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Review Article

Prevention, treatment and cure for COVID-19

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Abstract

Few months ago, COVID-19 was totally foreign to all but now it has spread its route in India. Starting from one case, the virus has spread in every corner of India. Coronavirus disease 2019 is an infection cause by Severe Acute Respiratory Syndrome coronavirus (SARS-CoV-2). The infection expresses as mild flu to severe acute respiratory infection. World health Organization (WHO) declared COVID-19 as a global pandemic disease. Even with the implementation of strong international travel restriction, by a large number of individuals exposed to SARS-CoV-2 has resulted in the spread of virus worldwide. At global level, scientific communities including various healthcare professionals are working to understand the virological, epidemiological and clinic aspects of COVID-19 in order to identify effective drugs and vaccines. Ministry of Health and Family Welfare, Government of India and Indian Council of Medical Research (ICMR) has formulated several guidelines, advisory for social distancing, diagnosis and management of the disease.

Keywords: COVID-19, Coronavirus, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2), Arsenicum Album, Ayush Kadha Immunity Booster, Sputnik-V, COVAXIN, Coronil, Convalescent Plasma Therapy, Nucleic Acid Amplification Test (NAAT) .

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1. Introduction

In early December 2019, a Pathogen has been identified as a novel enveloped RNA beta coronavirus that has currently been named as Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2).

(1) There are 7 strains of coronavirus that are reported as:

- Human Coronavirus 229E (HCoV-229E)
- Human Coronavirus NL63 (HCoV-NL63)
- Human Coronavirus OC43 (HCoV-OC43)
- Human Coronavirus HKU1
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV)
- Novel Coronavirus (2019-nCoV) (SARS-CoV-2)

Amongst this, Novel Coronavirus (2019-nCoV) (SARS-CoV-2) causes Coronavirus disease known as COVID-19. (2) Infection mediated by SARS-CoV-2 also known as COVID-19 is a new viral infection characterized by dry cough, fever, fatigue, dyspnea, lymphopenia which can be further complicated by interstitial pneumonia leading to Severe Acute Respiratory Distress Syndrome (ARDS). (3)

Pro-inflammatory Cytokines induces Pneumonia and Cytokine Storm Syndrome in patients with severe Coronavirus disease 2019 (COVID-19) which might lead to multiorgan failure and eventually death of the patient. (4,5)

2. Case Definition-

Table 1. Case definition of the disease (6,7)

S.No	Term	Case Definition
1	Suspect case	A patient with acute respiratory illness {fever and at least one sign/symptom of respiratory disease (e.g. cough, shortness of breath or diarrhoea), AND a history of travel to or residence in a country/area or territory reporting transmission of COVID-19 disease during the 14 days prior to symptom onset

		<p>A patient/Health care worker with any acute respiratory illness AND having been in contact with a confirmed COVID-19 in the last 14 days prior to onset of symptoms</p> <p>A patient with severe acute respiratory infection {fever and at least one sign/symptom of respiratory disease (e.g. cough, shortness breath)} AND requiring hospitalization AND with no other etiology that fully explains the clinical presentation</p> <p>A case for whom testing for COVID-19 is inconclusive</p>
2	Lab confirmed case	A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms
3	Contact	<p>A contact is a person that is involved in any of the following:</p> <p>Providing direct care without proper personal protective equipment (PPE) for COVID-19 patient</p> <p>Staying in the same close environment of a COVID-19 patient (including workplace, classroom, household, gatherings)</p> <p>Travelling together in close proximity (within 1 m) with a symptomatic person who later tested positive for COVID-19</p>
4	High Risk Contact	<p>Contact with a confirmed case of COVID-19</p> <p>Travel to a province where COVID-19 LOCAL TRANSMISSION is being reported as per WHO daily situation report</p> <p>Touched body fluids of patients (respiratory tract secretions, blood, vomitus, saliva, urine, faeces)</p> <p>Touched or cleaned the linens, clothes or dishes of the patient</p> <p>Close contact, within 3 feet (1 metre) of the confirmed case</p> <p>Co-passengers in an airplane/vehicle seated in the same row, 3 rows in front and behind of a confirmed COVID-19 case</p>
5	Low Risk Contact	<p>Shared the same space (same classroom/same room for work) or similar activity and not having high risk exposure to the confirmed/suspected case</p> <p>Travel in the same environment (bus/train/flight/any mode of transit) but not having high risk exposure as cited above</p> <p>Any traveller from abroad not satisfying high risk criteria</p>

3. Clinical Syndromes associated with SARS-CoV-2 infection

Table 2. Clinical Syndromes of the disease (8)

Syndrome	Definition
Uncomplicated illness	Patients with uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache, muscle pain or malaise. The elderly and immunosuppressed may present with atypical symptoms. These patients do not have any signs of dehydration, sepsis or shortness of breath.
Mild Pneumonia	<p>Patient with pneumonia and no signs of severe pneumonia.</p> <p>Child with non-severe pneumonia has cough or difficulty breathing + fast breathing: fast breathing (in breaths/min) : <2 months, ≥ 60; 2–11 months, ≥ 50; 1–5 years, ≥ 40 and no signs of severe pneumonia.</p>
Severe Pneumonia	<p>Adolescent or adult: fever or suspected respiratory infection, plus one of respiratory rate >30 breaths/min, severe respiratory distress, or SpO₂ <90% on room air.</p> <p>Child with cough or difficulty in breathing, plus at least one of the following: central cyanosis or SpO₂ <90%; severe respiratory distress (e.g. grunting, very severe chest indrawing); signs of pneumonia with a general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions. Other signs of pneumonia may be present: chest indrawing, fast breathing (in breaths/min) : <2 months, ≥ 60; 2–11 months, ≥ 50; 1–5 years, ≥ 40.</p>
Acute respiratory Distress Syndrome	<p>Onset: new or worsening respiratory symptoms within one week of known clinical insult.</p> <p>Chest imaging (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by effusions, lobar or lung collapse, or nodules.</p> <p>Origin of oedema: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of oedema if no risk factor present.</p> <p>Oxygenation (adults):</p> <p>Mild ARDS: $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$ (with PEEP or CPAP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated)</p> <p>Moderate ARDS: $100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}$ with PEEP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated)</p> <p>Severe ARDS: $\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mmHg}$ with PEEP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated)</p> <p>When PaO₂ is not available, SpO₂/FiO₂ ≤ 315 suggests ARDS (including in non-ventilated patients)</p>

	Oxygenation (children; note OI = Oxygenation Index and OSI = Oxygenation Index using SpO ₂): Bilevel NIV or CPAP ≥ 5 cmH ₂ O via full face mask: PaO ₂ /FiO ₂ ≤ 300 mmHg or SpO ₂ /FiO ₂ ≤ 264 Mild ARDS (invasively ventilated): $4 \leq OI < 8$ or $5 \leq OSI < 7.5$ Moderate ARDS (invasively ventilated): $8 \leq OI < 16$ or $7.5 \leq OSI < 12.3$ Severe ARDS (invasively ventilated): $OI \geq 16$ or $OSI \geq 12.3$
Sepsis	Adults: life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction. Children: suspected or proven infection and ≥ 2 SIRS criteria, of which one must be abnormal temperature or white blood cell count.
Septic Shock	Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L. Children: any hypotension (SBP 2 SD below normal for age) or 2-3 of the following: altered mental state; tachycardia or bradycardia (HR 160 bpm in infants and HR 150 bpm in children); prolonged capillary refill (> 2 sec) or warm vasodilation with bounding pulses; tachypnea; mottled skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia.

4. Chronological development of symptoms of COVID-19

Table 3. Chronological development of symptoms (9)

Symptoms	Min % to max %	Duration in survivors (days)	Duration in non survivors (days)
Fever	43.8 - 98.6	0 – 12	0 – 13
Cough	59.4 - 82	0 – 19	0 – 16
Shortness of breath	18.7 - 55	7 – 19	7 – 18
Fatigue	38.1 - 69.6		
Headache	8 - 13.6		
Respiratory rate > 24 beats per minute	29		
Sore throat	5		
Chest pain	2		
Nausea and Vomiting	1 - 10.1		
Nasal congestion	4.8		
Chills	11.5		
Throat congestion	1.7		
Tonsil swelling	2.1		
Enlargement of lymph nodes	0.2		
Rash	0.2		
Dizziness	9.4		
Abdominal pain	2.2		
anorexia	39.9		

5. Laboratory diagnosis

Guidance on specimen collection, processing, transportation, including related biosafety procedures, is Available from:

https://www.mohfw.gov.in/pdf/5Sample%20collection_packaging%20202019-nCoV.pdf

Table 4. Specimen types and Collection details (10)

Specimen type	Collection materials	Transport to laboratory	Storage temperature till testing	Comments
Nasopharyngeal and oropharyngeal swab	Dacron or polyester flocced swabs	4°C	≤ 5 days : 4°C > 5 days : -70°C	To increase the viral both Nasopharyngeal and oropharyngeal swab should be placed in the same tube
Bronchoalveolar lavage	Sterile container	4°C	≤ 48 hours : 4°C > 48 hours : -70°C	Some dilution of pathogen may be there but an important specimen in patients with serious infection.
Tracheal aspirate, nasopharyngeal aspirate or nasal wash	Sterile container	4°C	≤ 48 hours : 4°C > 48 hours : -70°C	–
Sputum	Sterile	4°C	≤ 48 hours : 4°C	To ensure if the material is from

	container		>48 hours : -70°C	lower respiratory tract
Tissue from biopsy or autopsy including from lung	Sterile container with saline or VTM	4°C	≤24 hours : 4°C >24 hours : -70°C	Important for post mortem diagnosis
Serum (acute and convalescent samples)	Serum separator tubes (adults: collect 3-5ml)	4°C	≤5 days : 4°C >5 days : -70°C	Paired samples to be collected: Acute- first week of illness Chronic- 2-3 weeks later
Whole blood	Blood in EDTA vial	4°C	≤5 days : 4°C >5 days : -70°C	-
Stool	Stool container	4°C	≤5 days : 4°C >5 days : -70°C	Important sample to rule out GI infection
Urine	Urine collection container	4°C	≤5 days : 4°C >5 days : -70°C	-

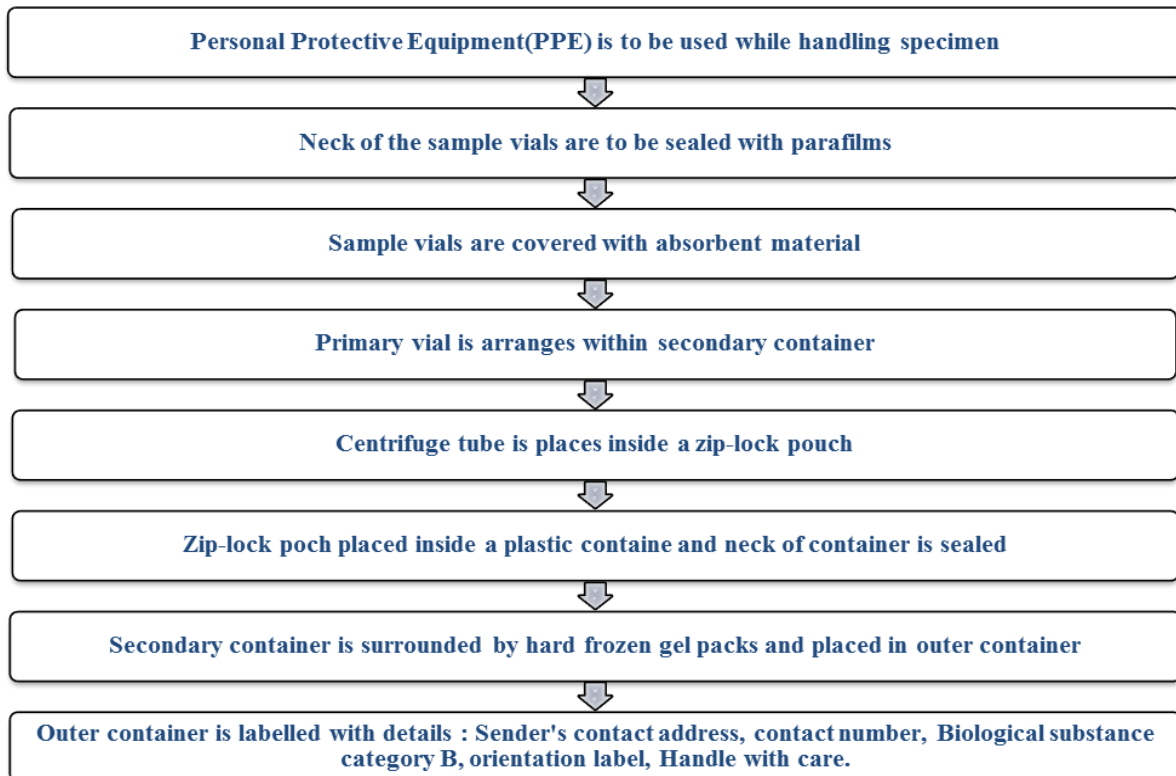


Figure 1. Procedure for specimen packaging and transport (10)

Other diagnostic method for the detection of SARS-CoV-2:

Nucleic Acid Amplification Test-

Nucleic acid amplification testing requires respiratory samples from the patient because SARS-CoV-2 is a respiratory virus.

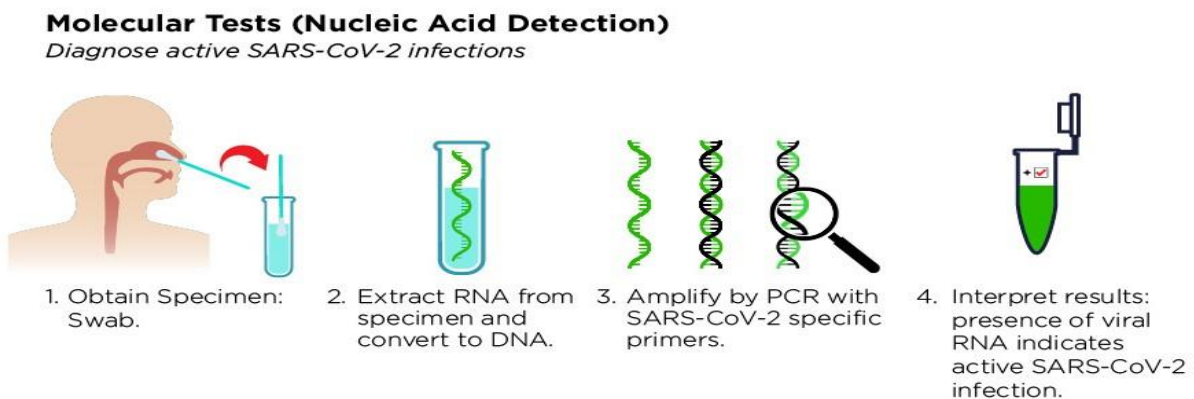


Figure 2. Nucleic Acid Amplification Test (NAAT)

Nasopharyngeal swabs are most commonly used. Lower respiratory secretions, such as sputum and bronchoalveolar lavage fluid, are also used if a patient has pneumonia or lung involvement with infection. Samples are then processed and tested for SARS-CoV-2 RNA. The test includes extraction of RNA from the patient specimen, conversion to DNA and PCR (Polymerase Chain Reaction) amplification with SARS-CoV-2-specific primers. (11)

RT-PCR (Real Time Polymerase Chain Reaction) involves the reverse transcription of SARS-CoV-2 RNA into complementary DNA (cDNA) strands, followed by amplification of specific regions of the cDNA. The design process generally involves two main steps: (1) sequence alignment and primer design, and (2) assay optimization and testing. (12)

Serology (11)

The immune system naturally produces protein known as Antibodies that is in response to infection. Antibodies bind to foreign molecules known as Antigens on the surface of pathogen. Whenever antibody binds to antigen, it disables pathogen through direct or indirect mechanisms.

Blood samples are used as specimen type for antibody testing. SARS-CoV-2 specific Antigen (spike or nucleocapsid protein) is mixed with patient’s blood. If antibodies are present in blood, the antigens will bind with antibodies which will result in colour change yielding positive result.

Major limitation of this test is that, this test only measures the amount of antibodies produced in response to SARS-CoV-2 infection but not for the test of the virus present. This test can even lead to false negative result in the situation if the test is conducted too early so that antibodies have not yet developed.

Antibody Tests (Serology)

Detect immune response to SARS-CoV-2 exposure

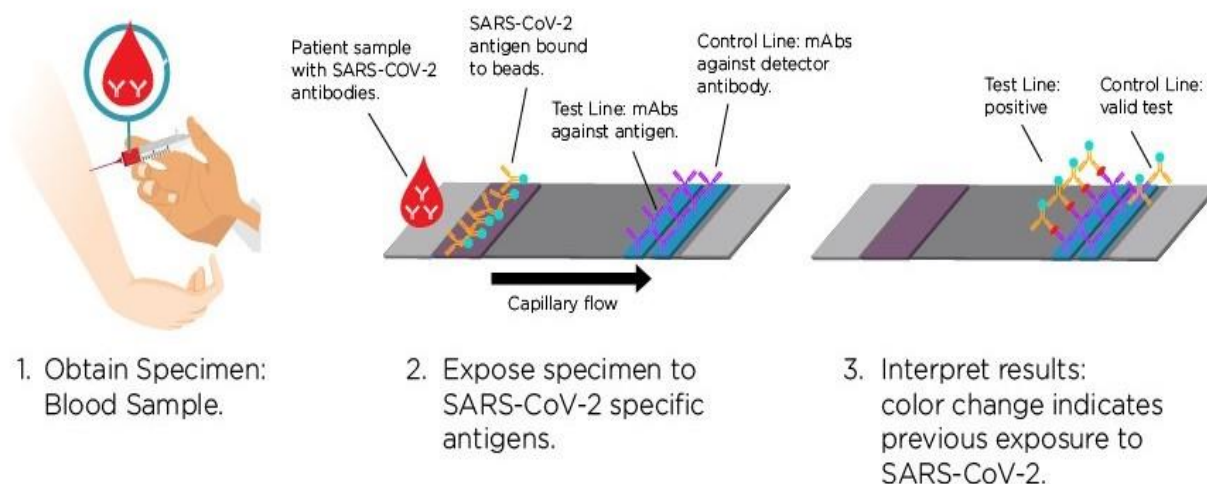


Figure 3. Serology Test

Comparison of Nucleic Acid Amplification Test and Serology-

Table 5. Comparison of NAAT and Serology

NAAT (PCR)	Serology (Antibody)
Also known as Swab test	Also known as Blood test
Detects- Viral RNA	Antibody (IgG, IgM)
Specimen- Nasal/oral	Blood (Serum)
Measures- Current infection with SARS-CoV-2	Past exposure to SARS-CoV-2
Time to obtain result- Few days or week	In an hour or less
Positive result indicates- Virus RNA present in sample – does not indicate if it is viable	Antibodies against virus present in blood (past infection)
Precaution- Nasal/throat swab reliable in 1 st week of disease only	Immune response not well/fully understood, no validated test available

6. Prevention of complication (13)

These interventions are generally based on Surviving Sepsis or other guidelines.

Implement the following interventions to prevent the complications that are associated with critical illness.

Table 6. Interventions to prevent complications

Anticipated Outcome	Interventions
Reduce days of invasive mechanical ventilation	<ul style="list-style-type: none"> Use weaning protocols that include daily assessment for readiness to breathe spontaneously Minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions
Reduce incidence of ventilator associated pneumonia	<ul style="list-style-type: none"> Oral intubation is preferable to nasal intubation in adolescents and adult Keep patient in semi-recumbent position (head of bed elevation 30-45°C) Use a closed suctioning system, periodically drain and discard condensate in tubing Use a new ventilator circuit for each patient; once patient is ventilated, change circuit if it is soiled or damaged but not routinely Change heat moisture exchanger when it malfunctions, when soiled, or every 5-7 days
Reduce incidence of venous thromboembolism	<ul style="list-style-type: none"> Use pharmacological prophylaxis (low molecular weight heparin [preferred if available] or heparin 5000 units subcutaneously twice daily) in adolescent an adults without contraindications. For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression devices)
Reduce incidence of catheter related bloodstream infection	<ul style="list-style-type: none"> Use a checklist with completion verified by a real-time observer as reminder of each step needed for sterile insertion and as a daily reminder to remove catheter if no longer needed
Reduce incidence of pressure	<ul style="list-style-type: none"> Turn patient every 2 hours
Reduce incidence of stress ulcers and gastrointestinal bleeding	<ul style="list-style-type: none"> Give early enteral nutrition (within 24-48 hours of admission) Administer histamine-2 receptor blockers or proton-pump inhibitors in patients with risk factors for GI bleeding. Risk factors for GI bleeding include mechanical ventilation for ≥48 hours, coagulopathy, renal replacement therapy, liver disease, multiple co-morbidities, and higher organ failure score
Reduce incidence of ICU-related weakness	<ul style="list-style-type: none"> Actively mobilize the patient early in the course of illness when safe to do so

7. Management of the disease

A. Management: General

As the world is struggling in responding to COVID-19 pandemic, WHO is recommending general public to reduce exposure and transmission of range of illness (14):

- Regularly cleaning hands with alcohol based hand rub or washing with soap and water.
- Maintaining at least 1 meter (3 feet) distance between 2 people.
- Avoid going to any crowded place.
- Avoid touching eyes, nose and mouth.
- Always cover mouth and nose with tissue while coughing and sneezing. The used tissue must be disposed immediately after use.
- Avoid close contact with anyone who has cough or fever.

- While visiting live markets in the areas that is currently experiencing cases of novel coronavirus, avoid any direct unprotected contact with animals.
- Avoid consumption of raw food or uncooked animal products. Raw milk, meat or any animal organ should be handled with much care to avoid cross-contamination with uncooked food.
- While having some of the symptoms like cough, fever and difficulty in breathing, immediately seek medical care.

Government of India has issued implementation guidelines for prevention and control measures of patient with suspected or confirmed COVID-19 (15):

Table 7. Guidelines for preventive measure of the disease

Precautions	Steps
At triage	Give suspect patient a triple layer surgical mask and direct patient to separate area, an isolation room if available. Keep at least 1 meter distance between suspected patients and other patient. Instruct all patients to cover nose and mouth during coughing or sneezing with tissue or flexed elbow for others. Perform hand hygiene after contact with respiratory secretions.
Apply standard precaution	Apply standard precautions according to risk assessment for all patients, at all times, when providing any diagnostic and care services. Standard precautions include hand hygiene and the use of Personal Protective Equipment (PPE) when risk of splashes or in contact with patients'

	blood, body fluids, secretions (including respiratory secretions) and non-intact skin. Standard precautions also include appropriate patient placement; prevention of needle stick or sharps injury; safe waste management; cleaning and disinfection of equipment; cleaning of environment. Best practices for safely managing health care waste should be followed.
Apply droplet precaution	Droplet precaution prevents large droplet transmission of respiratory viruses. Use a triple layer surgical mask if working within 1-2 meters of the patients. Place patients in single rooms, or group together those with same etiological diagnosis. If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation. When providing care in contact with a patient with respiratory symptoms (eg. coughing or sneezing), use eye protection (face mask or goggles), because sprays of secretions may occur. Limit patient movement within the institution and ensure that patients wear triple layer surgical masks when outside their rooms.
Apply contact precautions	Droplet and contact precautions prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces). Use PPE (triple layer surgical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving. If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers). If equipment needs to be shared among patients, clean and disinfect between each patient use. Ensure that health care workers refrain from touching their eyes, nose and mouth with potentially contaminated gloved or ungloved hands. Avoid contaminating environmental surfaces that are not directly related care (e.g. door handles and light switches). Ensure adequate room ventilation. Avoid movement of patients or transport. Perform hand hygiene.
Apply airborne precautions when performing an aerosol generating procedure	Ensure that healthcare workers performing aerosol-generating procedures (i.e. open suctioning of respiratory tract, intubation, bronchoscopy, cardiopulmonary resuscitation) use PPE, including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95). Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures, meaning negative pressure rooms with minimum of 12 air change per hour or at least 160 liters/sec/patient in facilities with natural ventilation. Avoid the presence of unnecessary individuals in the room. Care for patient in the same type of room after mechanical ventilation commences. Because of uncertainty around the potential for aerosolization, high flow nasal oxygen (HFNO), NIV, including bubble CPAP, should be used with airborne precautions until further evaluation of safety can be completed. There is insufficient evidence to classify nebulizer therapy as an aerosol-generating procedure that is associated with transmission of COVID-19.

B. Management: Homeopathy

Homeopathy plays an important role in case of epidemic disease. In many several epidemics like fever, cholera etc Homeopathic medicines have proved successful result. Number of ways is present which will boost the person's immunity for specified infectious disease. One way to improve vitality of a person is by raising good health through a balanced lifestyle as well as through homeopathic treatment. Other way is by the

use of vaccination and homeopathically prepared substances. (16)

Many homeopathic physicians worldwide are observing and prescribing successfully for COVID-19 patients which indicate improvement results from a range of medicine. Certain homeopathic medicine lie Arsenicum Album, Bryonia and Gelsemium have helped frequently for the symptomatic management during the epidemics of Cholera, Spanish influenza, Yellow fever, Scarlet fever, Diphtheria, Typhoid etc. (17)

Table 8. Homeopathic drugs and their uses

Drug	Active ingredient	Purpose
Arsenicum Album	Arsenic trioxide 30C HPUS*	Anti-inflammatory Pain killer Generic tonic Cough
Bryonia	Bryonia alba 30C	Anti-inflammatory Cough
Eupatorium Perfoliatum	Eupatorium perfoliatum 1m HPUS*	Anti-inflammatory Anti-oxidative Anti-plasmodial Immunomodulator Common cold Stiffness and bone pain associated with flu symptoms
Gelsemium Sempervirens	Gelsemium sempervirens 6C	Pain killer

	HPUS*	Asthma Fever
Antimonium Tartaricum	Antimonium potassium tartarate 6X HPUS*	Thick mucous Non productive cough

*HPUS- Homeopathic Pharmacopoeia of United States

Most efficient route of administration for Homeopathic medicine is oral or sublingual. For better absorption, homeopathic medicine should be taken in a mouth free of strong flavor or any other thing that may coat the mouth. It is been recommended to take the medicine 15 minutes before or after eating, drinking or brushing teeth. The food particles or any flavor remaining in the mouth interfere or delay the absorption

as the absorption takes place through mucous membrane inside the mouth. (18)

Food item like coffee, mint, garlic etc are to be avoided during the homeopathic treatment. Few remedies can be antidote by coffee. In such cases, the intake of coffee will aggravate the symptoms. The patient soon will experience a sensitive reaction after taking coffee and may inhibit the therapeutic measure.

Arsenicum Album 30C



Figure 4. Arsenicum Album 30C

Scientific Advisory Board of Central Council for Research in Homeopathy (CCRH) opened that “Arsenicum Album 30” could be taken as Prophylactic medicine against coronavirus infection. CCRH released a factsheet stating that this medicine is only a “possible prevention” against flu. Ayush Ministry recommended taking Arsenicum Album 30, daily dose once in empty stomach for 3 days. The dose should be repeated after one month following same schedule. Arsenicum Album is considered to correct inflammation in body. It also takes care of diarrhoea, cough and cold. It is used by several homeopaths to treat anxiety, restlessness, cold, ulceration and burning pains. (19)

disease can be focused from the ancient texts on ayurveda like Charaka Samhita, Sushruta Samhita and Ashtanga Hrudaya. These are the oldest known texts on ayurveda. Ayurveda documented the pandemics/epidemics under the Charaka Samhita Vimana sthana. The 3rd chapter of Charaka Samhita Vimana sthana is “Janapadoddhvamsaneeya Vimanam”. Janapada meand Community and Udhwamsa means Destruction. *Janapadodhvansa* (destruction of human settlements or communities by the means of natural or man-made calamities including epidemics) occurs when communities/towns/countries do not follow their *dharma* (eternal duties) in the past or/and present lives and commits such acts that are even more harmful.

C. Management: Ayurveda (20-28)

Ayurveda is an ancient system of medicine knowing about the herbs and trees. Prevention and cure for the



Figure 5. Divya Coroil Kit

In India, Ministry of AYUSH organization works in the field of Ayurveda, Siddha, Homeopathy, Unani and Yoga. One of the organization which works in the field of Ayurveda is "Patanjali Ayurveda", who recently developed a drug kit called "Coronil". Coronil has been developed in a Joint Research by Patanjali Research Institute and National Institute of Medical Science, Jaipur.

The drug named Coronil is in the form of kit that contains-

- Divya Coronil Tablet
- Divya Swasari Vati
- Divya Anu Taila

Major ingredients in the Coronil drug are Giloy, Ashwagandha, Tulsi, Black pepper, Amaltas, Bhringraj.

Table 9. Benefits of the ingredients used in Coronil

Ingredient	Part of the plant used	Benefits
Giloy (<i>Tinospora cordifolia</i>)	Stem, root	<ul style="list-style-type: none"> • Immunity booster • Treat chronic fever • Treat Respiratory problem • Reduces stress and anxiety • Reduces Asthmatic symptoms • Improves digestion
Ashwagandha (<i>Withania somnifera</i>)	Root	<ul style="list-style-type: none"> • Reduces inflammation • Increases muscle mass and strength in body • Reduces depression • Lowers cholesterol level • Lowers triglyceride level • Reduces cortisol level • Anti-cancer
Tulsi (<i>Ocimum sanctum</i>)	Leaves	<ul style="list-style-type: none"> • Strengthens immunity • Reduces breathing and lung related problem • Anti-bacterial • Anti-inflammatory • Anti-oxidant • Anti-carcinogenic • Beneficial in treating Malaria, TB and Dengue • Treatment of various skin related problems • Controls blood sugar level • Insect repellent
Black Pepper (<i>Piper nigrum</i>)	Dried unripe fruits	<ul style="list-style-type: none"> • Anti-oxidant • Anti-inflammatory • Piperin, an extract of black pepper is beneficial for brain • Boosts absorption of nutrients • Aids digestion • Stabilizes blood sugar metabolism
Amaltas (<i>Cassia fistula</i>)	Leaf, root, fruit, bark	<ul style="list-style-type: none"> • Anti-pyretic • Anti-inflammatory • Anti-bacterial • Hepatoprotective • Regulates hormonal imbalance in body
Bhringraj (<i>Eclipta alba</i>)	Whole plant	<ul style="list-style-type: none"> • Gastrointestinal infection treatment • Respiratory tract infection treatment • Cure fever, hairloss and skin disorder • Anti-inflammatory • Anti-carcinogenic • Anti-microbial

Other ingredients include-

- Sonth (*Zingiber officinale*)
- Lavang (*Syzygium aromaticum*)
- Dalchini (*Cinnamomum zeylanicum*)
- Mulethi (*Glycyrrhiza glabra*)

Patanjali Ayurveda claimed the medicine will be an immunity booster as the herbal ingredients have medicinal properties like anti-oxidant, Anti-inflammatory, Anti-viral and Bronchodilator. They also claimed that the ingredients will help to reduce symptoms like fever, cough and cold.

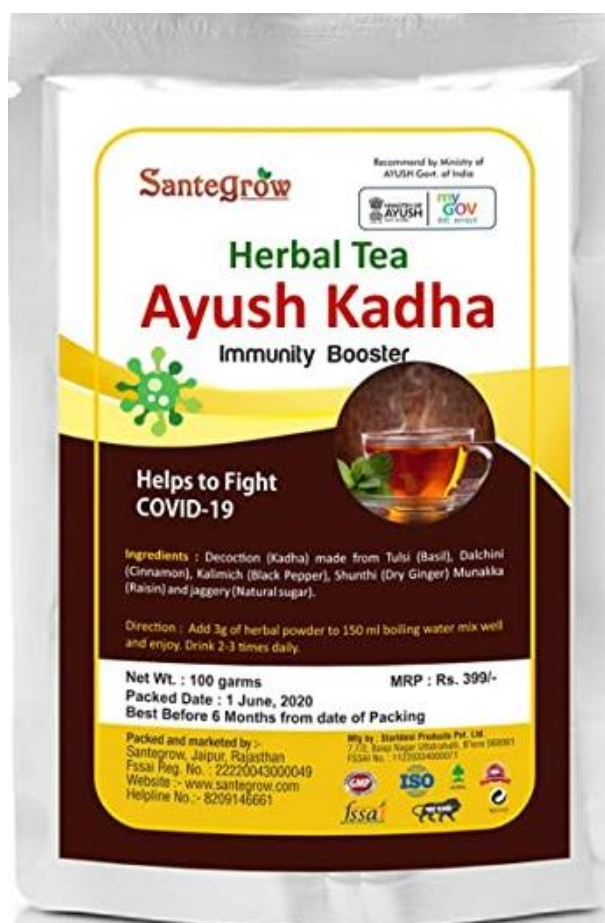


Figure 6. Ayush Kadha Immunity Booster

Ministry of AYUSH recommended drinking Herbal Tea/Decoction (Kadha) based on Ayurvedic literature and scientific publication for preventive measures and boosting immunity. This decoction (kadha) is made from Tulsi (Basil), Dalchini (Cinnamon), Kalimirch (Black Pepper), Sunthi (Dry ginger) and Munakka (Raisin). As

Table 10. Ayurvedic measures for symptom

per taste Jaggery (Natural sugar) or lemon juice can be added. This powder helps to enhance the immunity across age groups. This is an easy herbal concoction to strengthen the immune system and make it able to fight illness.

Symptoms	Measures
Cold, Running nose, Nasal congestion	<ul style="list-style-type: none"> • Steam inhalation with Tulsi, Peppermint, Eucalyptus oil • Nasal irrigation with warm saline water
Sore throat	<ul style="list-style-type: none"> • Gargle with Neem water decoction with Honey • Coriander and Turmeric Kashayam with Black pepper
Cough	<ul style="list-style-type: none"> • Chew Ginger
Dry cough	<ul style="list-style-type: none"> • Ginger Kashayam with Honey, Cloves, Cinnamon, Turmeric and Pepper in Milk
Wheeze, Chest congestion	<ul style="list-style-type: none"> • Steam inhalation with Tulsi or Eucalyptus oil
Headache	<ul style="list-style-type: none"> • Aromatherapy with Tulsi or Lavender oil
Malaise and Fatigue	<ul style="list-style-type: none"> • Lemon water with Honey
Stress, Anxiety, Depression	<ul style="list-style-type: none"> • Aromatherapy with Tulsi, Lavender or Lemon grass oil (steam inhalation)

D. Management: Drugs and Vaccines

Table 11. List of investigational drugs for treatment of COVID-19

Drug	Category	Marketed under brand name	Same drug for non-coronavirus candidate
Baricitinib	Anti-inflammatory	Olumiant	Rheumatoid Arthritis
Bemcentinib	Anti-viral	BerGenBio	Cancer, Ebola, Zika virus
Chloroquine	Anti-malarial	Aralen Phosphate, Aralen Hydrochloride	Malaria, Amoebiasis
Colchicine	Anti-inflammatory	Colcrys, Mitigare, Gloperba	Gout

Dexamethasone	Corticosteroid	Baycordon, Decadron, Dexamethasone Intensol, Zonacort	Arthritis, Ulcerative colitis, Lupus, Psoriasis, Breathing disorder
EIDD 2801	Anti-viral	Merck, Ridgeback Biotherapeutics	Influenza, Chikungunya, Ebola, Equine encephalitis
Favipiravir	Anti-viral	Avigan	Influenza
Hydroxychloroquine Sulfate	Anti-malarial	Plaquenil, Plaquenil sulfate, Quineprox	Malaria, Arthritis
Ivermectin	Anti-viral Anti-parasite	Stromectol	Many parasite infection including head lice, scabies, river blindness, ascariasis, lymphatic filariasis
Lopinavir and Ritonavir	Anti-viral	Kaletra	HIV
Methylprednisolone	Glucocorticoid	Medrol, Medrol Dosepak	Arthritis, Psoriasis, Lupus, Allergic disorder, Endocrine disorder, condition affecting eyes, skin, lung, stomach, nervous system or blood cells
Remdesivir	Anti-viral	Veklury	Ebola, Marburg virus, Filovirus, Pneumovirus
Sarilumab	Anti-inflammatory	Kevzara	Rheumatoid Arthritis
Tocilizumab	Anti-inflammatory	Actemra	Rheumatoid Arthritis, Polyarticular Juvenile Idiopathic Arthritis, Giantcell Arthritis, Inflammation of lining of arteries
Umefenovir	Anti-viral	Arbidol	Influenza, Chikungunya, Ebola, Zika virus, Hepatitis B and C, Herpes simplex, Foot and mouth disorder

Table 12. List of candidate vaccine in clinical evaluation

Platform	Type of candidate vaccine	Developer	Corona virus target	Current stage of clinical evaluation/regulatory status corona virus candidate	Same platform for non-corona virus candidate
Inactivated	Inactivated + alum	Sinovac	SARS-CoV2	Phase 3 NCT04456595 Phase 1/2 NCT04383574 NCT04352608	SARS
Non-Replicating Viral Vector	ChAdOx1-S	University of Oxford/AstraZeneca	SARS-CoV2	Phase 3 ISRCTN89951424 Phase 2b/3 2020-001228-32 Phase 1/2 PACTR202006922165132 2020-001072-15	MERS, influenza, TB, Chikungunya, Zika, MenB, plague
RNA	LNP-encapsulated mRNA	Moderna/NIAID	SARS-CoV2	Phase 2 NCT04405076 Phase 1 NCT04283461	Multiple candidates
DNA	DNA plasmid vaccine	Cadila Healthcare Limited	SARS-CoV2	Phase 1/2 CTRI/2020/07/026352 (not yet recruiting)	
Inactivated	Whole-Virion Inactivated	Bharat Biotech	SARS-CoV2	Phase 1/2 CTRI/2020/07/026300	
Protein Subunit	Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M	Novavax	SARS-CoV2	Phase 1/2 NCT04368988	RSV; CCHF, HPV, VZV, EBOV
RNA	3 LNP-mRNAs	BioNTech/Fosun	SARS-	Phase 1/2	

		Pharma/ Pfizer	CoV2	2020-001038-36 NCT04368728	
DNA	DNA Vaccine (GX-19)	Genexine Consortium	SARS-CoV2	Phase 1 NCT04445389	
Non-Replicating Viral Vector	Adeno-based	Gamaleya Research Institute	SARS-CoV2	Phase 1 NCT04436471 NCT04437875	
Protein subunit	Native like Trimeric subunit Spike Protein vaccine	Clover Biopharmaceutical Inc/GSK/Dynavax	SARS-CoV2	Phase 1 NCT04405908	HIV, REV Influenza
VLP	Plant-derived VLP adjuvanted with GSK or Dynavax adjs.	Medicago Inc	SARS-CoV2	Phase 1 NCT04450004	Flu, Rotavirus, Norovirus, West Nile virus, Cancer

Table 13. List of candidate vaccine in pre-clinical evaluation

Platform	Type of candidate vaccine	Developer	Corona virus target	Current stage of clinical evaluation/regulatory status corona virus candidate	Same platform for non corona virus candidate
DNA	DNA plasmid vaccine S,S1,S2,RBD &N	National Research Centre, Egypt	SARS-CoV2	Pre-Clinical	
DNA	Plasmid DNA, Needle-Free Delivery	Immunomic Therapeutics Inc/ EpiVax Inc/ PharmaJet	SARS-CoV2	Pre-Clinical	SARS
DNA	DNA with electroporation	Chula Vaccine Research Center	SARS-CoV2	Pre-Clinical	
Inactivated	Inactivated + alum	K.M Biologics	SARS-CoV2	Pre-Clinical	JE, Zika
Inactivated	Inactivated whole virus	National Research Centre, Egypt	SARS-CoV2	Pre-Clinical	
Inactivated	Inactivated + CpG 1018	Sinovac/Dynavax	SARS-CoV2	Pre-Clinical	
Live attenuated virus	Codon deoptimized live attenuated vaccines	Codagenix/ Serum Institute of India	SARS-CoV2	Pre-Clinical	HAV, InfA, ZIKV, FMD, SIV, RSV, DENV
Live attenuated virus	Codon deoptimized live attenuated vaccines	Indian Immunologicals Ltd/ Griffith University	SARS-CoV2	Pre-Clinical	
Non-Replicating Viral Vector	Sendai virus vector	ID Pharma	SARS-CoV2	Pre-Clinical	
Non-Replicating Viral Vector	[E1-, E2b-, E3-] hAd5- COVID19-Spike/Nucleocapsid	Immunity Bio Inc/ Nantkwest Inc	SARS-CoV2	Pre-Clinical	LASV, EBOV, MARV, HIV
Non-Replicating Viral Vector	Oral Ad5 S	Stabilitech Biopharma Ltd	SARS-CoV2	Pre-Clinical	Zika, VZV, HSV-2 and Norovirus
Non-Replicating Viral Vector	Recombinant deactivated rabies virus containing S1	Bharat Biotech/ Thomas Jefferson University	SARS-CoV2	Pre-Clinical	HeV, NiV, EBOV, LASSA, CCHFV, MERS
Protein Subunit	Adjuvanted protein subunit (RBD)	Biological E Limited	SARS-CoV2	Pre-Clinical	
Protein Subunit	Peptide	Flowpharma	SARS-CoV2	Pre-Clinical	Ebola, Marburg, HIV, Zika, Influenza, HPV therapeutic vaccine,

					BreastCA Vaccine
Protein Subunit	Adjuvanted microsphere peptide	VIDO Intervac/ University of Saskatchewan	SARS-CoV2	Pre-Clinical	
Protein Subunit	Orally delivered, heat stable subunit	Applied Institute of Biotechnology Inc	SARS-CoV2	Pre-Clinical	
Replicating Viral Vector	Measels vector	Cadila Healthcare Ltd	SARS-CoV2	Pre-Clinical	
Replicating Viral Vector	Live viral vectored vaccine based on attenuated influenza virus backbone (intranasal)	BiOCAD and IEM	SARS-CoV2	Pre-Clinical	Influenza
Replicating Viral Vector	Recombinant vaccine based on Influenza A virus, for the prevention of COVID-19 (intranasal)	FBRI SRC VB Vector, Rospotrebnadzor Koltsovo	SARS-CoV2	Pre-Clinical	Influenza
Replicating Viral Vector	M2-deficient single replication (M2SR) influenza vector	Bharat Biotech	SARS-CoV2	Pre-Clinical	Influenza
RNA	Liposome-encapsulated mRNA	BiOCAD	SARS-CoV2	Pre-Clinical	
RNA	mRNA in an intranasal delivery system	eTheRNA	SARS-CoV2	Pre-Clinical	
VLP	Enveloped Virus-Like Particle (eVLP)	VBI Vaccine Inc	SARS-CoV2	Pre-Clinical	CMV, GBM, Zika
VLP	Virus-like particle, based on RBD displayed on virus-like particles	Saiba GmbH	SARS-CoV2	Pre-Clinical	



COVAXIN, India's indigenous COVID-19 vaccine by Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). The vaccine received DCGI approval for Phase I & II Human Clinical Trials. At present, phase 1 human trials of the vaccines are being conducted across the country. <https://www.bharatbiotech.com/covaxin.html>

Figure 7. Covaxin

Sputnik-V (29-38)

After many years of coronavirus outbreak all over the world, world's first coronavirus vaccine has been reported successfully. Moscow State Medical University has completed the clinical study first coronavirus vaccine on volunteers. **Gam-COVID-Vac** trade name

Sputnik-V is a COVID-19 vaccine candidate. It was developed by Gamaleya Research Institute of Epidemiology and Microbiology in Russia and registered on 11th August 2020 by Russian Ministry of Health. Route of Administration is Intramuscular.

Gam-COVID-Vac is a viral two vector vaccine which is based on Human Adenovirus that is a common cold virus fused with spike protein of SARS-CoV-2 to stimulate an immune response. The recombinant Adenovirus type-5 (Ad5) and Adenovirus type-26 (Ad26) both are used as vectors in vaccine. Ad26 vaccine is used on the first day while Ad5 vaccine is used on 21st day to boost response.

Clinical Trial reveals that 100% volunteers developed immunity within 21 days.



Figure 8. Russian Ministry of Health image of Gam-COVID-Vac vials

After second vaccination, immunity response further was boosted and provides long lasting immunity. All volunteers are feeling well with no observed unwanted side effects. No one of the participant of the clinical trial had caught COVID-19 after administration of vaccine.

Plasma therapy: Convalescent Plasma constitutes the first option in the current scenario, since it has been successfully used in other coronavirus outbreak. Convalescent Plasma Therapy uses Blood from the people who have recovered from illness to help others recover.

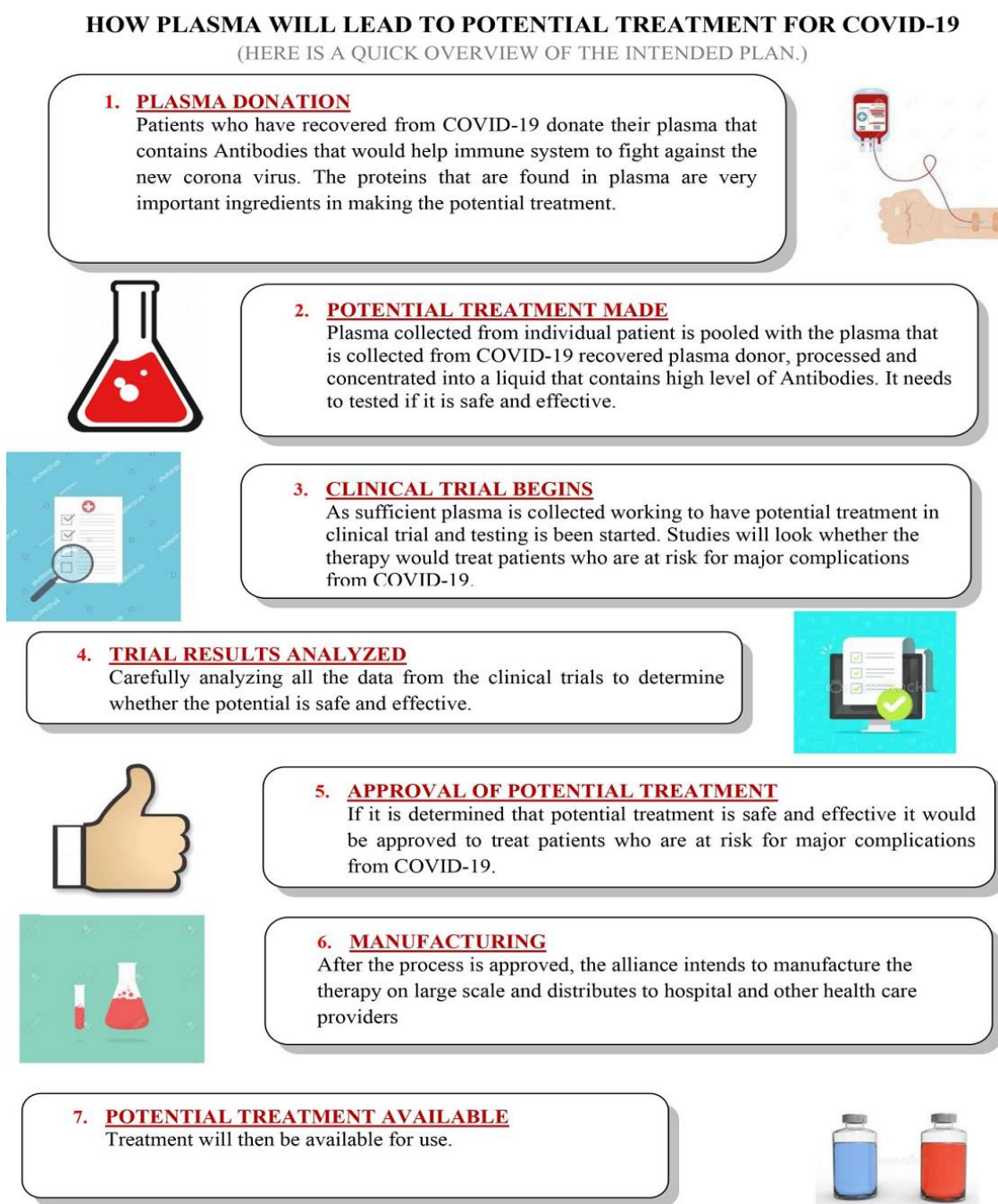


Figure 9. The above flowchart aims to provide plasma donors with general overview of the process so that they can well understand their role in donating their plasma.

Blood which is donated by an individual who have recovered from COVID-19 has Antibodies to virus that causes it. The donated blood is then processed to remove the blood cells, which will then leave the liquid (plasma) and the Antibodies behind. These can be given to the

people suffering from COVID-19 to boost their ability to fight the virus. Convalescent Plasma Therapy may help the people recover from COVID-19. It may lessen the severity or shorten the length of the disease

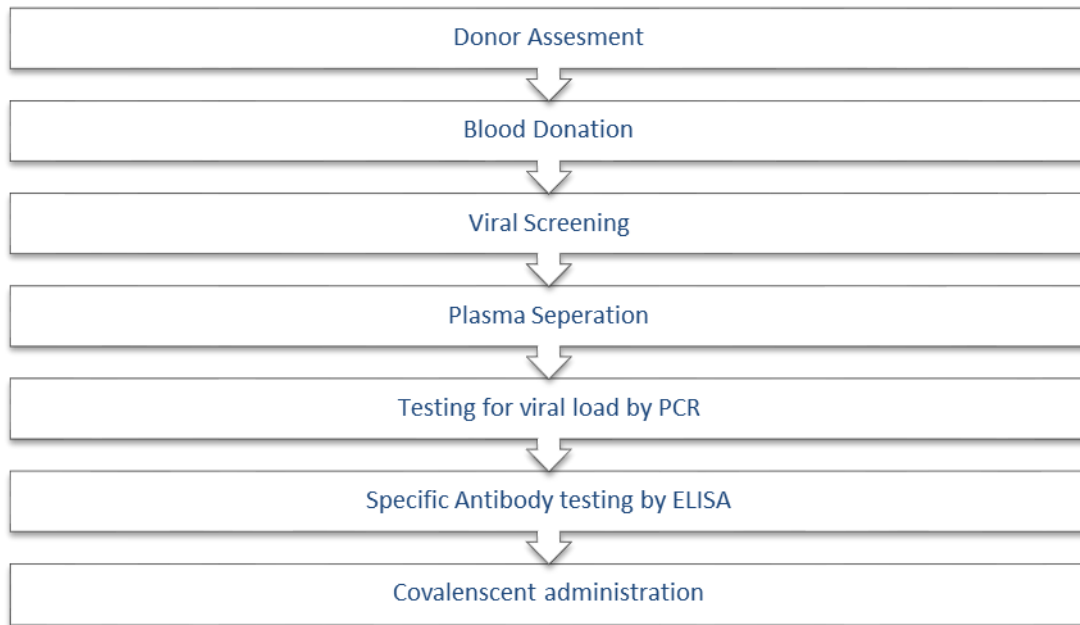


Figure 10. Flowchart of Convalescent Plasma Preparation in COVID-19 patients.

Advisory to start rapid antibody based blood test for COVID-19

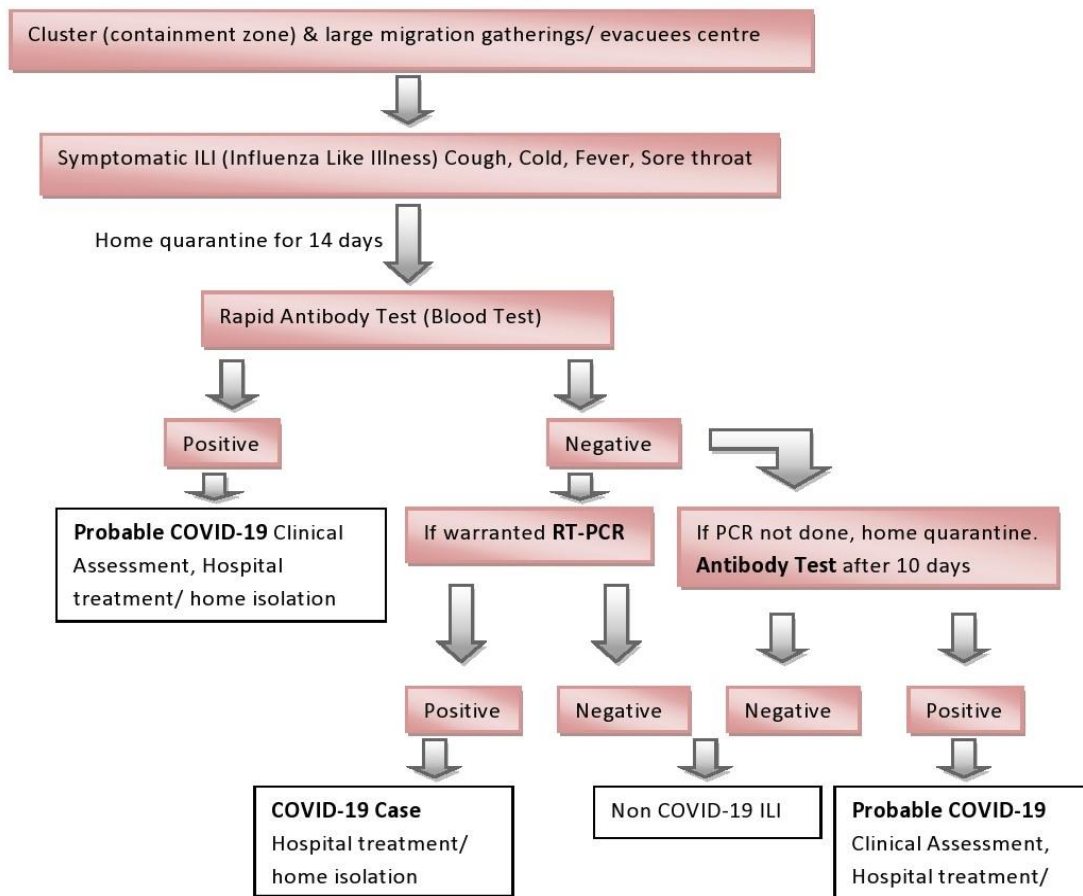


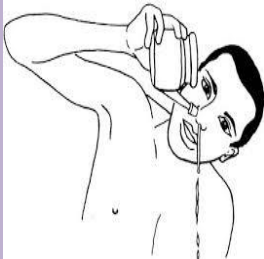
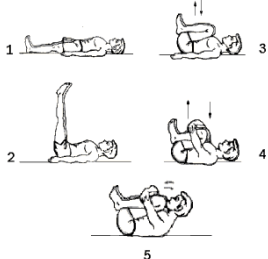
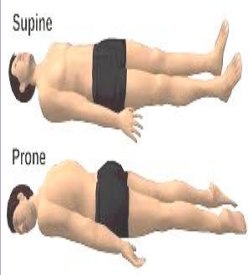
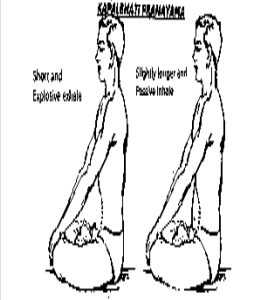
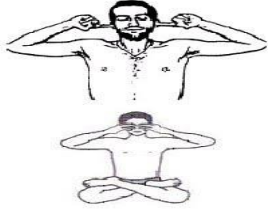
Figure 11. Advisory to start Rapid Antibody Blood Test for COVID-19 patients

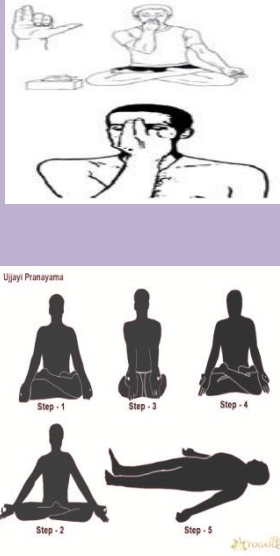


E. Management: Yoga (39-43)

Yoga is an ancient mind-body practice that has health benefits on many clinical as well as non-clinical conditions. Yoga can improve the symptoms of Anxiety, Stress, Depression, Post-traumatic stress disorder and many other psychological problems as well as promote well-being of the person. Toga will help to build up the

Table 14. Yoga practices for prevention, rehabilitation and increase immunity.

psycho-physiological health, emotional harmony and manage stress. Yoga may play significant role in psycho-social care and rehabilitation of COVID-19 patients during isolation and quarantine. They are particularly useful in reducing their anxiety and fear.

Yoga Practices	Steps	Do's	Don'ts	Benefits
ShodhanaKriya (Yogic cleansing practices) Jalaneti, Sutraneli		Use lukewarm water for cleansing. Jalaneti must be followed by Kapalbhata to remove all the water from nasal passage.	Should be avoided in case of epistaxis, middle ear infection and recent ENT surgery.	Neti helps in cleansing sinuses, beneficial in allergic conditions and reduces upper airway reactivity.
Yogic SuksmaVyayamas/ Pawanamuktasana series: Neck movement, Shoulder movement, Trunk movement, Knee movement		Do it slowly with breath awareness.	Do not over strain. Avoid this in case of severe joint pain and illness.	Joint movement help increase blood circulation and reduce stiffness which enhance joint flexibility.
Yogasana: Standing, Sitting, Prone and Supine lying		Do it with breath awareness. Cardiac patients shall do with care as advised by Yoga experts. Asanas that involve chest expansion preferred.	Avoid this practice in case of cardiac disorders, abdominal hernia, inflammation, ulcers, recent abdominal surgery.	Improves chest expansion and cardiopulmonary functions
Kapalbhati		40-60 strokes per minute	Hypertensive, cardiac problems, patients with respiratory distress, slipped disc should avoid it. Better to practice early in morning on an empty stomach	Improves pulmonary functions and reduces secretions. Helps to cleanse frontal sinuses.
Breathing and Pranayama: Sectional breathing Nadishodhana Ujjayi Bhramari		Breath should be slow, steady and controlled. It should not be forced or restricted in anyway. Initially start the practice with few repetitions and	In case of any cardiac disorders start with few repetitions and gradually increase the number of repetitions. Don't practice retention or hold at initial	Nadishodhan pranayama reduces the sympathetic activity and stimulate vagal (parasympathetic) activity and decreases stress and anxiety

		<p>gradually increase the number of repetitions. If possible, maintain the ratio of 1:2 for inhalation and exhalation.</p>	<p>stage.</p>	<p>Ujjayi increases the oxygen saturation in body. Bhramari pranayama similar to humming may increase Nasal Nitric Oxide (NO), which may improve blood flow to the ciliary epithelium and has anti-inflammatory action.</p>
<p>Yoga Nidra (Pratyahar)</p>		<p>Follow mentally with awareness as per the instructions given during practices. Keep the eyes closed during practices and avoid body movements.</p>	<p>Don't open the eye until asked. Don't sleep. Gradually increase the duration of the practice.</p>	<p>Reduction in sympathetic arousal and reduced emotional distress and improves quality of sleep. Rejuvenate the body and helps to keep the mind calm.</p>
<p>Meditative practices Breath awareness, Dharana and Dhyana</p>		<p>For beginners, soothing music may be played in the background during meditation or to observe the breath. Practice it as long as one can</p>	<p>Don't open the eye. Don't shake the body. Don't be judgemental with thoughts.</p>	<p>Meditation helps to reduce anxiety and stress by reducing the cortisol level and enhance the alpha brain wave. Makes body stable and calm the mind. Balances the functions of neuroendocrine system thereby enhances the immune system.</p>

8. Medical devices (44)

The below table lists the COVID-19 essential Medical Devices.

Table 15. List of Medical Devices

Device	Types	Definition
<p>Gloves</p>	<p>Patient examination gloves Latex patient examination gloves Polymer patient examination gloves Vinyl Patient examination gloves Surgeon gloves Powder free Non-Natural Rubber Latex Surgeon gloves</p>	<p>They are single-use sterile devices used to cover healthcare professionals' hands during surgery or other procedures (eg. examination). They could be made up of latex or synthetic materials such as polychloroprene, nitrile, polyisoprene or another synthetic latex free material not otherwise classified in this nomenclature.</p>

Gowns and other dressing elements for non surgical use (e.g. cover boots and shoes, caps and coglets)	Non Surgical Gowns	These include devices that can be both sterile and non-sterile which are used in the course of non-surgical procedures by medical and paramedical staff in order to ensure protection for the patient and the operator. They can be composed of both synthetic and natural material and are available in various shapes and sizes. The devices described can be disposable or reusable.
Mask	Surgical mask N95 Respirator mask Cloth mask	Multiple definitions applied
Ventilator for critical care	Invasive and Non-invasive	Multiple definitions applied depending on device function/modes and if invasive/non-invasive.
Non-invasive ventilators for ventilator dependent patients	Continuous Positive Airway Pressure Bilevel Positive Airway Pressure Autotitrating Positive Airway Pressure	Multiple definitions applied depending on device function/modes
Ventilator for transport and emergency	-	Pulmonary ventilators specifically built for ventilation of the patient during transport or during out-of-hospital emergency.
Anaesthetic ventilator	-	Devices which allow to anaesthetise and ventilate the patient with suitable gas mixtures.
Oxygen delivery devices	Oxygen masks, venturi masks, oxygen tents, oxygen head boxes, bag valve masks	Multiple definitions applied
Blood Pressure monitoring kits	-	Multiple definitions applied
Pulse Oximeter	Masimo Nellor Nihon Kohden Philips	Device generally used in operating rooms and in intensive care units, they allow non-invasive measurement of oxygen saturation in the blood (spo2), exploiting the partial transparency of the tissues. A photodetector converts a light signal (led) into an electrical signal proportional to the absorption. They could be produced in a handy compact version which is battery operated rendering it suitable for emergency use. When equipped with appropriate sensors, (for the finger, the forehead etc.) they can also be intended for paediatric use.
COVID-19 Test Kit PCR	-	Diagnostic kits for the in vitro detection of the presence of the Coronavirus genome in samples coming from from the human body. The presence of the genome is used in the diagnosis of respiratory infections.
COVID-19 Test Kit Antigen, including rapid tests	-	Diagnostic kits for the in vitro serological diagnosis of Coronaviruses in samples from the human body. There Serological diagnosis (antigen research and antibody titration) is used in the diagnosis of respiratory infection.
COVID-19 Test Kit Antibody, including rapid tests	-	Diagnostic kits for the in vitro one-step qualitative determination of antibodies against other viruses in samples coming from the human body. They are rapid tests for the detection of other viruses that do not find a place in specific terminal branches of the nomenclature.

9. Conclusion-

SARS-CoV-2 has been revealed as pandemic that causes COVID-19. Infected individuals have been reported with cytokine storm syndrome and most common flu-like symptoms in severe cases. Diagnosis of COVID-19 depends upon the detection of Nucleic Acid

tests by RT-PCR. Currently the treatment depends on the symptomatic relief. Several drugs like Remdesivir, Favipiravir and Chloroquine have shown to be effective. Personal Protective measures are to be accompanied in order to prevent COVID-19 infection. Clinical trials of COVID-19 vaccine are ongoing.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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