## OVERVIEW of COVID-19 & Case Management Department of Health Services University of Embu

## **Presentation Outline**

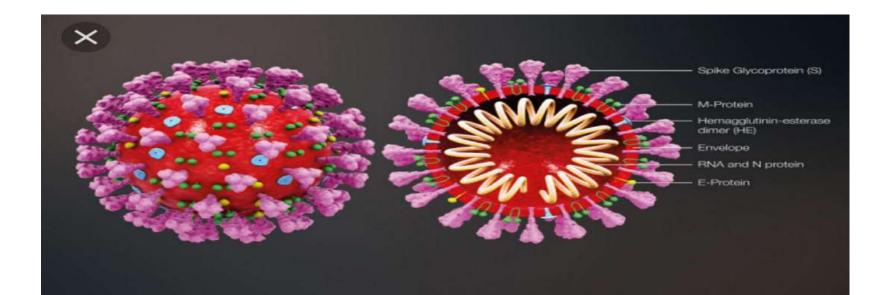
- Introduction
- Epidemiology
- Pathogenesis.
- Transmission
- Signs and symptoms
- Lab reviews.
- Diagnosis
- Case management
- Prognosis
- Donning and doffing of PPE.
- Prevention/ how to make chlorine.

## introduction

- Coronaviridae family, RNA virus, ss RNA genome.
- The initial cases were presumably linked to direct exposure to infected animals (animal-to human transmission) at a seafood market in Wuhan, China. Bat-pangolin
- known to cause diseases of the respiratory, hepatic, nervous system, and gastrointestinal systems in humans.
- CoVs are responsible for 5-10% of acute respiratory infections. It has been estimated that 2% of the population are deemed healthy carriers of these viruses.
- Some common human CoVs include; HCoV-OC43, HCoV-HKU1, HCoV-229E, HCoV-NL63, SARS-CoV, MERS-CoV and COVID 19.
- Causes of urti ; rhinovirus (major), coronavirus, influenza..
- Emerging resp. Viruses;1. SARS COV 1 2002 2.H1N1(swine flu) 2009 3. MERS COV 2012 4. nCoV( SARS COV 2).
- How do they emerge?; human health , animal health & the ecocystem are interlinked. 70-80% are zoonotic.Population change ,climate change ,increased urbanization , international travel and migration.
- Declared a pandemic in march 12th by WHO.

## introduction

- Sars cov 2002, mers cov 2012 case mortality ratio 10%(800/8000) and 35%(858/2494) respectively.
- Reservior bat-intermediate host pangolin. Incubation 2-14 days(ave 5/7 for symptoms). Zoonotic, Spillover event?
- These viruses are very fragile ,thus ,can be functionally inactivated with the use of ethanol (60%), ether (75%), and chlorine-containing disinfectants.
- Virus components: S spike protein, hemaglutin esterase protein, E protein, M protein, neuclocapsid, envelope, ssRNA.



## SARS COV 2

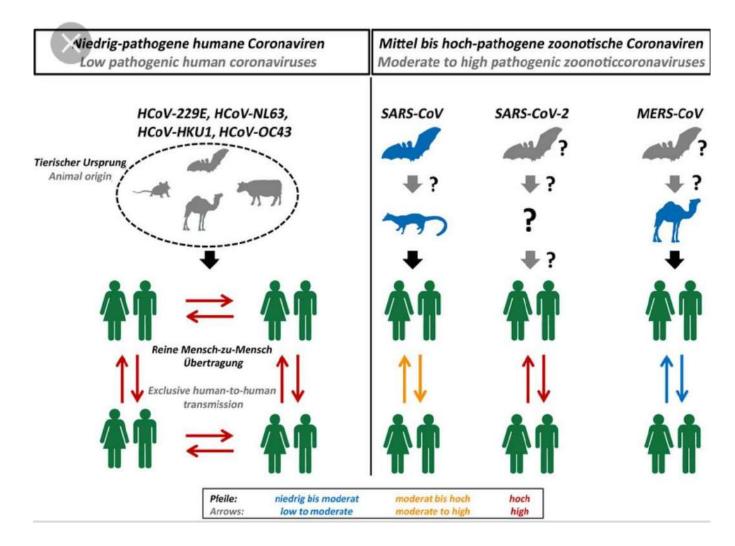
S TYPE	L type
30%	70%
LESS SEVERE, LESS AGGRESIVE	MORE SEVERE, MORE AGGRESIVE
ZOONOTIC CONNECTION	EVOLVED FROM S TYPE

	INCIDENCE	FATALITY	Recovered	CFR%
KENYA	27,425	438	13,867	1,6
WORLD	20,514,016	746,154	13,457,0354	3,6

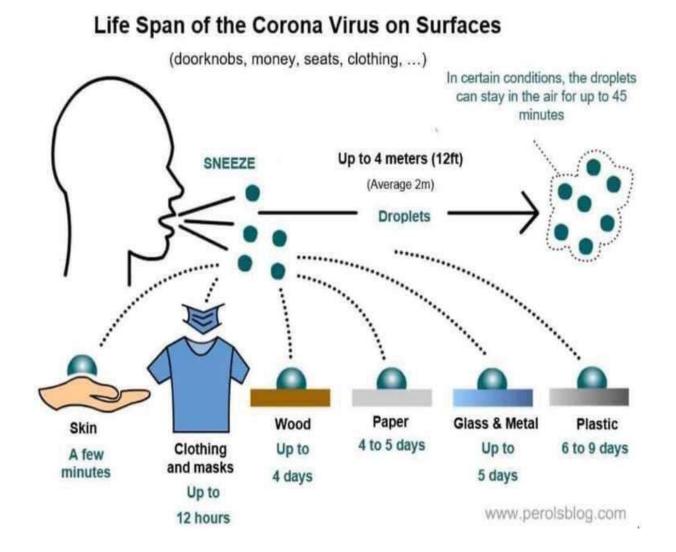
## Transmission

- 3 modes of transmission;
- 1.Contact-a. close personal contact e.g shaking hands, b. Touching contaminated surfaces then touching T ZONE
- 2.droplet-droplets from coughing and sneezing can reach the t zone(mucus membranes).
- 3.airborne- possible transmission in closed spaces due to elevated aerosol concentrations..
- Fecal-oral
- Human-to-human transmission is now considered the main form of transmission. Individuals who remain asymptomatic could also transmit the virus. However, the most common source of infection is symptomatic people.
- Ro (R naught) (infectivity) of 2.2. This suggests that a patient can transmit the infection to two other individuals. Ro 2-3, influenza 1,3.

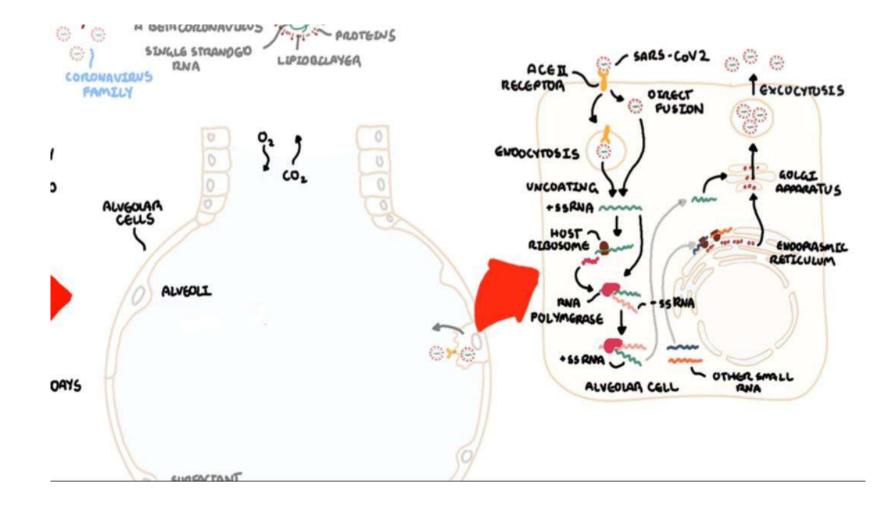
## Transmission



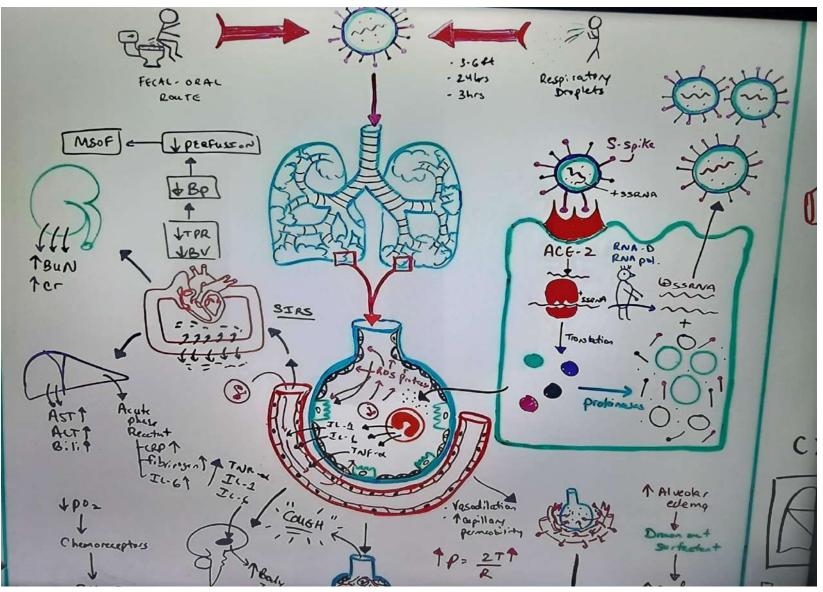
## Covid 19



## pathogenesis



## pathogenesis

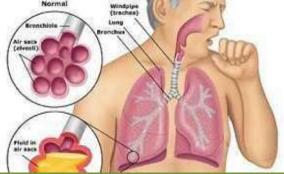


## pathogenesis

- Type 1(gaseous exchange) and type 2 pneumocyte(surfactant production).
- SARS COV 2, s spike binds to ACE 2 receptor, ss RNA combines with the cell cell ribosome ;a. ssRNA replication by RNA dependent RNA polymerase, b. Translation to protein fragments, proteseases cleaves the proteins to covid 19 components.
- Damaged type 2 pneumocyte releases prostaglandin and other components than invites macrophages ,Macrophages- releases cytokines like IL 6, TNF apha, IL 1-vasodilation,increased capillary permeability.
- Neutrophil- ros(reactive o2 radicals), proteases-which damages pneumocytes.
- SIRS, MOFS.

## Sırs/sepsis/septic shock/mods

SIRS	Two or more of: • Temperature >38°C or <36°C • Tachycardia >90bpm • Respiratory rate >20bpm or PaCO <sub>2</sub> <4.3kPa • White blood count >12x10 <sup>9</sup> /l or <4x10 <sup>9</sup> /l or >10% immature (band) forms	
Sepsis	SIRS due to severe infection, positive evidence of bacteria within the bloodstream, confirmed by cultures	
Bacteraemia	Presence of bacteria in the bloodstream (+/- SIRS)	
Sepsis induced hypotension	SBP <90mmHg or a reduction of >40mmHg from baseline in the absence of other causes of hypotension (NB this may be responsive to resuscitation)	
Septic Shock	Sepsis induced hypotension despite adequate fluid/vasopressic resuscitation along with the presence of perfusion abnormalities that may include but are not limited to • Lactic acidosis • Oliguria • Altered mental state	
MODS (Multiple Organ Dysfunction syndrome)	Dysfunction of the kidneys, liver, lungs, heart, genitourinary tract etc. caused by a severe hypoperfusion; and other complications of SIRS including physiological derangements in which organ function is not capable of maintaining homeostasis	



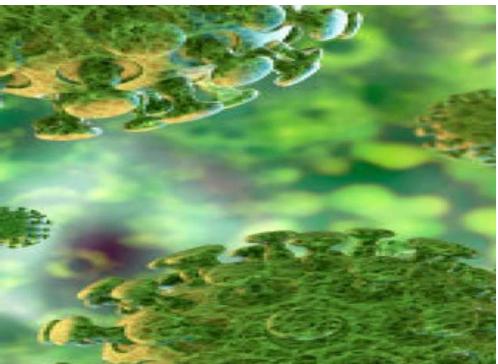
# **Clinical Features**

- Incubation period 2 14 days.
- The duration of hospitalization to discharge 7 days and to died 9 days, median time 4 days.
- Clinical range from asymptomatic to very severe Pneumonia.
- 1/3 patients had gastrointestinal symptoms.

Asymptomatic	Pneumonia	ARDS	Septic shock	Multi organ failure
13.5%	44.1%	12.4%	4%	
Gastrointestinal symptoms				
26%				

## Signs & symptoms

- COVID-19 manifests with a wide clinical spectrum ranging from asymptomatic patients to septic shock and multiorgan dysfunction.
- The most common symptoms of patients include fever (98.6%), fatigue (69.6%), dry cough, and diarrhea.
- The disease may be classified into mild, moderate, severe, and critical based on severity;
- 1.mild covid 19
- 2. moderate covid 19
- 3.severe covid 19/critical.



## Mild/moderate COVID 19

- Patients with mild illness may present with symptoms of an upper respiratory tract viral infection.
- These include dry cough, mild fever, nasal congestion, sore throat, headache, muscle pain, and malaise . It is also characterized by the absence of serious symptoms such as dyspnea.
- The majority (81%) of COVID-19 cases are mild in severity.
- Radiograph features are also absent in such cases. Patients with mild disease can quickly deteriorate into severe or critical cases.
- MODERATE
- Moderate covid 19 patients present with respiratory symptoms of cough, shortness of breath, and tachypnea. However, no signs and symptoms of severe disease are present

## SEVERE covid 19

- Patients with severe disease present with severe pneumonia. acute respiratory distress syndrome (ARDS), sepsis, or septic shock.
- Dx is clinical, and complications can be excluded with the help of radiographic studies.
- Clinical presentations include the presence of severe dyspnea, tachypnea (respiratory rate > 30/minute), respiratory distress, SpO2 ≤93%, PaO2/FiO2 < 300, and/or greater than 50% lung infiltrates within 24 to 48 hours. Even in severe forms of the disease, fever can be absent or moderate.

## Case study published in 18th june 2020

 Study via Nature Medicine reveals that asymptomatic individuals with <u>#COVID19</u> have longer duration of viral shedding than those who're symptomatic; they also have lower levels of virus-specific IgG antibodies & show rapid reduction earlier in the acute phase of infection.

The study of asymptomatic individuals with PCRconfirmed <u>#SARSCoV2</u> infections but without any relevant clinical symptoms in the preceding 14 days showed that the median duration of viral shedding in the asymptomatic group was 19 days

The asymptomatic group had a significantly longer duration of viral shedding than the symptomatic group.

The virus-specific IgG levels in the asymptomatic group were significantly lower relative to the symptomatic group in the acute phase.

## CASE STUDY

Of asymptomatic individuals, 93.3% and 81.1% had reduction in IgG and neutralizing antibody levels, respectively, during the early convalescent phase, as compared to 96.8% and 62.2% of symptomatic patients.

Forty percent of asymptomatic individuals became seronegative and 12.9% of the symptomatic group became negative for IgG in the early convalescent phase.

In addition, asymptomatic individuals exhibited lower levels of 18 proand anti-inflammatory cytokines. These data suggest that asymptomatic individuals had a weaker immune response to SARS-CoV-2 infection.

The reduction in IgG and neutralizing antibody levels in the early convalescent phase might have implications for immunity strategy and serological surveys.

### Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections

Quan-Xin Long<sup>1,8</sup>, Xiao-Jun Tang<sup>2,8</sup>, Qiu-Lin Shi<sup>2,8</sup>, Qin Li<sup>3,8</sup>, Hai-Jun Deng<sup>1,8</sup>, Jun Yuan<sup>1</sup>, Jie-Li Hu<sup>1</sup>, Wei Xu<sup>2</sup>, Yong Zhang<sup>2</sup>, Fa-Jin Lv<sup>4</sup>, Kun Su<sup>3</sup>, Fan Zhang<sup>5</sup>, Jiang Gong<sup>5</sup>, Bo Wu<sup>6</sup>, Xia-Mao Liu<sup>7</sup>, Jin-Jing Li<sup>7</sup>, Jing-Fu Qiu <sup>2,28</sup>, Juan Chen<sup>2,18</sup> and Ai-Long Huang<sup>1,28</sup>

The clinical features and immune responses of asymptomatic individuals infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have not been well described. We studied 37 asymptomatic individuals in the Wanzhou District who were diagnosed with RT-PCR-confirmed SARS-CoV-2 infections but without any relevant clinical symptoms in the preceding 14 d and during hospitalization. Asymptomatic individuals were admitted to the government-designated Wanzhou People's Hospital for centralized isolation in accordance with policy'. The median duration of viral shedding in the asymptomatic group was 19 d (interquartile range (IQR), 15-26 d). The asymptomatic group had a significantly longer duration of viral shedding than the symptomatic group (log-rank P = 0.028). The virus-specific lgG levels in the asymptomatic group (median S/CO, 3.4; IQR, 1.6-10.7) were significantly lower (P = 0.005) relative to the symptomatic group (median S/CO, 20.5; IQR, 5.8-38.2) in the acute phase. Of asymptomatic individuals, 93.3% (28/30) and 81.1% (30/37) had reduction in IgG and neutralizing antibody levels, respectively, during the early convalescent phase, as compared to 96.8% (30/31) and 62.2% (23/37) of symptomatic patients. Forty percent of asymptomatic individuals became seronegative and 12.9% of the symptomatic group became negative for IgG in the early convalescent phase. In addition, asymptomatic individuals exhibited lower levels of 18 proand anti-inflammatory cytokines. These data suggest that asymptomatic individuals had a weaker immune response to SARS-CoV-2 infection. The reduction in IgG and neutralizing antibody levels in the early convalescent phase might have implications for immunity strategy and serological surveys.

As of May 24, 2020, the coronavirus disease 2019 (COVID-19) pandemic, caused by SARS-CoV-2, has affected more than 5 million people around the world. Most patients with SARS-CoV-2 infections have reportedly had mild to severe respiratory illness with symptoms such as fever, cough and shortness of breath, which might appear 2–14 d after exposure. However, there are other patients who are diagnosed by a positive RT-PCR test but are either asymptomatic or minimally symptomatic<sup>-0</sup>. Increasing evidence has shown that asymptomatic individuals can spread the virus efficiently, and the emergence of these silent spreaders of SARS-CoV-2 has caused difficulties in the control of the epidemic<sup>-0</sup>. However, our understanding of the clinical features and immune responses of asymptomatic individuals with SARS-CoV-2 infection is limited. Here we describe the epidemiological and clinical characteristics, virus levels and immune responses in 37 asymptomatic individuals.

#### Results

Demographic characteristics. On February 6, 2020, the National Health Commission of China updated the COVID-19 Prevention and Control Plan (4th edition) for the management of close contacts, emphasizing identification and quarantine of asymptomatic individuals'. To identify asymptomatic individuals, the Wanzhou District Centers for Disease Control and Prevention (CDC) then conducted extensive RT-PCR screening for 2,088 close contacts under guarantine. Individuals with positive RT-PCR results then were screened by point prevalence surveys carried out by the local CDC and symptoms assessments reported by clinicians. Of these, 60 individuals claimed no symptoms in the preceding 14 d, according to local CDC records, and were transferred to a government-designated hospital for centralized isolation. On admission, 17 individuals were excluded for mild or atypical symptoms based on symptoms assessments reported by clinicians; six individuals who developed symptoms 4-17 d after admission were also excluded. Finally, 37 asymptomatic cases, defined as individuals with a positive nucleic acid test result but without any relevant clinical symptoms in the preceding 14 d and during hospitalization, were included in this study. A total of 178 patients with confirmed SARS-CoV-2 infections were identified in the Wanzhou District before April 10, 2020, as tracked by CDC surveillance systems. In this study, the proportion of patients with asymptomatic infections was 20.8% (37/178).

For antibody detection and cytokine measurements, 37 sex-, age-frequency- and comorbidity-matched mild symptomatic patients were selected for comparison with the asymptomatic individuals (Supplementary Table 1). Thirty-seven sex- and age-frequency-matched control individuals from the Wanzhou District with negative RT-PCR results for SARS-CoV-2 were also selected for cytokines comparison.

Of the 37 asymptomatic individuals, the median age was 41 years (range, 8–75 years) and 22 were female. Twenty-eight individuals had a confirmed history of contact with an RT-PCR-confirmed patient with COVID-19, and nine were Wuhan residents or had a

Key Laboratory of Molecular Biology on Infectious Diseases, Ministry of Education, Chongqing Medical University, Chongqing, China. "Echool of Public Health and Management, Chongqing Medical University, Chongqing, China. "Chongqing Center for Disease Control and Prevention, Chongqing, China. "Department of Radiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China. "Wanzhou People's Hospital, Chongqing, China. "Wanzhou District Center for Disease Control and Prevention, Chongqing, China. "The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China. "These authors contributed equally: Quan-Xin Long, Xiao-Juin Tang, Qiu-Lin Shi, Qin Li, Hai-Jun Deng. "Re-mail: Isqual 126 com; chenjuan2014/scomuedu.cr; ahuang.scomi.edu.cn

## What You Can do if You are at Higher Risk of Severe Illness from COVID-19

### Are You at Higher Risk for Severe Illness?



Based on what we know now, those at high-risk for severe illness from COVID-19 are:

· People aged 65 years and older

×

· People who live in a nursing home or long-term care facility

People of all ages with underlying medical conditions, particularly if not well controlled, including:

- People with chronic lung disease or moderate to severe asthma
- · People who have serious heart conditions
- · People who are immunocompromised
  - Many conditions can cause a person to be immunocompromised, induding cancer treatment, smoking, bone marrow or organ transplantation, immune deficiencies, poorly controlled HIV or AIDS, and prolonged use of corticosteroids and other immune weakening medications.
- · People with severe obesity (body mass index [BMI] of 40 or higher)
- People with diabetes
- People with chronic kidney disease undergoing dialysis
- People with liver disease

### Here's What You Can do to Help Protect Yourself



Stay home if possible.



Wash your hands often.



Avoid close contact (6 feet, which is about two arm lengths) with people who are sick.



Clean and disinfect frequently touched surfaces.



Avoid all cruise travel and non-essential air travel.

## Acute Respiratory Distress Syndrome(ARDS)

- The development of ARDS indicates new-onset or worsening respiratory failure. It occurs as a complication within one week of known clinical insult.
- The values of PaO2/FiO2 are used to distinguish ARDS based on varying degrees of hypoxia;
- 1. Mild ARDS- PaO2/FiO2 values between 200 mmHg and 300 mmHg
- 2. Moderate ARDS PaO2/FiO2 values between 100 mm Hg and 200 mm Hg.
- 3. Severe ARDS-  $PaO2/FiO2 \le 100 \text{ mm}$
- Levels of AST (aspartate transaminase) and ALT (alanine transaminase) at the time of admission correlate with clinical deterioration to ARDS. Higher levels at admission result in rapid clinical deterioration to ARDS
- In addition to the clinical and ventilatory criteria; chest imaging modalities such as chest X-ray, HRCT and lung ultrasound can be used to support the diagnosis.
- The most frequent finding on CT scan includes ground-glass opacity (86%), consolidation (29%), crazy paving (19%), bilateral disease distribution (76%), and peripheral disease distribution (33%). It is important to note that a chest X-ray has a lower sensitivity (59%) to detect subtle opacities.

## Septic shock

- Patients with COVID-19 and sepsis are deemed the most critical of them all. The accompanying multiorgan dysfunction results as a consequence of dysregulated host response to infection.
- Signs of organ dysfunction include severe dyspnea, low oxygen saturation Spo2, reduced urine output, tachycardia, hypotension, cold extremities and altered mentation.
- Laboratory evidence of other homeostatic dysregulation includes acidosis, high lactate, hyperbilirubinemia, thrombocytopenia, and evidence of coagulopathy.
- Patients with septic shock are persistently hypotensive despite volume resuscitation.
- They may also have an accompanying serum lactate level of >2 mmol/L.

## Lab Features

- Laboratory findings specific to COVID-19 include elevated prothrombin time, LDH (lactate dehydrogenase), D-dimer, ALT, C-reactive protein (CRP), and creatine kinase.
- Patients in the intensive care unit have shown higher levels of interleukin (IL) 2, IL-7, IL-10, GCSF (granulocyte colony-stimulating factor), TNF-α (tumor necrosis factor-α).
- They also displayed other abnormal findings indicative of coagulation activation, cellular immune deficiency, myocardial injury, renal injury, and hepatic injury .
- In critical patients, amylase and D-dimer levels are significantly elevated. lymphopenia.
- Elevated level of procalcitonin may suggest an alternative diagnosis such asbacterial pneumonia. Levels of CRP correlate directly with disease severity and progression
- Cbc,uecs,lfts,pti/inr,acute phase reactants e.g crp,esr. , procalcitonin, ckmb, troponins.



## Common Laboratory Findings

- <u>Complete blood count:</u>
- Leukopenia, particularly lymphopenia.
- Viral load:
- Greatest in lower respiratory tract, found in upper respiratory tract and some in blood, urine, stool.
- Co-infection with other respiratory viruses:
- Parainfluenza, rhinovirus, influenza, herpes simplex.
- Secondary nosocomially bacterial infection:
- Klebsiella pneumoniae, Staphylococcus aureus, Acinetobacter spp.

# Chest Radiograph

- Findings vary but are consistent with
- viral pneumonitis and ARDS:
- □ Bilateral hilar infiltration.
- □ Bilat or unilateral patchy infiltration.
- Segmented or lobar opacities.
- Ground glass appearance.
- **Small pleural effusion.**
- **Lower lobes tend to be affected early**
- in the course of illness.
- **Progressive rapidly.**



V05032020



### MINISTRY OF HEALTH Division of Disease Surveillance and Response

### Case Definition for Novel Coronavirus (COVID-19)

The case definition is based on the current information available and may be revised as new information accumulates.

### Suspect Case

Any person with any acute respiratory illness (fever or cough or difficulty in breathing) **AND** at least one of the following:

- A history of travel from or residence in countries with presumed widespread transmission\* in the 14 days prior to symptom onset, or
- Close contact<sup>\*\*</sup> with a confirmed or probable case of COVID-19 in the 14 days prior to illness onset, or
- Close contact\*\* with an individual with a history of respiratory illness and travel to countries with presumed widespread transmission\* within the last 30 days, or
- Worked or attended a health care facility in the 14 days prior to onset of symptoms where patients with hospital-associated COVID-19 infections have been reported.

### **Probable Case**

Probable case: A suspect case for whom testing for COVID-19 is inconclusive\*\*\* or for whom testing was positive on a pan-coronavirus assay.

### **Confirmed Case**

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

### \*China, South Korea, Italy and Iran

\*\*Close contact is defined as:

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

\*\*\*Inconclusive being the result of the test reported by the laboratory.



V25032020

### MINISTRY OF HEALTH

### Case Definition for Novel Coronavirus Disease (COVID-19)

The case definition is based on the current information available and may be revised as new information accumulates.

### Suspect case

A. A patient with acute respiratory illness (fever or cough or shortness of breath), AND

- A history of travel to a foreign country during the 14 days prior to symptom onset; OR
- Having been in contact\* with a confirmed or probable COVID-19 case (see definition of contact) in the last 14 days prior to symptom onset
- B. A patient with severe acute respiratory illness (fever or cough or shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.

### Probable case

- A. A suspect case for whom testing could not be performed for any reason OR
- B. A suspect case for whom testing for the COVID-19 virus is inconclusive.

### Confirmed case

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

#### \*Definition of a Contact

A contact is a person who experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case.

Close contact is defined as:

Working together in close proximity or sharing the same environment with a COVID-19 patient

- Face-to-face contact within 1 meter and for more than 15 minutes .
- Traveling together with a COVID-19 patient in any kind of conveyance
- Living in the same household as a COVID-19 patient
- Health care associated exposure, including providing direct care for COVID-19 patients, working with health care workers infected with novel coronavirus, visiting patients or staying in the same close environment as a COVID-19 patient.

Note: for confirmed asymptomatic cases, the period of contact is measured as the 2 days before through the 14 days after the date on which the sample was taken which led to confirmation.

### Lay/Community Case Definition

Any person presenting with hotness of the body or cough or difficulty in breathing having history of travel from outside the country OR lived with or visited somebody known to have Coronavirus disease.

Mondo

Dr. PATRICK AMOTH Ag. DIRECTOR GENERAL FOR HEALTH 25th March, 2020

## Diagnosis

- The CDC has developed criteria for persons under investigation (PUI). If a person is deemed a PUI, immediate prevention and infection control measures are undertaken. Suspected case, probable case and confirmed case. Detection;1.Working case defination 2. standard case defination 3.signals
- Epidemiological factors are used to assess the requirement of testing. These include close contact with a laboratory-confirmed patient within 14 days of symptoms or travel history to an infected area within 14 days of symptom onset.
- The WHO recommends collecting samples from both the upper and lower respiratory tracts.
- This can be achieved through expectorated sputum, bronchoalveolar lavage, endotracheal aspirate, NP & OP.
- These samples are then assessed for viral RNA using polymerase chain reaction(PCR). GOLD STANDARD. If a positive test result is achieved, it is recommended to repeat the test for reverification purposes.
- A negative test with a strong clinical suspicion also warrants repeat testing within 24hrs.

## Case management

- Isolation remains the most effective measure for containment of COVID-19.
- No specific antiviral medication or vaccine is currently available. Therefore, the treatment of COVID-19 includes symptomatic care and oxygen therapy.
- Patients with mild infections require early supportive management. This can be achieved with the use of acetaminophen, external cooling, oxygen therapy, nutritional supplements, and anti-bacterial therapy.

## Management of Critically ill patients

- Critically ill patients require high flow oxygen, intubation & mechanical ventilation and extracorporeal membrane oxygenation (ECMO),
- ECMO should be considered in patients with refractory hypoxemia despite undergoing protective ventilation. Patients with respiratory failure may require intubation and mechanical ventilation.
- High-flow nasal oxygen and non-invasive ventilation may aerosolize the virus.
- Treatment of septic shock requires hemodynamic support with the administration of vasopressors. Organ function support is necessary for patients with multiple organ dysfunction.
- Stress ulcer prophylaxis-omeprazole/esomeprazole.
- Thromboprophylaxis-pharmacological and mechanical. LMWH-clexane enoxaparın, unfrationated heparin. Pneumatic stockings.
- Antibiotics -co-infections.
- Hydration , prevention/correction of electrolyte imbalance.
- psychosocial support.
- convalesent plasma therapy- antibodies from those who recovered has been found to be protective on those with severe disease.

## RCTs

- According to the World Health Organization (WHO), there is no existing data from randomized clinical trials to advocate any specific anti-nCoV therapy for patients either suspected or diagnosed with SARS-CoV-2.
- Unlicensed treatments can only be given in the circumstance of ethically approved clinical trials or under the Monitored Emergency Use of Unregistered Interventions System (MEURI), with strict supervision (World Health Organization 2020a).
- However, researchers have tested a number of FDA-approved drugs against SARS-CoV-2 infection, and these drugs have shown promising antiviral activity in both cell culture and animal models.
- Some of these drugs are also in clinical trial for SARS-CoV-2 (Li and De Clercq 2020). In the past 2 months, drugs from various classes such as nucleoside analogs, protease inhibitors, and host-targeted agents have been tested to discover an authorized antiviral agent against SARS-CoV-2 infection (Table 10.2). The National Medical Products Administration of China has recently approved favipiravir as the first antiviral medication for the treatment of SARS-CoV-2.
- 3CLpro 3-chymotrypsin-like cysteine protease enzyme controls covid 19 replication and is essential for the life cycle.

Tocilizumab-IL 6 inhibitor.

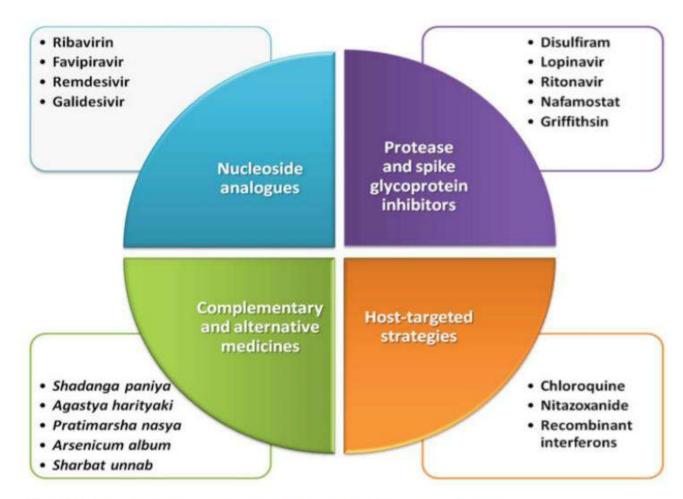


Fig. 10.1 Investigational treatment approaches for COVID-19 infection

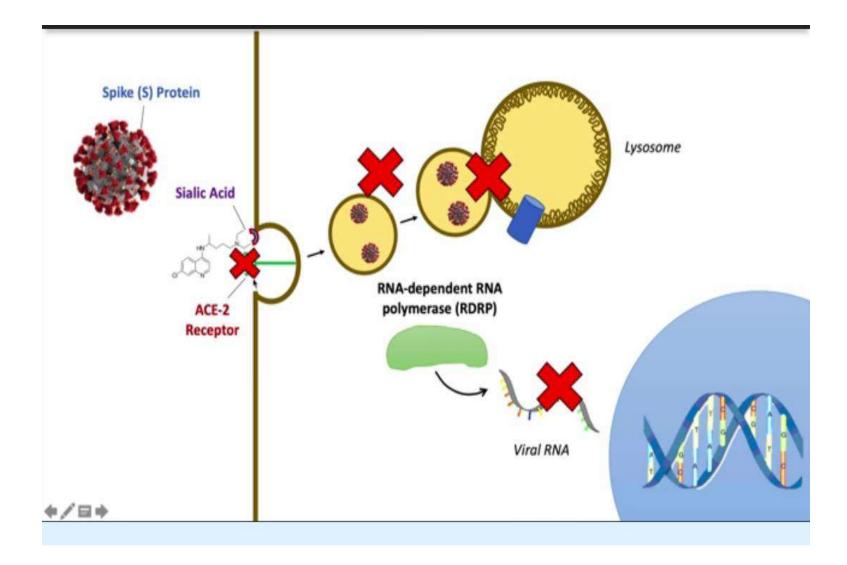
## Updates of drugs on RCTs

- 1, Dexamethasone-steroid given in low dose as an anti-inflammatory. In SEVERE COVID 19 cases Cytokine storm occurs. Cytokines are released causing excessive inflammation. Dexa acts on the immune system to dampen the response and reduce cytokine storm. Has shown biggest benifit in patients on ventilators, it reduced risk of death by 30%. For those requiring oxygen there was 20% reduction.
- 2. Hydroxychloroquine- has shown increased risk of death despite being promoted by POTUS. ANTIMALARIAL. 1.Immunomodulatory effects used to treat rheumatological conditions, 2. Alkalanizes vacuolar(lysosomal) ph – chloroquine is alkaline, inhibits protozoal food vacuole functioning, inhibits endocytosis, lysosomal fusion 3, zinc ionophore –allows influx of zinc into cells, may have anticancer effects. 4. binds to sialic acid. All these has been shown invitro.
- 3. FAVIPIRAVIR- shows improvement on mild and moderate covid 19 patients. Used in Japan. Oral medication, RNA polymerase enzyme inhibitor, which is responsible for viral replication, reducing the viral load. Trial claims improvement of patients in 4 days.
- 4. Remdesivir-antiviral- targets RNA dependent RNA polymerase, shuts down viral replication, reduce viral replication. 30% improvement compared to patients on placebo, also o mortality.

Antiviral agents	Drug targets Reported mechanism of action		
Virus-based treatment	t approaches		
Favipiravir	RdRp	Inhibits RdRp	
Ribavirin	RdRp	Inhibits viral RNA synthesis and mRNA capping	
Penciclovir	RdRp	Inhibits RdRp	
Remdesivir (GS-5734)	RdRp	Terminates the non-obligate chain	
Lopinavir	3CLpro	Inhibits 3CLpro	
Ritonavir	3CLpro	Inhibits 3CLpro	
Darunavir and cobicistat	3CLpro	Inhibits 3CLpro	
ASC09F (HIV pro- tease inhibitor)	3CLpro	Inhibits 3CLpro	
Nafamostat	Spike glycoprotein	Inhibits spike-mediated membrane fusion	
Griffithsin	Spike glycoprotein	Inhibits spike-mediated membrane fusion	
Arbidol (umifenovir)	-	-	
Oseltamivir			
Host-based treatment	approaches		
Recombinant interferons	Interferon response	Exogenous interferons	
Chloroquine	Endosomal acidification	A lysosomotropic base that appears to disrupt intrace lular trafficking and viral fusion events	
Nitazoxanide	Interferon response	Induces the host innate immune response to produce interferons by the host's fibroblasts and protein kinase R (PKR) activation	

Table 10.2 List of drugs that have antiviral activity compounds against SARS-CoV-2

## Chloroquine and HCQS



## Drugs on trial





# MOFS and complications **orevention**

#### Organ support and prevention of complication

- Lung-protective ventilatory strategies for ARDS.
- Sepsis early directed goal therapy.
- Antimicrobial treatment for co-infection.
- Renal replacement therapy.
- Cardiovascular support.

Lung protective vent strategies; setting low tidal volume 4-6ml/kg, high frequency and PEEP, bipap high therapeutic peep, prone position to increase surface are and ventilation perfusion match.

### Non-Invasive Multi-Parameters Patient Monitor



#### prognosis

Data from the

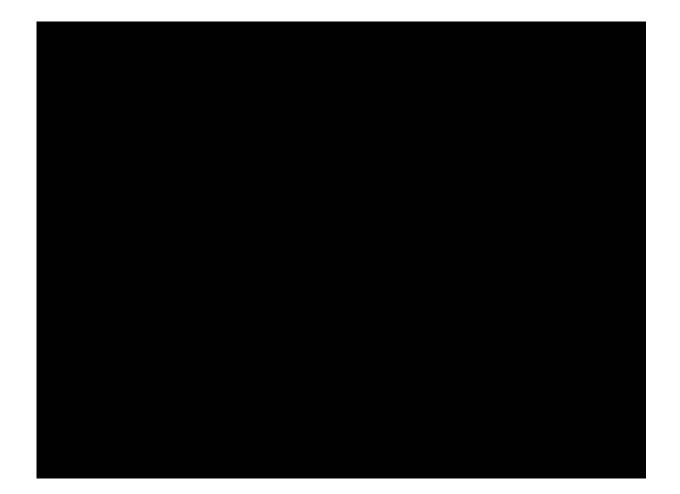
- Chinese Centers for Disease Control and Prevention (CDC) suggest that the case fatality rate for critical patients is 49%. Patients with preexisting comorbidities have a higher case fatality rate.
- These comorbidities include diabetes (7.3%), respiratory disease (6.5%), cardiovascular disease (10.5%), hypertension (6%), and oncological complications (5.6%).
- Patients without comorbidities have a lower case fatality rate (0.9%).
- 5% of patients can develop a critical disease with features of respiratory failure, cardiac injury, septic shock, or multiple organ dysfunction.

How to Put on and Remove Personal Protective Equipment

# PERSONAL PROTECTIVE EQUIPMENT

- 1. GLOVES
- 2. FACE SHIELD/GOGGLES
- 3. N95 MASK/ SURGICAL MASK
- 4. COVERALL
- 5. APRON
- 6. RUBBER BOOTS AND BOOT COVER
- 7. SCRUBS/HEAD COVER
- 8. 0.5% CHLORINE SOLUTION
- 9. ANTISEPTIC SOAP AND WATER
- 10. CHLORINE BATH





### **PPE Donning Steps**

- 1. Wash hands
- 2. Wear first layer of protective clothing
- 3. Put on rubber boots
- 4. Put on first pair of gloves
- 5. Put on the outer gown/coverall
- 6. Put on the plastic apron
- 7. Put on the second pair of gloves
- 8. Put on the mask
- 9. Put on the goggles
- 10. Put on a head cover

### PPE Removal / doffing Steps

- 1. Disinfect the outer pair of gloves
- 2. Disinfect the apron and boots\*\*\*
- 3. Remove the outer pair of gloves-then disinfect gloved hand
- 4. Remove the apron
- 5. Disinfect the gloved hands
- 6. Remove the head cover. -then disinfect gloved hand
- 7. Remove the outer coverall. -then disinfect gloved hand
- 8. Remove the goggles -then disinfect gloved hand
- 9. Remove the mask. -then disinfect gloved hand
- 10. Remove the inner pair of gloves.
- 11. Remove the boots.
- 12. Wash hands with bleach solution or soap and clean water.

## General guide on disinfection with chlorine

Concentratior	n Use
1%	Disinfection of heavily soiled linen
0.5%	Disinfection of body fluids
	Disinfection of surfaces
	Disinfection of toilets and bathrooms
	Disinfection of gloved hands
	Disinfection of floors
	Disinfection of beds and mattress covers
	Footbaths
0.05%	Disinfection of bare hands and skin
	Disinfection of medical equipment
	Disinfection of laundry
	Disinfection of eating utensils

# **Preparing chlorine solutions**

- 1. How do you constitute required chlorine solutions from liquid compounds?
- 2. How do you constitute required chlorine solutions from granule compounds?
- 3. How do you constitute required chlorine solutions from tablet compounds?

#### How to make chlorine solutions for environmental disinfection

#### Example I - Using Liquid Bleach

Chlorine in liquid bleach comes in different concentrations. Any concentration can be used to make a dilute chlorine solution by applying the following formula:

```
\left[\begin{array}{c} \frac{\% \text{ chlorine in liquid bleach}}{\% \text{ chlorine desired}}\right] - 1 = \text{Total parts of water for each part bleach}^{+}
```

Example: To make a 0.5% chlorine solution from 3.5%<sup>‡</sup> bleach:

 $\begin{bmatrix} \frac{3.5\%}{0.5\%} \end{bmatrix} - 1 = 7 - 1 = 6$  parts water for each part bleach

Therefore, you must add 1 part 3.5% bleach to 6 parts water to make a 0.5% chlorine solution.

- \* "Parts" can be used for any unit of measure (e.g. ounce, litre or gallon) or any container used for measuring, such as a pitcher.
- In countries where French products are available, the amount of active chlorine is usually expressed in degrees chlorum. One degree chlorum is equivalent to 0.3% active chlorine.

#### Example II - Using Bleach Powder

If using bleach powder,<sup>†</sup> calculate the amount of bleach to be mixed with each litre of water by using the following formula:

 $\begin{bmatrix} \frac{\% \text{ chlorine desired}}{\% \text{ chlorine in bleach powder}} \end{bmatrix} x 1 000 = \text{Grams of bleach powder for each litre of water}$ 

Example: To make a 0.5% chlorine solution from calcium hypochlorite (bleach) powder containing 35% active chlorine:

$$\frac{0.5\%}{35\%} \left[ x \ 1 \ 000 = 0.0143 \ x \ 1 \ 000 = 14.3 \right]$$

Therefore, you must dissolve 14.3 grams of calcium hypochlorite (bleach) powder in each litre of water used to make a 0.5% chlorine solution.

t When bleach powder is used; the resulting chlorine solution is likely to be cloudy (milky).

# For disinfection, remember!

- Always dilute disinfectants according to manufacturers instructions
- Add chlorine compounds to water not the other way round
- Change in-use disinfectant solution every 24hrs
- Disinfectants do not sterilise. Cannot be used for surgical instruments.
- Use gloves when mixing chlorine

## Waste segregation

Infectious waste	Pathological waste	Sharp Waste
Gauze/dressing Used IV/ fluid lines Used gloves Infusion set	Anatomical waste - Teeth - Placenta Pathological waste - Sputum container	Cannula/branula Retractables Broken slides Scalpels Broken vial Blades Broken ampules Needles Lancet Suture needle
Reflections Waste	Pathwasplant	SAFETY BOX
	Gauze/dressing Used IV/ fluid lines Used gloves Infusion set	Bauze/dressing Used IV/ fluid lines Used gloves Infusion set

