibited markedly more resistance to neutralization by convalescent plasma obtained from individuals previously infected with the ancestral SARS-CoV-2 strains compared to the B.1.1.7 variant, which was not more resistant to neutralization.

- b) REGN-COV2 (Casirivimab and Imdevimab):** REGN-COV2 is an antibody cocktail containing two noncompeting IgG1 antibodies (casirivimab and imdevimab) that target the RBD on the SARS-CoV-2 spike protein that has been shown to decrease the viral load *in vivo*, preventing virus-induced pathological sequelae when administered prophylactically or therapeutically in non-human primates. Results from an interim analysis of 275 patients from an ongoing double-blinded trial involving non-hospitalized patients with COVID-19 who were randomized to receive placebo, 2.4 g of REGN-COV2 (casirivimab 1,200 mg and imdevimab 1,200 mg) or 8 g of REGN-COV2 (casirivimab 2,400 mg and imdevimab 2,400 mg) reported that the REGN-COV2 antibody cocktail reduced viral load compared to placebo. This interim analysis also established the safety profile of this cocktail antibody, similar to that of the placebo group. Preliminary data from a Phase 3 trial of REGN-COV2 (casirivimab/imdevimab) revealed a 70% reduction in hospitalization or death in non-hospitalized patients with COVID-19. *In vitro* data is available regarding the effect of REGN-COV2 on the two new SARS-CoV-2 variants of concern (B.1.1.7; B.1.351 variants) that reveal retained activity.
- c) Bamlanivimab and Etesevimab (LY-CoV555 or LY3819253 and LY-CoV016 or LY3832479)** are potent anti-spike neutralizing monoclonal antibodies. Bamlanivimab is a neutralizing monoclonal antibody derived from convalescent plasma obtained from a patient with COVID-19. Like REGN-COV2, it also targets the RBD of the spike protein of SARS-CoV-2 and has been shown to neutralize SARS-CoV-2 and reduce viral replication in non-human primates. *In vitro* experiments revealed that etesevimab binds to a different epitope than bamlanivimab and neutralizes resistant variants with mutations in the epitope bound by bamlanivimab. In Phase 2 of the BLAZE-1 trial, bamlanivimab/etesevimab was associated with a significant reduction in SARS-CoV-2 viral load

compared to placebo. Data from the Phase 3 portion of BLAZE-1 is pending release, but preliminary information indicates that therapy reduced the risk of hospitalization and death by 87%. *In vitro* data is available regarding the effect of bamlanivimab/etesevimab on the new SARS-CoV-2 variants of concern (B.1.1.7; B.1.351) reveals retained activity.

- d) Sotrovimab (VIR-7831):** is a potent anti-spike neutralizing monoclonal antibody that demonstrated *in vitro* activity against all the four VOCs Alpha (B.1.1.7), Beta (B.1.351), Gamma (P1), and Delta (B.1.617.2). Results from a preplanned interim analysis (not yet peer-reviewed) of the multicenter, double-blind placebo-controlled Phase 3, COMET-ICE trial by Gupta *et al.* that evaluated the clinical efficacy and safety of sotrovimab demonstrated that one dose of sotrovimab (500 mg) reduced the risk of hospitalization or death by 85% in high-risk non-hospitalized patients with mild to moderate COVID-19 compared with placebo.
- e) REGN-COV2 (casirivimab and imdevimab), bamlanivimab/etesevimab, and sotrovimab:** were approved for clinical use by the FDA under three separate EUAs issued in November 2020, February 2021, and May 2021, respectively, that allowed the use of these drugs only in non-hospitalized patients (aged  $\geq 12$  years and weighing  $\geq 40$  kg) with laboratory-confirmed SARS-CoV-2 infection and mild to moderate COVID-19 who are at high risk for progressing to severe disease and/or hospitalization.

#### 4. Immunomodulatory Agents

- a) Corticosteroids:** Severe COVID-19 is associated with inflammation-related lung injury driven by the release of cytokines characterized by an elevation in inflammatory markers. During the pandemic's early course, glucocorticoids' efficacy in patients with COVID-19 was not well described. The Randomized Evaluation of Covid-19 Therapy (RECOVERY) trial, which included hospitalized patients with clinically suspected or laboratory-confirmed SARS-CoV-2 who were randomly assigned to receive dexamethasone (n=2104) or usual care (n=4321), showed that the use of dexamethasone resulted in lower 28-day mortality in patients who were on invasive mechanical ventilation or oxygen support but not in patients who were not receiving any respiratory support. Based on the results of this landmark trial, dexamethasone is currently considered the standard of care either alone or in combination with remdesivir based on the severity of illness in hospitalized patients who require supplemental oxygen or non-invasive or invasive mechanical ventilation.
- b) Interferon- $\beta$ -1a (IFN- $\beta$ -1a):** Interferons are cytokines that are essential in mounting an immune response to a viral infection, and SARS-CoV-2 suppresses its



release *in vitro*. However, previous experience with IFN-  $\beta$ -1a in acute respiratory distress syndrome (ARDS) has not benefited. Results from a small randomized, double-blind, placebo-controlled trial showed the use of inhaled IFN-  $\beta$ -1a had greater odds of clinical improvement and recovery compared to placebo. Another small randomized clinical trial showed that the clinical response using inhaled IFN-  $\beta$ -1a was not significantly different from the control group. The authors reported when used early, this agent resulted in a shorter length of hospitalization stay and decreased 28-day mortality rate. However, four patients who died in the treatment group before completing therapy were excluded, thus making the interpretation of these results difficult. Currently, there is no data available regarding the efficacy of interferon  $\beta$ -1a on the four SARS-CoV-2 VOCs Alpha (B.1.1.7), Beta (B.1.351), Gamma (P1), and Delta (B.1.617.2). Given the insufficient and small amount of data regarding this agent's use and the relative potential for toxicity, this therapy is not recommended to treat COVID-19 infection.

- c) **Interleukin (IL)-1 Antagonists:** Anakinra is an interleukin-1 receptor antagonist that is FDA approved to treat rheumatoid arthritis. Its off-label use in severe COVID-19 was assessed in a small case-control study trial based on the rationale that the severe COVID-19 is driven by cytokine production, including interleukin (I.L.)-1 $\beta$ . This trial revealed that of the 52 patients who received anakinra and 44 patients who received standard of care, anakinra reduced the need for invasive mechanical ventilation and mortality in patients with severe COVID-19. There is no data available regarding the efficacy of interleukin-1 receptor antagonists on the three new SARS-CoV-2 variants (B.1.1.7; B.1.351, and P.1). Given the insufficient data regarding this treatment based on case series only, this is not currently recommended to treat COVID-19 infection.

##### 5. Anti-IL-6 receptor Monoclonal Antibodies:

Interleukin-6 (IL-6) is a pro inflammatory cytokine that is considered the key driver of the hyper inflammatory state associated with COVID-19. Targeting this cytokine with an IL-6 receptor inhibitor could slow down the process of inflammation based on case reports that showed favorable outcomes in patients with severe COVID-19. The FDA approved three different types of IL-6 receptor inhibitors for various rheumatological conditions (Tocilizumab, Sarilumab) and a rare disorder called Castleman's syndrome (Siltuximab).

- a) **Tocilizumab** is an anti-interleukin-6 receptor alpha receptor monoclonal antibody that has been indicated for various rheumatological diseases. The data regarding the use of this agent is mixed. A randomized control trial involving 438 hospitalized patients with severe COVID-19 pneumonia, among which 294 were randomized to receive tocilizumab

and 144 to placebo, showed that tocilizumab did not translate into a significant improvement in clinical status or lower the 28-day mortality compared to placebo. Results from another randomized, double-blind placebo-controlled trial involving patients with confirmed severe COVID-19 that involved 243 patients randomized to receive tocilizumab or placebo showed that the use of tocilizumab was not effective in preventing intubation or death rate. The REMAP-CAP and RECOVERY trials (not yet published), two large randomized controlled trials, showed a mortality benefit in patients exhibiting rapid respiratory decompensation.

- b) **Sarilumab and Siltuximab** are IL-6 receptor antagonists that may potentially have a similar effect on the hyper inflammatory state associated with COVID-19 as tocilizumab. Currently, there are no known published clinical trials supporting the use of siltuximab in severe COVID-19. Conversely, a 60-day randomized, double-blind placebo control multinational phase 3 trial that evaluated the clinical efficacy, mortality, and safety of sarilumab in 431 patients did not show any significant improvement in clinical status or mortality rate. Another randomized, double-blind placebo-controlled study on sarilumab's clinical efficacy and safety in adult patients hospitalized with COVID-19 is currently ongoing.

##### 6. Janus kinase (JAK) inhibitors

- a) **Baricitinib** is an oral selective inhibitor of Janus kinase (JAK) 1 and JAK 2 currently indicated for moderate to severely active rheumatoid arthritis (RA) patients. Baricitinib was considered a potential treatment for COVID-19 based on its inhibitory effect on SARS-CoV-2 endocytosis *in vitro* and on the intracellular signaling pathway of cytokines that cause the late-onset hyper inflammatory state that results in severe illness. This dual inhibitory effect makes it a promising therapeutic drug against all stages of COVID-19. A multicenter observational, retrospective study of 113 hospitalized patients with COVID-19 pneumonia who received baricitinib combined with lopinavir/ritonavir (baricitinib arm, n=113) or hydroxychloroquine and lopinavir/ritonavir (control arm, n=78) reported significant improvement in clinical symptoms and 2-week mortality rate in the baricitinib arm compared with the control arm. Results from the ACTT-2 trial, a double-blind, randomized placebo-controlled trial evaluating baricitinib plus remdesivir in hospitalized adult patients with COVID-19, reported that the combination therapy of baricitinib plus remdesivir was superior to remdesivir therapy alone in not only reducing recovery time but also accelerating clinical improvement in hospitalized patients with COVID-19, particularly who were receiving high flow oxygen supplementation or noninvasive ventilation.



Baricitinib, in combination with remdesivir, has been approved for clinical use in hospitalized patients with COVID-19 under a EUA issued by the FDA. The efficacy of baricitinib alone or in combination with remdesivir has not been evaluated in the SARS-CoV-2 variants, and there is limited data on the use of baricitinib with dexamethasone.

- b) **Ruxolitinib** is another oral selective inhibitor of JAK 1 and 2 that is indicated for myeloproliferative disorders, polycythemia vera, and steroid-resistant GVHD. Similar to baricitinib, it has been hypothesized to have an inhibitory effect on cytokines' intracellular signaling pathway, making it a potential treatment against COVID-19. Results from a small prospective multicenter randomized controlled phase 2 trial evaluating the efficacy and safety of ruxolitinib reported no statistical difference than the standard of care. However, most of the patients demonstrated significant chest C.T. improvement and faster recovery from lymphopenia. A large randomized, double-blind, placebo-controlled multicenter trial (**NCT04362137**) is ongoing to assess ruxolitinib's efficacy and safety in patients with severe COVID-19.
- c) **Tofacitinib** is another oral selective inhibitor of JAK 1 and JAK3 that is indicated for moderate to severe RA, psoriatic arthritis, and moderate to severe ulcerative colitis. Given its inhibitory effect on the inflammatory cascade, it was hypothesized that its use could ameliorate the viral inflammation-mediated lung injury in patients with severe COVID-19. Results from a small randomized controlled trial that evaluated the efficacy involving 289 patients who were randomized to receive tofacitinib or placebo showed that tofacitinib led to a lower risk of respiratory failure or death (PMID:34133856).

### 7. Bruton's tyrosine kinase inhibitors:

Such as **acalabrutinib**, **ibrutinib**, **rilzabrutinib** are tyrosine kinase inhibitors that regulate macrophage signaling and activation currently FDA approved for some hematologic malignancies. It is proposed that macrophage activation occurs during the hyper inflammatory immune response seen in severe COVID-19. Results from a small off-label study of 19 hospitalized patients with severe COVID-19 who received acalabrutinib highlighted the potential clinical benefit of BTK inhibition. Clinical trials are in progress to validate the actual efficacy of these drugs in severe COVID-19 illness.<sup>63</sup>

### AYURVEDIC TREATMENT OF COVID-19

#### 1. Prophylactic care (high risk population primary contacts)

- **Ashwagandha:** (aqueous extract of *Withania somnifera* IP) or its powder

**Dosage and timing:** 500 mg extract or 1-3 g powder twice daily with warm water for 15 days or one month or as directed by Ayurveda physician

- **Guduchi Ghanvati:** (samshamani vati or giloy Ghana vati)

**Dosage and timing:** having Aqueous extract 500 mg extract or 1-3 g powder twice daily with warm water for 15 days or one month or as directed by Ayurveda physician

- **Chyawanprasha:** **Dosage and timing:** 10 g with warm water /milk once a day

#### 2. Asymptomatic covid-19 positive:

For prevention of disease progression to symptomatic and severe form and to improve recovery rate

- **Guduchi Ghanvati** (samshamani vati or giloy Ghana vati having Aqueous extract of *Tinospora cordifolia* IP) or the powder of *Tinospora cordifolia*.

**Dosage and timing:** 500 mg extract or 1-3 g powder twice daily with warm water for 15 days or one month or as directed by Ayurveda physician.

- **Guduchi + Pippali** (aqueous extracts *Tinospora cordifolia* IP and *piper longum* IP)

**Dosage and timing :** 375 Mg twice daily with warm water for 15 days or as directed by Ayurveda physician

- **AYUSH 64 :dosage and timing:** 500 mg twice daily with warm water for 15 days or as directed by Ayurveda physician

#### 3. Mild covid-19 positive:

##### Symptomatic management

Fever, headache, tiredness dry cough, sore throat nasal congestion

**Guduchi + Pippali** (aqueous extracts *Tinospora cordifolia* IP and *piper longum* IP)

**Dosage and timing:** 375 mg twice daily with warm water for 15 days or as directed by Ayurveda physician

**AYUSH 64 Dosage and Timing:** 500 mg twice daily with warm water for 15 days or as directed by Ayurveda physician.<sup>64</sup>

### HOMEOPATHIC TREATMENT FOR COVID-19

1. **Anas barbariae hepatis et cordis extractum (Oscillocoquinum®):** Dry cough, sore throat, fever, given in case of no symptoms

2. **Bryonia alba:** Dry deep cough, unilateral pneumonia, fever, dyspnea

3. **Sulphur\*\*:** Irritability, and selfishness, loose putrid cough, gastrointestinal symptoms; important follow-up to many acute homeopathic medicinal products to bring about further improvement

4. **Kalium carbonicum\*\*:** down-to-earth, simple, peasant character, very irritable, full of fear and imaginations, and hypersensitive to pain, noise, touch



**5. Camphora:** debilitating diarrhea, fever

**6. Nux vomica:** upper abdominal symptoms including pain, nausea, fever

**7. Gelsemium sempervirens\*\*\*:** trembling with fever, apathy, vertigo, head pain extending from temple to ear, muscle weakness.

**8. Ipecacuanha:** dry cough with nausea/vomiting, rapidly descending infection/bronchitis, shortness of breath.

**9. nfluenzinum:** frequent colds, catarrhs, influenza, weakness, tiredness, headache, joint pain and body aches, pharyngitis, laryngitis, gastroenteritis, nerve and muscle diseases after flu, consequences of flu (“never well since”), given in Case of no symptoms

**10. Tuberculinum Koch\*\*:** weakness in fever; respiratory symptoms with cough; shortness of breath; and low type fever

**11. yrogenium\*\*\*:** septic fever, offensive discharges, frequent pulse, palpitation, bed appears too hard.<sup>65</sup>

## SIDDHA TREATMENT FOR COVID-19

### 1. Adathodai Manapagu

This preparation is based on the *Adhatoda vasica* (AV) leaf juice. *Adhatoda vasica* belongs to the Acanthaceae family. The aqueous extract of *J. adhatoda* at 10 and 5 mg/mL concentrations shows reduced HA to 33% and 16.67%, respectively, in the simultaneous assay. These results showed that aqueous and methanolic extracts of *J. adhatoda* have strong antiviral activity that can inhibit viral attachment and/or viral replication, and may be used for viral prevention. The compound vasicine shows the excellent antiviral property in Dock assay. Adathodai Manapagu has Antipyretic activity, anti-inflammatory activity, antioxidant activity, antiviral activity, and hepatoprotective activity.

### 2. Kabasura Kudineer

The Siddha classical formulation kabasura kudineer chooranam consists of 15 ingredients of herbs. The mechanism of action of the phytochemicals present in the kabasura kudineer Siddha formulation attracting/binding multiple amino acids at different sites of viral proteins which corroborated with the well-known antimalarial drug, artemisinin. This showed the synergistic activity of phytochemicals not only against the viral proteins but also modulate the immune system for fighting against viral replication. The active molecules of the respective medicinal plants, *Trichosanthes cucumerina*, *T. cordifolia*, *H. auriculata*, *A. pyrethrum*, *A. paniculata*, *AV*, *S. lappa*, *C. serratum*, *S. aromaticum*, and *Z. officinale*, might inhibit the viral pathogenesis at various levels spanning from prevention to cure. It revealed that the functionally significant formulations against corona viral protein showed a more efficient inhibitory effect against viral replication. Kabasura Kudineer has Antipyretic activity, expectorant, antispasmodic, anti-asthmatic activity,

antiviral activity, immunomodulatory activity, hepatoprotective activity, and antioxidant activity.

### 3. Thontha Sura Kudineer

Thontha sura kudineer chooranam consists of 10 ingredients of herbs was studied for antiviral activity by in silico docking analysis. The phytochemicals in thontha sura kudineer had promising activity against the viral spike glycoprotein which prevents the spike proteins binding with host cell receptor. Thontha Sura Kudineer has Antiviral activity, anti-inflammatory activity, anti-asthmatic activity, hepatoprotective activity, and immunomodulatory activity.

### 4. Vajra Kandi Chenduram

It is a herbomineral preparation broadly utilized particularly in Siddha practitioners regards the management of several acute and chronic illnesses ranging from fever to chronic inflammatory disorders and immune-mediated diseases. This formulation is made of purified lingam, veeram, pooram, and rasa sindhuram. This component shows antipyretic, anti-inflammatory, and antioxidant activity. Vajra kandi chenduram through its antipyretic and anti-inflammatory activity can be the potential to prevent the release of the inflammatory mediators and cytokine storm of COVID-19 which is a major cause for severe lung complication. Therefore, this formulation can be advised as a safe and effective supportive therapy in the absence of any specific target treatment measures.

### 5. Visha Sura Kudineer

Visha sura kudineer (VSK) is a polyherbal formulation from Siddha literature “Kaaviya Sura Nool”. The components were *Azadirachta indica*, *Indigofera tinctoria*, *Z. officinale*, *Hemidesmus indicus*, *Aristolochia bracteata*, *V. zizanioides*, *Glycyrrhiza glabra*, *E. cardamomum*, and *Santalum album*. Each of the component shows antiviral activity against wide range of viruses.

### 6. Nilavembu Kudineer (NVK)

“Nilavembu kudineer is a polyherbal formulation with *A. paniculata* as the main ingredient that controls all types of fever related to body pain. Other components include *Vetiveria zizanioides*, *V. zizanioides*, *Santalum album*, *T. cucumerina*, *C. rotundus*, *Zingiber officinale*, *Piper nigrum*, and *M. cerviana*. All these plants are utilized traditionally in the treatment of pyretic, “inflammation, arthralgia, arthritis, gastric ulcer, jaundice, and general debility conditions”. Nilavembu kudineer extensively controls fever through its managing consequences effects on temperature, inflammation control, body pain, and it also acts in a way to improve immunity. All the components in this formulation have the bioactive molecules that show excellent activity against dengue, chikungunya, herpes simplex virus (HSV), and influenza virus.<sup>66</sup>





**UNANI TREATMENT FOR COVID-19**

1. **Behi dana (*Cydonia oblonga*)-** Antioxidant, immunomodulator, antiallergic and antiinfluenza (dose 3-5 gm).
2. **Unnab (*Zizyphus jujube*)-** Anti-influenza, immunomodulator, antioxidant (dose 5 pcs )
3. **Sapistan (*Cordia myxa*)-** Immunomodulator, tracheal smooth muscle relaxant, anti-oxidant (dose 9 pcs)
4. **Karanjwa (*Caesalpinia bonducella*)-** Antipyretic, antimicrobial, antiinflammatory, immunomodulator (dose 3 to 5 gm).
5. **Imli (*Tamarindus indica* L)-** Analgesic, anti-inflammatory.
6. **Halela (*Terminalia chebula* Retz) -** Anti-bacterial .
7. **Amaltas (*Cassia fistula* L )-**Immunomodulatory, antioxidant .
8. **Tukhm-eKasoo (*Cuscuta reflexa*)-** Anti viral (dose 15 gm) .
9. **Turanjabeen (*Alhagi pseudalhagi*)-** Anti-microbial, anti-oxidant.
10. **Kalonji (*Nigella sativa*)-** Anti viral (dose 1-2 gm) .
11. **Aslassus (*Glycyrrhiza glabra* )-**Anti viral (dose 5-10 gm).
12. **Khayar shamber (*Cassia fistula*)-** Anti viral (dose 10-20 gm).
13. **Gilo (*Tinospora cordifolia* )-**Anti viral (dose 5-10 gm) .
14. **Asgandh (*Withania somnifera*) –** Immunomodulator.<sup>67</sup>

**CONTROL MEASURE OF COVID-19****1. Wear a mask**

- If you are not fully vaccinated and aged 2 or older, you should wear a mask in indoor public places.
- In general, you do not need to wear a mask in outdoor settings.
- In areas with high numbers of COVID-19 cases, consider wearing a mask in crowded outdoor settings and for activities with close contact with others who are not fully vaccinated.
- People who have a condition or are taking medications that weaken their immune system may not be fully protected even if they are fully vaccinated. They should continue to take all precautions recommended for unvaccinated people, including wearing a well-fitted mask, until advised otherwise by their healthcare provider.

**2. Stay 6 feet away from others**

- Inside your home: Avoid close contact with people who are sick. If possible, maintain 6 feet between the person who is sick and other household members.
- Outside your home: Put 6 feet of distance between yourself and people who don't live in your household. Remember that some people without symptoms may be able to spread virus.
- Stay at least 6 feet (about 2 arm lengths) from other people.
- Keeping distance from others is especially important for people who are at higher risk of getting very sick

**3. Avoid crowds and poorly ventilated spaces**

- Being in crowds like in restaurants, bars, fitness centers, or movie theaters puts you at higher risk for COVID-19.
- Avoid indoor spaces that do not offer fresh air from the outdoors as much as possible.
- If indoors, bring in fresh air by opening windows and doors, if possible.

**4. Wash your hands often**

- Wash your hands often with soap and water for at least 20 seconds especially after you have been in a public place, or after blowing your nose, coughing, or sneezing.
- It's especially important to wash:
  - Before eating or preparing food
  - Before touching your face
  - After using the restroom
  - After leaving a public place
  - After blowing your nose, coughing, or sneezing
  - After handling your mask
  - After changing a diaper
  - After caring for someone sick
  - After touching animals or pets
- If soap and water are not readily available, use a hand sanitizer that contains at least 60% alcohol. Cover all surfaces of your hands and rub them together until they feel dry.

**5. Cover coughs and sneezes**

- If you are wearing a mask: You can cough or sneeze into your mask. Put on a new, clean mask as soon as possible and wash your hands.
- If you are not wearing a mask: Always cover your mouth and nose with a tissue when you cough or



sneeze, or use the inside of your elbow and do not spit. Throw used tissues in the trash.

- Immediately wash your hands with soap and water for at least 20 seconds. If soap and water are not readily available, clean your hands with a hand sanitizer that contains at least 60% alcohol.

## 6. Clean and disinfect

- Clean high touch surfaces daily. This includes tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks.
- If someone is sick or has tested positive for COVID-19, disinfect frequently touched surfaces. Use a household disinfectant product from EPA's List N: Disinfectants for Coronavirus (COVID-19) according to manufacturer's labeled directions. If surfaces are dirty, clean them using detergent or soap and water prior to disinfection.

## 7. Monitor your health daily

- Be alert for symptoms. Watch for fever, cough, shortness of breath, or other symptoms of COVID-19. Especially important if you are running essential errands, going into the office or workplace, and in settings where it may be difficult to keep a physical distance of 6 feet.
- Take your temperature if symptoms develop. Don't take your temperature within 30 minutes of exercising or after taking medications that could lower your temperature, like acetaminophen.
  - Follow CDC guidance if symptoms develop.

## 8. Get Vaccinated

- Authorized COVID-19 vaccines can help protect you from COVID-19.
- You should get a COVID-19 vaccine as soon as you can.<sup>68</sup>

### • VACCINES

#### a) Pfizer-BioNTech

Pfizer-BioNTech was the first COVID-19 vaccine to receive full Food and Drug Administration (FDA) approval for people ages 16 and older in August 2021

**Recommended for:** Anyone 12 or older.

**Dosage:** Two shots, 21 days apart; fully effective two weeks after second shot. Single-shot booster doses can be administered to those who are eligible at least six months after completion of the primary doses.

**How it works:** Unlike vaccines that put a weakened or inactivated disease germ into the body, the Pfizer mRNA vaccine delivers a tiny piece of genetic code from the SARS CoV-2 virus to host cells in the body, essentially giving those cells instructions, or blueprints, for making copies of spike proteins (the spikes you see sticking out of the

coronavirus in pictures online and on TV). The spikes do the work of penetrating and infecting host cells. These proteins stimulate an immune response, producing antibodies and developing memory cells that will recognize and respond if the body is infected with the actual virus.

#### How well it works:

Experts continue to learn about Pfizer's efficacy both in the laboratory and in the real world. Pfizer's initial Phase 3 clinical data presented in December showed its vaccine to have 95% efficacy.

In April, the vaccine had 91.3% efficacy against COVID-19, based on measuring how well it prevented symptomatic COVID-19 infection seven days through up to six months after the second dose. It also found it to be 100% effective in preventing severe disease as defined by the CDC, and 95.3% effective in preventing severe disease as defined by the FDA. Another study, not yet peer-reviewed, provided that brought the efficacy number down to 84% after 6 months, although efficacy against severe disease was 97%. In August, the CDC also published studies that showed mRNA vaccine protection against infection may be waning, although the vaccines were still highly effective against hospitalization. In one CDC study, data from the state of New York showed vaccine effectiveness dropping from 91.8 to 75% against infection.

#### How well it works on viral mutation :

A number of studies have focused on the vaccine and the mutations. In early May, the Pfizer vaccine was found to be more than 95% effective against severe disease or death from the Alpha variant (first detected in the United Kingdom) and the Beta variant (first identified in South Africa) in two studies based on real-world vaccinations. As far as the Delta variant, two studies reported by Public Health England that have not yet been peer reviewed showed that full vaccination after two doses is against symptomatic disease and against hospitalization. But Israel later reported the vaccine's effectiveness to be 90% effective against severe disease, and 39% against infection in its population in late June and early July, based on an analysis of the country's national health statistics.

#### b) Moderna

Moderna's vaccine was authorized for emergency use in the U.S. in December 2020, about a week after the Pfizer vaccine. Moderna uses the same mRNA technology as Pfizer and has a similarly high efficacy at preventing symptomatic disease. It also needs to be stored in freezer-level temperatures. In mid-August, the FDA approved a third dose of the Moderna vaccine for certain immunocompromised individuals, including solid organ transplant recipients and those with conditions that give them an equally reduced ability to fight infections and other diseases.

**Recommended for:** Adults 18 and older. While the vaccine is not yet available for children, the company says its



vaccine provides strong protection for children as young as 12, and it is testing its efficacy for children ages 5-11.

**Dosage:** Two shots, 28 days apart; fully effective two weeks after the second dose.

**Common side effects:** Similar to Pfizer, side effects can include chills, headache, pain, tiredness, and/or redness and swelling at the injection site, all of which generally resolve within a day or two. On rare occasions, mRNA vaccines have appeared to trigger anaphylaxis, a severe reaction that is treatable with epinephrine (the drug in Epipens®). For that reason, the CDC requires vaccination sites to monitor everyone for 15 minutes after their COVID-19 shot, and for 30 minutes if they have a history of severe allergies.

**How it works:** Similar to the Pfizer vaccine, this is an mRNA vaccine that sends the body's cells instructions for making a spike protein that will train the immune system to recognize it. The immune system will then attack the spike protein the next time it sees one (attached to the actual SARS CoV-2 virus).

**How well it works:** Moderna's initial Phase 3 clinical data in December 2020 was similar to Pfizer's—at that point, both vaccines showed about 95% efficacy. This figure has changed over time. At six months after vaccination, the Moderna vaccine was shown to have efficacy of 90% against infection and more than 95% against developing a severe case, according to the company. In addition, while both Pfizer and Moderna still are considered highly effective, several recent studies showed Moderna to be more protective. One study published in *The New England Journal of Medicine* found Moderna vaccine to be 96.3% effective in preventing symptomatic illness in health care workers compared to 88.8% for Pfizer. Another, from the CDC, found Moderna's effectiveness against hospitalization held steady over a four-month period, while Pfizer's fell from 91% to 77%. This research is still limited and more data is needed to fully understand the differences between the two vaccines.

**How well it works on virus mutations:** Some research has suggested that Moderna's vaccine may provide protection against the Alpha and Beta variants. In June, Moderna reported that studies showed its vaccine is effective against the Beta, Delta, Eta, and Kappa variants, although it did show it to be about two times weaker against Delta than against the original virus.

### c) Johnson & Johnson

The FDA granted EUA for Johnson & Johnson's vaccine in February, 70 days after Pfizer and Moderna. Unlike the mRNA vaccines, this is a carrier, or virus vector, vaccine. It can be stored in normal refrigerator temperatures, and because it requires only a single shot, it is easier to distribute and administer.

**Status:** Emergency use in the U.S. and other countries, including in the European Union (under the name Janssen). In October, an FDA panel recommended

authorization of a Johnson & Johnson booster for adults 18 and older to be given at least two months after their initial J&J shot. (But there are additional steps to be completed before a J&J booster EUA is finalized).

**Recommended for:** Adults 18 and older.

**Dosage:** Single shot. Fully effective two weeks after vaccination.

**Common side effects:** Fatigue, fever headache, injection site pain, or myalgia (pain in a muscle or group of muscles), all of which generally resolve within a day or two. It has had noticeably milder side effects than the Pfizer and Moderna vaccines, according to the FDA report released in late February. No one suffered an allergic reaction in clinical trials for the vaccine, according to the company.

**FDA warnings:** The FDA has attached two warnings to the Johnson & Johnson vaccine. In July, the FDA attached a warning after rare cases of the neurological disorder Guillain-Barré syndrome were reported in a small number of vaccination recipients. Most of the cases occurred within 42 days after vaccination.

In April, the FDA added a warning label after ending a pause on the vaccine it had recommended "out of an abundance of caution" over an uncommon, but potentially serious, blood clotting disorder that occurred in a small number of recipients.

**How it works:** This is a carrier vaccine, which uses a different approach than the mRNA vaccines to instruct human cells to make the SARS CoV-2 spike protein. Scientists engineer a harmless adenovirus (a common virus that, when not inactivated, can cause colds, bronchitis, and other illnesses) as a shell to carry genetic code on the spike proteins to the cells (similar to a Trojan Horse). The shell and the code can't make you sick, but once the code is inside the cells, the cells produce a spike protein to train the body's immune system, which creates antibodies and memory cells to protect against an actual SARS-CoV-2 infection.

**How well it works:** 72% overall efficacy and 86% efficacy against moderate and severe disease in the U.S., according to analyses posted by the FDA in February. In early October, J&J reported in a company press release that clinical trial data showed that a booster shot given about two months after the first shot increased protection to 94% against moderate to severe disease in the U.S.

**How well it works on virus mutations:** Johnson & Johnson reported in July that its vaccine is also effective against the Delta variant, showing only a small drop in potency compared with its efficacy against the original strain of the virus, although one recent study suggested that the J&J vaccine is less effective against Delta.

But the first study to assess the vaccine against Delta in the real world reported the vaccine to be 71% effective against hospitalization and up to 95% effective against death. The vaccine's performance was slightly lower against the Beta



variant in the study. This preliminary research was reported in August at a news conference by the Ministry of Health in South Africa. These studies have not yet been peer-reviewed or published in a scientific journal.<sup>69</sup>

#### d) ZyCoV-D vaccine

- India has given a boost to its vaccination programme by approving its first vaccine for those under 18.
- The three-dose ZyCoV-D vaccine prevented symptomatic disease in 66% of those vaccinated, according to an interim study quoted by the vaccine maker Cadila Healthcare.
- The ZyCoV-D vaccine is also the world's first DNA vaccine against Covid-19.

Like other vaccines, a DNA vaccine, once administered, teaches the body's immune system to fight the real virus.

- ZyCoV-D uses plasmids - or small rings of DNA that contain genetic information - to deliver the jab between two layers of the skin.
- ZyCoV-D is also India's first needle-free Covid-19 jab. It is administered with a disposable needle-free injector, which uses a narrow stream of the fluid to penetrate the skin and deliver the jab to the proper tissue
- The key third phase of clinical trials was conducted at the peak of the deadly second wave of the virus. The vaccine maker believes this reaffirmed the jab's "efficacy against the mutant strains", especially the highly infectious Delta variant.
- The other potential drawback is that ZyCoV-D requires three doses, instead of two as is the case with the other two candidates being used in India. The vaccine maker says it is evaluating at a two-dose jab.

#### e) Sputnik V

- The vaccine, developed by Moscow's Gamaleya Institute, initially generated some controversy after being rolled out before the final trial data had been released. But scientists say its benefits have now been demonstrated.
- It uses a cold-type virus, engineered to be harmless, as a carrier to deliver a small fragment of the coronavirus to the body. After being vaccinated, the body starts to produce antibodies especially tailored to the virus.
- It can be stored at temperatures of between 2 and 8°C degrees (a standard fridge is roughly 3-5°C degrees) making it easier to transport and store.
- But unlike other similar jabs, the Sputnik jab uses two slightly different versions of the vaccine for the first and the second dose - given 21 days apart.

#### f) Covaxin

- Covaxin is an inactivated vaccine which means that it is made up of killed coronaviruses, making it safe to be injected into the body.
- Bharat Biotech, a 24-year-old vaccine maker with a portfolio of 16 vaccines and exports to 123 countries, used a sample of the coronavirus isolated by India's National Institute of Virology.
- When administered, immune cells can still recognise the dead virus, prompting the immune system to make antibodies against the pandemic virus.
- The two doses are given four weeks apart. The vaccine can be stored at 2C to 8C.
- The vaccine has an efficacy rate of 81%, preliminary data from its phase 3 trial shows.

#### g) Covishield

- The Oxford-AstraZeneca vaccine is being manufactured locally by SII.
- The vaccine is made from a weakened version of a common cold virus (known as an adenovirus) from chimpanzees. It has been modified to look more like coronavirus - although it can't cause illness.
- When the vaccine is injected into a patient, it prompts the immune system to start making antibodies and primes it to attack any coronavirus infection.
- The jab can be safely stored at temperatures of 2C to 8C, and is administered in two doses given between four and 12 weeks apart.
- International clinical trials of the Oxford-AstraZeneca vaccine showed that when people were given a half dose and then a full dose, effectiveness hit 90%.
- But there was not enough clear data to approve the half-dose, full-dose idea.
- However, unpublished data suggests that leaving a longer gap between the first and second doses increases the overall effectiveness of the jab - in a sub-group given the vaccine this way it was found to be 70% effective after the first dose.
- It can be stored at temperatures of between 2 and 8C degrees (a standard fridge is roughly 3-5C degrees) making it easier to transport and store.<sup>70</sup>

#### CONCLUSION

The global health and economic consequences of the SARS-CoV-2 pandemic are severe. Although many therapies have been suggested, at present there are no specific options capable of treating COVID-19 disease or preventing SARS-CoV-2 infection. The only intervention currently viable and proven to decrease the contagion rate seems to be strict quarantine measures for the general





population. Specifically designed randomized clinical trials are urgently needed to determine the most appropriate evidence based treatment modality to reduce the spread of this disease and prevent the burden of any future outbreak.

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