

# **HOMOEOPATHIC PERSPECTIVES IN COVID-19 CORONAVIRUS Infection**

## **FACT SHEET**



### **CENTRAL COUNCIL FOR RESEARCH IN HOMOEOPATHY**

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## **1. Introduction**

The global public health emergency of COVID-19 pandemic disease caused by severe acute respiratory syndrome coronavirus 2 (will be referred as SARS-CoV-2 hereafter) has been unfolding rapidly that emerged in Wuhan, China and has now spread to at least 180 countries. Detailed investigations found that SARS-CoV in 2003 was transmitted from civet cats to humans and MERS-CoV in 2012 from dromedary camels to humans.<sup>1</sup> The genetic sequence of the SARS-CoV-2 enabled the rapid development of point-of-care real-time RT-PCR diagnostic tests specific for SARS-CoV-2 which is based on full genome sequence data on the Global Initiative on Sharing All Influenza Data [GISAID] platform.<sup>2</sup> Though in a scorching pace, the scientist of China shared its genome sequence, it is the Australian scientists who have for the first time recreated the virus.<sup>3</sup> It is suggested that even though patients of all ages are susceptible to this disease, individuals developing critical illness were older with greater number of co morbid conditions.<sup>4</sup>

### **1.1 Historical Background**

On 31 December 2019, World Health Organization (will be referred as WHO hereafter) was alerted about an outbreak of several cases of pneumonia in Wuhan City, Central Hubei Province of China raising concern since the affected patients were geographically linked with a local wet market as a potential source with 12% risk of death.<sup>5</sup> On 7 January 2020, Chinese authorities confirmed identification of a novel coronavirus, named “2019-n CoV” from the family of viruses that include SARS-CoV and MERS-CoV.<sup>6</sup> China reported its first death of a 61 year old patient from SARS-CoV-2 on 11 January 2020. Further, on 20 January 2020, WHO situation report detailed the first confirmed cases outside China in Thailand, Japan and South Korea. However, on 31 January 2020, WHO declared the outbreak a global public health emergency as more than 9,000 cases were reported from all over the world. The Diamond Princess Cruise ship on 1 February 2020 with 3,711 people on board was found to have the epidemic of SARS-CoV-2.<sup>7</sup> On 9 February 2020, the death toll in mainland China surpassed number of fatalities from SARS outbreak in 2003.<sup>8</sup> Italy on 24 February 2020 became the worst-hit country in Europe by this virus.<sup>9</sup> On 28 February 2020, Iran reported 34 deaths out of 388 confirmed coronavirus cases, making it the country with the highest number of deaths from the virus outside China. President Trump of USA signed an \$8.3 billion emergency spending package on 6 March 2020 to combat the coronavirus outbreak, as the number of global cases hit 1,00,000.<sup>10</sup> Henceforth, on 11 March 2020 WHO made the assessment of Coronavirus as pandemic. Spain recorded a spike of nearly 2,000 new cases on 14 March 2020.<sup>11</sup> Italy on 16 March 2020 announced that confirmed cases rose to nearly 28,000, an increase of more than 3,000 from the day before, while the death toll hit 2,158.<sup>12</sup>

### **1.2.Epidemiology**

So far, as on date 23 March 2020, 3,39,039 globally confirmed cases<sup>13</sup> are reported and 81,093 confirmed cases from China but 3,270 deaths making China “Very High” under WHO risk assessment.<sup>14</sup> Between lockdowns and quarantines, the COVID-19 epidemic in China peaked and plateaued by early February, to even decline from there. Person-to-person transmission of SARS-CoV-2 in hospital and family settings may be suggested, as reports of infected travellers in other geographical regions surfaced.<sup>15</sup> In India, 415 cases are reported till 23 March 2020, according to Ministry of Health & Family Welfare. Therefore, the Government of India has asked travellers from China to immediately report to nearest health facility in case they do not feel well.<sup>16</sup>

### **1.3.Causative Agent**

SARS-CoV-2 is a type of RNA virus which is zoonotic in origin and it is estimated that Coronavirus infections are likely to emerge periodically in humans due to frequent cross-species infections and occasional spillover events.<sup>17</sup> Coronaviruses are a large family of viruses that cause the common cold as well as more serious respiratory illness. There are six known human coronaviruses which were first identified in the 1960s from patients with the common cold.<sup>18</sup> The transmission of coronavirus is reported through respiratory droplets, human contact and fecal-oral route.<sup>19 20 21</sup>

#### **1.4. Incubation period**

Median incubation period is 5.8 days<sup>22</sup> with range reported from 2.1 days to 11.1 days. This implies that under conservative assumption, length of quarantine or active monitoring can be up to 14 days.<sup>23</sup>

### **2. Pathogenesis**

The pathological features of SARS-CoV-2 of family Coronaviridae measuring from 60 to 140 billionths of a metre across, having median  $R_0$  2.79<sup>24</sup> with early outbreak data following exponential growth<sup>25</sup> have been shown to greatly resemble those seen in SARS and MERS coronavirus infection.<sup>26 27</sup> First described in 1960s, the coronavirus gets its name from a distinctive corona or “crown” of sugary-proteins projecting from envelope surrounding the particle. Following the entry of coronavirus into the cell, the uncoated particle and the RNA genome is deposited into the cytoplasm. The coronavirus RNA genome has a 5' methylated cap and a 3' polyadenylated tail, which allows the RNA to attach to ribosomes for translation. Coronaviruses also have a protein known as a replicase encoded in its genome which allows the RNA viral genome to be transcribed into new RNA copies using the host cell's machinery.<sup>28</sup> Coronaviruses have a non-structural protein – a protease – which can separate the proteins in the chain.<sup>29 30</sup> The excess production of type 2 cytokines and an age dependant defect in T-cell and B-cell function could lead to a deficit in control of viral replication and more prolonged proinflammatory responses, potentially leading to a poor outcome in patients of COVID-19.<sup>31</sup> The main pathogenesis of SARS-CoV-2 as a respiratory system targeting virus is severe pneumonia, RNAemia and acute cardiac injury. In a first-hand data reported from Hospital of China, it was found that, by Jan 2, 2020, 41 laboratory- confirmed SARS-CoV-2 infection admitted hospital patients had a higher plasma level of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNF $\alpha$ .<sup>32</sup>

#### **2.1. Histopathology**

From the histopathological data obtained on the lungs of two patients undergoing lung lobectomies for adenocarcinoma who were retrospectively found to have had SARS-CoV-2 infection at the time of surgery, the lungs of both 'accidental' cases showed oedema, exudates as large protein globules, vascular congestion combined with inflammatory clusters of fibrinoid material, multinucleated giant cells and hyperplasia of pneumocytes.<sup>33</sup>

#### **2.2. Case Definition**

| S.No. | Term         | Case definition <sup>34 35 36 37</sup>                                                                                                                                                                                                                                                                                  |
|-------|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 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), <b>AND</b> 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 |
|       |              | A patient/Health care worker with any acute respiratory illness <b>AND</b>                                                                                                                                                                                                                                              |

|    |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|----|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                    | having been in <i>contact</i> with a confirmed COVID-19 in the last 14 days prior to onset of symptoms                                                                                                                                                                                                                                                                                                                                                                                                                      |
|    |                    | A patient with severe acute respiratory infection {fever and at least one sign/symptom of respiratory disease (e.g. cough, shortness breath)} <b>AND</b> requiring hospitalization <b>AND</b> with no other etiology that fully explains the clinical presentation                                                                                                                                                                                                                                                          |
|    |                    | A case for whom testing for COVID-19 is inconclusive                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| 2. | Lab confirmed Case | A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 3. | Contact            | A contact is a person that is involved in any of the following: <ul style="list-style-type: none"> <li>• Providing direct care without proper personal protective equipment (PPE) for COVID-19 patient</li> <li>• Staying in the same close environment of a COVID-19 patient (including workplace, classroom, household, gatherings)</li> <li>• Travelling together in close proximity (within 1 m) with a symptomatic person who later tested positive for COVID-19</li> </ul>                                            |
| 4. | High risk contact  | Contact with a confirmed case of COVID-19<br>Travel to a province where COVID-19 LOCAL TRANSMISSION is being reported as per WHO daily situation report<br>Touched body fluids of patients (respiratory tract secretions, blood, vomitus, saliva, urine, faeces)<br>Touched or cleaned the linens, clothes or dishes of the patient<br>Close contact, within 3 feet (1 metre) of the confirmed case<br>Co-passengers in an airplane/vehicle seated in the same row, 3 rows in front and behind of a confirmed COVID-19 case |
| 5. | Low risk Contact   | Shared the same space (same classroom/same room for work) or similar activity and not having high risk exposure to the confirmed/suspected case<br>Travel in the same environment (bus/train/flight/any mode of transit) but not having high risk exposure as cited above<br>Any traveller from abroad not satisfying high risk criteria                                                                                                                                                                                    |

Severe Acute Respiratory Infection suspected of SARS-CoV-2 infection may be defined as-<sup>38</sup>

1. Patients with severe acute respiratory infection (fever, cough, and requiring admission to hospital), AND with no other aetiology that fully explains the clinical presentation AND at least one of the following:

- a history of travel to or residence in the city of Wuhan, Hubei Province, China in the 14 days prior to symptom onset, or
- Patient is a health care worker who has been working in an environment where severe acute respiratory infections of unknown aetiology are being cared for.

2. Patients with any acute respiratory illness AND at least one of the following:

- close contact\* with a confirmed or probable case of COVID-19 in the 14 days prior to illness onset, or
- visiting or working in a live animal market in Wuhan, Hubei Province, China in the 14 days prior to symptom onset, or

- Worked or attended a health care facility in the 14 days prior to onset of symptoms where patients with hospital associated COVID-19 infections has been reported.

\*Close contact is defined as:

- Health care associated exposure, including providing direct care for COVID-19 patients, working with health care workers infected with novel coronavirus, visiting patients or staying in the same close environment as a COVID-19 patient.
- Working together in proximity or sharing the same classroom environment with a COVID-19 patient.
- Travelling together with a COVID-19 patient in any kind of conveyance.
- Living in the same household as COVID-19 patient.

### **2.3. Clinical Syndromes associated with SARS-CoV-2 Infection**

| 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) : &lt;2 months, <math>\geq 60</math>; 2–11 months, <math>\geq 50</math>; 1–5 years, <math>\geq 40</math> and no signs of severe pneumonia.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Severe pneumonia                    | <p>Adolescent or adult: fever or suspected respiratory infection, plus one of respiratory rate <math>&gt;30</math> breaths/min, severe respiratory distress, or SpO<sub>2</sub> <math>&lt;90\%</math> on room air.</p> <p>Child with cough or difficulty in breathing, plus at least one of the following: central cyanosis or SpO<sub>2</sub> <math>&lt;90\%</math>; 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) : &lt;2 months, <math>\geq 60</math>; 2–11 months, <math>\geq 50</math>; 1–5 years, <math>\geq 40</math>.</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> <ul style="list-style-type: none"> <li>• Mild ARDS: <math>200 \text{ mmHg} &lt; \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}</math> (with PEEP or CPAP <math>\geq 5 \text{ cmH}_2\text{O}</math>, or non-ventilated)</li> <li>• Moderate ARDS: <math>100 \text{ mmHg} &lt; \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}</math> with PEEP <math>\geq 5 \text{ cmH}_2\text{O}</math>, or non-ventilated)</li> <li>• Severe ARDS: <math>\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mmHg}</math> with PEEP <math>\geq 5 \text{ cmH}_2\text{O}</math>, or non-ventilated)</li> </ul> |

|              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              | <ul style="list-style-type: none"> <li>When PaO<sub>2</sub> is not available, SpO<sub>2</sub>/FiO<sub>2</sub> ≤315 suggests ARDS (including in non-ventilated patients)</li> </ul> <p>Oxygenation (children; note OI = Oxygenation Index and OSI = Oxygenation Index using SpO<sub>2</sub>):</p> <ul style="list-style-type: none"> <li>Bilevel NIV or CPAP ≥5 cmH<sub>2</sub>O via full face mask: PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 300 mmHg or SpO<sub>2</sub>/FiO<sub>2</sub> ≤264</li> <li>Mild ARDS (invasively ventilated): 4 ≤ OI &lt; 8 or 5 ≤ OSI &lt; 7.5</li> <li>Moderate ARDS (invasively ventilated): 8 ≤ OI &lt; 16 or 7.5 ≤ OSI &lt; 12.3</li> <li>Severe ARDS (invasively ventilated): OI ≥ 16 or OSI ≥ 12.3</li> </ul> |
| Sepsis       | <p>Adults: life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction.</p> <p>Children: suspected or proven infection and ≥2 SIRS criteria, of which one must be abnormal temperature or white blood cell count.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Septic Shock | <p>Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate level &gt;2 mmol/L.</p> <p>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 (&gt;2 sec) or warm vasodilation with bounding pulses; tachypnea; mottled skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia.</p>                                                                                                                                                                               |

### 3. Clinical features

The first fatal case of SARS-CoV-2 infection had continuous exposure to Wuhan Market; China was admitted with a 7-day history of fever, cough and dyspnoea. After 5 days of onset of illness, the wife of the patient who had no known history of exposure to the market, also had pneumonia and hospitalized in the isolation ward. The SARS-CoV-2 infection has so far caused clusters of severe respiratory illness like severe acute respiratory syndrome coronavirus and was associated with ICU admission and high mortality in China. Patients with SARS-CoV-2 infection are exhibiting a wide range of symptoms. Most cases reported have mild disease, and nearly 20% appear to progress to severe disease, including pneumonia, respiratory failure and in some cases death.<sup>39</sup> Fever, cough, myalgia or fatigue is most common symptoms reported whereas less common symptoms include sputum production, headache, haemoptysis and diarrhoea.<sup>40</sup> The Chinese CDC report<sup>41</sup> divided the clinical manifestations of the disease with a spectrum of illness severity by following:

| S.No. | Disease severity | Symptoms                                                                                                                                                                                        | Occurred in % cases |
|-------|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| 1.    | Mild Disease     | Non-pneumonia and mild pneumonia                                                                                                                                                                | 81%                 |
| 2.    | Severe disease   | Dyspnea, respiratory frequency ≥ 30/min, blood oxygen saturation (SpO <sub>2</sub> ) ≤ 93%, PaO <sub>2</sub> /FiO <sub>2</sub> ratio < 300, and/or lung infiltrates > 50% within 24 to 48 hours | 14%                 |
| 3.    | Critical Disease | Respiratory failure, septic shock, and/or multiple organ dysfunction (MOD) or failure (MOF)                                                                                                     | 5%                  |

### 3.1. Chronological Development of symptoms of COVID-19

| Symptoms <sup>42 43 44 45 46 47</sup>   | Min % to max % | Duration in survivors <sup>48</sup> | Duration in non survivors <sup>49</sup>  |
|-----------------------------------------|----------------|-------------------------------------|------------------------------------------|
| Fever                                   | 43.8 to 98.6   | Day 0 to 12                         | Day 0 to 13                              |
| Cough                                   | 59.4 to 82     | Day 0 to 19                         | Day 0 to 16<br>Day 0 to 14 <sup>50</sup> |
| Shortness of breath                     | 18.7 to 55     | Day 7 to Day 19                     | Day 7 to 18 <sup>1/2</sup>               |
| Myalgia                                 | 11 to 44       |                                     |                                          |
| Fatigue                                 | 38.1 to 69.6   |                                     |                                          |
| Sputum production                       | 26.8 to 33.7   |                                     |                                          |
| Headache                                | 8 to 13.6      |                                     |                                          |
| Hemoptysis                              | 0.9 to 5       |                                     |                                          |
| Diarrhea                                | 2 to 10.1      |                                     |                                          |
| Respiratory rate >24 breaths per minute | 29             |                                     |                                          |
| Confusion                               | 9              |                                     |                                          |
| Sore throat                             | 5              |                                     |                                          |
| Rhinorrhea                              | 4              |                                     |                                          |
| Chest pain                              | 2              |                                     |                                          |
| Nausea and Vomiting                     | 1 to 10.1      |                                     |                                          |
| Conjunctival congestion                 | 0.8            |                                     |                                          |
| Nasal congestion                        | 4.8            |                                     |                                          |
| Chills                                  | 11.5           |                                     |                                          |
| Throat congestion                       | 1.7            |                                     |                                          |
| Tonsil swelling                         | 2.1            |                                     |                                          |
| Enlargement of lymph nodes              | 0.2            |                                     |                                          |
| Rash                                    | 0.2            |                                     |                                          |
| Pharyngalgia                            | 17.4           |                                     |                                          |
| Dizziness                               | 9.4            |                                     |                                          |
| Abdominal pain                          | 2.2            |                                     |                                          |
| Anorexia                                | 39.9           |                                     |                                          |

Symptomatic representation (graphical)

| Days ☞              | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
|---------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|
| Symptom ☞           |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |
| Fever               |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |
|                     |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |
| Cough               |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |
|                     |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |
| Shortness of breath |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |
|                     |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |

Survivors: 

Non Survivors: 

### 3.2. Clinical Outcomes of survivors and non survivors<sup>51 52</sup>

| S.No. | Clinical Outcome                    | Survivor (Days) | Non survivor (Days) |
|-------|-------------------------------------|-----------------|---------------------|
| 1.    | Sepsis                              | 9               | 10                  |
| 3.    | Acute Respiratory Distress Syndrome | 10              | 12                  |

|    |                      |  |    |
|----|----------------------|--|----|
| 4. | Acute Cardiac injury |  | 15 |
| 5. | Acute Kidney injury  |  | 15 |
| 6. | Secondary infection  |  | 17 |

### 3.3. Co-morbidities associated with SARS-CoV-2 Infection<sup>53</sup>

| S.No. | Survivor (with percentage) | Non-survivor (with percentage) |
|-------|----------------------------|--------------------------------|
| 1.    | Hypertension (23%)         | Hypertension (48%)             |
| 2.    | Diabetes (14%)             | Diabetes (31%)                 |
| 3.    |                            | Coronary Heart Disease (24%)   |

## 4. Investigations and Diagnosis

The CT scan of patients of COVID-19 shows ground-glass opacities in the lung and bilateral pulmonary infiltrates which is known to be compatible with changes in viral pneumonia. Predominance in lower lung is highly suspicious of COVID-19 in the first week of disease onset.<sup>54</sup> Duration of viral shedding ranged between 8 and 37 days with median duration found to be 20 days in survivors, but continued until death in terminal cases. The longest viral shedding in survivors was seen to be 37 days. Prolonged viral shedding provides the basis for a strategy of isolation of infected patients and optimal antiviral interventions in the future.<sup>55</sup> Elevated levels of blood IL-6, high sensitivity cardiac troponin I, lactate dehydrogenase and lymphopenia are seen in severe COVID-19.<sup>56</sup> Although, the US Food and Drug Administration (FDA) has issued an emergency use authorization for point-of-care detection of SARS-CoV-2 within approximately 45 minutes<sup>57</sup>, the following investigations based on changes seen in lab parameters can be done.

| S.No. | Lab Investigations                    |
|-------|---------------------------------------|
| 1.    | White Blood cells                     |
| 2.    | Neutrophil count                      |
| 3.    | Absolute neutrophil count             |
| 4.    | Lymphocyte count                      |
| 5.    | Absolute Lymphocyte count             |
| 6.    | Platelet count                        |
| 7.    | Activated partial thromboplastin time |
| 8.    | TNF-alpha                             |
| 9.    | Interferon-gamma                      |
| 10.   | IGM                                   |
| 11.   | IGG                                   |

| Who should be referred for testing of COVID-19             | Who should not be referred for testing of COVID-19               |
|------------------------------------------------------------|------------------------------------------------------------------|
| Suspect case                                               | Patient having mild fever with cough but no respiratory distress |
| High risk contact                                          |                                                                  |
| Patient reporting of fever, cough and respiratory distress |                                                                  |

## 5. WARNING SIGNS

### 5.1. WARNING SIGNS FOR DOCTORS

1. Pre-existing underlying serious illness such as cardiovascular disease

2. Greater severity of pneumonia at presentation marked by increased score of Pneumonia Severity Index and/or CURB score- 65
3. Radio opacity and/or pulmonary infiltrates in chest X-ray
4. Higher Sequential Organ Failure Assessment (SOFA) score on admission of patient

## **5.2. WARNING SIGNS FOR PATIENTS**

1. Pre-existing underlying serious illness such as cardiovascular disease
2. Older age group
3. Immunocompromised medical condition

## **6. MANAGEMENT**

### **6.1. MANAGEMENT- GENERAL**

WHO encourages all countries to continue with epidemic preparedness and charges china's success in stanching the crisis to its unprecedented lockdowns and cordon sanitaires.<sup>58</sup> Currently there is no specific antiviral treatment or any vaccine against COVID-19 infection. There is no current evidence from RCTs to recommend any specific anti-nCoV treatment for patients with suspected or confirmed nCoV. Preliminary trials of chloroquine in the treatment of COVID-19 have been encouraging, prompting to several new trials.<sup>59</sup> As the world struggles to respond to the COVID-19 pandemic, WHO's standard recommendations<sup>60</sup> for the general public to reduce exposure to and transmission of a range of illnesses are as follows, which include hand and respiratory hygiene, and safe food practices:

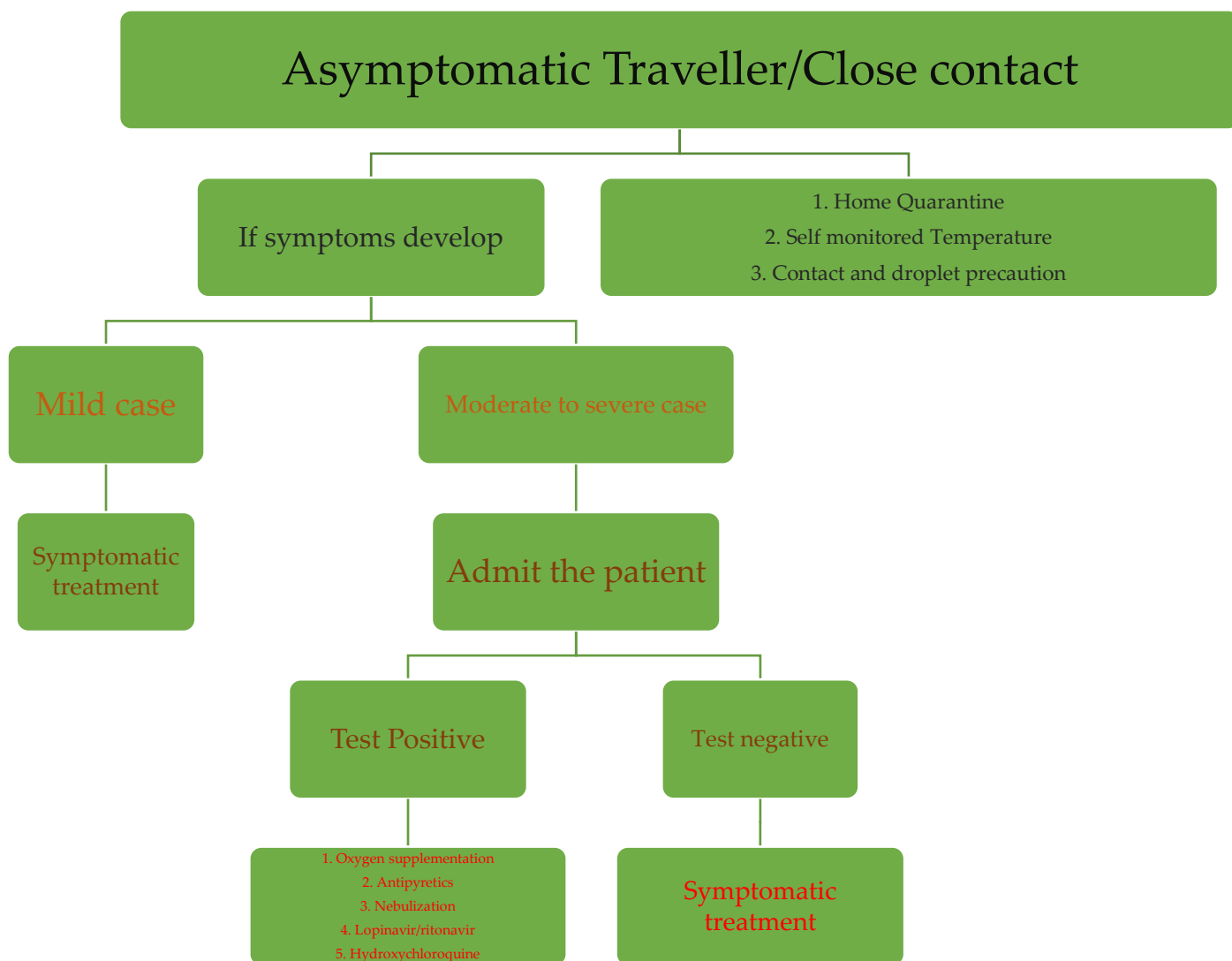
1. Frequently clean hands by using alcohol-based hand rub or soap and water.
2. When coughing and sneezing cover mouth and nose with flexed elbow or tissue – throw tissue away immediately and wash hands.
3. Avoid close contact with anyone who has fever and cough. Promote social distancing.
4. If you have fever, cough and difficulty breathing seek medical care early and share previous travel history with your health care provider.
5. When visiting live markets in areas currently experiencing cases of novel coronavirus, avoid direct unprotected contact with live animals and surfaces in contact with animals.
6. The consumption of raw or undercooked animal products should be avoided. Raw meat, milk or animal organs should be handled with care, to avoid cross-contamination with uncooked foods, as per good food safety practices.

India already suffers from poor medical infrastructure with only 2.3 critical beds per lakh population<sup>61</sup> and has reached stage 2 of coronavirus outbreak although no documentation of community transmission of the disease as on 23 March 2020.<sup>62</sup> Therefore, India cannot afford to lose its vigil. Identification at early stages and effective containment is required to slow down the spread of the disease which will allow confidence in public health response. Special attention is necessary to protect or reduce transmission in susceptible populations. The Government of India has also issued implementation guidelines for prevention and control measures of patients with suspected or confirmed COVID-19 patient.

| S.No. | Precaution | Steps                                                                                                                                                                                                                                                                                                          |
|-------|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1.    | At triage  | Give suspect patient a medical mask and direct patient to an isolation room if available. Keep at least 1meter distance between suspected patients and other patients. Instruct all patients to cover nose and mouth during coughing or sneezing with tissue or flexed elbow for others. Perform hand hygiene. |

|    |                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|----|-----------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2. | Apply Droplet precaution                                                    | Use a medical mask if working within 1-2 metres of the patient. Place patients in single rooms, or group together those with the same etiological diagnosis, similar clinical diagnosis and/or based on epidemiological risk factors, with a spatial separation. When providing care in close contact with a patient with respiratory symptoms, use eye protection (face-mask or goggles). Limit patient movement within the institution and ensure that patients wear medical masks when outside their rooms.                                                                                                                                                                                                                                         |
| 3. | Apply contact precaution                                                    | Use PPE (medical 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 to patient care (e.g. door handles and light switches). Ensure adequate room ventilation. Avoid movement of patients or transport. Perform hand hygiene.                                                |
| 4. | Apply Air-borne 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 or equivalent, or higher level of protection). Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures, meaning negative pressure rooms with minimum of 12 air changes per hour or at least 160 litres/second/patient in facilities with natural ventilation. Avoid the presence of unnecessary individuals in the room. Care for the patient in the same type of room after mechanical ventilation commences. |

Below is a flowchart for management of case of COVID-19 patient.



There are 52 testing sites and 57 laboratories for helping in sample collection for COVID-19.

| 52 testing sites for COVID -19 in India <sup>63</sup> |       |                                                                          |
|-------------------------------------------------------|-------|--------------------------------------------------------------------------|
| State/UT                                              | S.No. | LIST OF VRDLs                                                            |
| Andhra Pradesh                                        | 1.    | Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh |
|                                                       | 2.    | Andhra Medical College, Visakhapatnam, Andhra Pradesh                    |
|                                                       | 3.    | GMC, Anantapur, Andhra Pradesh                                           |
| Andaman & Nicobar islands                             | 4.    | Regional Medical Research Centre, Port Blair, Andaman and Nicobar        |
| Assam                                                 | 5.    | Gauhati Medical College, Guwahati, Assam                                 |
|                                                       | 6.    | Regional Medical Research Center, Dibrugarh, Assam                       |
| Bihar                                                 | 7.    | Rajendra Memorial Research Institute of Medical Sciences, Patna, Bihar   |
| Chandigarh                                            | 8.    | Post Graduate Institute of Medical Education & Research, Chandigarh      |
| Chhattisgarh                                          | 9.    | All India Institute Medical Sciences, Raipur, Chhattisgarh               |
| Delhi-NCT                                             | 10.   | All India Institute Medical Sciences, Delhi                              |

|                          |     |                                                                            |
|--------------------------|-----|----------------------------------------------------------------------------|
|                          | 11. | National Centre for Disease Control, Delhi                                 |
| <b>Gujarat</b>           | 12. | BJ Medical College, Ahmadabad, Gujrat                                      |
|                          | 13. | M. P. Shah Government Medical College, Jamnagar, Gujrat                    |
| <b>Haryana</b>           | 14. | Pt. B.D. Sharma Post Graduate Inst. of Med. Sciences, Rohtak, Haryana      |
|                          | 15. | BPS Govt Medical College, Sonapat, Haryana                                 |
| <b>Himachal Pradesh</b>  | 16. | Indira Gandhi Medical College, Shimla, Himachal Pradesh                    |
|                          | 17. | Dr. Rajendra Prasad Govt. Med. College, Kangra, Tanda, Himachal Pradesh    |
| <b>Jammu and Kashmir</b> | 18. | Sher-e- Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir |

| <b>DHR/ICMR 57 laboratories helping in Sample Collection for COVID -19 in India<sup>64</sup></b> |     |                                                                     |
|--------------------------------------------------------------------------------------------------|-----|---------------------------------------------------------------------|
| <b>State/UT</b>                                                                                  |     | <b>LIST OF VRDLs</b>                                                |
| <b>Andhra Pradesh</b>                                                                            | 1.  | Siddhartha Medical College, Vijayawada, Andhra Pradesh              |
|                                                                                                  | 2.  | Rajeev Gandhi Institute of Medical Sciences, Kadapa, Andhra Pradesh |
|                                                                                                  | 3.  | Rangaraya Medical College, Kakinada, Andhra Pradesh                 |
|                                                                                                  | 4.  | Guntur Medical College, Guntur, Andhra Pradesh                      |
| <b>Assam</b>                                                                                     | 5.  | Silchar Medical College, Silchar, Assam                             |
|                                                                                                  | 6.  | Jorhat Medical College, Jorhat, Assam                               |
|                                                                                                  | 7.  | Tezpur Medical College, Tezpur, Assam                               |
|                                                                                                  | 8.  | Fakhruddin Medical College, Barpeta, Assam                          |
| <b>Bihar</b>                                                                                     | 9.  | Patna Medical College, Patna, Bihar                                 |
|                                                                                                  | 10. | Darbhanga Medical College, Darbhanga, Bihar                         |
|                                                                                                  | 11. | S K Medical College, Muzaffarpur, Bihar                             |
| <b>Chandigarh</b>                                                                                | 12. | Government Medical College & Hospital, Chandigarh                   |
| <b>Chhattisgarh</b>                                                                              | 13. | Late SBK Memorial Govt. Medical College, Jagdalpur, Chhattisgarh    |
| <b>Delhi-NCT</b>                                                                                 | 14. | Lady Hardinge Medical College, New Delhi                            |
| <b>Gujrat</b>                                                                                    | 15. | Government Medical College, Surat, Gujrat                           |
|                                                                                                  | 16. | GMC, Bhavnagar, Gujrat                                              |
|                                                                                                  | 17. | PDU GMC, Rajkot, Gujrat                                             |
|                                                                                                  | 18. | Government Medical College & SSG Hospital, Vadodara                 |
| <b>Jammu &amp; Kashmir</b>                                                                       | 19. | Government Medical College, Srinagar                                |
| <b>Jharkhand</b>                                                                                 | 20. | Rajendra Institute of Medical Sciences, Ranchi, Jharkhand           |
| <b>Karnataka</b>                                                                                 | 21. | Vijayanagar Institute of Medical Science, Bellary                   |
|                                                                                                  | 22. | Gulbarga Institute Of Medical Sciences, Gulbarga                    |

## 6.2. MANAGEMENT-HOMOEOPATHIC

During Ebola outbreak in 2014 expert group of WHO recommended that “it is ethical to offer unproven interventions with as yet unknown efficacy and adverse effects, as potential treatment or prevention” keeping in view no vaccine or anti-virals were available.<sup>65</sup>

The preventive aspect of Homoeopathy is well known, and historically, Homoeopathy has reportedly been used for prevention during the epidemics of Cholera, Spanish Influenza, Yellow fever, Scarlet fever, Diphtheria, Typhoid etc.<sup>66</sup> The genus epidemicus is the remedy found to be most effective for a particular epidemic once data have been gathered from several cases. This concept was first put forth by Samuel Hahnemann in the Organon of Medicine, Aphorism 241, as “...each single epidemic is of a peculiar, uniform character common to all the individuals attacked, and when this character is found in the totality of the symptoms common to all, it guides us to the discovery of homoeopathic (specific) remedy suitable

for all the cases....”<sup>67, 68</sup> There is anecdotal evidence that homeopathy was successful during the Spanish flu epidemic of 1918 to 1919, in which at least 20 million people died worldwide, more than 500,000 in the United States alone. According to the historian Julian Winston, the death rates for patients treated with homeopathy (genus epidemicus) were 1 to 2% compared with a 30 to 60% mortality for those treated by conventional physicians.<sup>69, 70</sup> As in all collective diseases, the image of the clinical picture emerges after observing a considerable number of patients; Hahnemann suggests observing several cases in order to paint “the full picture of the disease”, “totality of characteristic signs and symptoms” or “epidemic genius”, according to the homeopathic connotation of this term. The *Genus epidemicus* is identified through observation of several cases of an epidemic disease, and analysing the symptomatology of those cases for the most indicated medicine. This medicine is the preventive medicine for the ongoing epidemic of that disease.<sup>71</sup> It was reported that, during recent past GE had been used during various disease outbreak for preventing the spreading of diseases like Chikungunya, Dengue Fever, Japanese Encephalitis and Cholera with good results.<sup>72</sup> The detailed account of use of homoeopathy in control of epidemics is given in recent publication.<sup>73</sup>

In Indian scenario, CCRH had so far undertaken clinical trials in Dengue and Acute Encephalitis syndrome/JE with Homoeopathy as an add-on to usual care in tertiary care setups. In Dengue Hemorrhagic fever, add on Homoeopathy could bring early improvement in platelet count and decrease in hospital stay by 2 days.<sup>74</sup> Similarly, in Acute Encephalitis Syndrome/Japanese Encephalitis homeopathy as an adjuvant to the Institutional Management protocol could decrease death rate by 15% in comparison to those who received only Institutional Management protocol.<sup>75</sup> In both the studies, adverse effect was not observed. Keeping in view the clinical success in above mentioned severe viral diseases, Homoeopathy as an adjuvant to the usual care may be tried in COVID-19 patients.

With regard to the positive results from the prophylactic homoeopathic medicine during epidemic outbreaks of various diseases during recent past, the Scientific Advisory Board of our Council in meeting held on 28 January 2020 discussed to find out possible genus epidemicus for recent outbreak of corona virus in China. The sign and symptoms of the patients were referred from the recent publication from the clinical history of patients of Wuhan, China in Lancet titled, “*Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China*”.<sup>76</sup> Therefore, the Health advisory given by Ministry of AYUSH against corona virus infection included Homoeopathic medicine *Arsenicum album* – 30 as a possible preventive for flu like illness such as coronavirus infection.<sup>77</sup> Scientific Advisory Board considered that the same medicine has been advised for prevention of Influenza Like Illness<sup>78, 79, 80</sup>. Arsenic album as one of the constituents in a formulation has been shown to affect HT29 cells and human macrophages. Also, it showed ↓NF-κB hyperactivity (reduced expression of reporter gene GFP in transfect HT29 cells), ↓TNF-α release in macrophages.<sup>81</sup> More over Arsenic album is a common prescription in the cases of respiratory infections in day to day practice. People however should also follow general measures as per the Health Advisory above.

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