Novel Corona –A review

Introduction

The 2019-novel coronavirus (2019-nCoV) has been declared a world pandemic by WHO on 11 March 2020. Clinical symptoms of 2019- nCoV have mostly resembled that of severe acute respiratory syndrome coronavirus (SARS-CoV) of 2003.

Severe acute respiratory syndrome coronavirus (SARS-CoV-2), initially named novel coronavirus or 2019-nCoV, is a single-stranded RNA virus which forms one of the seven coronaviridae - 229E, OC43, NL63, HKU1, severe acute respiratory syndrome coronavirus (SARS-CoV), and Middle East respiratory syndrome coronavirus (MERSCoV)) - now known to infect humans.

It is the virus responsible for causing coronavirus disease 2019 (COVID-19), a type of lower respiratory tract infection with the potential to cause severe and possibly fatal atypical novel coronavirus (2019-nCoV) – infected pneumonia (NCIP) in humans

Both shared the same receptor, angiotensin converting enzyme 2 (ACE2).

Therefore, this virus was named SARS-CoV-2. By 28 March 2020, a total of 593 735 SARS-CoV-2 infected cases have been confirmed in 200 countries worldwide. In addition to the respiratory system involvement, recent evidence has shown that SARS-CoV-2 can affect other organ systems including nervous, vascular, digestive, urinary, haematological and so on.

The pathological findings confirmed the nature of multiorgan damaged by SARS-CoV-2, which include pulmonary lesion and cerebral oedema, microvascular steatosis and thrombosis.

Neurological symptoms can be trivial or non-specific at the early stage of the COVID-19 infected patients, which have often been delayed and misdiagnosed and led to inappropriate management. These patients then become silent contagious sources or 'virus spreaders'. Although neurological involvement is uncommon in patients with COVID-19, it can be seen in those with severe infection.

The first human coronavirus was isolated from the nasal discharge of patients in 1965. In humans, CoVs infections primarily involve the upper respiratory and gastrointestinal tracts. Under the electronic microscope, there are many evenly arranged protrusions on the

surface of viral particles. The entire virus particle resembles a ‘crown’ of a medieval European emperor. Hence, it was given the name of ‘coronavirus’.

A coronavirus particle is usually enclosed by an envelope, and its membrane surface has three proteins: spike (S), envelope (E) and membrane (M). Protein spike (S), projecting from the virus membrane and resembling a crown, is the key structure for its infectivity and pathogenicity. These spikes can have open access can recognise and bind to receptors on the surface of host cells and subsequently invade the host cells.

Overview

Severe acute respiratory syndrome (SARS) is a contagious and sometimes fatal respiratory illness. SARS first appeared in China in November 2002. Within a few months, SARS spread worldwide, carried by unsuspecting travelers.

SARS showed how quickly infection can spread in a highly mobile and interconnected world. On the other hand, a collaborative international effort allowed health experts to quickly contain the spread of the disease. There has been no known transmission of SARS anywhere in the world since 2004.

Etymology

The name "coronavirus" is derived from Latin *corona*, meaning "crown" or "wreath", itself a borrowing from Greek κορώνη *korṓnē*, "garland, wreath".

The name was coined by June Almeida and David Tyrrell who first observed and studied human coronaviruses. The word was first used in print in 1968 by an informal group of virologists in the journal *Nature* to designate the new family of viruses.

The name refers to the characteristic appearance of virions (the infective form of the virus) by electron microscopy, which have a fringe of large, bulbous surface projections creating an image reminiscent of the solar corona or halo. This morphology is created by the viral spike peplomers, which are proteins on the surface of the virus.

Classification

Phylogenetic tree of coronaviruses

The scientific name for coronavirus is *Orthocoronavirinae* or *Coronavirinae*.

Coronaviruses belong to the family of *Coronaviridae,* order *Nidovirales,* and realm *Riboviria.* They are divided into **alphacoronaviruses** & **betacoronaviruses** which infect mammals – and gammacoronaviruses and deltacoronaviruses which primarily infect birds.

- Genus: ***Alphacoronavirus***; type species: *Alphacoronavirus 1* (TGEV)
    - Species: *Alphacoronavirus 1,*
    - *Human coronavirus 229E*,
    - *Human coronavirus NL63*,
    - *Miniopterus bat coronavirus 1*, *Miniopterus bat coronavirus HKU8*,
    - *Porcine epidemic diarrhea virus*, *Rhinolophus bat coronavirus HKU2*, *Scotophilus bat coronavirus 512*
    -
- Genus ***Betacoronavirus***;[55] type species: *Murine coronavirus* (MHV)
    - Species: *Betacoronavirus 1* (*Bovine Coronavirus*, *Human coronavirus OC43*), *Hedgehog coronavirus 1, Human coronavirus HKU1*, *Middle East respiratory syndrome-related coronavirus, Murine coronavirus*, *Pipistrellus bat coronavirus HKU5*, *Rousettus bat coronavirus HKU9*, *Severe acute respiratory syndrome-related coronavirus* (*SARS-CoV*, *SARS-CoV-2*), *Tylonycteris bat coronavirus HKU4*
    -
- Genus ***Gammacoronavirus***;] type species: *Avian coronavirus* (IBV)
    - Species: *Avian coronavirus, Beluga whale coronavirus SW1*
- Genus ***Deltacoronavirus***; type species: *Bulbul coronavirus HKU11*
    - Species: *Bulbul coronavirus HKU11*, *Porcine coronavirus HKU15*

ZOONOSIS

Corona viruses can, however, cause severe disease in animals, and that's why scientists suspected that the SARS virus might have crossed from animals to humans. It now seems likely that that the virus evolved from one or more animal viruses into a new strain.

SARS is caused by a coronavirus (SARS-CoV) that exists in bats and palm civets in Southern China.

How deadly is COVID-19?

Most patients have only mild symptoms and the death rate appears to be between 2% and 5%. By comparison, seasonal flu has an average mortality rate of about 0.1%, but is highly infectious — with up to 400,000 people dying from it each year.

The mortality rate associated with COVID-19 may be "considerably less than 1%," instead of the 2% reported by some groups, write Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases, and colleagues in an editorial published February 28 in the *New England Journal of Medicine*.

The editorial appeared alongside a report by Wei-jie Guan, PhD, and colleagues that characterized 1099 patients with laboratory-confirmed COVID-19 from 552 hospitals in China through January 29, 2020. Guan is with the Guangzhou Institute of Respiratory Health, First Affiliated Hospital of Guangzhou Medical University in China.

Is the Corona virus same as SAARS?

No. The virus that causes COVID-19 and the one that caused the outbreak of Severe Acute Respiratory Syndrome (SARS) in 2003 are related to each other genetically, but the diseases they cause are quite different.

Severe Acute Respiratory Syndrome (SARS)

Virus is SAARS-Cov-2

Emerged in southern China (Guangdong) in 2002

Spread to 30 countries

Cases: 8473

Deaths: 813

Fatality rate: 9.5%

Route of transmission

Although SARS-CoV-2, SARS and Middle East respiratory syndrome corona viruses belong to the same large family of corona viruses, their genetic characteristics are significantly different. For COVID-19, transmission through respiratory droplets and contact are the main routes of transmission.

In aerosols the virus can survive for about af an hour then trickles down on surfaces.

On Cardboard surface it can last upto 4 hrs, but maximum survival is over plastic and copper where it can survive upto even 72 hrs.

One important issue to be remembered here is even if one virus enters the body (theoretically only possible, as in droplets plenty of viruses are present) it immediateately in seconds multiply and hence no particular infective dose can be predicted. However here 2 points are important:

1)If less dose enters the manifestations are less

2)If more dose enters, as in healthcare workers, manifestations are more.

But in whom less dose enters and later they are somehow exposed to a larger dose their manifestations will be extremely severe due to relative lack of immunity in past.

It has also been confirmed that live virus and virus nucleic acid can be detected **in human stool**. Thus, we speculated that the digestive tract might be another transmission route. Moreover, SARS-CoV-2 can be transmitted through aerosols under a prolonged exposure in a relatively closed environment. Clinical characteristics and manifestations COVID-19 is highly contagious and has a long latency period. The incubation period is generally 3–14 days, but the most extended period was reported to be 24 days. Local news in Wuhan has reported a case of asymptomatic SARS-CoV-2 infection that had a 38-day incubation period. People who have visited the epidemic area or have a contact history with patients or suspected cases should consider self-quarantine and closely monitor body temperature and related symptoms along with Systemic and respiratory symptoms.

Patients with COVID-19 often have a fever, dry cough and fatigue as the primary manifestations, and in some patients, pharyngeal pain, abdominal pain, diarrhoea and

conjunctivitis are common. **Therefore, if a patient has any of these symptoms, even if the symptoms are mild, testing for COVID-19 is recommended.**

Symptoms

SARS usually begins with flu-like signs and symptoms — fever, chills, muscle aches, headache and occasionally diarrhoea. After about a week, signs and symptoms include:

- Fever of 100.5 F (38 C) or higher
- Dry cough
- Shortness of breath

- Most patients with COVID-19 have a low grade fever, but a few would have high temperature. It is worth noting that some patients may have difficulty breathing*. In some patients, their lung CT scans may have signs of severe damage from the infection, but their temperature remains within normal limit.* In these patients, feeling weak or exhaustion was their main complaint.
- **In other patients, their temperature may drop, but their pneumonia actually progressed. Therefore, to judge the progression of the disease, lung CT is essential**

In more severe cases infection can cause pneumonia, severe acute respiratory syndrome, and even death. Many people with SARS develop pneumonia, and breathing problems can become so severe that a mechanical respirator is needed. SARS is fatal in some cases, often due to respiratory failure.

Other possible complications include heart and liver failure. The period within which the symptoms would appear is 2-14 days.

In addition to the attacking the alveoli (air sacs) in the lungs, the virus also infects other organs in the body, causing kidney failure, inflammation of the heart sac (pericarditis), or severe systemic bleeding from disruption of clotting system (disseminated intravascular coagulation), reduced lymphocyte cell counts (lymphopenia), inflammation of the arteries (**vasculitis**), and inflammation of the gut with diarrhoea.

People with compromised immune systems such as severe rheumatoid arthritis or organ transplantation may not experience respiratory symptoms but can have fever or diarrhoea.

PREVENTION

If SARS infection is suspected, follow these safety guidelines if you're caring for someone who may have a SARS infection:

- Wash your hands. Clean your hands frequently with soap and hot water or use an alcohol-based hand rub containing at least 60% alcohol.

- Wear disposable gloves. If you have contact with the person's body fluids or feces, wear disposable gloves. Throw the gloves away immediately after use and wash your hands thoroughly.

- Wear a surgical mask. When you're in the same room as a person with SARS, cover your mouth and nose with a surgical mask. Wearing eyeglasses also may offer some protection.Ordinary surgical masks,if used shoul not be re-used but n-95 masks can be sterilised by ETO for reuse.

- Wash personal items. Use soap and hot water to wash the utensils, towels, bedding and clothing of someone with SARS.

- Disinfect surfaces. Use a household disinfectant to clean any surfaces that may have been contaminated with sweat, saliva, mucus, vomit, stool or urine. Wear disposable gloves while you clean and throw the gloves away when you're done.

- Diet. It has been seen that a low carbohydrate diet, with high content of salads, fruits (containing Vitamin-C), vitamin –D supplements with calcium and in non-veg, chicken soups improve immunity. In China, they have found certain herbs which also improve immunity. Overall a healthy balanced diet, which may not worsen risk factors like diabetes or hypetension or hypercholeteolomia and improve immunity is advisable.

- **Extensive laboratory tests should be requested to confirm diagnosis of COVID19.**

- **RT-PCR should be performed in isolated samples of throat swabs, sputum, stool, and blood samples.**

Follow all precautions for at least 10 days after the person's signs and symptoms have disappeared.

Keep children home from school if they develop a fever or respiratory symptoms within 10 days of being exposed to someone with SARS.

SPREAD

Most respiratory illnesses, including SARS, spread through droplets that enter the air when someone with the disease coughs, sneezes or talks. Most experts think SARS spreads mainly through close personal contact, such as caring for someone with SARS. Most respiratory illnesses, including SARS, spread through droplets that enter the air when someone with the disease coughs, sneezes or talks. Most experts think SARS spreads mainly through close personal contact, such as caring for someone with SARS. **The virus may also be spread on contaminated objects — such as doorknobs, telephones and elevator buttons.**

RISK FACTORS

What are risk factors for SARS?

SARS-CoV can infect a person regardless of their health status or age group. However, it was clear that some people were at increased risk during the 2002-2003 outbreaks. This included people over the age of 50 (some reported mortality rates of about 50%), **pregnant** women, and those with underlying diabetes, heart disease, or liver disease. A major risk factor is simply close association with any person infected with SARS-CoV since the virus can be spread through droplets sprayed into the air by coughing, sneezing, **or even talking.**

Other risk factors include the following:

- Recent travel to mainland China, Hong Kong, or Taiwan or close contact with ill people with a history of recent travel to these areas

- Employment in an occupation at risk for SARS-CoV exposure, including a health care worker with direct contact with a patient having SARS-CoV, or a worker in a laboratory that contains live SARS-CoV

How do health care professionals diagnose SARS?

SARS-CoV is detected using enzyme-linked immunoassays (EIA) or reverse transcriptase polymerase chain reaction (RT - PCR) tests, which are available through the CDC. These tests are performed on respiratory secretions or blood.

These tests are performed only when the patient's history makes SARS likely and usually in consultation with infectious-disease doctors, public-health authorities, and the Centres for Disease Control and Prevention. If a test is positive, it will be confirmed by the CDC. Other tests may be abnormal, but they are not specific for SARS. The chest X-ray shows pneumonia, which may look patchy at first.

White blood cells and platelet (clotting cell) counts in the blood are usually decreased.

Pulmonary progress on axial chest CT.

(A) During the first few days, a single lesion;

(B) during the first week, multiple lesions;

(C) during the first and second week, nearly 50% involvement of bilateral lungs;

(D) after the second week, diffuse lesion of bilateral lungs.

Novel- Corona - High Risk Groups

Current reports suggest that all demographics of the global population could be susceptible to infection of COVID-19, however there are some groups that are at higher risk of severe disease .

According to the CDC, older adults –

1]Age over 65 years of age - are more at risk of severe disease than younger people.

2]Patients with serious chronic underlying medical conditions, namely cardiovascular disease, *diabetes*, cancer (especially of the lung), Chronic Liver or Kidney disease.

3] Chronic obstructive pulmonary disease, interstial lung disease etc.

4] *Hypertension*

5] History of smoking

6] **Those patients with a higher maximum body temperature on admission**.

7] Occupational risks have also been identified by various authorities. During the preliminary stages of the COVID-19 outbreak, employees of seafood and wet animal wholesale markets in Wuhan were most at risk of contracting the virus in addition to any customers who had visited these markets.

8] This was closely followed by the subsequent epidemic which posed a high risk to healthcare workers who regularly came into contact with patients with suspected COVID-19. As a result, healthcare workers with pre-existing risks such as an increased age or chronic respiratory disease are advised to ask colleagues who are not in high risk groups to care for patients with potential COVID-19 where possible.

There is currently no evidence to suggest that either sex is more at risk of severe disease, nor that children are more susceptible to infection.

Differential diagnosis

1.Other viral respiratory infections caused by SARS virus, influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus and metapneumovirus. These patients present with similar clinical presentations, except for normal or decreased leukocyte count in some patients.

2.Patients may also present with pneumonia due to bacterial causes, which may be accompanied by high fever, cough and moist rales (crepitations) on auscultation.

3.Mycoplasmal pneumonia is another common type of false presentation. Chest X-ray images for such patients may indicate reticular shadows and small patchy or large consolidations. Mycoplasma-specific IgM are helpful for this differential diagnosis.

Epidemiological exposure and blood or sputum culture will be helpful for ensuring the correct diagnosis of COVID-19 .

Management:

1] Prevention

Although spread via an airborne route, *air disinfection of communities* (as is done in protozoal infections like malaria or other viral illness like dengue) is currently not known to be effective in halting further viral transmission and spread. Human-to-human transmission should be limited in order to prevent transmission amplification events. The use of personal protective equipment should be carefully considered since resources are currently in short supply. Surgical masks in particular are utilised widely within the general population, but have not been clinically proven to reduce or prevent the acquisition of COVID-19.

Within the hospital setting, however, high-filtration masks including N95, goggles, and gowns / PPE should be worn by healthcare professionals working in direct contact (within 1-2 metres) of infected patients.

If an infected individual has been identified, rapid isolation and the administration of optimised care should be provided. Suspected patients should also be given a medical mask and placed in an isolation room/ CALLED Bay unit in most private settings if available. Wherever possible, the use of adequately ventilated single rooms when performing aerosol-generating procedures (eg nebulisation) should be employed.

All patients should be instructed to cover their nose and mouth during coughing or sneezing with tissue.

Hand hygiene after contact with respiratory secretions should be enforced. No specifications regarding sanitisers are required, simple regular hand-washes are enough.

If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs, and thermometers) for suspected cases, and avoid contaminating environmental surfaces (e.g. door handles).

Lockdown

In mid-January of 2020, Chinese authorities implemented an array of unprecedented containment strategies, including restriction of human movement, **Hubei province lockdown, and the suspension of flights and trains.** These time-critical measures have contributed grossly to the decline in reported cases, and the WHO has since congratulated China on a “unique and unprecedented public health response that reversed escalating cases”. Moreover, between 16th and 30th January 2020 the number of people infected by an individual host dropped to an estimated 1.05, **and data from other cities having**

implemented lockdown measures reported approximately 37% fewer cases in comparison to cities without.

Notably, the implementation of control measures a week earlier could have prevented approximately 67% of all Chinese cases according to a model simulation from the University of Southampton, UK.

Non-pharmaceutical interventions (NPIs) like this have been addressed in an attempt to suppress and/or mitigate the disease, with suppression defined as a reduction in the Reproduction Number (R0) - the average number of individuals one infected person can infect - to less than 1, and mitigation defined as a reduction of the effects of the pandemic on health, ultimately reducing mortality and morbidity.

Lab tests

Key laboratory results on admission include leucocytes below or above the normal range; neutrophils above the normal range; lymphocytes, haemoglobin and platelets below the normal range.

Key liver findings may include elevated alanine aminotransferase, aspartate aminotransferase.

C-reactive proteinelevation, creatine kinase, lactate dehydrogenase, blood urea nitrogen, and serum creatinine levelsshould be regularly monitored. **Regarding the infection index, procalcitonin levels may be above the normal range**.(surprisingly similar to bacterial infections).

Radiological findings may also aid the diagnosis of pneumonia in virally infected patients. Bilateral and multi lobe lung involvement were common in over 75% and 71% of adult patients, respectively.

Covid testing

Blood

Bio-Medomics has developed and launched one of the world's first rapid point-of-care lateral flow immunoassays to aid in the diagnosis of coronavirus infection. The test detects early marker and late marker, IgM/IgG antibodies in human finger-prick (capillary) or venous whole blood, serum, and plasma samples.

Although critically important, *PCR tests are only positive during the brief window of acute infection, after which they become negative.* And while serology tests are not as effective as PCR early in acute infection, they are able to detect COVID-19 antibodies for a prolonged period of time after disease resolution, which enables identification of prior infection. **Knowledge of prior infection is epidemiologically important.**

BioMedomics Rapid IgM-IgG Combined Antibody Test for COVID-19 is immunochromatography based. The test card contains Colloidal gold-labeled recombinant novel coronavirus antigen and quality control antibody colloidal gold marker, two detection lines (G and M lines) and one quality control line (C) fixed on a nitrocellulose membrane. M is fixed with monoclonal anti-human IgM antibody for detecting the novel coronavirus IgM antibody. G is fixed with monoclonal antihuman IgG antibody for detecting the novel coronavirus IgG antibody. The quality control antibody is fixed on the C line. When an appropriate amount of test sample is added to the sample well of the test cassette, the sample will move forward along the test card via capillary action. If the sample contains IgM antibody, the antibody will bind to the colloidal gold-labeled novel coronavirus antigen.

The antibody/antigen complex will be captured by the anti-human IgM antibody immobilized on the membrane, forming a red M line and indicating a positive result for the IgM antibody. If the sample contains IgG antibodies, the antibody will bind to the colloidal gold-labeled novel coronavirus antigen and the antibody/antigen complex will be captured by the antibody immobilized on the membrane, forming a red G line and indicating a positive result for the IgG antibody. If neither antibody is present, a negative result is displayed. However false negativity is common in this method.

Throat swab tests are done and remains the gold standard, (discussedealier).

Many different companies provide different method of collection.

CentoSwab™ (Germany) has certain Key Benefits:

- Extensively validated with patient and control samples for the detection of SARSCoV2 RNA
- Sterilized, ready to use swabs and collection tubes

- Medical device class I – CE labeled
- Sensitivity of ≤ 5 virus particles as demonstrated with validated SARSCoV2 RT-PCR assay
- Easy logistics – can be sent without stabilization buffer

Strict social isolation and distancing measures and include:

1. *Case isolation at home*: Symptomatic cases to remain at home for 7 days which is expected to reduce the number of contacts outside the household by 75% during this timeframe.All forms of social contact must be avoided by symptomatic individuals.

2. *Voluntary home quarantine*: If a symptomatic case is identified in the household, the entire household must remain at home for 14 days. This is thought to decrease contacts outside of the household by 75% and household contact to increase two-fold.

3. *Social distancing* for those above 70 years old: Individuals over 70 years of age are to practice social distancing i.e. must maintain a **2 meter distance** from other individuals when possible and to avoid gatherings or congregations. This measure is targeted to reduce contacts by 50% in the workplace and decrease other contacts by 75%, while inadvertently increasing household contacts by 25%.

4. *Social distancing for the entire population*: All individuals are to practice social distancing as described above, this way reducing all household contacts by 75% and workplace contacts by 25%. School contact rates remain the same and household contacts increase by 25%.

Non-essential use of public transport must be avoided and, if possible, arrangements to work from home should be made. Individuals should use remote technology to keep in touch with friends and family, as all large and small gatherings must be avoided. Telephone and online services should be used to contact healthcare professionals and other essential services.

5. ***Closure of schools and universities***: All schools to remain closed and only 25% of universities to remain open, in essence increasing household contact for families of students by 50% and community contacts by 25% during the time of closure **for a duration of 5 months**, with maximum effects felt if all four interventions plus complete lockdown (i.e. individuals prevented from going to work) are implemented.

6. Additionally, strict hand washing habits and respiratory hygiene must be followed by individuals to curb the spread of the respiratory viruses, including COVID-19. Of note, Ferguson et al. warn that lifting the measures in the absence of a vaccine is likely to lead to a second peak of infection due to the absence of or insufficient herd immunity, with cases reaching the predicted figures in the no-intervention scenario mentioned above. In order to minimise this effect, social distancing policies must be in place until a vaccine is made readily available- a timeframe of at least 18 months.

7.As a response to this predicted, prolonged period of social distancing, the study examined an 'adaptive triggering' strategy with 'on' and 'off' thresholds 'On' triggers are to include the implementation of social distancing and closures of schools and Universities. Case isolation and household quarantine are to be implemented throughout the on/off periods.

Supportive Management

Supportive management received by a patient is dependent upon the observed severity of disease, feasibility of quarantine, and possible need for hospitalisation. For asymptomatic neonates and young children with suspected COVID-19 infection, monitoring and supportive care in a quarantined ward are essential. Vital observations including heart rate, respiration rate, SpO2 should be closely monitored. Neonatal feeding should be considered if the mother is COVID-19 positive. For symptomatic neonates, medical management and intervention are necessary.

For adults with mild infection - typically characterised by an uncomplicated illness with absence of a severe acute respiratory infection (SARI) - management at home is deemed appropriate and a patient may be isolated in an outpatient setting. Key aspects of delivered care involve monitoring for any clinical deterioration that may require hospitalisation as well as preventing the transmission to other people in the household.

For patients with severe disease

WHO defines early supportive therapy and monitoring as follows:

Intravenous Fluid Administration

● Use conservative fluid management in patients with SARI with no evidence of shock. Treat carefully with IV fluids as aggressive resuscitation can impact oxygenation where mechanical ventilation availability is limited.

Oxygen Therapy

● Provide supplemental oxygen therapy immediately if patients present with SARI, hypoxaemia or shock. Give oxygen therapy at 5L/min to reach target SpO2 of at least 90% in non-pregnant adults (over 92% in pregnant patients).

Children with severe breathing difficulties should have a target SpO2 of over 94%.

● Closely monitor patients with SARI in case of rapid respiratory failure or sepsis and intervene immediately.

This is of utmost importance for patients with COVID-19. **Patients with increased work of breathing or hypoxemia despite oxygen therapy may be developing hypoxemic respiratory failure seen in ARDS. Clinicians should consider mechanical ventilation at this point.**

● Appreciate a patient's co morbidities to enable management to be tailored and prognosis realised. Communicate this early with both the patient and relatives.

Corticosteroids ● Routinely administer corticosteroids in the treatment of viral pneumonia unless in a clinical trial or if steroids are indicated for another condition.

Their use in studies on influenza have been found to exacerbate the infection and increase mortality rates.

Management of critical COVID- Admission to ICU With 5% of all COVID-19 cases becoming seriously or critically unwell and 20-30% of hospitalised patients requiring intensive care support, it is imperative that up-to-date guidelines are in place to aid management.

Patients with failing standard oxygen therapy are likely to require advanced oxygen therapy or ventilatory support.

With hospital admissions overwhelming healthcare systems worldwide, the National Institute of Health and Care Excellence (NICE) has published an algorithm to ensure appropriate ICU admissions. Factors taken into consideration when making such decisions are age over sixty-five, frailty - accessed via the Clinical Frailty Scale (CFS) - and co morbidities.

Special considerations should be made in patients with long-term disabilities, learning disabilities and autism. In such cases an individual assessment of frailty must be performed.

Critical care treatment should be withdrawn when the outcomes set at initiation of treatment are not reached and the patient fails to improve. Decisions must be communicated with the patient when possible and their family, carers and/or independent mental capacity advocate, if appropriate.

Non-invasive ventilation (NIV) Initial reports did not favour the use of NIV in COVID-19, over fears of large tidal volumes and high transpulmonary pressures causing further lung damage. NIV methods - continuous positive airway pressure (CPAP) or Bilevel Positive Airway Pressure (BiPAP)- were also not recommended as they are aerosol-generating medical procedures and therefore increase the risk of spread of COVID-19.

There is now emerging evidence to support CPAP use during the pandemic.

Reports from Italy and China claim that many patients benefited from receiving non-invasive mechanical ventilation. Specifically in Italy, 50% of patients who received CPAP did not require invasive ventilation.

The WHO recommends that patients receiving CPAP should be supervised by experienced clinicians who are able to perform endotracheal intubation if the patient fails to improve or rapidly deteriorates. Teams have adapted the existing CPAP model making it better suited for mass production. This will make the machines readily available for COVID-19 patients.

National Health Service (NHS) England has specified that CPAP should be used for hypoxaemic respiratory failure and BiPAP for hypercapnic states in cases of acute on chronic respiratory failure.

Indications include : ● As a ceiling of care option ● In an attempt to avoid intubation ● In an attempt to aid extubation

Endotracheal Intubation

If endotracheal intubation is deemed appropriate, the WHO recommends endotracheal intubation to be performed by an experienced clinician using protective equipment.

● Preoxygenate the patient with 100% Fi02 for 5 minutes using a face mask, bag-valve mask, High-flow nasal oxygen (HFNO) or Non-invasive ventilation (NIV) prior to attempting intubation. Invasive Mechanical Ventilation Summation of evidence from a recent review by King's College Hospital NHS Trust as well as guidelines issued by the WHO conclude that severe cases requiring mechanical ventilation may benefit from the following principles:

1) Usage of low tidal volumes (4-8 ml/kg predicted body weight (PBW)) and target plateau pressure 90%.

Settings for Positive End-Expiratory Pressure (PEEP), based on the required Fraction of Inspired Oxygen (FiO2) derived from the ARDS net trial.

3) Early airway pressure release ventilation should be considered in certain patients.

4) **Consideration of early prone ventilation in patients where there is no improvement observed after twelve hours of ventilator optimisation (i.e. PaO2/**

In paediatric patients, the following criteria for rapid respiratory rate should be followed for diagnosis of COVID-19 associated pneumonia: ≥60 times/min for less than 2 months old; ≥50 times/min for 2–12 months old, ≥40 times/min for 1–5 years old, ≥30 times/min for >5 years old (after ruling out the effects of fever and crying) In paediatric patients, the following criteria for rapid respiratory rate should be followed for diagnosis of COVID-19 associated pneumonia: ≥60 times/min for less than 2 months old; ≥50 times/min for 2–12 months old, ≥40 times/min for 1–5 years old, ≥30 times/min for >5 years old (after ruling out the effects of fever and crying) the following criteria for rapid respiratory rate should be followed for diagnosis of COVID-19 associated pneumonia: ≥60 times/min for less than 2 months old; ≥50 times/min for 2–12 months old, ≥40 times/min for 1–5 years old, ≥30 times/min for >5 years old (after ruling out the effects of fever and crying) In paediatric patients, the following criteria for rapid respiratory rate should be followed for diagnosis of COVID-19 associated pneumonia: ≥60 times/min for less than 2 months old; ≥50 times/min for 2–12 months old, ≥40 times/min for 1–5 years old, ≥30 times/min for >5 years old (after ruling out the effects of fever and crying)

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3) 3) Early airway pressure release ventilation should be considered in certain patients.
4) Consideration of early prone ventilation in patients where there is no improvement observed after twelve hours of ventilator optimisation (i.e. PaO2/FiO2)

When does a patient declared cured

Recovery and clearance of the virus is thought to be achieved when ≥2 negative oral swabs are confirmed in an infected individual. Emerging evidence, however, has speculated the complete clearance of the virus in such cases as anal swabs and blood cultures may remain positive despite having negative oral swabs and supports that the main modes of spread of the virus include respiratory droplets, bodily fluids, fecal-oral, direct contact, and transmission through environmental surfaces.

Hence even after the patient is declared cured should stay in home isolation for about 10 days, as per some studies.

Current evidence supports that there is no vertical transmission of the virus (mother to foetus).

Drug trials – Treatment options

Remdesivir most promising COVID-19 drug, say researchers.

A review of potential COVID-19 therapeutics revealed that the most effective are likely to be those directly targeting SARS-CoV-2, such as remdesivir and tilarone.

According to the authors, SARS-CoV-2 is easily transmissible because Spike (S) proteins on the surface of the virus bind exceptionally efficiently to the angiotensin-converting enzyme 2 (ACE2) on the surfaces of human cells. One clinical study is already underway, testing if recombinant ACE2 can act as a decoy, binding the S proteins and preventing SARS-CoV-2 infecting cells in patients with severe COVID-19.

Onearticle suggests the most promising COVID-19 antiviral is remdesivir, which gets incorporated into viral RNA and prevents it being synthesised, halting viral replication. Remdesivir inhibited SARS-CoV-2 replication in laboratory studies and was tested in one patient with COVID-19 in US. The patient's symptoms improved following intravenous remdesivir administration; however, more clinical data is required before the drug can be approved for use.

Tilarone is a broad-spectrum antiviral that may also be active against SARS-CoV-2. The synthetic small molecule is used in some countries, including Russia and neighbours, to treat several viruses, including acute respiratory viral infection, influenza and hepatitis. Other studies suggest tilarone may be active against Middle Eastern Respiratory Syndrome (MERS-CoV); however, the studies do not meet US Food and Drug Administration (FDA) standards for safety.

Plasma transfusion

A further treatment option currently being explored, according to the authors, is the transfusion of blood from a recovered COVID-19 patient into someone with an active viral infection. This has primarily been used for patients in critical condition as it has a lack of high quality randomised clinical trial data to back up its efficacy. Several clinical trials investigating its effectiveness and safety against COVID-19 are now in progress.

Use of Hydroxychloroquine and Chloroquine During the COVID-19 Pandemic: What Every Clinician Should Know

Jinoos Yazdany, MD, MPH; Alfred H.J. Kim, MD, PhD

Could the old generic malaria drug hydroxychloroquine (*Plaquenil*, Sanofi-Aventis, among others), which is also used for the treatment of rheumatic disease, be an essential treatment for COVID-19?

This hypothesis, put forward by some, including Professor Didier Raoult of the IHU Méditerranée Infection in Marseille, **was dismissed by other eminent infectious disease specialists and dismissed as fake news recently by the Ministry of Health.**

Cause:

Plaquenil has been shown to have the side effect of sudden unexplained death.

In the desperate search to find effective treatments for coronavirus disease 2019 (COVID-19), 2 generic drugs, used largely by rheumatologists and dermatologists to treat immune-mediated diseases, have entered the spotlight. The antimalarials hydroxychloroquine (HCQ) and chloroquine (CQ) have demonstrated antiviral activity against severe acute respiratory syndrome–coronavirus 2 (SARS–CoV-2) in vitro **(not in vivo) and in small, poorly controlled or uncontrolled clinical studies (1–3). Normally, such research would be deemed hypothesis-generating at best**.

Data to support the use of HCQ and CQ for COVID-19 are limited and inconclusive. The drugs have some in vitro activity against several viruses, including coronaviruses and influenza, but previous randomized trials in patients with influenza have been negative.

In COVID-19, one small nonrandomized study from France(discussed elsewhere in *Annals of Internal Medicine*) demonstrated benefit **but had serious methodological flaws, and a follow-up study still lacked a control group.** Yet, another very small, randomized study from China in patients with mild to moderate COVID-19 **found no difference in recovery rates** . *Sadly, reports of adverse events have increased, with several countries reporting poisonings and at least 1 death reported in a patient* who drank fish tank cleaner because of its CQ content. **Antimalarial drugs can cause ventricular arrhythmias, QT prolongation, and other cardiac toxicity, which may pose particular risk to critically ill persons.**

Given these serious potential adverse effects, the hasty and inappropriate interpretation of the literature by public leaders has potential to do serious harm. At this time of crisis, it is our ethical obligation as physicians and researchers to organize and refer patients to

expedited, well-performed randomized trials that can clarify if, when, and for whom antimalarial medications are helpful in COVID-19. As of this writing, 10 such trials are under way, and information should be forthcoming within weeks.

Inclusion Criteria for use of Cloroquin / Hydroxychoroquin :

Presently based on non randomised trials and clinical experience:

- Household contact of index case: currently residing in the same household as an individual evaluated at NYP via outpatient, emergency department (ED), or inpatient services who (1) test positive for COVID-19, or (2) are defined as suspected cases, or persons under investigations (PUI), by the treating physician.
- Willing to take study drug as directed for 5 days.

Exclusion Criteria for use of Cloroquin / Hydroxychoroquin

- Age <18 years old
- Suspected or confirmed current COVID-19, defined as: (1) temperature > 38 Celsius; (2) cough; (3) shortness of breath; (4) sore throat; or, if available (not required), (5) positive confirmatory testing for COVID-19
- Suspected or confirmed convalescent COVID-19, defined as any of the above symptoms within the prior 4 weeks.
- Inability to take medications orally
- Inability to provide written consent
- Known sensitivity/allergy to hydroxychloroquine
- Current use of hydroxychloroquine for another indication
- Pregnancy
- Prior diagnosis of retinopathy
- Prior diagnosis of glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Major comorbidities increasing risk of study drug including:

i. Hematologic malignancy, ii. Advanced (stage 4-5) chronic kidney disease or dialysis therapy, iii. *Known history of ventricular arrhythmias*, iv. Current use of drugs that prolong the QT interval

Anti-TNF therapy as potential treatment for COVID-19

Authors writing in *Lancet* propose that there is sufficient evidence and an urgent need for anti-TNF therapy trials in the fight against COVID-19.

Deaths from COVID-19 are chiefly due to a major immune inflammatory response and diffuse alveolar damage. The pro-inflammatory cytokine upregulation (interleukin (IL)-1, IL-6, TNF, and interferon γ) documented in this disease is a valid target for anti-TNF therapy.

Among the many anti-inflammatory candidates for COVID-19, only a few anti-TNF antibodies such as (infliximab or adalimumab) are potentially effective, widely available, and have a well-established safety profile. This treatment should be evaluated in patients with COVID-19 on hospital admission to prevent progression to the requirement of intensive care support.

Blockade of TNF alone is clinically effective in many diseases, despite the presence of other pro-inflammatory cytokines and mediators.

A single infusion of anti-TNF antibody might reduce some of the processes that occur during COVID-19 lung inflammation, reducing TNF and other inflammatory mediators, cellularity, and exudate.

The best time for this therapy in patients with COVID-19 is as early as possible after hospital admission because patients will already have initiated anti-viral immunity for several days.

There is sufficient evidence to support clinical trials of anti-TNF therapy in patients with COVID-19. Study subjects should be initiated on this therapy as early as possible. If anti-TNFs are beneficial and safe in hospitalised subjects, out of hospital treatment of COVID-19 patients at high risk could be considered.

Analgesics:

It has been proven that Paracetamol is the only safe analgesic. However, contrary to the current belief, The European Medicines Agency (EMA) says there is currently "no scientific evidence" that nonsteroidal anti-inflammatory drugs (NSAIDs), such as Ibuprofen, could worsen coronavirus disease.

EMA adds that it "is monitoring the situation closely" and will review any new information that becomes available on this issue in the context of the pandemic.

Although there is currently no known effective treatment for COVID-19, reports of the use of oseltamivir, lopinavir/ritonavir (protease inhibitors) and antibiotics have been reported despite the WHO making no recommendation for the use of antiviral drugs, antibiotics, or glucocorticoids.

Care should therefore be taken to not administer medication with unknown efficacy to patients of critically-ill status. Consequently, efforts to prevent and control COVID-19 require an evidence-based and likely multifactorial approach. Fundamentally, successful prevention requires an in-depth understanding of the clinical severity of COVID-19, extent of transmission and infection, and the efficacy of treatment options in order to accelerate the development of diagnostics and therapeutic modalities.

VACCINES

NIH-funded trial of Moderna mRNA vaccine is first of any for COVID-19

The trial will involve 45 healthy adults.

Study participants must be healthy adults age 18 to 55 years. To be eligible, they can't have certain health conditions that affect the immune system, and they can't be taking medications that affect the immune system.

The initial trial will involve just 45 participants—28 at KPWHRI and 17 at Emory University. It is a "phase I" test of a 3-phase process examining the potential vaccine. In this first phase, researchers are testing the safety of various doses and whether these doses produce an immune response.

Phase I trials don't study the effectiveness of the vaccine in preventing coronavirus infection. That work comes at a later phase of the vaccine research.

Response to study recruitment efforts has been very positive, so the study teams no longer need to identify potential study participants. Online study recruitment is now closed.

KPWHRI's path to this important role

KPWHRI's vaccine research team began preparations for the possibility of a trial as soon as they got the call on January 28. The team has expertise in conducting these kinds of trials, including testing other investigational vaccines against "swine" and "bird" flu. KPWHRI became a VTEU site in 2007, and it is the only one of the nation's 9 VTEU centers not housed at a university medical center. Since 1962, the VTEUs have played a key role in developing new and improved vaccines and therapies against infectious diseases.

Currently there is no vaccine proven to protect against SARS-CoV-2 infection

Two coronavirus vaccine candidates enter human trials, 60 in pre-clinical stage:

India's Zydus Cadila, Serum Institute and Bharat Biotech are among the global firms working on COVID-19 vaccine.

Two candidate vaccines for COVID-19 have entered the first phase of human clinical trials and another 60 candidate vaccines are in pre-clinical studies, the World Health Organisation (WHO) has confirmed.

The vaccine candidate jointly developed by CanSino Biological Inc and Beijing Institute of Biotechnology uses the non-replicating viral vector as the platform, same as the non-corona candidates like Ebola, to develop a vaccine with a 'Adenovirus Type 5' candidate, a draft landscape of COVID-19 vaccine candidates brought out today.

Sources say adenoviruses are common viruses that cause pneumonia and can deliver potential antigens to stimulate the production of antibodies that work against the disease. CanSino Biological Inc, in association with the Chinese Academy of Military Medical Science's Bioengineering Institute, had developed an Ebola vaccine in 2017.

The other vaccine that has entered the first phase of trials is from the US-based biotech firm Moderna and the National Institute of Allergy and Infectious Diseases (NIAID) combine. This lipid nanoparticle (LNP) encapsulated mRNA candidate vaccine uses an RNA platform

with multiple candidates. In this, the virus's genetic information is de-coded from the DNA to make proteins. mRNA, or messenger RNA, acts as an intermediary between the genetic information in DNA and the amino acid sequence of proteins, which gives cells command to make proteins that fight the viruses.
But such vaccines have not yet been approved for human use, said sources.

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Scientists at the University of Oxford are promising a super fast vaccine against the novel coronavirus and say it will be available by September.
At a virtual press conference on Friday, the lead researcher of the vaccine development programme, Prof. Sarah Gilbert, said she and her team were confident that the ChAdOx1 vaccine can work against the coronavirus.
The Oxford vaccine group has promised one million doses of the vaccine by September.
FOURTH TO ENTER CLINICAL TRIAL PHASE
ChAdOx1 is only the fourth Covid-19 vaccine candidate in the world to enter the clinical trial phase. But what separates it from others is the minimum time it will take to deliver mass quantities.
The other three contenders besides the Oxford group -- two American and one Chinese -- are expected to take at least 12 to 18 months to mass produce the vaccine.
"With ChAdOx1 technology, already 12 clinical trials have been conducted against different diseases; we consistently see a very good vaccine safety and very strong immune response with single dose, while some other vaccine technologies such as RNA and DNA need two or more." "With ChAdOx1 technology, already 12 clinical trials have been conducted against different diseases; we consistently see a very good vaccine safety and very strong immune

response with single dose, while some other vaccine technologies such as RNA and DNA need two or more."

Individual systemic involvement of Corona

Neurological symptoms and signs

Neurological symptoms have been observed in patients with COVID-19.6 It has been reported that more than one third of patients experienced various neurological symptoms including the involvement of central nervous system (dizziness, headache, impaired consciousness, acute cerebrovascular disease, ataxia and epilepsy), peripheral nervous system *(taste impairment, smell impairment, vision impairment and neuralgia)* and skeletal muscular damage.

Skeletal muscle injury was defined when a patient had skeletal muscle pain and elevated serum creatine kinase level above 200 U/L.

In patients with central nervous system manifestations, the most common complaints were dizziness and headache. In patients with peripheral nervous system manifestations, the most common complaints were taste and smell impairment.

The nervous system manifestations were significantly more common in patients with severe infection, manifested as ischaemic stroke and cerebral haemorrhage diagnosed by clinical symptoms and head CT, impaired consciousness and skeletal muscle injury. Rapid clinical deterioration or worsening could be from a neurological event such as stroke, which may have contributed to its high mortality rate. The main reason of clinical worsening is the hyperactivation of inflammatory factors that eventually causes a fatal inflammatory storm as the disease progresses.

In addition, coagulation system is damaged causing the D-dimer and platelet abnormalities, which increases the risk of cerebrovascular disease. During the epidemic period of COVID-19, when seeing patients with above neurological manifestations especially more develop nervous system manifestations, doctors should consider SARS-CoV-2 infection as a differential diagnosis so to avoid misdiagnosis and seize the opportunity of stopping it from infecting the others. Issues require special attention in laboratory inspection Brain CT and

chest CT images from a critically ill patient with COVID-19. Brain CT showing cerebral infarction.. Diffuse lesion of bilateral lungs from the same patient.

In laboratory examinations, their premorbid routine blood test may show lymphopaenia. For older patients and those with comorbidities, clinicians should pay more attention to possible secondary infection. These patients should be treated quickly in order to halt the progression. Some may develop acute cerebrovascular disease, which could account for sudden clinical worsening. During this period, increased inflammatory response and blood coagulation abnormalities could be the main causes of clinical worsening. These patients are more likely to convert into critical stage. Someone has tried to use the immune modulation treatment, including small doses of methylprednisolone, gamma globulin, haemodialysis and anticoagulation, and found that was effective.

Possible causes of neurological symptoms and precautions for neurologists Symptoms related to the development of acute cerebrovascular diseases.

Among patients with SARS-CoV-2 infection, middle-aged and elderly people accounted for the majority of strokes, especially in critically ill patients. Serum D-dimer level is generally increased, which could be the source of embolic vascular events.

Many of these patients may already have other cerebrovascular risk factors, such as hypertension, diabetes mellitus, hyperlipidaemia, smoking or previous stroke history. Some may develop their firstever acute ischaemic stroke.Therefore, medical staff should pay close attention to the manifestation of neurological symptoms. If an acute ischaemic stroke patient with suspected or confirmed diagnosis of COVID-19 are admitted, emergency treatment should be jointly offered by neurologists and infectious disease specialists.

Since SARS-CoV-2 specifically binds to ACE2 receptors, 2 patients with hypertension may encounter blood pressure fluctuations following SARS-CoV-2 infection, which may increase the risk of intracranial haemorrhage. Furthermore, some critically ill patients with SARS-CoV-2 infection have severe thrombocytopaenia, another highrisk factor for cerebral haemorrhage. **For hypertensive patients with SARS-CoV-2 infection, it is recommended to stop using ACE inhibitors or angiotensin II receptor blockers (ARBs) as antihypertensive drugs, and consider calcium channel blockers, diuretics and other classes of antihypertensive drugs.**

Symptoms related to intracranial infection.Based on the previous discovery, coronavirus may invade the central nervous system. Researchers have detected SARS coronavirus nucleic acid in patients' cerebrospinal fluid, and SARS coronavirus was also verified in brain tissue on autopsy.

For this SARS-CoV-2 outbreak, some patients have had symptoms similar to thosePresentation with status, without fever or with intracranial infections such as headache, seizure and disturbance of consciousness.

Few patients had central nervous system symptoms before having pulmonary symptoms. Therefore, neurologists should be vigilant when seeing COVID-19 infected patients and look for any signs suspicious for intracranial infection, and if possible, MRI of head with and without contrast should be performed. **A lumbar puncture to look for SARS-CoV-2 nucleic acid by using PCR is recommended.**

For these COVID-19 patients with intracranial infection, treatment strategies such as controlling cerebral oedema, treating and preventing seizures and treating psychotic symptoms should be considered and the guidelines should be followed.

Presentation with status epilepticus has been reported, without fever or chest symptoms. The patient displayed ongoing myoclonic jerks of the right eyelid and upper-lip, started two hours before.The neurological examination showed fluent aphasia, right central facial nerve palsy, pronation of the right arm and drift of the right leg. The patient displayed ongoing myoclonic jerks ofthe right eyelid and upper-lip, started two hours before.

Only clue was lymphopenia and thrombocytopenia.

Brain MRI confirmed extensive gliosis and atrophy involving the left temporo-parietal lobe, in the absence of new cerebral lesions as documented by both diffusion weighted imaging and post-gadolinium sequences. These pts should be kept in isolation, tested for Covid and along with management of status should be started on protease inhibitors (lopinavir-ritonavir) with Hydroxychloroquin.

Symptoms related to muscle damage Historically, SARS coronavirus was involved in the myocardial inflammation. In clinical observation, some patients with COVID-19 may experience symptoms of skeletal muscle damage, such as fatigue or limb aches, and mild **elevation of serum creatine kinase level. They are due to inflammatory reaction caused by**

the SARS-CoV-2 infection or direct muscle damage by the virus. For patients with muscle damage symptoms, screening for SARS-CoV-2 infection is recommended.

MS(mutiplesclerosis) disease modifying therapies (DMTs) and coronavirus

DMTs affect your immune system, which can make your chances of infection, or complications from infection, higher. These risks are different for different DMTS, but generally they are moderate.

If you're taking a DMT and think you have coronavirus, you should be able to continue taking it if your symptoms are mild.

In addition to active treatment of COVID-19, strengthening nutritional support is recommended.

Cautions in neurology clinic

1. Neurologists need to wear disposable work caps, medical protective masks, work clothes such as scrubs, disposable latex gloves and carry hand sanitiser that contains ethanol, hydrogen peroxide or sodium hypochlorite.
2. Patients and their companions must have temperature measured in triage routinely before entering the consulting room. To reduce cross-infection, companions should avoid entering the room. Everyone must wear disposable medical masks.
3. For patients with neurological symptoms but also highly suspicious of COVID-19, it is recommended that the patient go to a fever clinic first and consult a neurologist later.
4. After work, doctors should remove the protective gear step by step according to the decontamination protocol. It is forbidden to leave the contaminated area wearing personal protective equipment for the purpose of preventing cross-infections. Management in neurological emergency and staffing acute stroke green pathway.

5. The protection level in the emergency room and stroke green pathway should be at least at level 2: wearing working clothes and caps, medical protective masks, goggles/face shields and disposable isolation gown. When treating suspected or confirmed cases of COVID-19 or patients with close contact history, the protection level should be appropriately raised: wearing medical protective masks, goggles/face shields, disposable medical protective clothing, disposable latex gloves and long shoe covers.
6. Neurological emergency and stroke green pathway (including consultation rooms, CT/MRI rooms, interventional operating rooms and so on) should be strictly separated from routine emergency and fever clinics to ensure no direct interaction with a patient with fever.
7. Doctors should ask patients and their companions whether they have typical symptoms of COVID-19, such as fever, sore throat and so on, within 14 days of exposure or a contact history with suspected or confirmed cases. Patients should have a chest CT at the same time of having a head CT. In any suspected conditions, a specialised medical staff should accompany the patient to the fever clinic and carry out stroke triage/emergency treatment in the fever clinic. The patient should be admitted to an isolation ward after treatment. Patients without suspected situations can be admitted to a buffer ward to receive the next treatment and do further screening for COVID-19 at the same time. A neurologist should round on these patients regularly. Patients will be transferred to the general ward of neurology only when COVID-19 has been definitely ruled out. on April 14, 2020 at India:BMJ-PG Sponsored.
8. Patients who receive thrombolysis or thrombectomy should avoid entering the neurological intensive care unit and should be treated in a private room first. Medical staff should pay close attention to those in isolation. If the body temperature (monitoring at least for 3 days), blood routine, chest CT and SARS-CoV-2 nucleic acid tests are negative, the patient can be transferred to a semiprivate or multiperson ward.

9. Medical staff treating neurological emergency and responsible for acute stroke green pathway must have a good work/life balance, avoid long working hours and sleep deprivation. Appropriate exercises and nutritional support are also very important to fend off infections.
10. It is recommended that to assess and treat those with severe infection in an intensive care unit (ICU), a team of two should be organised to enter the areas and depart together. Forming such partnership can help healthcare providers to look out for and assist each other. In case one healthcare provider feels ill, which make him unable to continue to work in the ICU, the other one can help evaluate and evacuate.
11. Only one family companion is permitted for each patient, and the companion must have had the same screening tests to exclude COVID-19 before entering the ward. A guard at the entrance of the ward is needed to take the temperature of anyone entering the ward. All people in the ward must wear disposable medical masks to avoid cross infection.
12. Everyone in the ward should monitor body temperature regularly. Patients and their companions should have COVID-19 screening test every few days until discharge. Once a person with fever has been identified, medical staff should notify the prevention and control team of the hospital immediately, then assist the treatment, examination, isolation and disinfection of wards.
13. If a highly suspected case has been identified during the monitoring, doctors should notify the prevention and control team and arrange for an in-hospital COVID-19 specialist consultation immediately. Other patients, their companions and medical staff who came in contact with should be separated. The temperature and COVID-19 related symptoms of all contacts should be closely monitored. The patient should be temporarily taken to a separate room and then quickly transferred to the isolation ward or a designated hospital once the diagnosis has been confirmed. The space where the patient stayed must be disinfected strictly.

Neurological Conclusion

COVID-19 is a highly contagious disease that has become a worldwide pandemic. Patients infected may show neurological symptoms first. Healthcare providers and neurologists should pay close attention to these symptoms and have a high index of suspicion when evaluating patients in an endemic area. Early recognition may help initiate treatment and isolation early so to prevent clinical worsening and spreading of virus.

Gastrointestinal manifestations

In a recently published, single-center case series of 138 consecutive hospitalized patients with confirmed COVID-19, investigators reported that approximately 10% of patients initially presented with GI symptoms, prior to the subsequent development of respiratory symptoms. Common and often very subtle symptoms included diarrhoea, nausea, and abdominal pain, with a less common symptom being nonspecific GI illness. New studies are expanding our understanding of the possible fecal transmission of COVID-19. Assessment by polymerase chain reaction (PCR) has provided evidence of the virus in the stool and the oropharynx outside the nasopharynx and respiratory tract. Virus in the stool may be evident on presentation and last throughout the course of illness resolution for up to 12 days after the respiratory virus evidence is gone.

Human coronaviruses, such as SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), are known to cause respiratory and enteric symptoms. In the SARS outbreak of 2002-03, 16%-73% of patients with SARS had diarrhoea during the course of the disease, usually within the first week of illness.

SARS-CoV ribonucleic acid (RNA) was only detected in stools from the fifth day of illness onwards, and the proportion of stool specimens positive for viral RNA progressively increased and peaked at day 11 of the illness, with viral RNA still present in the feces of a small proportion of patients even after 30 days of illness.

Till now, infection control and surveillance focus on the respiratory system. The ignorance of SARS-CoV-2 in the digestive system may cause difficulty with disease control.

Gastrointestinal symptoms seem to be uncommon in patients with COVID-19 when compared with SARS.

However, they should not be ignored as the increasing rate of diarrhoea occurs in confirmed COVID-19 patients according to a recent report that 14 of 138 confirmed patients had diarrhea. One possible route for the movement of SARS-CoV-2 into the digestive system may be the “trachea-esophagus-ileum-colon” as single-cell transcriptome analysis showed ACE2, the entry receptor for SARS-CoV-2, highly expressed in lung AT2 cells, esophagus upper and stratified epithelial cells, and enterocytes from the ileum and colon.

Another similarity that may be noted between SARS and COVID-19 is that mild to moderate liver injury has existed in patients.

Xiao F et al. examined the viral RNA in feces from 71 patients with confirmed COVID-19 during their hospitalization from February 1-14, 2020.They collected serum, nasopharyngeal and oropharyngeal swabs, urine, stool, and tissues (from endoscopy) from the patients. The age of the patients ranged from 10 months to 78 years. The duration of positive stool tests ranged from 1 to 12 days, they added, and patients remained positive via stool tests after showing negative in respiratory samples. The researchers found that 53.4% of patients had SARS-CoV-2 RNA in their stool and 23% of patients tested positive in their stool despite testing negative for the virus in respiratory samples.

This finding indicates that viral gastrointestinal infection and the potential fecal-oral transmission can last even after viral clearance in the respiratory tract.

The author strongly recommends that rRT-PCR testing for SARS-CoV-2 from feces should be performed routinely in SARS-CoV-2 patients, and transmission-based precautions for hospitalized SARS-CoV-2 patients should continue if the feces tests positive by rRT-PCR testing.

Fecal occult blood testing indicated an upper gastrointestinal bleed; subsequent endoscopy found mucosal damage to the esophagus, and esophageal, gastric, duodenal, and colonic samples were taken for testing. Hematoxylin and eosin staining showed no significant damage, but numerous infiltrating plasma cells and lymphocytes, as well as interstitial edema, were seen in the lamina propria of the stomach, duodenum, and rectum. Most significantly, results demonstrated positive ACE2 protein staining, mainly in

the cytoplasm of gastrointestinal epithelial cells. It has been previously shown that SARS-CoV-2 uses this protein as a viral receptor for its entry process.

Immunofluorescence testing showed that ACE2 was abundantly expressed in the glandular cells of the gastric, duodenal and rectal epithelia of the above-mentioned patient, as well as other patients. These data demonstrated that infectious virions are being secreted from the gastrointestinal cells of people with SARS-CoV-2 infection, and thus support the potential for fecal-oral transmission of the virus. The discharge guideline depending on the respiratory tract test also meets the challenge.

Gastroenterological Conclusions

Clinicians should recognize that digestive symptoms, such as diarrhea, may be a presenting feature of COVID-19, and that the index of suspicion may need to be raised earlier in at-risk patients presenting with digestive symptoms rather than waiting for respiratory symptoms to emerge. It should also be considered before discharge that viral gastrointestinal infection and potential fecal-oral transmission can last even after viral clearance from the respiratory tract.

Final note

This review has been written by myself keeping in mind both doctors/scientists and common people's queries.

Although this does not cover every detail.yet many issues can be clear to doctors, paramedics and common people.

NB:

2] If any reader has any suggestions, comments or queries, kindly do not hesitate to mail me, giving ref of, ' Query on Novel Corona' in website.