INTERNATIONAL **PULMONOLOGIST'S** CONSENSUS ON **COVID-19**

Chief Editors

Dr. Tinku Joseph (India), **Dr. Mohammed Ashkan Moslehi** (Iran)

Editors Note

The novel Corona virus disease (COVID-19) has been spreading at a rapid rate across the world, which made World health organization (WHO) to declare it as a pandemic disease. A lot is still unknown about this virus. In view of this Pulmonologist's from different nations affected by this disease joined hands to frame this consensus on prevention and treatment aspects of this disease. I would like thank all of them who have contributed to this article. This handbook is available to everyone for free. I would also like to request all readers to excuse all the contributors of this handbook for the minor errors; this was purely due to the shortage of time we got for framing this COVID -19 consensuses. Also on behalf of all contributors I would like to dedicate this handbook to every health care worker who has been contributing immensely in the fight against this deadly disease. Let us all join and fight against COVID-19.

Together we can. "Never stop. Do your best. Today you are someone's hope and one day someone's hero"

Dr.Tinku Joseph

Editor in chief
International pulmonologist's consensus group on **COVID-19**
Associate Prof. & Interventional Pulmonologist
Amrita Institute of Medical Sciences, Kochi, Kerala, India

Chief Editors

Dr. Tinku Joseph (India)
Associate Prof & Interventional Pulmonologist
Bronchoscopy course director
Amrita Institute of Medical Sciences &
Research center. Kochi, Kerala.
(Corresponding Author)
Email: tinkujoseph2010@gmail.com
Mob: +91 7034564871

Dr. Mohammed Ashkan Moslehi (Iran)
Head of Pediatric Pulmonary Division
Shiraz University Of Medical Sciences
Chair of Pediatric section in World Association for
Bronchology and Interventional pulmonology (WABIP)

Contributors

Dr.Kyle Hogarth (USA)
Prof. of Medicine
Director of Bronchoscopy services
University of Chicago, Chicago, IL

Dr.Chen Meng (China)
Director of pediatric Respiratory division
Qilu children's Hospital
Shandong university, Jinan.

Dr. Adnan Majid (USA)
Chief of Interventional pulmonary
BIDMC (Harvard)
Boston,MA

Dr. Renato Cutrera (Italy)
Head of Pediatric Pulmonology
Pediatric Hospital, Bambino Gesù, Rome

Dr. Aji Kavidasan (UK)
Consultant Chest Physician &
Interventional Pulmonologist
at Croydon University Hospital, London

Dr. Ali Sadoughi (USA)
Director, Interventional Pulmonology & Bronchoscopy.
Montefiore Medical Center
Divisions of Pulmonary and Critical Care
Albert Einstein College of Medicine

Dr.Mayank Vats (UAE)
Senior Pulmonologist
Rashid Hospital, Dubai health authority
Dubai.

Dr. Lucia Carolina (Columbia)
Faculty of Medicine
University Del sinu, Cartagena

Contributors

Dr. Jasleen Pannu (USA)
Director of Interventional Pulmonary
Translational Research
Ohio State University Werner Medical Center

Dr. Nader Faseeh (Egypt)
Prof. of Pediatrics, Head of Respiratory and
Allergy Unit, Faculty of Medicine.
Alexandria University.

Dr. Michela Bezzi (Italy)
Director of Interventional Pulmonology
University hospital Careggi.
Florence

Dr.Lili Zhong (China)
Director of Pediatric Respiratory division
Hunan provincial peoples hospital, Hunan.

Dr. Anantham Devanand (Singapore)
Senior consultant
Respiratory & Critical care Medicine,
Singapore General hospital

Dr.Elena Mitrofan (Romania)
Consultant Pulmonologist
Hospital of Pulmonary Diseases, Lasi county

Dr. Calvin NG (China)
Division of Cardiothoracic Surgery,
The Chinese University of Hong Kong.
Prince of Wales Hospital. Hong Kong

Dr.Henri Colt (USA)
Founder chairman of WABIP
Professor Emeritus
Pulmonary & Critical care Medicine
University of California

Dr. Jamalul Azizi (Malaysia)
Head of Respiratory Medicine &
chief Interventional Pulmonologist
Hospital Serdang, Kualalumpur.

Dr. Basil Elnazir (Ireland)
Senior Pediatric Respiratory consultant
Tallaght University Hospital, Tallaght

Dr.Antonio Gonzalo (Bolivia)
Consultant Pulmonologist
Hospital Elizabeth seton

Dr.Samaher Hashim (Saudi Arabia)
Consultant Pulmonologist
University of Tabuk, Tabuk city, KSA

Dr.Omer Elgaili (Sudan)
Associate professor
Faculty of Medicine Alneelain university

Dr. Kostas Priftis (Greece)
Associate Prof. in pediatric Pulmonology
National & Kapodistrian university of Athens

Contents

	Title	Page No.
1	Introduction	01
2	Mode of Transmission	02
3	Epidemiology	03
4	Clinical Features	03
5	Diagnosis	06
6	Initial management	11
7	Treatment Options	15
8	Progonostic Factors	25
9	Prevention	26
10	Conclusion	33

1 Introduction

Corona virus comprises of a large family of viruses that are common in human beings as well animals (camels, cattle, cats, and bats). There are seven different strains of corona virus. [15]

- 229E (alpha coronavirus)
- NL63 (alpha coronavirus)
- OC43 (beta coronavirus)
- HKU1 (beta coronavirus)
- MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS)
- SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS)
- SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19)

Sometimes corona virus from animals infect people and spread further via human to human transmission such as with MERS-CoV, SARS-CoV, and now with this COVID 19 (Corona disease 2019). The virus that causes COVID-19 is designated severe acute respiratory syndrome corona virus 2 (SARS-CoV-2); previously, referred to as 2019-nCoV.

Towards December 2019, this novel corona virus was identified as a cause of upper and lower respiratory tract infections in Wuhan, a city in the Hubei Province of China. It rapidly spread, resulting in an epidemic throughout China and then gradually spreading to other parts of the world in pandemic proportions. It has affected almost every continent in this world, except Antarctica. In February 2020, the World Health Organization designated the disease COVID-19, which stands for corona virus disease 2019 [1].

Objectives:

- Mode of transmission
- Epidemiology
- Clinical features
- Diagnostic modalities
- Treatment
- Prevention
- Frequently asked questions

2 Transmission

Our understanding of the mode of transmission is currently incomplete. Epidemiologic investigation in Wuhan at the beginning of the outbreak identified an initial association with a seafood market where most patients had worked or visited [2]. The seafood market also sold live rabbits, snakes and other animals. The initial concept was that the virus originated from snakes, however later studies proved that it had more similarity with bats. However, as the outbreak progressed, person-to-person transmission through droplets and fomites became the primary mode of transmission.

2A How does Person-to-person transmission occur?

Droplet transmission

The virus is released in the respiratory secretions when an infected person coughs, sneezes or talks. These droplets can infect others if they make direct contact with the mucous membranes. Infection can also occur by touching an infected surface and followed by eyes, nose or mouth. Droplets typically do not travel more than six feet (about two meters) and do not linger in the air. However, given the current uncertainty regarding transmission mechanisms, airborne precautions are recommended routinely in some countries and in the setting of specific high risk procedures. Patients are thought to be most contagious when they are symptomatic [6]. Some spread might be possible before symptoms appear, but this is not thought to be a common occurrence [3-5].

Other possible modes of transmission

It may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes, but this is not thought to be the main way the virus spreads.

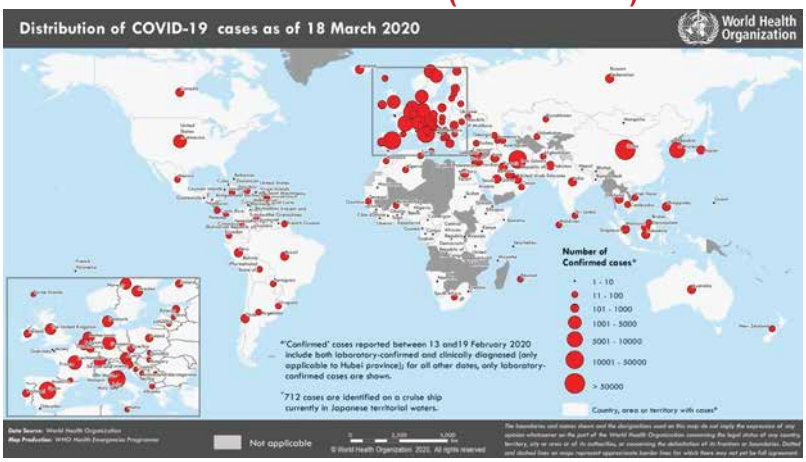
One study suggested that the **virus may also be present in feces** and could contaminate places like toilet bowls and bathroom sinks [60]. But the researchers noted the possibility of this being a mode of transmission needs more research.

In February a Chinese **newborn** was diagnosed with the new coronavirus just 30 hours after birth. The baby's mother tested positive before she gave birth. It is unclear how the disease was transmitted - in the womb, or after birth [61]. Recently in London another newborn was tested positive for the coronavirus, marking what appears to be the second such case as the pandemic worsens. [62].

3 Epidemiology

Since the first reports of cases from Wuhan, at the end of 2019, more than 80,000 COVID-19 cases have been reported in China; including all laboratory-confirmed cases as well as clinically diagnosed cases in the Hubei Province. Increasing numbers of cases have also been reported in other countries across all continents except Antarctica. The rate of new cases outside of China has outpaced the rate in China which led world health organization (WHO) to declare COVID-19 as a pandemic.

COVID-19 OUTBREAK (WORLD DATA)



Coronavirus Map: Distribution of COVID-19 cases as of March 18, 2020. Credit: WHO
(Image reproduced with permission from WHO)

Updated till: March 21st 2020

COVID-19 Cases	Deaths	Recovered
2,77,049	11,422	91,986

Courtesy: worldometers.info

4 Clinical Features

4A Incubation period

The exact incubation period is not known. It is presumed to be between 2 to 14 days after exposure, with most cases occurring within 5 days after exposure [8, 9, and 10].

4B The spectrum of illness severity

Most infections are self limiting. COVID-19 tends to cause more severe illness in elderly population or in patients with underlying medical problems. As per the report from Chinese center for disease control and prevention that included approximately 44,500 confirmed Infections with an estimation of disease severity [11]

- Mild illness was reported in 81% patients
- Severe illness (Hypoxemia, >50% lung involvement on imaging within 24 to 48 hours) in 14%
- Critical Disease (Respiratory failure, shock, multi-organ dysfunction syndrome) was reported in 5 percent
- Overall case fatality rate was between 2.3 to 5%

4C Age affected

- Mostly middle aged (>30 years) and elderly.
- Symptomatic infection in children appears to be uncommon, and when it occurs, it is usually mild [42]

4D Clinical Presentation

In a study describing 1099 patients with COVID-19 pneumonia in Wuhan, the most common clinical features at the onset of illness were: [41]

- Fever in 88%
- Fatigue in 38%
- Dry cough in 67%
- Myalgias in 14.9%
- Dyspnea in 18.7%

Pneumonia appears to be the most common and severe manifestation of infection. In this group of patients breathing difficulty developed after a median of five days of illness. Acute respiratory distress syndrome developed in 3.4% of patients.

Other symptoms

- Headache
- Sore throat
- Rhinorrhea
- Gastrointestinal symptoms

About 80% of confirmed COVID-19 cases suffer from only mild to moderate disease and nearly 13% have severe disease (dyspnea, respiratory frequency ≥30/minute, blood oxygen saturation≤93%, PaO2/FiO2 ratio <300, and/or lung infiltrates >50% of the lung field within 24-48 hours).

Critical illness (respiratory failure, septic shock, and/or multiple organ dysfunction/failure) is noted in only in less than 6% of cases.

4E COVID 19 IN PEDIATRIC POPULATION

In this outbreak, compared with adult cases, there are relatively fewer cases of children, milder symptoms and better prognosis. Also, children are less frequently exposed to the main sources of transmission. Most infected children recover one to two weeks after the onset of symptoms, and no deaths had been reported by February 2020. According to the recent report of the China-WHO Joint Mission Expert Group, the current domestic case data show that children under 18 years of age account for 2.4% of all reported cases, and no deaths have been reported.[21]

Probable reasons Why COVID-19 is less affected in children

- The time period of the outbreak, is the winter vacation time of the university, middle school and kindergarten. It is a good time for everyone to stay in their own families, which is equivalent to active home isolation. It is a good time to avoid the collective cluster disease by chance.
- Secondly, humoral and cellular immune development in children is not fully developed. This may be one of the mechanisms that lead to the absence of severe immune responses after viral infection.
- As COVID-19 virus exploits the ACE2 receptors to gain entry inside the cells, under expression, immaturity of ACE2 receptors in children is another hypothesis in this regard.
- Moreover, recurrent exposure to viruses like respiratory syncytial virus in winters can induce more immunoglobulins levels against the new virus infection compare to adults.There is no direct evidence of vertical mother-to-child transmission, but new borns can be infected through close contact.

In recent studies in china, there was no significant gender difference in children and it was suggested that alleges ranged from 1 day to 18 years were prone to infected by the COVID-19[49]. The symptoms of COVID-19 are similar in children and adults. However, children with confirmed COVID-19 have generally presented with mild symptoms and usually recover within 1 to 2 weeks. Reported symptoms in children may include cold-like symptoms, such as fever, dry cough, sore throat, runny nose, and sneezing. Gastrointestinal manifestations including vomiting and diarrhea have also been reported.

In the 13 pediatric patients (13/20, 65%) that had an identified history of close contact with COVID-19 diagnosed family members. Fever (12/20, 60%) and cough (13/20, 65%) were the most common symptoms. [15] Children with underlying medical conditions and special healthcare needs may be at higher risk for severe illness. There is much more to be learned about how the disease impacts children.

For laboratory findings, in the early stage of the disease, the total number of peripheral white blood cells is normal or decreased, the lymphocyte count is reduced, and some children have increased liver enzymes, lactate dehydrogenase (LDH), muscle enzymes, and myoglobin; some critically ill patients have increased troponin, D-dimer and ferritin and the number of peripheral blood lymphocytes have progressively reduced. Like adults, the children with severe and critical illness may be accompanied by elevated levels of inflammatory factors such as interleukin (IL)-6, IL-4, IL-10, and tumor necrosis factor (TNF)-α. [50]

There are no abnormal findings in the early stages of the disease in the children's plain X-rays with COVID-19 thus plain X-rays it is not recommended especially in the early stages and in whom without symptoms or any positive risk factors. Suspected cases should undergo chest CT examination as soon as possible. The most important finding in early stages is a single or multiple limited ground-glass opacity which mostlylocated under the pleura or near the bronchial blood vessel bundle especially in the lower lobes. Severe period is very rare, manifested by diffuse unilateral or bilateral consolidation of lungs and a mixed presence of ground glassopacities. [51]
Also compared to adults, consolidation with surrounding halo signs is more common in pediatric patients and was suggested as a typical sign in pediatric patients. [16]For now, treatment is supportive; no specific antiviral medications are available for children.

5 Diagnosis

5A CASE DEFINITION [23] *(As per WHO-China joint commission report)*

5.1.1Suspected case

Based on the epidemiologic characteristics observed so far in China, everyone is assumed to be susceptible, although there may be risk factors increasing susceptibility to infection.

- A patient with acute respiratory tract infection (sudden onset of at least one of the following: cough, fever, shortness of breath) AND with no other aetiology that fully explains the clinical presentation AND with a history of travel or residence in a coun try/area reporting local or community transmission* during the 14 days prior to symp tom onset;

OR

- A patient with any acute respiratory illness AND having been in close contact with a confirmed or probable COVID-19 case in the last 14 days prior to onset of symptoms;

OR

- A patient with severe acute respiratory infection (fever and at least one sign/symptom of respiratory disease (e.g., cough, fever, shortness breath)) AND requiring hospital isation (SARI) AND with no other aetiology that fully explains the clinical presentation.

5.1.2 Probable Case

A suspected case for whom testing for virus causing COVID-19 is inconclusive (according to the test results reported by the laboratory) or for whom testing was positive on a pan-coronavirus assay.

5.1.3 Confirmed Case

A person with laboratory confirmation of virus causing COVID-19 infection, irrespective of clinical signs and symptoms

5.1.4 Close Contacts

Close contact of a probable or confirmed case is defined as

- A person living in the same household as a COVID-19 case;
- A person having had direct physical contact with a COVID-19 case (e.g. shaking hands);
- A person having unprotected direct contact with infectious secretions of a COVID-19 case (e.g. being coughed on, touching used paper tissues with a bare hand);
- A person having had face-to-face contact with a COVID-19 case within 2 metres and > 15 minutes;

- A person who was in a closed environment (e.g. classroom, meeting room, hospital waiting room, etc.) with a COVID-19 case for 15 minutes or more and at a distance of less than 2 metres;
- A healthcare worker (HCW) or other person providing direct care for a COVID-19 case, or laboratory workers handling specimens from a COVID-19 case without recommended personal protective equipment (PPE) or with a possible breach of PPE;
- A contact in an aircraft sitting within two seats (in any direction) of the COVID-19 case, travel companions or persons providing care, and crew members serving in the section of the aircraft where the index case was seated (if severity of symptoms or movement of the case indicate more extensive exposure, passengers seated in the entire section or all passengers on the aircraft may be considered close contacts). [24]

5B LABORATORY FINDINGS

White Blood Cell Count

- White blood cell count can vary. It does not provide accurate information about COVID-19. [40]
- Leukopenia, leukocytosis, and lymphopenia have been reported.
- Lymphopenia is more common, seen in more than 80% of patients [40]
- Mild thrombocytopenia is commonly seen. However thrombocytopenia is considered as a poor prognostic sign. [40, 41]

INFLAMMATORY MARKERS

Serum Procalcitonin

- Serum procalcitonin is often normal at the time of admission; however it increases in patients who require ICU care. In one study high D-Dimer and lymphopenia are asso ciated with poor prognosis. [40, 41]

C - reactive protein (CRP)

- COVID-19 increases CRP. This seems to track with disease severity and prognosis. In patients suffering from with severe respiratory failure with a normal CRP level an alternative diagnosis should always be sought. [40, 41]

Patients who meet the criteria for suspect cases, as discussed above, should undergo testing for SARS-CoV-2 and also respiratory pathogens. Respiratory specimen collection from the upper and in particular lower respiratory tract should be performed under strict airborne infection control precautions (25). Preferably these samples should be obtained as early as symptom onset, since it yields higher virus concentrations.

5C RECOMMENDATIONS FOR SAMPLE COLLECTION

- Collection of specimens to test for SARS-CoV-2 from the upper respiratory tract (nasopharyngeal and oropharyngeal swab) is the preferred method for diagnosis
- Induction of sputum collection is not recommended
- Bronchoscopy being an aerosol generating procedure has got the potential to trans mit infection to others. In view of this preferably avoid performing it and limit its usage clearing secretions/mucous plugs in intubated patients [46]
- All respiratory specimen collection procedures should be done in negative pressure rooms
- Additional specimens (eg: Blood, stool, urine) can also be collected to rule out alter native/supportive diagnosis.

5D CURRENT RECOMMENDED DIAGNOSTIC MODALITY FOR COVID 19

- SARS-CoV-2 RNA is detected by polymerase chain reaction (RT-PCR) (25)
- Results are generally available within a few hours to 2 days
- A single positive test should be confirmed by a second RT-PCR assay targeting a different SARS-CoV-2 gene
- If initial testing is negative but the suspicion for COVID-19 remains, the WHO recom mends re-sampling and testing from multiple respiratory tract sites
- For safety reasons, specimens from a patient with suspected or documented COVID-19 should not be submitted for viral culture.
- Samples should also be tested for other viral/bacterial pathogens.

5E COVID 19- RAPID TESTS

COVID-19 Rapid Test qualitatively detects IgG and IgM antibodies to SARS-CoV-2 in human whole blood, serum and plasma samples. This test applies lateral flow immuno-chromatog-raphy and is a tool to assist in the diagnosis of SARS-CoV-2 infections. . The IgM-IgG com-bined assay has better utility and sensitivity compared with a single IgM or IgG test. It can be used for the rapid screening of SARS-CoV-2 carriers, symptomatic or asymptomatic, in hospitals, clinics, and test laboratories. [26]

Recommendation:
Despite the promise, there is no definitive definitive evidence regarding the utility of rapid kits for testing COVID 19 suspected patients respiratory/serum samples .

Photograph
COVID-19 Rapid Test kit

5F BRONCHOSCOPY

Benefits

- Helps in obtaining BAL samples in patients who are not able to expectorate sputum for checking bacterial culture/AFB smear/gene Xpert
- Bronchoscope can be used to clear out mucous plugs in ventilated patients.

Risks

- May cause some deterioration in clinical condition, especially in patients who are on high oxygen support
- High risk of transmission of infection to providers.
- Significant utilization of valuable resources at this point (N95 respirators, physi cians, respiratory therapists) – Supply of all these resources will be limited during the time of a pandemic.

Recommendations

- Bronchoscopy should not be done only for the purpose of ruling COVID-19 [28 &46]. Risk of transmission of infection to others is extremely high through aerosols.
- It can be performed when sputum sample cannot be obtained to rule out alternative diagnosis like (Tuberculosis, bacterial/fungal pneumonias)
- It can be performed to suction out mucous plugs in ventilated patients
- Consideration for use of a disposable bronchoscope if available
- Consider bronchoscopy in patient's place of care to minimize the exposure
- Minimize staff in room during procedure.
- Negative pressure room if available
- All Personal Protective equipment should be used: Face shield/goggles, N95 mask, Contact isolation gown, Gloves
- Standard disinfection protocols should be followed for cleaning your flexible bron choscopes and video monitors.

5G RADIOLOGY IN COVID-19 INFECTION

In this section, we are about to describe the imaging features in COVID-19 infection. The information we have available until now, it is based on Chinese registries and publications of recently knowledge.

It is good to know that the American College of Radiology have released recommendations for the use of Chest Radiography and computed Tomography in the last two weeks (March 11st). And the official paper emphasize that knowledge of the infection is rapidly evolving. Also there is the recommendation of the CDC, supporting the fact that chest radiography or computed tomography are not recommended to diagnose the COVID-19 infection. CDC link. www.cdc.gov

The findings on chest imaging are not specific of the infection, and could overlap with other entities, such as Influenza. There are also recommendations about the performance of the chest radiography, including the fact that it is better to avoid the movement of the patient within the hospital.

Chest Radiography (CXR).

The findings on CXR are not specific, and in the initial phases of the disease the studies could be normal. The most common features include lobar/ multi-lobar / bilateral lung consolidation. [64]

Computed Tomography (CT Chest).

Recent studies have reported the features on CT imaging. Pan et al [65] described the tomographic changes of 21 patients with mild to moderate disease who recovered from the disease, and they described **four stages:**

- **Early stage** (0-4 days after the onset of the symptoms), in which ground glass opaci ties (GGO) are frequent, with sub-pleural distribution and involving predominantly the lower lobes. Some patients in this stage could have a normal CT.
- **Progressive stage** (5-8 days after the onset of the symptoms), the findings usually evolved to rapidly involvement of the two lungs or multi-lobe distribution with GGO, crazy-paving and consolidation of airspaces.
- **Peak stage** (9-13 days after the onset of the symptoms), the consolidation becomes denser and it was present in almost all of the cases. Other finding was residual parenchymal bands.
- **Absorption stage** (>14 days after the onset of the symptoms), no crazy paving pattern was observed, the GGO could remain.

Shi et al [66] also described the CT findings in 81 patients in Wuhan, China. All of the patients had an abnormal CT, and the features include: GGO, smooth and irregular interlobular septal thickening, crazy paving pattern, air bronchogram and irregular pleural thickening. Usually affecting the subpleural regions and the lower lobes.

Lung ultrasound. (USG

The USG findings are also not specific for COVID-19 infection. Little information is available to date on this matter. The findings include: Irregular pleural lines, sub-pleural areas of consolidation, areas of White lung and thick B lines [67]. It is a tool that could be used at bed side avoiding the need for shifting infected patients to a Radiology suite [68].

Pulmonary function tests (PFT)

Sources of cross infection in pulmonary function lab can occur due to close contact, direct contact and through aerosolized particles. Among these Droplets/aerosolized particles is the most common mode of transmission of infection. Numerous factors play a role in the virulence of an organism: source & strain of pathogen, route of infectivity, particle size, room temperature and infective dose of pathogen. [47&48]

Recommendations:

- All kinds of pulmonary function tests should be avoided among patients with a strong suspicion of upper or lower Respiratory tract infection.
- In COVID 19 endemic zones it would be wise to avoid PFTs for a major proportion of patient to avoid spread of infection and usage of PFT should be limited for time being for only pre-operative fitness assessment.
- All patients who are enrolled to perform a PFT should be segregated, since this helps in preventing the spread of infection. Performing a chest x-ray prior to PFT would help to rule out Respiratory infections to certain extent. [47]
- Contact in waiting room with potentially infectious patients should be minimized. Surgical facemasks, tissues, and waste container, alcohol-based sanitizers should be made easily available for infectious patients.
- All connections between the patient and the PFT machine (tubing's & valves) should be cleaned and disinfected before re-use.
- Disposable items in PFT lab like mouth pieces can be a reservoir of microorganisms and hence should be disposed carefully.
- Usage of personal protective equipments helps in reducing the risk of cross contami nation.

6 Initial Management

6A COVID 19 INFECTED PATIENTS

At the moment, the therapeutic strategies to deal with the infection are only supportive, and prevention aimed at reducing transmission in the community is our best weapon. Aggressive isolation measures in China have led to a progressive reduction of cases in the last few days. In Italy, in geographic regions of the north, political and health authorities are making incredible efforts to contain a shock wave that is severely testing the health system.

6B WHO ALL NEEDS ISOLATION?

1. Any person diagnosed with SARS CoV 2 infection by means of laboratory testing at a government recommended testing laboratory.
2. Anyone who has symptoms of fever and respiratory illness, and has a history of close contact of a person who has either been diagnosed as COVID-19, or has a history of travel to a COVID affected region within the last 14 days.
3. Any health care worker with symptoms of fever and respiratory illness who has been involved directly in treating COVID- 19 patients, or has close contact with persons involved in treating COVID- 19 patients during the last 14 days.

6C IF NEEDED WHERE TO ISOLATE?

- Asymptomatic cases with exposure to Covid-19 positive patients can be quarantined at their homes, but to be under strict surveillance by the government authorities
- Suspected patient to be isolated in well ventilated, preferably separate rooms.
- Symptomatic COVID- 19 positive patients should be hospitalized in isolation room and also should be monitored adequately by medical team
- Sputum/BAL samples (if needed) should be collected from isolation rooms or a separate space with HEPA filters/negative pressure ventilation

6D PREPARATION OF ISOLATION ROOM

- Ensure that appropriate hand washing facilities and hand-hygiene supplies are avail able.
- Stock the sink area with suitable supplies for hand washing, and with alcohol-based hand rub, near the point of care and the room door.
- Ensure adequate room ventilation.
- Post signs on the door indicating that the space is an isolation area.
- All visitors should consult the health-care worker in charge before being allowed into the isolation areas. Keep a roster of all staff working in the isolation areas, for possible outbreak investigation and contact tracing. Some centers have banned all visitors.
- Remove all non-essential furniture and ensure that the remaining furniture is easy to clean.
- Stock the PPE supply and linen outside the isolation room or area (e.g. in the change room). Setup a trolley outside the door to hold PPE. A checklist may be useful to ensure that all equipment is available.
- Place appropriate waste bags in a bin. If possible, use a touch-free bin. Ensure that used (i.e. dirty) bins remain inside the isolation rooms.
- Place containers for disposal of sharps inside the isolation room or area.
- Keep the patient's personal belongings to a minimum.
- Dedicate non-critical patient-care equipment (e.g. stethoscope, thermometer, blood pressure cuff and sphygmomanometer) to the patient, if possible. Thoroughly clean and disinfect patient-care equipment every time before using in next patient.
- Adequate equipment required for cleaning or disinfection inside the isolation room should be kept and room should be cleaned on a daily basis
- Set up a telephone or other method of communication in the isolation room or area to enable patients, family members or visitors to communicate with health-care workers. This may reduce the number of times the workers need to don PPE to enter the room or area.

6E WEARING AND REMOVING PERSONAL PROTECTIVE EQUIPMENT (PPE)

Before entering the isolation room or area:

- Collect all necessary items.
- Ensure to perform hand hygiene with an alcohol-based hand rub or soap and water;
- Use PPE in the order that ensures adequate placement of PPE items and prevents self-contamination and self-inoculation while using and taking off PPE.
- Figure 1 & 2 illustrates an example of the order in which to don PPE and what all are required.

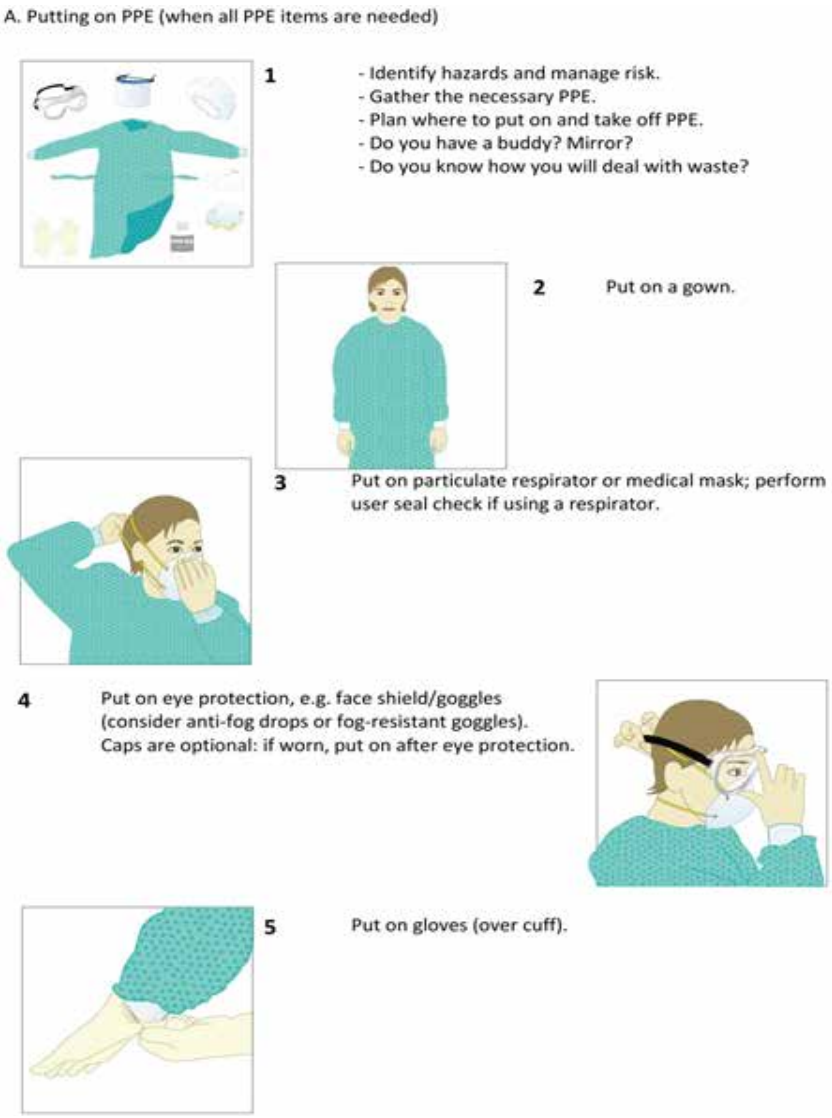


***Figure 1**: Steps of putting personal protective equipments*

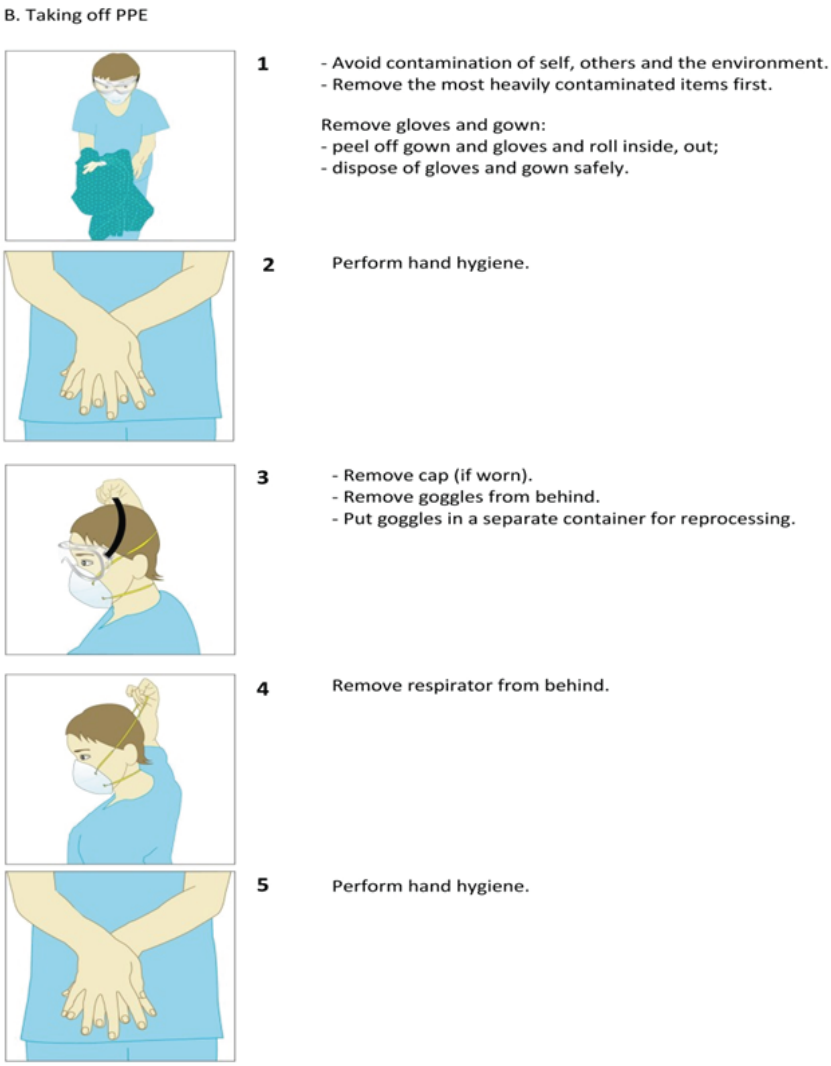


Figure 2: *Steps of removing personal protective equipments*

6F LEAVING THE ISOLATION ROOM AREA

- Either remove PPE in the anteroom or, if there is no anteroom, make sure that the PPE will not contaminate either the environment outside the isolation room or area, or other people.
- Remove PPE in a manner that prevents self-contamination or self-inoculation with contaminated PPE or hands. General principles are:
- Remove the most contaminated PPE items first;

- Perform hand hygiene immediately after removing gloves
- Remove the mask or particulate respirator last (by grasping the ties and discarding in a rubbish bin);
- Discard disposable items in a closed rubbish bin;
- Put reusable items in a dry (e.g. without any disinfectant solution) closed container; an example of the order in which to take off PPE when all PPE items are needed is gloves (if the gown is disposable, gloves can be peeled off together with gown upon removal), hand hygiene, gown, eye protection, mask or respirator, and hand hygiene

Perform hand hygiene with an alcohol-based hand rub (preferably) or soap and water whenever ungloved hands touch contaminated PPE items.

6G PATIENT IN ISOLATION ROOM

- Preferably wear face mask as much as time possible in a day
- Restrict movement of patient for chest xays/CT scans/labs as this lead to dissemination of infection to other places
- Attached urinals/wash room facility in all isolation rooms
- Separate portable stethoscopes/xray/CT units/USG machines should be dedicated for patients suffering from COVID-19
- Patient needs to be kept in isolation till his both respiratory samples turns out to be negative.

7 Treatment Options - COVID 19

There is no specific antiviral treatment recommended for COVID-19, and no vaccine is currently available at time of writing this article. [28]

Mild Disease

These patients usually present with symptoms of

- An upper respiratory tract viral infection
- Low grade fever , cough, malaise, rhinorrhoea, sore throat without any warning signs
- Shortness of breath
- Haemoptysis
- Gastro-Intestinal symptoms: Nausea, vomiting, Diarrhea
- Without change in mental status (ie: confusion, lethargy)
- Non immunocompromised

Recommendation: Consider for home isolation in asymptomatic/mild disease

7A WHO ALL NEEDS ADMISSION IN COVID-19?

Severe Disease (14%)

- Respiratory rate > 30/min
- SPo2- <93%
- PaO2/FiO2 <300
- Lung infiltrates >50% within 24- 48 hours

Critically ill (5%)

- Respiratory failure (need of mechanical ventilation)
- Septic shock
- MODS

Is there a definitive therapy?

- No drug of choice
- Oxygen support
- Oxygen saturation to be maintained above 90%
- Conservative fluid management
- Give empirical antibiotics (As per institution based CAP guidelines)/ anti-viral (Osel tamivir)
- High dependency / ICU care when needed

7B ANTI-VIRAL THERAPY

No anti-viral therapy has been proven to work for COVID-19 in humans. Multiple RCTs are ongoing; hopefully they will bring us further information soon. [28]

Whenever possible, patients should be enrolled in RCTs.

- Information is provided below about some of the more popular agents which are being used by some practitioners.
- Inclusion in this chapter is not a recommendation to use one or more of these medi cations. This information is simply provided as a background to help us understand these therapies.
- A focus is placed on lopinavir/ritonavir and chloroquine since these agents are currently available.
- Practitioners are encouraged to review available evidence and reach their own conclusions regarding whether to use these medications.

INDICATIONS FOR ANTI-VIRAL THERAPY

Retrospective data from SARS suggests that earlier treatment (e.g. within 1-2 days of admission) may be more effective than reserving therapy until severe organ failures occur (Chan 2003). This is consistent with data from influenza that suggests a finite treatment window occurring relatively early in the disease course.

- The vast majority of patients will do fine without any therapy, so in most cases there's no need for antiviral therapy.
- However, waiting until patients are severely ill before initiating therapy could cause us to miss an early treatment window, during which the disease course is more mod ifiable.
- Predictors of adverse outcome might be useful in predicting who will do poorly and thus who might benefit most from early anti-viral therapy, but data is limited.

ANTI-VIRAL MOLECULES UNDER TRIAL (Experimental options)

REMDESIVIR (compassionate use only)

- Investigational antiviral drug with reported in vitro activity against SARS-CoV-2
- **No published phase 3 trials**
- Mechanism of action: Extrapolated from MERS CoV
- Premature termination of viral RNA transcription
- Has been found to reduce pulmonary pathology in in vitro studies
- Remdesivir cannot be used in combination with other experimental antiviral agents
- Tried in Ebola virus too
- Side effects- Hepatotoxicity
- **Dose: Adult:** 200mg IV on day 1(loading dose) followed by 100mg IV OD x 9 days[32]
- **Pediatric:** < 40 kg: 5 mg/kg IV on day 1, then 2.5 mg/kg IV q24h

Lopinavir/Ritonavir (29)

- In vitro reduces replication by 50% in MERS corona virus
- **Definite efficacy not proven**
- WHO has mentioned as an agent that can be tried
- May be also tried in combination with Interferon alpha orRibavirin
- Potent CYP3A4 inhibitor – monitor for drug interactions
- Oral and liquid formulation is available
- Dose: Adult: 400/100mg PO Q12h
- Pediatric: Pediatric (based on lopinavir): Oral solution

- < 15kg: 12mg/kg/DOSE q12h
- 15-40kg: 10mg/kg/DOSE q12h
- >40kg: 400mg q12h
- Oral tablet
- ≥15-25kg: 200mg q12h
- ≥25-35kg: 300mg q12h
- >35kg: 400mg q12h

Ribavirin

- Inhibitor of RNA polymerization [30]
- Studies done in MERS
- Concentration required to inhibit MERS-CoV in vitro exceeds peak levels in the blood after therapeutic doses in humans.
- High risk of toxicity
- Renal dose adjustment is necessary
- Boxed warning for hemolytic anemia
- No study results yet in SARS CoV2
- **Dose (Oral):** 2 grams x 1 dose, then 600mg q8h

Oseltamivir

- Neuraminidase enzyme inhibitor in influenza
- Not seen in SARS CoV2
- No trials on COVID-19
- Many patients with similar presentation of COVID 19 might be influenza
- **Hence better to give the drug to avoid patient worsening due to influenza**
- **Dose: 150mg BD x 5 days**

7C OTHER AVAILABLE TREATMENT OPTIONS

ACE INHIBITORS (ACEi) /ANGIOTENSIN RECEPTOR BLOCKERS (ARBS)

- Off late there is lot of interest in the potential role of ACE-inhibitors (ACEi) / angioten sin receptor blockers (ARBs) in the pathophysiology of this disease since the SARS-CoV-2 virus binds to the ACE2 receptor for cellular entry
- Theoretically it can be blocked by ARBs
- But ACE2 is a negative regulator of RAS(It inactivates angiotensin 2), hence the suggestion might be counterintuitive
- ACE (CD143) appears on the macrophage plasma membrane during activation
- **Proposed reduction of cytokine storm**

- Currently there are no data to support either starting or stopping ACEi/ARBs on any patients with COVID-19.

INTERFERONS

- IFN-α2a, IFN-α2b orIFN-β1a
- SARS CoV2 attenuates the interferon (IFN) response of the innate immune system
- **Impair the antiviral adaptive type 1 T-helper cell**
- But in vitro effects hasn't been fully shown to be working

CHLOROQUINE/HYDROXYCHLOROQUINE

- Proposed mechanism- Hampers the low pH dependant steps of viral replication
- No renal or hepatic dose adjustments necessary
- Has been even proposed for prophylaxis- however lacks evidence
- Side effects: QT prolongation
- **Dose (Adult) :** 400mg PO Q12h x 1 day, 200mg PO Q12h x 4 days
- **Pediatric:** 6.5mg/kg/DOSE PO q12h x 1 day, then 3.25mg/kg/DOSE PO q12h x
- 4 days (up to adult maximum dose)

TOCILIZUMAB (optional)

- IL-6 inhibitor
- Proposed to reduce the cytokine storm in COVID-19
- Reports of tocilizumab use in COVID-19 infections have been mostly anecdotal from Italy or case series data from China.
- Adverse effects: elevation of liver enzymes, Increased risk of re-activation of other Respiratory infections.
- **Dose: 4-8 mg/kg (max 400mg) IV x 1**

CORTICOSTEROIDS

- **Not indicated in treating SARS CoV2 as per available evidence**
- Might prolong viral shedding
- Use as per indicated in septic shock/if patient has other indications for steroid use

ASCORBIC ACID

- Ascorbic acid did appear to improve mortality in the multi-center CITRIS-ALI trial. [31]
- Extremely limited evidence suggests that ascorbic acid could be beneficial in animal models of corona virus (Atherton 1978).
- Administration of a moderate dose of IV vitamin C could be considered (e.g. 1.5 grams IV q6 ascorbic acid plus 200 mg thiamine IV q12). This dose seems to be safe. However, there is no high-quality evidence to support ascorbic acid in viral pneumonia.

ANTI BACTERIAL THERAPY

Initial empirical antibiotics [28]

- COVID-19 itself is not an indication to start antibiotics.
- However antibiotics can be initiated to treat secondary bacterial pneumonia.
- Broad spectrum antibiotics to be initiated according to the institution based guide lines

Delayed bacterial super infection [28]

- Bacterial pneumonia can emerge during the hospital course (especially ventilator-as sociated pneumonia in patients who are intubated).
- This may be investigated and treated similarly to other ventilator-associated pneu monias, or hospital-acquired pneumonias.

OTHER AGENTS

- BaricitinibDarunavir/Cobicistat
- Umifenovir(Arbidol)- 200 mg TDS
- Favilavir- first approved drug in china
- Galidesivir
- Leronlimab
- Brilacidin
- Combination of monoclonal antibody
- Traditional medicines in different countries

7D WHAT WE CAN ADOPT FOR TREATMENT?

- Patient to be classified as mild/severe/critical
- Decide whether he/she requires only home isolation
- Assess oxygenation on room air
- Consider referral to a nodal center if requiring admission
- Home care advise in mild/asymptomatic cases

7E COVID -19 MANAGEMENT IN A NUT SHELL

There are no proven or approved treatments for COVID-19. The following treatment plan is suggested on the on the basis of information available till date on various investigational treatment approaches.

SEVERITY OF ILLNESS	PLAN
Mild illness without any risk factors/ Co-morbidities	• Outpatient care • Strict Home Quarantine monitored by government/health authorities • Supportive care • Assess patient's clinical condition via telephonic conversation/ using telemedicine facility
Moderate Illness: • Dyspnoea • Hypoeximia • Infiltrates/ consolidation on chest xray/ CT scan	• Admit in Hospital isolation room • Supportive care • Start empirical antibiotics as per local community acquired pneumonia treatment guidelines • Oseltamivir 75/150mg BD • Consider starting Hydroxychloroquine Or Lopinavir/Ritonavir (If evident risk factors for progression of disease are present)
Critical Illness: • Mechanically ventilated patient's • Multi lobar/ bilateral lung consolidation *Careful using these drugs in patients with multi-organ damage*	• Remdesivir (for compassionate use only) • **Tocilizumab** can be considered (check IL-6 level prior to starting Tocilizumab). Especially in patients with evidence of cytokine release syndrome. • Continue IV antibiotics and supportive care • Rule out ventilator associated pneumonia/ catheter related infections and other secondary bacterial/viral/fungal infections • Always keep in mind the to rule out differentials of non –resolving pneumonia • In ventilated patients: follow ARDS NET protocol strategy • Consider ECMO if need arises • Refractory or progressive cases in ICU: **Interferon beta B1** can be considered. However it should be combined with an anti-viral (Lopinavir/Ritonavir) and hydroxychloquine

Summary of currently available drugs which can be potentially used for treatment of COVID-19

Disclaimer: *The options listed below are NOT licensed for the treatment of COVID-19*

Agent	Classification	Mechanism of action	Dosage	Side effects
Hydroxychloroquine	Off label use	Hampers low PH dependant steps of viral replication	400 mg BID x 2 doses, then 200 mg BID for 5 days	QT prolongation
Oseltamivir	No trials on COVID-19	Neuraminidase enzyme inhibitor in influenza	150mg BID for 5 days	GI intolerance Headache Insomnia
Remdesivir	Investigational (can be used only on compassionate basis)	RNA dependent RNA polymerase inhibitor	200 mg IV loading dose, then 100 mg IV daily, up to 10 days	GI intolerance Hepatotoxicity
Lopinavir/Ritonavir	Off label use	3CLpro (viral protease) inhibitor	400/100 mg BID for up to 10 days	QT prolongation Hepatotoxicity
Ribavirin	Off label use	Inhibitor of RNA polymerization	2 grams (loading dose) then 600mg TID	High risk of toxicity Boxed warning for haemolytic anaemia
Interferon Beta B1	Off label use	Immunomodulatory; enhancement of innate and adaptive viral immunity		Flu like syndrome depression
Tocilizumab	Off label use	Monoclonal antibody to IL6 receptor / treats cytokine release syndrome		Elevation of liver enzymes Increased risk of re-activation of other Respiratory infections
Antibiotics (Broad spectrum)	Initiate as per institution based CAP/VAP policy	Secondary bacterial infection (CAP)/VAP	-	-
Corticosteroids	Not indicated in treating SARS CoV2 as per available evidence. Might prolong viral shedding. Use as per indicated in septic shock/if patient has other indications for steroid use			
IV Immunoglobulin (IVIG)	Off label use	Antibodies from convalescent plasma might suppress viraemia. Theoretically: Better to start at early stage of disease	Consider IVIG at standard dose of 1 gm/kg daily x 2 doses	Might interact with antivirals/

7F CRITICAL CARE MANAGEMENT OF ICU PATIENTS AND THOSE WHO NEED MECHANICAL VENTILATION

Role of Noninvasive positive pressure ventilation (NIPPV):

- NIPPV have Limited role as patients are usually very much tachypneic / hypoxic and starting and maintaining NIPPV with frequent interruption by patient may cause more aerosolization of the virus with the consequent risk to medical personal.
- Avoid high flow Nasal Oxygen (HFNO) or NIPPV for the above mentioned reasons unless individualized patient's related factors exists such as (e.g. COPD, Do Not Intubate / Do Not Resuscitate status etc[54]
- If use of NIPPV cannot be avoided (less ICU beds / or non-availability of mechanical ventilator then use NIPPV with helmet mask interface (Preferred)
- NIV use has been found to be associated with worse outcome

Patients who require intubation and Mechanical Ventilation

Caution while Intubation / resuscitation the patient

- Try to do with the minimum possible number of people (high aerosol generation risk) with full PPE precautions
- Standard intubation and resuscitation protocols to be followed with utmost impor tance of prevention of infection.
- Intubate early under controlled conditions if possible / Low threshold for watchful wait
- Need a separate cubicle/patient roomfor intubated patients
- Continuous hemodynamic and oxygenation monitoring
- Use a conservative fluid management strategy for ARDS patients who are not in shock to shorten the duration of mechanical ventilation [55]
- early appropriate empiric Broad spectrum antibiotics

Ventilation Strategy: Manage as per ventilator management in ARDS NET protocol

- Lung Protective ventilation (Low Tidal Volume, Low Plateau pressure, High PEEP for getting adequate Spo2 targets and Permissive Hypercarbia to protect lung ventilation from ventilation induced injury and follow ARDS protocol.
- Implementing a low-volume, low-pressure ventilation strategy/protocol, which targets a tidal volume of 6 ml/kg (predicted body weight), a plateau airway pressure (Pplat) of ≤ 30 cm H2 O and SpO2 88–93% or PaO2 55–80 mm Hg (7.3–10.6 kPa) has been shown to reduce mortality in a heterogeneous population of ARDS patients. [56]

- Sedation and Paralytics to relax patient and facilitate ventilation with daily interruption of sedation and paralytics. Administration of neuromuscular blockade for initial 48 hours has been associated with improved survival and increased time off the ventila tor without causing significant weakness [56]
- Prone positioning (Take care of accidental removal of line, tubes, and catheter) [56]
- Inhaled prostacyclins may be tried
- In selected cases ECMO can be an option too (unclear who are the ideal candidate, however can be used for refractory hypoxemia).

- Investigational therapies should be continued despite lack of significant evidence Corticosteroids may reduce inflammation. None of these investigational therapies are of proven benefit but literature is evolving rapidly and we hope that specific medicines would be available soon.

7G RISK OF VIRAL SHEDDING

- Exact dynamics unknown
- First COVID 19 case was detected in USA on the 4 of patient's illness. It is suggestive of high viral loads and potential for transmissibility. They also detected 2019-nCoV RNA in a stool specimen collected on day 7 of the patient's illness. [43]
- However, extra pulmonary detection of viral RNA does not necessarily mean that infectious virus is present, and the clinical significance of the detection of viral RNA outside the respiratory tract is unknown at this time
- As a precautionary measure treated/isolated patient should be discharged only after 2 samples are negative (more than 24 hours apart)

7D WHEN TO DISCHARGE PATIENT

- Resolution of symptoms
- Radiological improvement
- Documented virological clearance in 2 samples at least 24 hours apart

8 Prognostic Factors

General prognosis [28]

The vast majority of infected patients (e.g. >80%) don't get significantly ill and don't require hospitalization.

- Among hospitalized patients (Guan et al 2/28)
- 10-20% of patients are admitted to ICU.
- 3-10% requires intubation.
- 2-5% dies.

Longer term outcomes: Prolonged ventilator stay? As the epidemic progresses, an issue which may arise is a large volume of patients unable to wean from mechanical ventilation.

Epidemiological risk factors

- Older Age
- Male sex
- Medical comorbidities
- Chronic pulmonary diseases
- Cardiovascular disease
- Chronic kidney disease
- Diabetes

9 Prevention

9A WHO IS A CONTACT?

- A contact is a person that is involved in any of the following: [33]
- Providing direct care without proper personal protective equipment (PPE)2 for COVID-19 patients
- Staying in the same close environment of a COVID-19patient (including workplace, classroom, household, gatherings).
- Traveling together in close proximity (1 m) with a COVID-19 patient in any kind of conveyance within a 14-day period after the onset of symptoms in the case under consideration
- According to a study published in NEJM by Sebastian Hoehl et.al a symptom-based screening process was ineffective in detecting SARS-CoV-2 infection in 2 persons who later were found to have evidence of SARS-CoV-2 in a throat swab and said that shedding of potentially infectious virus may occur in persons who have no fever and no signs or only minor signs of infection [44]

9B CAN THE VIRUS STAY ON INANIMATE SURFACES?

- COVID-19 virus can persist on inanimate surfaces like metal, glass or plastic for up to 9 days, but can be efficiently inactivated by surface disinfection procedures with 62–71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite within 1 minute. [45]
- Other biocidal agents such as 0.05–0.2% benzalkonium chloride or 0.02% chlorhexi dine digluconate are less effective.
- Hence terminal disinfection is important even after the patient getting discharged [39]

9C WHAT SHOULD INCLUDE IDEAL PERSONAL PROTECTIVE EQUIPMENT (PPE)?

PPE for at-risk health facilities

Airborne precautions for aerosolized generating procedures:

Gloves

Gloves nitrile, powder-free, non-sterile. (eg. minimum 230mm total length. Various sizes ranging from small, medium , large

Mask (healthcare worker)

Medical mask, good breathability, internal and external faces should be clearly identified

Face Shield

Made of clear plastic and provides good visibility to both the wearer and the patient, Adjustable band to attach firmly around the head and fit snuggly against the forehead, Fog resistant (preferable), Completely cover the sides and length of the face, May be re-usable (made of robust material which can be cleaned and disinfected) or disposable.

Particulate respirator, grade N95 or higher

N95 or FFP2 respirator or higher Good breathability with design that does not collapse against the mouth (e.g. duckbill, cup-shaped)

Figure: Mask vs. Respirator

N95 vs. FFP3 & FFP2

The most commonly discussed respirator type is N95. This is an American standard managed by NIOSH – part of the Center for Disease Control (CDC). [34] Europe uses a "filtering face piece" score (FFP). This comes from EN standard 149:2001 – drafted and maintained by CEN (European Committee for Standardization).

Figure: Different types of Respirators commonly used

Respirator standard	Filter capacity(removes x% of all particles that are 0.3 microns in diameter or larger
FFP1	80%
FFP2	94%
N95	95%
FFP3	99.95%
N100	99.97%

Table 1: Filter capacity of different types of Respirators

Are N95/N100 actually better than FFP2/FFP3?

Whilst the specifications for the NIOSH (N95/N100) are marginally higher than FFP, that doesn't mean the respirators are any better. [34]

Can Surgical Masks Filter the Corona virus?

Whilst FFP2/FFP3 or N95/N100 are the gold standard as far as face protection goes, **what about surgical masks,** do they provide any protection? [35-36]

Surgical masks are **primarily** designed to protect vulnerable patients from medical professionals. Stopping the wearer from spreading their germs when coughing/sneezing/speaking. So they're designed to protect patients, **not** to protect the wearer. There isn't currently research available on the efficacy of surgical masks (or even respirators), for protecting wearers against the corona virus.

RECOMMENDATIONS FOR USAGE OF SURGICAL TRIPLE LAYER MASK/ RESPIRATORS

1. Asymptomatic individuals wearing masks of any type is not recommended
2. Wearing masks when they are not indicated results in unnecessary cost and a procurement burden especially during the time of an epidemic/pandemic
3. People with respiratory symptoms or who are taking care of COVID-19 patients at home should receive triple layer surgical masks. [57-59]
4. Respirators(N95, FFP2 or equivalent standard) should be reserved for aerosol gener ating procedures (Tracheal intubation, non-invasive ventilation, tracheostomy, bron choscopy and cardio pulmonary resuscitation) along with other personal protective equipments (PPE)
5. Health care workers who are involved in direct care of COVID -19 patients should use three layered surgical mask/ Respirator (only if available in sufficient quantity) and other PPE (eye protection, gloves and gowns/fluid resistant aprons)
6. Medical and Nursing staff involved in Intensive care unit should use Respirators(N95/FFP2 or an equivalent)
7. During the present pandemic situation respirators (e.g., N95, FFP2 or equivalent stan dard) can be used for an extended time, especially while caring for multiple patients who have the same diagnosis without removing it. Evidence shows that respirators maintain their protection when it is been used for extended periods. [57-59]
8. Always prioritize the use of N95 respirators for those personnel at the highest risk of contracting infections.
9. Most often an N95 mask can be used for up to 8hours on a continuous or intermittent basis and ideally it needs to be removed after that.
10. Avoid touching the inside of the respirator. If inadvertent contact is made with the inside of the respirator, perform hand hygiene.
11. Used mask should be considered as a potentially infected material and it should be disposed separately in an infectious waste disposable bag.
12. Health care system at every locality should adopt appropriate steps for disposal of used masks. [63]

Scrubs, tops

Tunic/tops, woven, scrubs, reusable or single use, short sleeved (tunic/tops), worn underneath the coveralls or gown.

Scrubs, pants

Trouser/pants, woven, scrubs, reusable or single use, short sleeved (tunic/tops), worn underneath the coveralls or gown.

Apron, heavy duty

Straight apron with bib, Fabric: 100% polyester with PVC coating, or 100% PVC, or 100% rubber, or other fluid resistant coated material, Waterproof, Sewn strap for neck and back fastening. Minimum basis weight: 300g/m2covering size: 70-90 cm (width) X 120-150cm (height) Reusable (provided appropriate arrangements for decontamination are in place)

Gown

Single use, disposable, length mid-calf.

Shoe cover, hood

Goggles, protective

Good seal with the skin of the face, Flexible PVC frame to easily fit with all face contours with even pressure, Enclose eyes and the surrounding areas, Accomodate wearers with prescription glasses, Clear plastic lens with fog and scratch resistant treatments, Adjustable band to secure firmly so as not to become loose during clinical activity, Indirect venting to avoid fogging, May be re-usable (provided appropriate arrangements for decontamination are in place) or disposable.

Less Protection More Protection

WHAT CAN YOU DO TO REDUCE RISK?
Social Distancing

Novel coronavirus are spread by people who have the virus coming in to contact with people who are not infected. The more you come in to contact with infected people, the more likely you are to catch the infection. Social distancing is infection control action that can be taken by public health officials to stop or slow down the spread of a highly contagious disease.

In addition to social distancing measures taken by governments, we can ourselves choose to reduce physical exposure to potentially sick people, for example:

- Exploring the option to work from home if your job allows for it.
- Avoiding large public gatherings such as sporting events. Or situations where you may come in to contact with crowds of people, for example in busy shopping malls.
- Interacting with people over the phone/video calls, instead of in person.

These types of steps may be an impediment to normal life. However the intention is that these will be a short term measure (not forever!).

A risk with a pandemic is that the initial spread is so quick that it overwhelms the health services. A key aim for any country should be to avoid that, and social distancing can help.

9D REGULAR HAND WASHING

The CDC recommends regular hand washing with soap and water for at least 20seconds.

Prioritize washing prior to eating and after being out.Regular hand washing dries the hands, which at an extreme, may make them vulnerable to infection. To mitigate this, regularly use a glycerin based moisturizer with pump or squeeze mechanism.

Alcohol Based Hand Sanitizer

– The CDC recommend that if soap and water are not available, use an alcohol-based hand sanitizer with **at least 60% alcohol.** Leave to air dry.

9E SANITIZE YOUR PHONE

Given how often we use our phones, this seems like the next logical priority to be sanitized. Using antibacterial wipes or alcohol swabs (typically 70% alcohol) to clean your phone and other items is a good option. If the antibacterial wipes claim to be able to kill the flu virus (H1N1) – that's a good sign they may be able to do similar for the corona virus. Once finished wiping, leave to air dry.

9F SANITIZE OTHER ITEMS YOU TOUCH REGULARLY, INCLUDING:

- Computer keyboard and mouse
- House and car keys
- Re-usable water bottles
- Car steering wheel
- Clothing pockets
- Door handles

9G KEEP YOUR IMMUNE SYSTEM HEALTHY

Examples of action you can take to maintain a healthy immune system:[37-38]

- **Sleep** – Get adequate, high quality sleep. For most people 'adequate' means 7-8 hours. It's no coincidence that "burning the candle at both ends" increases risk of illness. A 2004 literature review concluded that "sleep deprivation has a considerable impact on the immune response" and "should be considered a vital part of the immune system"
- **Exercise** – Exercise regularly, but don't overdo it. To quote a 2007 study on exercise and the immune system – "moderate exercise seems to exert a protective effect, whereas repeated bouts of strenuous exercise can result in immune dysfunction

9H VACCINES FOR SARS COV 2

- Altimmune's intranasal coronavirusvaccine
- INO-4800 by InovioPharmaceuticals
- mRNA-1273 vaccine byModerna
- Avian Corona virus Infectious Bronchitis Virus (IBV) vaccine by MIGAL and many more
- All vaccines are in developing stage only

9i IMPORTANT STEPS FOR PREVENTING TRANSMISSION IN THE COMMUNITY

- Diligent hand washing, particularly after touching surfaces in public. Use of hand sanitizer that contains at least 60 percent alcohol is a reasonable alternative if the hands are not visibly dirty.
- Respiratory hygiene (e.g.: covering the cough or sneeze).
- Use triple layer disposable surgical mask if you have any Respiratory symptoms.
- Avoiding crowds (particularly in poorly ventilated spaces) if possible and avoiding close contact with ill individuals. Also try to maintain a safe distance of 1 metres.
- Avoid handshakes, hugs and kisses
- Avoid non essential travels/gatherings
- Avoid holding on railings of steps
- May use pens for switching on lights in common areas, lift buttons
- At hospitals, avoid keeping patients files on the bed
- Use gloves
- Used mask and other personal protective equipments should be considered as a potentially infected material and it should be disposed separately in an infectious waste disposable bag.

10 Conclusion

- Corona virus disease 2019 (COVID-19) was reported as cluster of disease in China in December 2019
- It has since spread to all continents except Antarctica and WHO declared COVID-19 as a pandemic.
- Elderly persons with co-morbidities are more affected
- It spreads mainly via Respiratory droplets
- Pneumonia is the most common complication
- Severe cases have a mortality rate of 2.3 to 5%
- Presently there is no standardized treatment or vaccine available for COVID-19
- Containment and prevention is the best option

REFERENCES

1. World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 (Accessed on February 12, 2020).
2. World Health Organization. Novel coronavirus situation report -2. January 22, 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200122-sitrep-2-2019-ncov.pdf (Accessed on January 23, 2020).
3. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. N Engl J Med 2020; 382:970.17.
4. Kupferschmidt K. Study claiming new coronavirus can be transmitted by people with out symptoms was flawed. Science. February 3, 2020. https://www.sciencemag.org/news/2020/02/paper-non-symptomatic-patient-transmitting-coronavirus-wrong (Accessed on transmission during the incubation period. J Infect Dis 2020.
5. Bai Y, Yao L, Wei T, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. JAMA 2020.
6. Li Z, Yi Y, Luo X, et al. Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis. J Med Virol 2020.
7. Centers for Disease Control and Prevention. Interim Clinical Guidance for Management of Patients with Confirmed 2019 Novel Coronavirus (2019-nCoV) Infection, Updated February 12, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html (Accessed on February 14, 2020).
8. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl JMed 2020.
9. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020
10. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to person transmission: a study of a family cluster. Lancet 2020; 395:514.
11. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020.
12. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395:497.
13. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395:507. Wang D, Hu B, Hu C,
14. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf
15. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases

16. .Pediatric Pulmonol. 2020 Mar 5. doi: 10.1002/ppul.24718. [Epub ahead of print]Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Xia W1, Shao J1, Guo Y1, Peng X1, Li Z2, Hu D2.
17. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf
18. https://www.ecdc.europa.eu/en/case-definition-and-europe an-surveillance-human-infection-novel-coronavirus-2019-ncov
19. Vital Surveillances: The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51
20. https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics/
21. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf
22. PediatrPulmonol. 2020 Mar 5. doi: 10.1002/ppul.24718. [Epub ahead of print] Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Xia W1, Shao J1, Guo Y1, Peng X1, Li Z2, Hu D2.
23. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf
24. https://www.ecdc.europa.eu/en/case-definition-and-europe an-surveillance-human-infection-novel-coronavirus-2019-ncov
25. https://www.ecdc.europa.eu/en/case-definition-and-europe an-surveillance-human-infection-novel-coronavirus-2019-ncov
26. https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25727 Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis
27. https://pubs.rsna.org/doi/10.1148/radiol.2020200823. Performance of radiologists in differentiating COVID-19 from viral pneumonia on chest CT
28. https://link.springer.com/content/pdf/10.1007/s00134-020-05967-x.pdf. Severe SARS-CoV-2 infections: practical considerations and management strategy for intensivists. Lila Bouadma1,2, Francois Xavier Lescure2,3, Jean Christophe Lucet2,4, Yazdan Yazdanpanah2,3 and Jean Francois Timsit1,
29. Treatment of Middle East respiratory syndrome with a combination of lopinavir/ ritonavir and interferon-β1b (MIRACLE trial): statistical analysis plan for a recursive twostage group sequential randomized controlled trial Yaseen M. Arabi1,2* , Ayed Y. Asiri3
30. Ribavirin and Interferon Therapy for Critically Ill Patients With Middle East Respiratory Syndrome: A Multicenter Observational Study. Yaseen M. Arabi, 1 Sarah Shalhoub, 2

31. Ascorbic Acid, Corticosteroids and Thiamine in Sepsis (ACTS) protocol and statistical analysis plan: a prospective, multicentre, double-blind, randomised, placebo-con trolled clinical trial. Ari Moskowitz1,2, Tuyen Yankama2
32. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Manli Wang, Ruiyuan Cao
33. https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov)
34. N95 Respirators vs Medical Masks for Preventing Influenza Among Health Care Personnel – A Randomized Clinical Trial – Lewis J. Radonovich Jr, MD et al. – JAMA – Sept 2019
35. Surgical Mask vs N95 Respirator for Preventing Influenza Among Health Care Workers – A Randomized Trial – Mark Loeb et al. – JAMA – Nov 2009
36. Face Mask Use and Control of Respiratory Virus Transmission in Households – Mac Intyre et al. – Emerging Infectious Diseases Journal – Feb 2009
37. Sick and tired: does sleep have a vital role in the immune system? – Bryant et al. (2004)
38. Exercise and the Immune System – Brolinson (2007)
39. Persistence of corona viruses on inanimate surfaces and their inactivation with biocidal agents. G. Kampfa
40. Clinical Characteristics of Coronavirus Disease 2019 in China. W. Guan, Z. Ni. Yu Hu, W. Liang, C. Ou, J. He, L. Liu
41. Clinical Characteristics of Coronavirus Disease 2019 in China. W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, B. Du, L. Li, G. Zeng, K.-Y. Yuen, R. Chen
42. Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang ZJ. Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China. JAMA. 2020 Feb 14. doi: 10.1001/ja ma.2020.2131. [Epub ahead of print]]
43. First Case of 2019 Novel Coronavirus in the United States. Michelle L. Holshue,M.P.H., Chas DeBolt, M.P.H., Scott Lindquist, M.D., Kathy H. Lofy, M.D., John Wiesman, Dr.P.H., Hollianne Bruce, M.P.H
44. Evidence of SARS-CoV-2 Infection in Returning Travelers from Wuhan, China. Sebas tian Hoehl, M.D.Holger Rabenau, Ph.D
45. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect.2020 Mar;104(3):246-251. doi: 10.1016/j.jhin.2020.01.022.]
46. American Association for Bronchology and Interventional Pulmonology (AABIP) State ment on the Use of Bronchoscopy and Respiratory Specimen Collection in Patients with Suspected or Confirmed COVID-19 Infection. Momen M. Wahidi;* Carla Lamb, MD,* MD, MBA; Septimiu Murgu, MD.

47. Vitalograph: Hygiene Considerat ions for Spirometry. First published in Primary Care Today. 2011. [Last accessed on 5 Jun 2014]. pp. 1–3. Available from https://vitalo graph.com/resources/article/hygiene-considerations-for-spirometry .

48. Infection control in the pulmonary function test laboratory. Shweta Amol Rasam, Komalkirti Keshavkiran Apte,1 and Sundeep Santosh Salvi. Lung India. 2015 Jul-Aug; 32(4): 359–366.

49. 1-Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020. doi: 10.1056/NEJMoa2002032. 2-The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team.

50. National Health Commission of the People's Republic of China. Diagnosis and treat ment plan of novel coronavirus pneumonia (Version 7) [EB/OL]. (2020-03-04)[2020-03-05].http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294 a7dfe4cef80dc7f5912eb1989.shtml.

51. Ma HJ, Shao JB, Wang YJ, et al. High resolution CT features of novel coronavirus pneu monia in children[J]. Chin J Radiol, 2020, 54, [Epub ahead of print]. DOI: 10.3760/c ma.j.issn.1005-1201.2020.0002

52. Sztrymf B, Messika J, Mayot T, Lenglet H, Dreyfuss D, Ricard JD. Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: a prospective observational study. Journal of Critical Care 2012;27:324 e9–13.

53. (The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. The New England Journal of Medicine 2006;354:2564–75)

54. Dellinger RP, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008. Critical Care Medicine 2008; 36:296–327. http://www.survivingsepsis.org/about_the_Campaign/Documents/Final%2008% 20SSC%20Guidelines.pdf

55. Papazian L, Forel JM, Gacouin A, et al. Neuromuscular blockers in early acute respira tory distress syndrome. The New England Journal of Medicine 2010;363:1107–16

56. Sud S, Friedrich JO, Taccone P, et al. Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. Intensive Care Medicine 2010;36: 585–99

57. Beckman S, Materna B, Goldmacher S, Zipprich J, D'Alessandro M, Novak D, et al. Evaluation of respiratory protection programs and practices in California hospitals during the 2009-2010 H1N1 influenza pandemic. Am J Infect Control. 2013;41(11):1024-31. doi:10.1016/j.ajic.2013.05.006.

58. Janssen L, Zhuang Z, Shaffer R. Criteria for the collection of useful respirator perfor mance data in the workplace. J Occup Environ Hyg. 2014;11(4):218–26. doi:10.1080/15459624.2013.852282.

59. Janssen LL, Nelson TJ, Cuta KT. Workplace protection factors for an N95 filtering facepiece respirator. J Occup Environ Hyg. 2007;4(9):698–707. doi:10.1080/ 15459620701517764. 6

60. Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomat ic Patient. Sean Wei Xiang Ong, MBBS1; Yian Kim Tan, PhD2; Po Ying Chia, MBBS1; et al

61. https://www.bbc.com/news/world-asia-china-51395655

62. https://nypost.com/2020/03/13/second-newborn-baby-tests-positive-for-coronavirus/

63. Guidelines on use of masks for health care workers, patients and members of public. Ministry of health and family welfare. Government of India.

64. Kanne JP, Little BP, Chung JH, Elicker BM, Ketai LH. Essentials for Radiologists on COVID-19: An Update-Radiology Scientific Expert Panel. Radiology [Internet]. 2020;200527. Available from:http://www.ncbi.nlm.nih.gov/pubmed/32105562

65. Pan, Fen; Ye, Tianhe; Sun, Peng; Gui, Shan; Liang, Bo; Li, Lingli; Zheng, Dandan; Wang, Jiazheng; Hesketh, Richard; Yang, Lian; Zheng C. Time Course of Lung Changes On Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. Radiology. 2020;77(8):1–15.

66. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis [Internet]. 2020;3099(20):1–10. Available from: http://ww w.ncbi.nlm.nih.gov/pubmed/32105637

67. Buonsenso D, Piano A, Raffaelli F, Bonadia N. Point-of-Care Lung Ultrasound findings in novel coronavirus disease-19 pnemoniae : a case report and potential applications during COVID-19 outbreak. Eur Rev Med Pharmacol Sci. 2020;24:2776–80.

68. Peng QY, Wang XT, Zhang LN, Critical C, Ultrasound C, Group S. Findings of lung ultra sonography of novel corona virus pneumonia during the 2019 – 2020 epidemic. Inten sive Care Med [Internet]. 2020;(87):6–7. Available from: https:// doi.org/10.1007/s00134-020-05996-6