HEART NEWS

...NHI Dialogue

Vol. No. LVII Since 1963 Health Magazine of All India Heart Foundation & National Heart Institute July–September 2021

USE OF ECMO IN COVID

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NATIONAL HEART INSTITUTE

HEART NEWS ...NHI Dialogue

Vol. No. LVII • Since 1963 • Health Magazine of All India Heart Foundation & National Heart Institute • July–September 2021

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स्वास्थ्य संवाद

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Post Covid Syndrome

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen responsible for coronavirus disease 2019 (COVID-19), has caused morbidity and mortality at an unprecedented scale globally. Scientific and clinical evidence has evolved and demonstrated the subacute and long-term effects of COVID-19, which can affect multiple organ systems. Early scientific data have suggested residual effects of SARS-CoV-2 infection, such as fatigue, dyspnea, chest pain, cognitive disturbances, arthralgia and decline in quality of life in various covid affected patients following recovery. This constellation of symptoms have been termed as Post Covid Syndrome.

Post-Covid Syndrome are a wide range of new, returning, or ongoing health problems that people can experience more than four weeks after first being infected with the virus that causes COVID-19. Even people who did not have symptoms when they were infected can have post-COVID conditions. These conditions can have different types and combinations of health problems for different lengths of time.

Based on recent literature, it is further divided into two categories:

(1) Subacute or ongoing symptomatic COVID-19- which includes symptoms and abnormalities present from 4-12 weeks beyond acute COVID-19

(2) Chronic or Post-COVID-19 syndrome-which includes symptoms and abnormalities persisting or present beyond 12 weeks of the onset of acute COVID-19 and not attributable to any alternative diagnoses.

Epidemiology

Early reports have now emerged on post-acute infectious consequences of COVID-19, with studies from the United States, Europe and China reporting outcomes for those who survived hospitalization for acute COVID-19. The findings from studies reporting various outcomes in subacute/ongoing symptomatic COVID-19 and chronic/post - COVID-19 syndrome are found in 35% of outpatient and 80-85% of hospitalized people.Various constellation of symptoms involving pulmonary, haematologic, endocrine, neurological, gastrointestinal and cardiovascular systems are usually involved.

Pathophysiology

Cellular damage, a robust immune response with inflammatory cytokine production, and a pro-coagulant state induced by SARS-CoV-2 infection may contribute to these sequelae. Depending on resources, prioritization may be considered for those at high risk for post-acute COVID-19, defined as those with severe illness during acute COVID-19 and/or requirement for care in an ICU, advanced age and the presence of organ comorbidities (pre-existing respiratory disease, obesity, diabetes, hypertension, chronic cardiovascular disease, chronic kidney disease, post-organ transplant or active cancer).

Potential mechanisms contributing to the pathophysiology of post-acute COVID-19 include:

(1) virus-specific pathophysiologic changes;

(2) immunologic aberrations and inflammatory damage in response to the acute infection; and

(3) expected sequelae of post critical illness

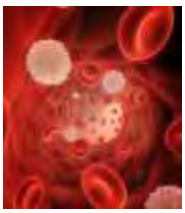
Clinical Syndromes

Pulmonary : The various symptoms and features seen of pulmonary Covid sequelae are :

Dyspnea, decreased exercise capacity and hypoxia in a persistent manner.

Reduced diffusion capacity, restrictive pulmonary physiology, ground-glass opacities and fibrotic changes on imaging noted at follow-up of COVID-19 survivors.

Hematologic



Thromboembolic events have been noted to be <5% in post-acute Covid-19 in various retrospective studies.

The duration of the hyper inflammatory state induced by infection with SARS-CoV-2 is unknown and often persistent.

Direct oral anticoagulants and low-molecular-weight heparin may be considered for extended thromboprophylaxis after risk–benefit discussion in patients with predisposing risk factors for immobility, persistently elevated d-dimer levels (greater than twice the upper limit of normal) and other high-risk comorbidities such as cancer.

Cardiovascular

Persistent symptoms may include palpitations, dyspnea and chest pain.

Long-term sequelae may include increased cardiometabolic demand, myocardial fibrosis or scarring

(detectable via cardiac MRI), arrhythmias, tachycardia and autonomic dysfunction.

Patients with cardiovascular complications during acute infection or those experiencing persistent cardiac symptoms require to be monitored with serial clinical, echocardiogram and electrocardiogram follow-up.

Neuropsychiatric

Persistent abnormalities may include fatigue, myalgia, headache, dysautonomia and cognitive impairment (brain fog).

Anxiety, depression, sleep disturbances and PTSD have been reported in 30–40% of COVID-19 survivors.

Renal

Resolution of AKI during acute COVID-19 occurs in the majority of patients; however, reduced e GFR has been reported.

COVID-19 survivors with persistent impaired renal function require early and close follow-up in AKI survivor.

Endocrine

Endocrine sequelae may include new or worsening control of existing diabetes mellitus, subacute thyroiditis and bone demineralization.

Patients with newly diagnosed diabetes in the absence of traditional risk factors for Type 2 Diabetes Mellitus, suspected hypothalamic–pituitary adrenal axis suppression or hyperthyroidism should undergo the appropriate laboratory testing and should be monitored.

Gastrointestinal and hepatobiliary

Prolonged viral fecal shedding can occur in COVID-19 even after negative nasopharyngeal swab testing.

COVID-19 has the potential to alter the gut microbiome, including increase of opportunistic organisms and depletion of beneficial commensals leading to lot of gastrointestinal symptoms.

Dermatologic

Hair loss is the predominant symptom and has been reported in approximately 20% of COVID-19 survivors.

MIS-C (Multi system inflammatory syndrome in children)

Diagnostic criteria: Seen in less than 21 years old, with fever, elevated inflammatory markers, multiple organ dysfunction, current or recent SARS-CoV-2 infection and exclusion of other plausible diagnoses.

Typically affects children >7 years and disproportionately of African, Afro-Caribbean or Hispanic origin.

Cardiovascular (coronary artery aneurysm) and neurologic (headache, encephalopathy, stroke and seizure) complications can occur in them.

Nutrition and rehabilitation considerations.

Severe COVID-19, similar to other critical illnesses, causes catabolic muscle wasting, feeding difficulties and frailty, each of which is associated with an increased likelihood of poor outcome. Malnutrition has been noted in 26–45% of patients with COVID-19, as evaluated by the Malnutrition Universal Screening Tool in an Italian study. Measure to study the nutritional deficits and provide adequate nutritional support are very often required.

Management and Future direction

Necessary active and future research should include the identification and characterization of key clinical, serological, imaging and epidemiologic features of COVID-19 in the acute, subacute and chronic phases of disease, which will help us to better understand the natural history and pathophysiology of this new disease entity.

The healthcare professionals caring for survivors of acute COVID-19 have the key role in carefully documenting, investigating and managing ongoing or new symptoms, as well as following up organ-specific complications that developed during acute illness. A dedicated follow up clinics for management of these Post Covid sequelae is necessary by the hospitals.

The various principles to be followed in the management of Post Covid Syndrome include :

1. Holistic support, adequate rest, gradual improvement of physical activity and monitoring of the functional status of the person.
2. Self monitoring of oxygen saturation and other parameters are to be encouraged and initiation of investigations if any significant change occurs.
3. Pulmonary and cardiac rehabilitation with a multidisciplinary approach is to be followed for patients with relevant sequelae.
4. Referral to a specialist in select few cases when relevant severe findings are present may also be necessary.
5. Mental and psychological support and guidance may be necessary specially for the geriatric age group of patients.

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कोरोना की दूसरी लहर

क्या है कोरोना ?

कोरोना एक प्रकार का आर एन ए प्रजाति का विषाणु है जिसकी बाहरी सतह पर मुकुट के आकार के सूक्ष्मतम प्रोटीनयुक्त कांटे होते हैं जो मानव कोशिकाओं में स्थित एस इन्हीबिटर रिसेप्टर एंजाइम से चिपक कर उसे निष्क्रिय कर देते हैं। ये विषाणु अल्कोहल युक्त या साबुन से पूर्णतः विनष्ट हो जाते हैं। विचारणीय बात यह है की यह विषाणु हमारे शरीर में नाक, गले या मुख से प्रवेश कर श्वसन पथ में पहुँचता है और फिर सम्पूर्ण शरीर में। इस विषाणु के विषय में हमें २०१९ में चीन के वुहान प्रांत में हुए अचानक संक्रमण से पता चला जिसने देखते ही देखते सम्पूर्ण विश्व को आपने आगोश में ले लिया। ग्यारह मार्च २०२० को विश्व स्वास्थ्य संघटन ने इसे वैश्विक महामारी घोषित कर दिया। भारत ने सत्वर लाकडाउन ,बचाव के प्रयास और जन जागरण के बल पर इस पर प्रारम्भिक नियंत्रण प्राप्त कर लिया और दिसंबर २०२० तक स्थिति काफी अनुकूल सी हो गयी थी। जनवरी २०२१ में जब कोवैक्सीन तथा कोवीशील्ड टीके का शुभारम्भ हुआ तब लगा हम इस महाआपदा के निराकरण के द्वार तक पहुँच गये है। परन्तु हमारी यह सदिच्छा बड़ी भूल साबित हुयी क्योंकि भारत में विदेशों से आये लोगों ने कोरोना के प्रत्यावर्तित उपबीजों (म्युटेंट स्ट्रेन) का संक्रमण यहाँ भी फैला दिया। फल यह हुआ की २८ दिसंबर २०२१ तक ये उपबीज हमारे देश में अपनी जड़ जमा चुके थे और यहीं से प्रारम्भ हुआ दूसरी लहर का प्रच्छन्न प्रारम्भ जो मार्च २०२१ तक भयंकर महामारी का रूप ग्रहण कर चुका है।

दूसरी लहर का प्रसार :

कहते हैं दूध का जला हुआ छाछ भी फूंक फूंक कर पीता है। पर हम हैं कि हमने कोविड -१९ द्वारा २०२० में हुयी जन-धन की तबाही से जो कुछ सीखा था उसे अप्रैल २०२१ के जाते जाते पूर्णतः गवां बैठे। आज स्थिति यह है कि जून २०२१ के प्रथम सप्ताहांत तक २.८९ करोड़ भारतीय लोग इस रोग से ग्रसित हो चुके हैं । गनीमत यह है कि इनमें से अधिकाँश लोग (२.७२ करोड़) रोग मुक्त हो चुके हैं। भारत के अधिकाँश महानगर मुंबई , पूने , नागपुर , दिल्ली , इंदौर,अहमदाबाद इस समय बुरी तरह कोरोना संक्रमण की चपेट में थे। प्रति दिन मरने वालों की संख्या ३५५ से बढ़ कर ३५०१ पहुँच गयी थी। अकेले महाराष्ट्र में एक दिन में हजारों लोगों की मृत्यु का समाचार है। अब तक सम्पूर्ण देश में तीन लाख उनचास हजार से ऊपर लोग अपने प्राण गवां चुके हैं। इससे स्थिति की भयावहता का सरलता से अंदाजा लगाया जा सकता है।

दूसरी लहर के विषाणु की विशेषताये :

१. अधिक आक्रामक,
२. अधिक विस्फोटक प्रसार,
३. विषाणु की वायु में उपस्थिति (वायु विलयता),
४. लाक्षणिक विविधतायें -अतिसार, पेट में दर्द ,बच्चों - किशोरों में कोरोना का प्रकोप,
५ युवकों में अधिक मारकता,
६ हृदय और फेफड़ों में इसके मारक प्रहार की क्षमता,
७. प्रत्यावर्तित स्ट्रेन की सी आर टी -पी सी आर की पकड़ से दूर,
८. आर टी -पी सी आर जांच की अपेक्षा क्लिनिकल / लक्षणों विशेषताओं की अधिक विश्वसनीयता,
९. परिवार का यदि एक व्यक्ति प्रभावित हुआ तो सम्पूर्ण परिवार के प्रभावित होने की सम्भावना,
१०. एक लाक्षणिक रोगी के पीछे कम से कम पांच अन्य अलाक्षणिक व्यक्तियों के संक्रमित होने की संभावना।

प्रश्न यह उठता है की जब हम कोरोना पर नियंत्रण के निकट पहुँच गए थे तब पुनः इस भयानक स्थिति में पहुंचे कैसे? वैज्ञानिकों द्वारा टीकान्वेषण का सफल प्रयास, चिकित्सकों का अथक परिश्रम और सरकारकी कार्य योजना कैसे मिट्टी में मिलती नजर आ रही है ? उत्तर है - कोरोना बचाव के प्रयत्नों में हमारी सामूहिक लापरवाही ,वैक्सीन की खबर आते ही अति आत्मविश्वास और उत्सव -महोत्सव के प्रति

हमारा व्यामोह। वैक्सीन आते ही हम भूल गये की मास्क पहनना जरुरी है -पहनना ही काफी नहीं वरन उसे ठीक से पहनना (सुमास्क), नाक मुंह दोनों ढक कर रखना आवश्यक है। भीड़ -भाड़, मेले -ठेले, रैली - महा रैली, मंदिर - मस्जिद, जुलूस जलसा, मजलिस-होटल-माल अनावश्यक रेल-हवाई जहाज की यात्रा से बचे। अपने घर को ही मंदिर - मस्जिद समझे।

टीका उसकी आक्रामकता को रोकने का प्रभावी तरीका है। वह हमें कोरोना विषाणु के प्रति प्रतिरक्षित करता है परन्तु वह अमोघ कवच नहीं है। कोरोना के खिलाफ इस जंग में सुमास्क धारण और दूरी का अनुपालन करना है। तभी तो कहा गया है:

(१) मास्क और दूरी, दोनों है जरुरी;

(२) दवाई भी, कड़ाई भी।

हमें अब क्या करना चाहिये:

दूसरी लहर की उपरिलिखित विशेषताओं की पृष्ठभूमि में हमें अब सामूहिक रूप से निम्नलिखित कार्य करना चाहिये:

१. लहर की श्रृंखला को तोड़ना : दो गज दूरी, मास्क पहनना है जरुरी। जान है तो जहान है को गाँठ में बाँध कर घर में ही रहना।

२. घर में अगर एक भी व्यक्ति को सर्दी / जुकाम / गले में खरांस / पेट खराब - बार बार टट्टी आने की शिकायत है तो अन्य अप्रभावित लोगों को घर में भी मास्क पहनना चाहिए और पृथक -पृथक रहना चाहिये।

३. अपने नित्य प्रति के व्यवहार में सुबह-शाम गरारे करना, भाप लेना और अनुलोम-विलोम प्राणायाम को सम्मिलित करें।

४. घर की खिड़कियों को खुला रक्खें जिससे शुद्ध वायु का प्रवेश हो सकें। वायु -आवागमन हो सके।

५. खाने में विटामिन सी प्रचुर पदार्थ जैसे नीबू, संतरा, टमाटर; हरित- खनिज युक्त आहार, फल- फूल, पर्याप्त जल ले।

६. टीकाकरण की प्रक्रिया पुनः प्रारम्भ होने पर टीका जरूर लगवायें। टीका लगवाते समय भी मास्क धारण करना और सामाजिक दूरी का ख्याल रक्खें। यह भी ध्यान रक्खें की टीका लगने का मतलब यह नहीं की आप निर्द्वन्द होकर बिना मास्क लगायें बिना पारस्परिक दूरी का ख्याल रक्खें भीड़,तमाशे, सिनेमा-मॉल में धक्का-मुक्की का हिस्सा बन सकते हैं।

कोरोना से कैसे बचे ?

१. घर में रहें -अपवाद कोरोना योद्धा जैसे चिकित्सक, नर्सेज, सफाई कर्मचारी, एम्बुलेंस-सेवा, पुलिस एवं आवश्यक सेवा में कार्यरत अन्य लोग।

२ भाप लें - दो बार

३. नमक का गरारा करें - दो बार

४. व्यायाम / योगासन

५. भोजन औषधिवत करें - जंक भोजन कदापि नहीं।

६. तम्बाकू निषेध

७. मदिरा अवांछनीय

८. विटामिन सी

९. डायबिटीज, ब्लड प्रेशर, हृदयाघात (हार्ट अटैक), प्रोस्टेट, थायरॉइड की अक्षमता या कैंसर सम्बन्धी अपनी पूर्वत औषधियां नियमित लेते रहें।

१०. सकारात्मक रहें / रचनात्मक शौक को बढ़ावा दे

११. कोरोना पराजित करने के लिए अपनी अपनी आस्था के अनुसार प्रार्थना करें। प्रार्थना में बहुत बल होता है।

सारांश : कोरोना काल में हम उपनिषद के श्लोक - सर्वे भवन्तु सुखिनः, सर्वे सन्तु निरामयाः, सर्वे भद्राणि पश्यन्तु, माँ कश्चिद् दुःख भागवेत ' के आप्त सन्देश से अनुप्राणित होकर 'संसार में सभी लोग निरोग हों 'की शुभाषा करें। प्रथम दृष्टया यह बहुत आदर्शपूर्ण बात लगती है परन्तु है अत्यंत श्लाघनीय और व्यवहारिक। अगर सभी लोग ऐसी मंगलकामना एक दूसरे के प्रति रक्खे और तदनुकूल आचरण करें तो अन्य लोग भी स्वस्थ सबल रह सकेंगें। आज के समय में इसका वैज्ञानिक स्वरूप यह होगा कि हम सब कोरोना सम्यक व्यवहार करें अर्थात मास्क पहनें, पारस्परिक दूरी बनायें रक्खें, हाथों को साबुन -पानी से धोते रहें। और संयोग से कोरोना से संक्रमित हो भी गये तो तुरंत अपने को अलग कर लें और पृथक वास करें।

सुमास्क यमदूत दूर,
कुमास्क यमदूत क्रूर।

डाक्टर श्रीधर द्विवेदी
वरिष्ठ हृदय रोग विशेषज्ञ
नेशनल हार्ट इंस्टिट्यूट, नई दिल्ली -११००६५

Commonly Used Drugs in COVID 19

SARS-CoV-2 through ACE2 receptors also directly damages on T-cells and produces lymphopenia, and dysfunction of granulocytes. There occurs and increased lactic acid levels that inhibits the proliferation and dysfunction of lymphocytes. Lymphopenia may lead to infection with microbe thereby promoting the activation and recruitment of neutrophils in the blood.

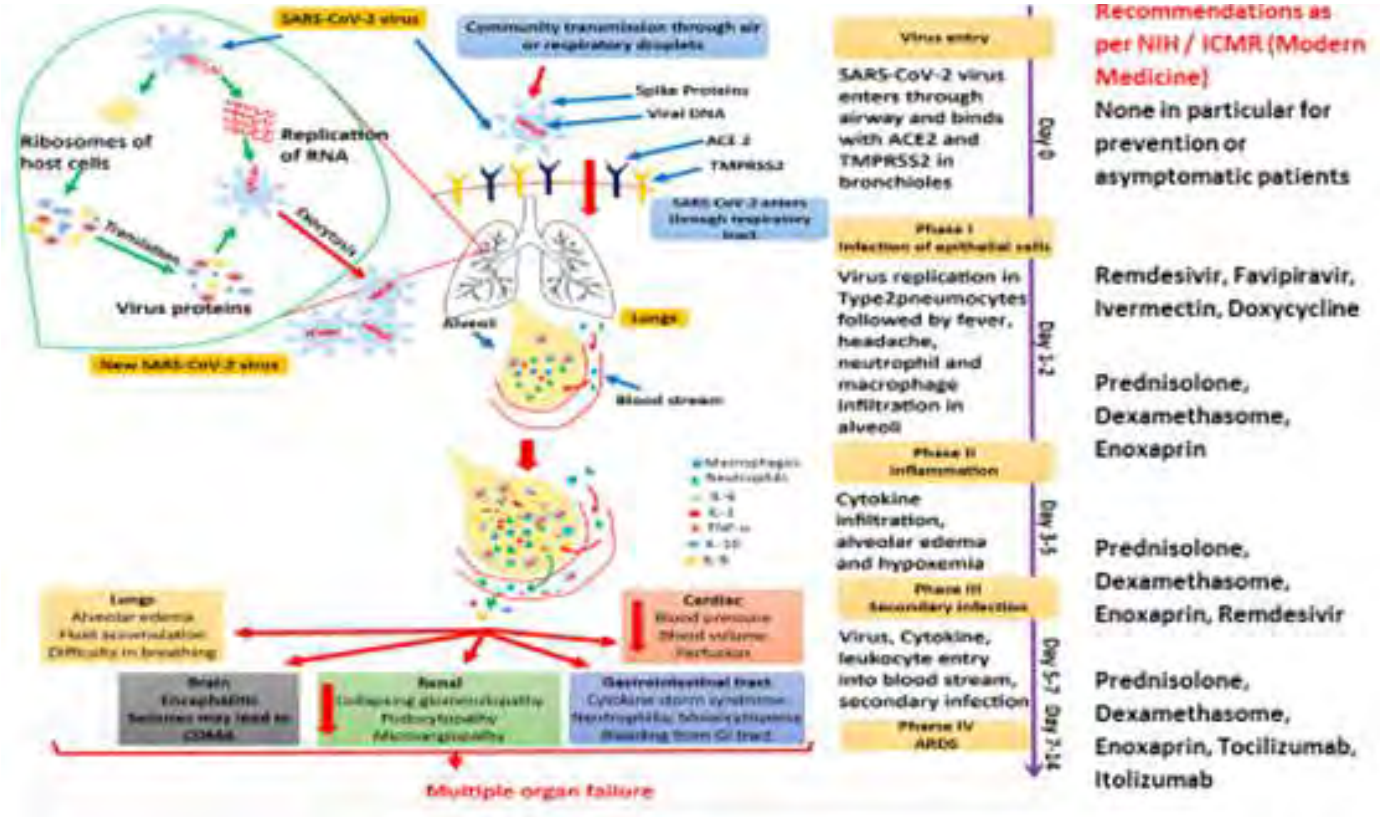
The resultant excessive infiltration of immune cells and dysfunctional immune response with the cytokine storm leads to a. multi-organ damage. In the alveoli severe endothelial injury is produced that increases vascular permeability and pulmonary edema. This abolishes hypoxic pulmonary vasoconstriction (vasoplegia) together with fluid-fill alveoli that finally cause Acute Respiratory Distress (ARDS)

Both entry of the virus and stimulation of immune mechanisms require ACE-2 as a consequence of which various systems associated with renin-angiotensin system get deranged because of high virus titer, strong cytokine surge and inflammatory response induced not only in the lungs but also the other organs where ACE-2 is highly expressed, leading to high morbidity and mortality. There are also secondary complications in cardiac, brain, kidney, gastrointestinal tract leading to multiple organ failure (**Fig. 1**).

Fig. 1: Pathogenesis and various stages of SARS-CoV-2 infection.

On the basis of above following are the drugs being used currently across the world and being investigated or are in the advanced stage of clinical Trials.:

1. **Antiviral drugs:**
   a. Viral Entry inhibitors like Interferons (Virafil), Camostat (TMPRSS2 inhibitor); Soluble r-ACE-2 (rhACE2;



APN01 of Apeiron) and Coroquil (DPSRU/Remedium)

b. RdRp inhibitors: (Remdesivir, Flavipiravil, Gladidesvir)

c. Nuclear Transport inhibitors (Ivermectin)

d. Miscellaneous:

i. Chloroquine/4-hydroxychloroquine

ii. 2-Deoxy-glucose(2DG)

iii. Convalescent Plasma therapy

iv. Neutralizing Monoclonal Antibodies like Regen-COV-2, JS016, Bamlanivimab, VIR 7631)

2. Immuno-modulators:

a. Corticosteroids like Dexamethasone and Prednisolone

b. IL-6 inhibitors like Tocilizumab

c. Antioxidants

3. Drugs for Symptomatic Treatment or Supportive Therapy:

a. Analgesics

b. Oxygen, Bronchodilators

c. Vitamins (Vitamin C, Vitamin D)

d. Minerals (Zinc, Magnesium)

Antiviral Drugs:

Remdesivir is given by intravenous injection. It was approved in May 2020 but later it was shown that as compared to placebo, the time of recovery, or mortality day were only marginally different on day 29. It should be started within 10 days of onset of symptom/s. The safety data is not available, but should not be given only to moderate to severe cases where supplemenal oxygen is not required and patient do not have any renal or hepatic dysfunction. Elevated transaminases (reversible) and kidney injury have been reported in some patients.

Flavipiravir has been shown to be more efficacious, safe and well tolerated. It clears virus within 4 days better than placebo and has been widely used. It is contraindicated during pregnancy, metabolite found in breast milk. Some adverse effects reported are hyperuricemia, diarrhea, elevated transaminases, reduction in neutrophil count.27

Ivermectin has been reported to reduce all cause mortality reduced, and the time to recovery. It retards progression to more advance disease.

Convalescent Plasma therapy emerged for last several months as therapy that provides neutralizing antibodies. Antibodies contained in plasma of donors who have recovered from COVID-19 may help suppress the virus and modify the inflammatory response There are opposing views about its efficacy. While some reports support its efficacy, no significant difference in 28-day time to clinical improvement and mortality between the convalescent plasma and standard treatment group. It may produce transfusion-associated circulatory overload and acute lung injury, allergic reactions and even lfe-threatening cardiac events and thrombotic events e.g. hypotension, thrombotic/ thromboembolic complications.

Although, Convalescent plasma therapy is controversial, it has become strategy for discovery for the development of new drugs as neutralizing antibodies like Regen-COV-2, JS016, Bamlanivimab, VIR 7631. Viral Spike Protein S1 and Host Cell Receptor ACE2 Interaction. mAb against RBD can prevent virus-ACE interaction and hence viral entry in the cell

Chloroquine and hydroxychloroquine as compared to supportive care only, was independently associated with lower mortality in hospitalized patients with COVID-19. They are however, **are reported to produce** Maculopathy, Retinopathy or visual field defect, QTc prolongation, Hemolysis in G6PD deficiency, hypoglycemia, nNeuropsychiatric and central nervous system effects.

Immuno-modulators

Involvement of excessive immune mechanisms in COVID-19 trigged repurposing research of many immunomodulators. Baricitiniban approved for rheumatoid arthritis having an inhibitory action on Janus kinase (JAK)1/JAK2, Imatinib mesylate and Dasatinib, inhibitors of the kinase signaling pathway, Trametinib, Selumetinib, a potent inhibitor of MEK, and many others came into the race. Tocilizumab, however, got a greater success among them.

Dexamethasone like other glucocorticoids produce anti-inflammatory, immunosuppressive, anti-proliferative, and vasoconstrictive effects

Tocilizumab is an IL-6 inhibitor and produces effective reduction in cytokine storm. In an open-label study of tocilizumab for severe COVID-19 without comparison group reported that earlier use of tocilizumab and reduced mortality.-In a cohort of mechanically ventilated COVID-19 patients, tocilizumab also showed reduction in the hazard of death, despite twice the frequency of superinfection. It is safe in pregnancy but hematologic effects, infections, hepatotoxicity, gastrointestinal perforations, hypersensitivity reactions (caution in patients with neutropenia (<500 cells/μL) or thrombocytopenia (<50 000/μL) have been reported.

Symptomatic and Supportive therapy:

Apart from respiratory failure and immune or cytokine surges, other clinical reports showed that in COVID-19 patients who are critically ill, patients have high incidences of thromboembolism and haemostatic abnormalities include mild thrombocytopenia and increased D-dimer levels leading to death. The use of anticoagulant drugs in COVID-19 patients became yet another strategy but only to the patients having higher D-dimer levels. Based on the clinical symptoms reported from time to time and then clarity of the pathophysiological consequences of COVID-19, the use of non-conventional antibiotics like azithromycin, steroids like dexamethasone & monoclonal antibodies for immunomodulation, antithrombotics, or thrombolytics, and certain food supplements were recommended by the statutory bodies in different countries.

Anticoagulants/Thrombolytics:

In view of high incidence of Vaso occlusive and thromboembolic episodes in moderate to severe Covid patients such cases are put on prophylactic anticoagulants. Patients suffering acute coronary events are treated with standard thrombolytic therapy .

Vitamins and Minerals – Role of vitamin C and Z though not conclusively proved to be use ful in acute Covid patients these agents are used empirically in most part of the world.

Zinc is said to shut down RNA dependent RNA polymerase or replicase. Small amount of chloroquine at 10 μM will increase the intracellular concentration of zinc ten-folds.

Limitations of Various drugs used for the treatment of COVID-19

Antivirals accelerate recovery but don't seems to save life. The virus rely on human cell machinery to copy themselves and antivirals interfere with copying viral gene and hence, antivirals don't eradicate virus but slow down multiplication. Thus an early treatment is the key to keep viral load low, faster you take antiviral drug, more you can limit its spread. However, early diagnosis is problem as by the time symptoms appear the patient have enough viruses. Hence reliance is more on body immune system/symptomatic treatment.

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USE OF ECMO IN COVID

Extra Corporeal Membrane Oxygenation (ECMO) is a much-discussed treatment modality for those patients with severe lung and/or heart problems following a variety of causes. These may be as varied as viral or bacterial pneumonias, severe heart failure, etc. The bottom line is that all of these conditions are not responding to other standard treatment modalities. ECMO basically is a technique designed to give rest to the heart and/or lungs, which are severely damaged by the disease process, while they recover. Hence if it is being used for a lung problem, it enhances the oxygen levels of the blood and removes excess carbon dioxide, thereafter returning the blood to the body. This form of ECMO is also known as VV-ECMO (Veno-venous ECMO) as it involves removal of blood from a major vein of the body, adding oxygen and removing carbon dioxide, then returning it back to the body by means of another major vein. From thereon, the blood goes to the lungs, then to the left side of the heart from where it is pumped to the rest of the body as usual. The advantage here is that the job of the lungs (adding of oxygen and removal of carbon dioxide) has already been done by the ECMO machine. Most cases of VV-ECMO are done for a generic group of lung disease called Respiratory Failure. These may be due to various underlying pathologies, like viral pneumonia. The outbreak of Swine flu with severe respiratory failure a few years ago led to a major rise in the use of ECMO, with good results. But what is Respiratory failure? This is a broad term that simply means an inability of the lungs to supply adequate oxygen to the blood, due to the inflammation caused by the viral infection or any other pathology.

In patients affected by COVID19, lung involvement, if extensive may lead to respiratory failure, which goes beyond a mere drop in oxygen saturation (SpO_2). Severe lung involvement may need to be tackled by various means, depending on the severity and clinical picture. Initially the patient may be put on inhaled oxygen through nasal prongs, face mask or reservoir bag. If adequate saturation is not able to be maintained on these modalities, High Flow Nasal Oxygen (HFNO) devices may have to be used. However, if despite these measures, the patient's oxygen saturation is falling and /or they are retaining carbon dioxide in their blood, invasive mechanical ventilation may have to be considered. In such a scenario, the patient is put under general anesthesia while the ventilator totally takes over the work of breathing. This enables the doctor to adjust the ventilator settings based on the clinical picture and the Arterial Blood Gas (ABG) analysis findings of the patient. The ABG gives the oxygen, carbon dioxide levels of the arterial blood of the patient, besides other parameters like the pH value and electrolyte levels of the blood. This informs us of the ability (or inability) of the lungs to oxygenate blood and remove carbon dioxide. Based on the oxygen levels on ABG, the Fraction of inspired oxygen (FiO_2) is set. This is nothing but the amount of oxygen being delivered to the patient via the ventilator. A normal person breathing room air is inhaling 21% oxygen. That is, the proportion of oxygen being inhaled out of all the gases present in the air is 21%. Most patients with severe lung involvement in COVID need a high level of FiO_2, some as high as 100%. But how do we decide what level of FiO_2 is adequate for the particular patient? This is decided on the basis of a simple ratio, known as the PaO_2: FiO_2 ratio, where the first value is the partial pressure of oxygen on the patient's ABG. Oxygen is a gas which is dissolved in liquids, and the unit by which the amount of oxygen dissolved in liquid blood is measured, is mm of mercury (mmHg), which is called the partial pressure of that particular gas. When the PaO_2: FiO_2 ratio is calculated, the latter value is expressed as a fraction, so that 40% of oxygen becomes 0.4. For example, a patient on ventilator maintaining a PaO_2 of 200mmHg on 40% of oxygen will have a PaO_2: FiO_2 ratio of 200:0.4, which comes out to be 500. A PaO_2: FiO_2 ratio of 300 and above means that the patient can be commenced on weaning from the ventilator. Unfortunately, things are never this rosy in COVID.

Most patients that get ventilated in COVID barely manage a PaO_2: FiO_2 ratio of 100-150. When this happens, other means are tried to improve the ratio, some of these are:

1. Proning, that is making the patient lie on his/her abdomen, face down, so as to improve the area of lung available for oxygen exchange,
2. Total muscular paralysis of the patient, by pharmacologic means, so that there is no struggling to breathe, which may cause fatigue, while the entire work of ventilation is borne by the machine,
3. Increase in positive pressure ventilation, that is the pressure exerted at the end of an expiratory cycle, which causes the smaller air passages to remain open and be available for oxygen uptake,
4. Inhalation of certain drugs, via the breathing tube, which may cause enlargement of lung blood vessels, thereby improving oxygen uptake.

When these measures lead to an improvement in the PaO_2: FiO_2 ratio to >150, ECMO may not be needed. However, after these measures for 12-24 hours, if the PaO_2: FiO_2 ratio further deteriorates to <80 for 6 hours or even 50 for 3 hours, ECMO may have to be considered. Please note that ECMO IS NOT A MIRACLE THERAPY FOR COVID LUNGS. IT IS MERELY A LAST-DITCH RESCUE THERAPY WHEN ALL OTHER MEASURES AT IMPROVING OXYGENATION AS GIVEN ABOVE, HAVE FAILED. In the above scenario, VV ECMO may be considered, provided there are no other contraindications to it. That is, there are no other conditions that may possibly make ECMO cause more harm to the patient. Some of these conditions are:

1. Non –consent by patient/attendants
2. Severe pre-existing neurological deficit, advanced dementia
3. Limited life expectancy <1 year due to underlying disease (e.g., cancer)
4. Active brain hemorrhage
5. Advanced age >75 years
6. Advanced terminal lung disease pre-existing
7. Advanced cancer spread all over body
8. Advanced liver failure

Prior to commencement of ECMO, if all other criteria have been met, the patient's family and caregivers must be counselled about the possibility of non-improvement of lungs following ECMO. This is because this technique is merely resting the lungs while awaiting spontaneous recovery from the damage due to the virus. As such the lung involvement, especially in the second wave of infections has been noted to be much more severe than the first. This means that even as ECMO is being used, the disease process and progression is in no way altered and the patient may, in fact deteriorate during ECMO. The deterioration may be two-fold: first, as mentioned above, as a result of the ongoing disease process; second, as a result of complication arising out of ECMO itself. Complications of ECMO may include:

1. Bleeding, as a result of the potent blood thinning medications required or ECMO. Bleeding may be minor, as in bruising spots all over the body, or serious as in new brain hemorrhage
2. Organ dysfunction that may involve liver, kidneys, intestines, etc.
3. Muscle wasting due to inadequate nutrition, despite intravenous and alimentary feeding
4. Damage to blood vessels due to placement of wide-bore cannula
5. Infection, which may be localised at sites of invasive monitoring lines, or generalised as in sepsis
6. Clot formation in ECMO circuit, which may cause breakdown of red blood cells and jaundice, this may even necessitate change of circuit.

In conclusion, it may be reiterated that COVID is an evolving situation, and ECMO is only a rescue modality, with attendant risks. It also carries financial implications, with high costs of circuits and maintenance involved. However, in the absence of anything better and its spectacular results during the Swine flu epidemic, it may still be used in selected cases with caution, after a thorough discussion with the patient's family members of all possible risks, need for prolonged post-ECMO rehabilitation and financial burdens.

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Pandemic which taught many lessons

An ounce of prevention is worth a **pound** of **cure**,
Namaste far better than hand shake and embrace,
Putting on snuggly fitting mask prevents deadly vice,
Wise to stand aloof than mill in the crowd for sure.
Virus punishes everyone flouting basic rules,
King pauper physician clergy stars might and mule,
Everyone must fall in line same bed day and night,
Gold diamond stones meaningless virus so might.
Nobility of health profession never so obvious,
Faceless silent moving fingers pacing ingenious,
Connecting oxygen watching each drop so precious,
Putting PPE drenched in sweat every bit courageous.
A timely lift lifeline prick saves precious life not the trick,
So many hands sweeping floors cleaning corners and pick,
The unsung real heroes braving COVID nineteen our brick,
Charged with positivity zeal missionary spirit service of sick.
'Little hands of love' latex glove Nightingales from Brazil,
Feeling of warm holding hands how sweet you little angel,
True to the spirits of Gurus oxygen- langars beds & morsels,
Commoners accompanying unknown last journey last rituals.
Black marketeer vultures foxy drum shell rotten seeds,
Man proposes God disposes bubble bursts in seconds,
When you depart carry nothing but your own good deeds,
Came empty handed return likewise penniless indeed,
Nature has its own system of reward and punishment,
Hang your ego power pelf outside hospital establishment,
Collect goodwill not ill will not the time for grandiloquent,
Master Orchestra plans for each & sundry so goes the testament.

No one knows the final journey its ultimate destination,
Each one must face ultimate fire sum of truth falsification,
Big salute to human instinct tender touch nature's dispensation,
COVID pandemic taught us many lessons humane revelations.

New-Onset Diabetes in Covid-19

There is a bidirectional relationship between Covid-19 and diabetes. On the one hand, diabetes is associated with an increased risk of severe Covid-19. On the other hand, new-onset diabetes and severe metabolic complications of pre-existing diabetes, including diabetic ketoacidosis and hyperosmolarity for which exceptionally high doses of insulin are warranted, have been observed in patients with Covid-19. These manifestations of diabetes pose challenges in clinical management and suggest a complex pathophysiology of Covid-19–related diabetes.

It's believed that the virus damages certain kinds of cells — known as beta cells — that are found in the pancreas. They are found within another kind of cell known as an islet cell (more on islet cells below).

The destruction of these beta cells prevent the body from making insulin — triggering hyperglycemia (or high blood sugar). Because, in this case, the body needs glucose as energy (but can't use it), it turns to ketones, chemicals the liver makes when you don't have enough insulin, for energy. The use of ketones signals the production of acids, which can also lead to a condition called diabetic ketoacidosis (DKA), a potentially-fatal condition.

People with prediabetes who have been infected with COVID-19 should also be aware of the general symptoms of diabetes.

That people with prediabetes should know that any added stress (such as a virus) can tax the metabolic system, which could lead to diabetes.

"Hypothetically, someone with prediabetes could get COVID-19 and be asymptomatic…but might experience the classic symptoms of the onset of diabetes a number of other patients were found to have spontaneously developed diabetes after having been infected with COVID-19. This development of diabetes also occurred due to the SARS virus.

"We need to keep an eye on diabetes rates in those with prior COVID-19, and determine if rates go up over and above expected levels,"

Beyond investigating the specifics of how the virus triggers diabetes, the researchers also trying to determine whether the diabetes cases are permanent.

COVID-19 can also worsen current diabetes

New data — found by comparing COVID-19 to SARS — has shown that COVID-19 can also worsen existing endocrine conditions, including diabetes.

So, how does it work? The virus binds to a receptor known as ACE2, which allows it to enter into endocrine cells. Once the virus takes hold, it can disrupt insulin production and cause blood glucose levels to go haywire, making it harder to fight off the virus.

According to The Endocrine Society, it all goes back to those islet cells mentioned above: "A study during the SARS epidemic demonstrated ACE2 expression in islet cells and a high incidence of hyperglycemia among SARS patients. The authors speculated that SARS-CoV-1 may directly infect islet cells causing their dysfunction, resulting in hyperglycemia or new-onset diabetes."

Additionally, viral infections can lead to dysfunctional immune response and circulatory issues, as well as increased inflammation (which is also known as internal swelling) in patients with diabetes. This is due to high blood sugar, which can lead to further complications, according to the American Diabetes Association (ADA).

The majority of diabetes patients already have an inflammatory state present, "so if they become infected with COVID-19, the virus can create an inflammatory storm with cytokines flying all over the place." This is known as a cytokine storm, which is an increase in cell-signalling proteins that create inflammation and can lead to organ failure or even death.

Some researchers also believe that an inflammatory state could lead to the development of new-onset diabetes as well.

Other risks to current diabetics? Diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome, both of which can be brought on by infection. These risks are high for patients who don't have well-controlled diabetes.

Diabetic ketoacidosis can also alter your electrolyte and fluid levels, which can be dangerous if sepsis —otherwise known as a life-threatening organ dysfunction due to infection — sets in. The ADA recommends checking for ketones (chemicals from ketoacidosis) if your blood sugar has registered high (greater than 240 mg/dl) more than twice in a row.

Symptoms of DKA include

- Increased thirst
- Bad (or fruity) breath
- Nausea
- Abdominal pain
- Fatigue
- Confusion

Another serious complication of COVID-19 and diabetes is called hyperosmolar hyperglycemic syndrome. It occurs when blood glucose is extremely high for a long period of time without intervention. The symptoms are similar to DKA, and include frequent urination and vision changes as well.

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Frequently asked questions about COVID Vaccine

Q.1. How many types of COVID-19 Vaccines are manufactured in India?

Ans: Following vaccines which are being manufactured in India.

a) ***Covishield***

Developed by : University of Oxford & AstraZeneca in collaboration with the SII

Vaccine type : Modified chimpanzee adenovirus vector

Efficacy : DCGI: 70.42% overall

Dosage : Two doses (Gap 2.5 – 3 months)

b) ***Covaxin***

Developed by : Bharat Biotech in associated with ICMR and NIV

Vaccine type : Inactivated whole virus

Efficacy : 78%

Dosage : Two doses (0, 14 days)

c) ***ZyCov-D***

Developed by : ZydusCadila

Vaccine type : Plasmid DNA Vaccine

Dosage : 3 doses (28 days apart each)

d) ***Biological E***

Developed by : Biological E

Vaccine Type : Subunit Vaccine

e) ***Mynvax***

Developed by : Mynvax – IISc

Vaccine type : Protein based vaccine

f) ***HGC019 – Gennova Biopharmaceuticals***

Developed by : Gennova Biopharmaceuticals

Vaccine type : mRNA vaccine

g) ***Sputnik V***

Developed by : Gamaleya Research Institute of Epidemiology & Microbiology, Russia (Approved to be used in India)

Vaccine type : Non-replicating viral vector (adenovirus)

Efficacy : 91.4%

Dosage : Two doses

Q 2. Which vaccine to choose?

Ans: As of now, we don't have enough vaccine to immunize everybody. So, whichever vaccine is available, one should take it. All the currently available vaccines have been demonstrated to be safe, efficacious and is being manufactured with high quality. All vaccines offer nearly similar protection.

Q 3. Is it necessary for people who do not have risk for severe complication of COVID-19 to take vaccine?

Ans: Regardless of your risk, you can still contract the infection and spread it to others, so it's important you get vaccinated. Once the vaccine is widely available, it's recommended that as many eligible adults as possible get the vaccine. It's not only to protect you but your family and community as well.

Q 4. If someone receive the COVID-19 vaccine, is he at greater risk become sick from another illness?

Ans: There is no evidence to suggest that getting the vaccine heightens your risk to become sick from another infection such as the flu.

Q 5. Certain blood types have less severe COVID-19 infections, is the vaccine necessary for them?

Ans: Research has shown there is no reason to believe being a certain blood type will lead to increased severity of COVID-19. By choosing to get vaccinated, you are protecting not only yourself and your family but your community as well.

Q 6. What is the degree of protection offered by various Vaccines?

Ans: Almost, all the available vaccines are highly protective against severe disease, which may lead to hospitalization and death. Vaccines may not completely prevent infection, but the immunity developed in body in response to vaccination is good enough to protect people from getting sick even if they get the infection. In countries like Israel & U.K., studies have found that people who have received the first dose have 70 – 80% protection against infection. Following second dose, this could be even higher. The degree of protection may vary from vaccine to vaccine.

Q 7. Should People with History of Allergy not have COVID Vaccine?

Ans: Person with simple allergy like common cold, allergy dermatitis can have COVID vaccine. However, it better to consult Physician, if someone has history of major form of allergy.

Q 8. Those who are allergic to egg products, do they need to avoid vaccination?

Ans: The Pfizer, Moderna and J&J COVID-19 vaccines do not contain egg products, and eggs are not used to produce the vaccines. The CDC recommends that people with a history of severe allergic reactions *not related to vaccines*—such as food, pet, venom, environmental or latex allergies—get vaccinated for COVID-19. If you have a history of vaccine reactions, talk to your Physician before getting the COVID-19 vaccine.

Some people have had serious allergic reactions—anaphylaxis—within about 15 minutes after receiving the Pfizer-BioNTech and Moderna vaccines. It also occurred in one person in the J&J COVID-19 vaccine trial. Based on data so far, severe allergic reactions are rare. However, due to the risk of anaphylaxis, vaccination locations must have epinephrine and other medical supplies on hand to treat anaphylaxis. The healthcare provider administering your vaccine may ask you to wait 15 to 30 minutes for observation after you receive the vaccine.

Q 9. Do we require booster dose following initial Vaccination?

Ans: As of now, there is no data to suggest that booster dose of COVID vaccination will be required or not. Persons who have received full course of vaccination develops protective immunity in the body to protect against severe disease even from newer variants of virus. Even in countries where there are a lot of variants of virus found, vaccinated people did not develop severe disease or succumb to death even if they develop infection.

Q 10. Which of the COVID vaccine is a DNA vaccine?

Ans: ZyCoV-D is a plasmid DNA vaccine, which produces spike protein of SARS-CoV-2 virus & elecits immune response mediated by both cellular & humoral immune system. It's a needle free vaccine. The vaccine shot given by spring powered device. It's very comfortable for children and people who have injection hesitancy. ZyCoV-D has a 3 dose regimen with an interval of 28 days each shot.

Q 10. What are the side effects of Vaccines?

Ans: The major adverse effect with vaccines is very rare, may be 1 – 10 / million frequency.

Temporary side effects of COVID vaccination includes headache, fatigue & fever. These are signs of revving up of immune system, which is a normal response to vaccine. The immune system has two main arms and the first one kicks in as soon as the body detects a foreign intruder. White blood cells swarm to the site, prompting inflammation i.e. responsible for chills, sourness, fatigue and other side effects. This rapid response steps up our immune system tends to wane with age and therefore younger people report side effects more often than older, adults. Some vaccine may elicit more reaction than others and every one reacts differently. If someone didn't feel anything a day or two after either dose, that does not mean the vaccine is not working.

Vaccination also sets in motion, the second part of our immune system, which will provide the real protection from the virus by producing antibody. Sometimes with activation of immune system, there may be temporary swelling in lymph node such as those under armpit & very rarely people have severe allergic reaction.

Q 11. How long to the COVID-19 vaccine protects people?

Ans: It has been found that the mRNA COVID-19 vaccine like Pfizer & Moderna reduce the risk of infection by 91% for fully vaccinated people. However, how long the protection will **lose**after full vaccination is still not clear. Fully or partially vaccinated people who become infected with COVID-19 might be less likely to spread the virus to others. In fully or partially vaccinated people, the virus was 40% less detectable in their noses.

Q 12. What is the chances of death following COVID-19 vaccination?

Ans: Number of deaths reported following vaccination in the country is only 0.0002% of 23.5 crore doses administered.

The mortality rate for those testing positive is over 1% and vaccination can prevent these deaths. Therefore, the risk of dying following vaccination is negligible compared to risk of dying due to COVID-19.

Q 13. Can pregnant woman take COVID vaccine?

Ans: As per the current guidelines in India, pregnant woman should not be given vaccine. However, in United States, FDA has approved Pfizer & Moderna vaccine for pregnant women also. Soon in India, we may get data regarding Covishield & Covaxin.

Q 14. Can a breast feeding mother get vaccination?

Ans: COVID Vaccination is safe in lactating mothers and they should receive vaccination.

Q 15. There has been some news regarding composition of Covaxin Vaccine, where it has been suggested that Covaxin vaccine contains the new-born calf serum?

Ans: These are misinterpreted facts. Covaxin does not contains new-born calf serum at all & calf serum is not an ingredient of the final vaccine product.

Q 16. Can vaccinated people transmit COVID-19 to others?

Ans: Fully vaccinated means someone has completed a COVID-19 vaccine course. "Fully vaccinated" does not mean "Immune to COVID-19". No vaccine offers 100% protection against illness yet it gives better chance to fight off the infectious consequences of being exposed to SARS-CoV2 virus. Fully vaccinated people can transmit the virus to others though at a lower rate. This could also be a reality for people who don't have good immune response to the vaccine.

Q 17. Can someone get COVID-19 from the vaccine?

Ans: You cannot get COVID-19 from the vaccine because it doesn't contain the live virus.

You must be exposed to the novel coronavirus to get COVID-19. The COVID-19 vaccines being distributed do not contain any virus particles, so one cannot get COVID-19 from the vaccine. After vaccination, some people develop a fever, muscle aches, headache, and fatigue—symptoms commonly associated with COVID-19. But, when these symptoms occur within three days of vaccination, they are almost always vaccine side effects. These side effects are a good sign the vaccine is working, as the symptoms are evidence that your body is developing an immune response.

If you get sick and test positive for the novel coronavirus soon after receiving the vaccine, it means you were exposed to the virus, such as being in close contact with an infected person.

Q 18. Can COVID-19 vaccination lead to positive test for COVID-19?

Ans: Viral tests used to diagnose COVID-19 check samples from the respiratory system for the presence of the virus that causes COVID-19. Since there is no live virus in the vaccines, the vaccines will not affect your test result. It is possible to get infected with the virus before the vaccine has had time to fully protect your body.

Q 19. Why are the vaccinated people still getting COVID-19?

Ans: Lot of people who are in between the doses or people who have received both doses are still testing positive or becoming infected with COVID-19. Immunization with COVID-19 vaccine provides the best protection within 2 weeks of being fully vaccinated. A person is considered fully vaccinated 2 weeks after receiving second dose of Pfizer, Moderna and Covishield vaccines or one dose of Johnson & Johnson, Covaxin and Sputnikc vaccine. If someone test positive for COVID-19, are becomes ill a few days later, they most likely were exposed before being fully vaccinated.

Q 20. Should I get COVID antibody tested after vaccination to assess antibody response following vaccination?

Ans: The effectiveness of vaccine antibody vaccine efficacy does not depend only on quantum of antibody production. There are other mechanisms like cell mediated immunity and protection through memory cells which helps in antibody production at higher rate on infection. Therefore, COVID antibody testing is not advisable.

Q 21. Those who already had COVID-19 do not require a Vaccine?

Ans: Due to severe health risk associated with COVID-19 and the fact that reinfection with COVID-19 is possible, people may be advised to get a COVID-19 vaccine even if they have recovered from COVID-19. There is not enough information currently available to say if or for how long one is protected from getting COVID-19 after they have had it (natural immunity). Early evidence suggests that the natural immunity from COVID-19 may not loss very long.

Q 22. How long after COVID infection one can get vaccinated?

Ans: Anybody who was infected with COVID-19 can receive COVID vaccination after 90 days of recovering from infection.

Q 23. COVID-19 vaccine enters the cells and may change DNA?

Ans: The COVID vaccines are designed to help our body's immune system to fight the corona virus. The messenger RNA of COVID-19 vaccine does enter cells, but not the nuclei of the cells where DNA resides. The mRNA does its job to cause the cells to make protein to stimulate immune system and then it quickly breakdown without affecting DNA.

Q 24. What is a Nasal Vaccine?

Ans: A nasal vaccine is given by the nose, rather than a needle through your arm. Its target is to directly deliver the dose to the respiratory pathway, much like a nasal spray. BBV154, an intranasal vaccine developed by Bharat Biotech, is already in the pre-clinical trial phase.

A) Advantages of Nasal Vaccine?

Benefits that make this kind of vaccine stand apart include the fact that this is a non-invasive vaccine. This means that there are no needless required to take the dose of this vaccine and it does not need health workers to administer.

B) How does Nasal Vaccine works?

The significant advantage of intranasal vaccine is that it creates a robust immune response at the site of virus entry – the nose. This helps in shielding against the virus and transmission. If the virus can be stopped from entering at this point, it will not be able to get into the lungs to cause damage. If one effective mucosal

immune response is generated, it would possibly prevent the coronavirus infection from the outset and more effectively reduce transmission of the virus.

Bharat Biotech's Nasal Vaccine

Bharat Biotech's nasal vaccine candidate is under Phase I trials. According to the manufacturer, as per the reports, the intranasal vaccine BBV154 creates an immune response at the site of infection (in the nasal mucosa). This helps to block both infection and transmission of COVID-19.

C) How is it different from existing COVID-19 vaccination?

The nasal spray is usually preferred for children but for adults too doctors found that the nasal spray works just as well as the flu shot.

Q 25. **Canthe COVID-19 vaccine cause infertility?**

Ans: There is no evidence that COVID-19 vaccination causes infertility or miscarriage, and the American Society for Reproductive Medicine states that patients who are undergoing fertility treatment should be encouraged to receive the COVID-19 vaccine based on eligibility criteria.

According to University of Missouri Health Care, "misinformation on social media suggests the vaccine trains the body to attack...a protein on the placenta;" however, this protein is different enough that COVID-19 vaccination will not affect it.

Q 26. Do we require to wear mask even after complete vaccination?

Ans: Masking, hand washing and physical distancing remain necessary in public until a sufficient number of people are immune. Fully vaccinated people can meet with other fully vaccinated people without wearing masks.

Q 27. Will a COVID-19 vaccine alter my DNA?

Ans: No. COVID-19 vaccines do not change or interact with your DNA in any way. There are currently two types of COVID-19 vaccines that have been authorized and recommended for use in the United States: messenger RNA (mRNA) vaccines and a viral vector vaccine. Both mRNA and viral vector COVID-19 vaccines deliver instructions (genetic material) to our cells to start building protection against the virus that causes COVID-19. However, the material never enters the nucleus of the cell, which is where our DNA is kept. This means the genetic material in the vaccines cannot affect or interact with our DNA in any way. All COVID-19 vaccines work with the body's natural defenses to safely develop immunity to disease.

Q 28. Is it possible to receive two different vaccinations as first and second shot?

Ans: As of now combination of vaccines have not been approved. Studies are underway to see the safety and efficacy of combing two different vaccines. One should stick to the same vaccine for second shot also.

Q 29. Is it risky for cardiac patients to receive COVID-19 Vaccines?

Ans: Cardiac patients are at higher risk of acquiring COVID infection and complication. Vaccine will reduce the chances of getting into serious illness and requirement for hospitalization. So all cardiac patients should receive vaccination as soon as possible.

Q 30. Is it true that COVID-19 Vaccine is leading to new heart disease?

Ans: The Centre of Disease Control, US and also from Israel, cases of inflammation of heart muscles following COVID vaccination has been reported, though the numbers are very low. It has been seen with Pfizer vaccine, more often in young males following second dose and typically within 4 – 5 days of vaccination. This needs follow up and with increasing number of vaccination in future, one will be able to know exactly the problem. After vaccination, anyone who feel chest pain, short of breath or feels that their heart or pulse is beating particularly fast, fluttering or pounding should see a Physician.

Q 31. What are the chances of developing clot in the brain following COVID vaccine?

Ans: Vaccine induced prothrombotic thrombocytopenia has been reported with administration of Johnson & Johnson and AstraZeneca COVID-19 vaccines. It is seen usually 5 – 28 days following vaccination. It presents as clotting in unusual site like cerebral sinuses of the brain or the splanchnic vein of abdomen. It is due to formation of antibody to platelet factor-4 heparin complex. The risk of developing a serious blood clot is 8 to 10 times higher in people with COVID than those who get a vaccine.

Q 32. Patients who are on blood thinner, should they have COVID – 19 Vaccine?

Ans. Patients with bleeding disorders or taking anticoagulants or antiplatelet medications, require special consideration as there is a slightly increased risk of bleeding due to the intra-muscular route of administration.

- Patients on standard intensity anticoagulation with Warfarin (target INR 2.0 – 3.0) can receive intra-muscular injections as long as the most recent INR is < 3.0. There is no need to re-check the INR solely for the purposes of vaccination.
- Patients on maintenance therapy with Direct Oral Anticoagulants (Apixaban, Dabigatran, Edoxaban and

Rivaroxaban) can delay the dose on the day of vaccination until after the intra-muscular injection but do not need to miss any doses.

- Patients on single agent anti-platelet therapy (e.g. aspirin or clopidogrel) can continue on these medications without any adjustment.
- Patients with higher intensity anti-thrombotic treatment, for example Warfarin with a target INR > 3.0 or dual antithrombotic medications, should be managed on an individual basis.
- The bleeding risk can be reduced by application of firm pressure at the injection site for at least 5 minutes afterwards.
- Patients on a full dose of Heparin or Fondaparinux injections, should also be able to have the vaccine. The daily dose can be delayed until after the injection but there is no need to miss any doses.

Q 33. **Patients suffered from cancer, should they have COVID – 19 Vaccine?**

Ans: Cancer is a high-risk condition – expected to be in one of the earlier priority groups able to receive the vaccine.

If a vaccine is available to you, it may be appropriate to delay the start of some non-urgent cancer treatments until vaccination has been completed.

Most cancer treatments, however should not be delayed for vaccination. Depending on the types of cancer treatment, you may have had or are receiving, there may be other special considerations.

- **For Patients receiving chemotherapy or other immune suppressing treatments –** In general, receiving either vaccine during chemotherapy is recommended. But because the vaccines can cause a fever within the first 24 to 48 hours, is is preferable to receive the vaccines at a time when your white blood counts are not expected to be low. This is because if a fever occurs when your blood counts are low, it may require hospitalization. In some circumstances, it may be appropriate to delay vaccination until after completion of very intensive chemotherapy treatments such as those given as induction therapy for acute leukemia.
- **For patients receiving immunotherapy** – For most patients receiving immunotherapy for cancer, it's fine to proceed with vaccination and immunotherapy need not be interrupted.
- **For Patients receiving steroids medications –** Corticosteroids may reduce the response to COVID-19 vaccination. If you require corticosteroids as a part of your cancer treatment, you should discuss the timing of vaccination with your Physician.
- **For patients receiving Rituximab, Blinatumomab, Anti-thymocyte Globulin, Alemtuzumab and other Lymphocyte – depleting therapies –** These treatments can affect the lymphocytes, which are an important part of the immune response to the COVID-19 vaccines. Vaccination may be more effective, if delayed for at least three months after completing these therapies. However, if COVID-19 rates are high in your community, the benefit of partial protection from vaccination during or soon after treatment should be considered.
- **For patients receiving hormonal treatments –** Endocrine or hormonal treatments for cancer including Tamoxifen, Aromatase inhibitors, LHRH analogs and anti-androgens are not expected to alter the safety or effectiveness of the vaccines.
- **For patients receiving IVIG** – For most patients receiving IVIG, it's fine to proceed with vaccination and IVIG therapy need not be interrupted.
- **For patients receiving Radiation Therapy** – For most patients receiving radiation treatment, it's recommended to proceed with vaccination and radiation treatment need not be interrupted.
- **For patients receiving Surgery –** For most patients receiving cancer related surgery, it's recommended to proceed with vaccination. Since fever can occur in the first 24 to 48 hours after vaccination, it's best to avoid scheduling your vaccination within a few days of planned surgery as a fever may result in cancellation of the surgery. For those undergoing splenectomy, you should receive the first vaccine dose at least two weeks or more before surgery if possible.
- **For patients who have had severe allergic reactions to chemotherapy or monoclonal antibody treatments –** the vaccine ingredients polyethylene glycol and polysorbate may be found in a variety of chemotherapy and monoclonal antibody drugs. If you experienced anaphylaxis or other severe allergic reactions to cancer therapies, consultation with an allergist is recommended prior to receiving the vaccine.

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"To live in the hearts of those
we love is never to die."

Prof (Dr) S Padmavati
(1917 – 2020)

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