

## Approach to the COVID 19 illness

Since January of 2020, COVID 19 has caused a global pandemic with millions of infections and millions of deaths. To date there is no accepted regimen of therapy established as a “Gold Standard” although clinical trials are currently ongoing. For the individuals who develop severe illness and need support with mechanical ventilation the mortality with the current treatment strategy has a poor outcome. In individuals who have clinical signs and symptoms due to COVID 19 infection early administration of anti-inflammatories will lead to better clinical outcomes. It is reported that individuals who have recovered from COVID 19 illness very often have a prolonged recovery with considerable long term disability which needs adequate evaluation.

COVID 19 is a newly describes Beta corona virus that was first noted to cause severe illness in Wuhan the capital of the Hubei province in the Peoples Republic of China, that rapidly evolved into a significant pandemic with a large number of infected people. In previously described (corona virus) outbreaks of serious illness due to SARS and MERS effective antiviral therapy has not been established. This has prompted multiple efforts to understand the mechanisms of infection with corona viruses, elucidating the role of the spike protein of corona viruses in cellular entry and the role of various antibodies in blocking the pathogenesis of corona virus infections. There has also been an effort to develop potential therapies (including small molecules) based on the understanding of the structure and pathogenesis of corona virus infections.

## COVID 19 Myths and Realities

COVID 19 has understandably created enormous despair, the news is full of reports of suffering and deaths combined with a lack of options for medical care of the sick. The epidemic is nowhere near control and the future uncertain. In this atmosphere of generalized confusion, it is no surprise that many myths have emerged that compound our problems. So, what to Do ??????????

We at SHARE INDIA suggest this as a guide to rational response to the COVID crisis:

1. **DO NOT PANIC !** know how to recognize the possibility of COVID illness by the following symptoms:

### Common Symptoms of COVID 19:

- Fever (Oral temperature of at least 100.5° F or 38. 5° C)
- Agusia/Dysgusia (loss of sensation of taste or unusual or bad taste in mouth)
- Anosmia (loss of sense of smell)
- Nausea/vomiting or Diarrhea
- Malaise (Feeling weak and tired)
- Myalgia (Muscle pain)
- Headache

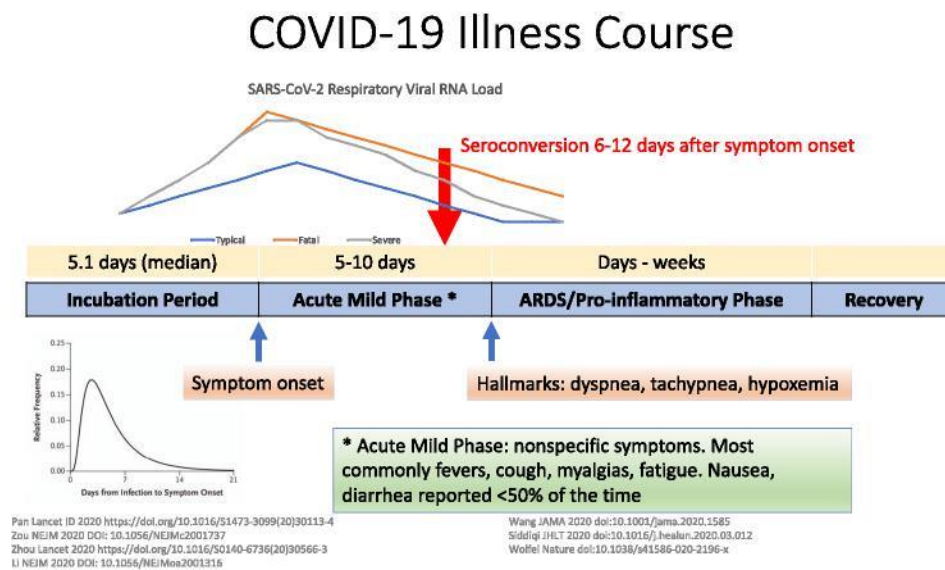
- Nasal congestion/coryza
- Cough
- Dyspnea (RR > 22) or blood oxygen saturation  $\leq 94\%$ , (Shortness of breath, breathing more than 20 times per minute)
- Tachycardia (HR > 80) Pulse rate

**Uncommon symptoms and signs also noted occasionally with COVID 19:**

- Skin rash of many different types
- Severe erythroderma (Diffuse redness of skin) suggestive of Kawasaki disease: Multisystem inflammatory syndrome of Children
- Discomfort in throat
- Neurologic illnesses including severe weakness of lower limbs (Guillain- Barre syndrome)
- Stroke
- Sudden inflammation of heart (Myocarditis)

**2. What to do ? what diagnostic tests are most useful?**

Diagnostic tests that look for evidence of the virus such as direct antigen test or the RTPCR tests are positive in the early stages of infection and may become negative in most instances after 14 days of symptom onset with a small number of individuals who remain RTPCR positive for months after complete clinical recovery. Antibody testing is primarily an epidemiologic tool and is not helpful in diagnosing acute infections. Considering the stage of the epidemic now, in the context of persistent symptoms a negative test should not deter further evaluation and possible treatment.



COVID-19 clinical course of illness. The first phase of COVID-19 infection involves an incubation period of variable duration, with a median of 5.1 days. The second is an acute mild phase that most commonly includes flu-like symptoms like cough, fevers, and myalgias, but can also

include gastrointestinal symptoms. Some patients progress to an ARDS hyperinflammatory phase that is often marked by dyspnea, tachypnea, and hypoxemia. The respiratory viral load rises before the onset of symptoms and peaks around the onset of symptoms. It declines over the first week. Severe cases have higher viral loads compared with mild cases. Prolonged viral shedding in severe and mild cases is reported.

**The tests most useful for guiding management are:**

- a) Pulse oximetry : Oxygen saturation of less than 94% is a sign of serious illness
- b) Complete Blood picture (Count)
- c) C reactive protein (CRP): A high value is consistent with inflammation
- d) D dimer: A high value indicates a risk for formation of blood clots that may lead to severe complications including death
- e) Ferritin: A remarkably high ferritin of over 800 suggests a risk of progression to severe illness

All other testing such as IL6; LDH; Liver enzymes; other blood tests; are not directly and specifically relevant to the routine management of COVID 19 and are indicated only when clinically required for the management of extremely ill individuals. CT scans are neither indicated nor essential for the diagnosis or management of COVID 19 except in cases of advanced lung disease not responding to treatment.

**3. Proven therapies for COVID 19:**

- a. Any individual with Oxygen levels falling (especially if less than 94%) would benefit from early treatment with Dexamethasone not exceeding 8 mg a day by mouth. Higher doses do not confer any advantage and increase complications such as increasing blood sugar levels; increasing blood pressure and reducing immunity to other infections such as tuberculosis and fungal infections known to complicate COVID 19 illness.
- b. Any individual with significant respiratory symptoms such as severe cough may benefit from inhaled budesonide
- c. Any individual with serious illness (such as low oxygen levels) or high D dimer should receive anticoagulation (blood thinner) such as Heparin, Enoxaparin, Apixaban or Rivaroxaban
- d. Individuals with Oxygen saturation below 90% will clearly need supplemental oxygenation and in most individuals high flow oxygen with a nasal cannula will suffice, in a few unfortunate individuals ventilators may be required (Noninvasive or conventional in a hospital)
- e. Duration of treatment is best guided by presence of clinical illness and persistence of markers of inflammation such as CRP and D dimer.

**4. Therapies proven not to be of any benefit in treatment or prevention:**

- a) Hydroxychloroquine
- b) Azithromycin
- c) Ivermectin
- d) Doxycycline
- e) Vitamin C
- f) Vitamin D
- g) Zinc
- h) Convalescent plasma

**5. Therapies with questionable benefit and possible complications:**

- a) Antivirals such as Remdesivir; Favipiravir
- b) Potent immunomodulators such as Tocilizumab
- c) Exceedingly high dose steroids
- d) Routine use of “prophylactic” antibiotics
- e) Any medication or special diet to boost the immune system

**6. Therapies of possible benefit in mild early illness**

- a) Low dose Colchicine (however can cause diarrhea in some individuals)
- b) Famotidine
- c) Statin class of medications such as “Atorvastatin”
- d) N acetylcysteine (reduces polymerization of von Willebrand factor and platelet thrombi)

**7. Medications that do not affect management of COVID 19**

- a) Antihypertensives
- b) Medications for management of Diabetes mellitus
- c) Medications for Asthma or another lung disease
- d) Any medications being used for treatment of underlying medical conditions should not be stopped without consulting the treating physician

**8. Best way to prevent COVID 19:**

- a) **Vaccines !** , all vaccines are equally beneficial, the best is, the first one available. All vaccines can cause minor side effects such as fever, malaise, headache, myalgias in some individuals and is easily managed with paracetamol. Although vaccines do not prevent all infections, they do substantially reduce the risk of illness and death. Vaccines have been shown to reduce the risk of transmission quite substantially.
- b) Clean air and Ventilation: Adequate ventilation is critical for ensuring clean uncontaminated air, since COVID 19 spreads easily through the air. Universal masking is known to substantially reduce the risk of spread of the virus in the air and acquiring

infection where the air is contaminated. Even plain cloth masks are quite effective but must be well fitting covering the entire nose and mouth. A poorly fitting mask (even N95) would not be effective. A cloth mask is easy to reuse after simple washing and is environmentally superior to nylon masks.

- c) Physical distancing of at least 2 meters. Avoid congregating in groups, being in a group of 10 individuals poses a 30% chance of getting infected! The risk rises to 90% in a group of 50 individuals!
- d) Clean hands: Many pathogens especially respiratory viruses such as Influenza, Parainfluenza and COVID 19 can be spread through handshakes, frequent cleansing with simple soap water and or alcohol based cleansers is effective. Gloves lose their effectiveness after 15-20 minutes and therefore have to be changed after each contact with infected persons and after 20 minutes of use even without any contact.
- e) Clean Environment: Cleaning with usual household cleansers (detergent and clean water) will suffice, using any kind of expensive cleansing solutions is not needed. Fogging is not required and potentially dangerous. Solutions such as sodium hypochlorite should be handled with great care and should certainly not be used as a spray in the house. Sources of ultraviolet radiation are potentially hazardous and should not be used. Sunshine inactivates the virus. The virus cannot be transmitted easily from environmental surfaces therefore using extreme measures to “Sanitize” the environment is not beneficial. Simple frequent cleansing (simple household detergent) of high touch surfaces such as door handles or some frequently used articles of furniture will suffice.
- f) Pets: There is the possibility that household pets can acquire COVID 19 from humans however transmission from household pets to humans has not been seen

## **9. How to interpret what I hear and see on various media:**

It is particularly important to depend on reliable evidence rather than opinions of so called self-styled “Experts” who are best characterized as “False Prophets”. It is important to understand that with COVID 19 the vast majority of infected people do not suffer any significant illness, it is only a small minority who develop significant illness and a small number of the symptomatic individuals have developed fatal illness. The reason anybody becomes ill is that COVID 19 triggers uncontrolled inflammation that persists even after the virus is no longer detectable. It is this inflammation that is responsible for damage to the body primarily the lungs and other vital organs. The only intervention that has been shown to reduce illness is anti-inflammatory medications. It is necessary to use only those treatment regimens that have proven to be beneficial in more than 95% of infected persons. Such kind of proof requires carefully designed scientific studies with several thousand subjects being evaluated by skilled experts. To date very few studies of such reliability have been completed and published. All of the large well designed studies that we can rely on, demonstrate proof of benefit only for Dexamethasone, Blood thinners and Oxygen. Unfortunately, many published studies that are being used to advocate all sorts of treatments are unreliable because of poor design and therefore scientifically unacceptable for broad application in the present epidemic.

## **10. A community based approach to Managing the COVID 19 crisis:**

### **IDENTIFY:**

Early Identification is key to optimum benefit from treatment. It is necessary to identify as quickly as possible those individuals who are candidates for treatment. Until rapid testing using point of care technology becomes available it may be necessary to institute treatment based on syndromic identification (presence of symptoms) of presumed COVID 19 illness and looking for markers of inflammation such as CRP, D dimer and Ferritin.

Individuals presumed to have COVID 19 illness may be additionally risk stratified for urgent treatment with dexamethasone and/or transport to inpatient treatment by screening for high risk attributes such as low oxygen saturation. Other indications for intense medical intervention are, advanced age and concurrent hypertension, diabetes, renal failure, lung disease, heart disease or other chronic illness.

### **TREAT:**

It is clear from current data that a large majority of the individuals with SARS-CoV2 infection are asymptomatic and at least some of the milder illness may be managed with appropriate home care, thus optimizing resource utilization.

Treatment that is appropriately designed is imperative to reduce complications and death and reduce the burden of over stretched hospitals. To the extent possible community treatment with dexamethasone and anticoagulants should be instituted as early as possible based on oximetry. This is a strategy that is simple enough for community level application.

There is an urgent need to implement a strategy of ensuring that all individuals who may have COVID 19 illness are provided appropriate early treatment and appropriate interventions such as anti-inflammatory treatment, prophylactic anticoagulation, adjunctive treatment approaches such as critical care support with high flow oxygen and/or support with ventilator/pressor etc.

### **TRACE:**

An intensive tracing strategy will assist in rapid identification of COVID illness at an early stage as well guide appropriate epidemic control interventions such as targeted testing with isolation of infected individuals to limit spread. In view of the rapidity of spread of SARS-CoV-2 in the vulnerable population innovations in tracing such as digital methods along with strong data analytics is desirable. Expeditious investigations of clusters along with contact tracing are invaluable.

## **Simplified Protocol for Community Based Strategy for COVID Infection:**

### **IDENTIFY:**

Current health condition:

1. Age and gender, blood group type if known.
2. Underlying conditions such as Hypertension; Diabetes; Heart problems; Lung problems such as asthma, bronchitis etc; Kidney problems; Liver Problems.
3. Ask about chronic conditions such as current treatment for HIV; Tuberculosis etc.
4. Ask about adherence to medical regimen, medications, diet exercise.
5. Ask about ease of access to health care provider (Doctor, Nurse, Pharmacist, Hospital)

### **Screen for symptoms of COVID:**

#### **Common Symptoms of COVID 19:**

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#### **Uncommon symptoms and signs also noted occasionally with COVID 19:**

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### **Evaluation:**

1. Blood pressure and heart rate and BMI
2. Pulse oximetry and respiratory rate (Number of breaths per minute)
3. Random blood sugar by glucometer finger prick
4. Blood tests:
  - a. Complete blood picture to look for Lymphopenia
  - b. CRP
  - c. Ferritin

- d. D dimer
- 5. If possible specific tests for COVID such as rapid antigen or RTPCR. Antibody tests are not indicated (Epidemiological tool)

**Intervention:**

1. Counseling about NPI (Masks, physical distancing, personal and environmental hygiene)
2. For all asymptomatic with high risk contact home isolation
3. For symptomatic without high risk such as serious underlying illness; high ferritin, low oxygen saturation < 94% with breathing more than 20 times per minute: Basic anti-inflammatory treatment with:
  - a. Colchicine 0.5 mg twice daily; Famotidine 40 mg twice daily; N acetylcysteine 600 mg twice daily.
  - b. For respiratory symptoms especially any cough Budesonide inhaled.
  - c. Daily monitoring of symptoms and oximetry
4. For symptomatic with high risk such as high ferritin, low oxygen saturation < 94% with breathing more than 20 times per minute, or exertional dyspnea:
  - a. Supplemental oxygen if oxygen saturation less than 90%
  - b. Colchicine 0.5 mg twice daily; Famotidine 40 mg twice daily; N acetylcysteine 600 mg twice daily. Dexamethasone 4 mg twice daily. Anticoagulation with Heparin, Enoxaparin, Apixaban or Rivaroxaban
  - c. Daily monitoring of symptoms and oximetry
  - d. Repeat markers of inflammation every week: Ferritin, D dimer, CRP
  - e. Treatment should be continued until resolution of symptoms and normalization of CRP
  - f. Failure to respond to above requires hospitalization for critical care
  - g. All affected by COVID illness/infection should be followed for at least 9 months for Post-acute sequelae of SARS Co V 2.

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**Any of above require hospitalization for critical care.**

**Conclusion:**

The ideal approach to COVID epidemic response is integrating a foundation of high quality clinical care with appropriate testing and epidemic control measures that provide broad acceptance of voluntary non pharmacologic interventions. In india the COVID epidemic response has been characterized largely by a state imposed coercive non pharmacologic intervention that has now entered into a state of diminishing returns. Considering the fact that 80% of all infected persons are asymptomatic and of those testing positive, less than 4% have a fatal outcome a more nuanced approach to addressing the epidemic is desirable. There is an



almost unreal and naïve expectation that a lockdown extended for a long enough period of time will provide the principal solution. There is insufficient recognition or acknowledgement that the lockdown can at best flatten the epidemic curve, buying necessary time for building crucial credible health care systems by augmenting infrastructure and human resources. The scientific and technical response (largely non state entities) to the epidemic in areas of diagnostic technology, vaccine and therapeutic options have far outpaced the cumbersome state regulatory apparatus in place, using legacy processes to evaluate newer modalities. The pandemic has exposed the stark and tragic inadequacy of the health care infrastructure and human resource capacity to respond to this unprecedented public health emergency. The socio-economic consequences of the lockdown threaten to cause greater damage than the current state of the epidemic. The chronic systemic neglect of public health, environmental degradation and complete disregard for the role of animals in human health needs a transformational paradigm shift towards the goal of “One Health” COVID 19 is a warning wakeup call from nature, we ignore it at our own peril.

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