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Review Article

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WORLD BIGGEST PROBLEM NOVEL CORONA VIRUS

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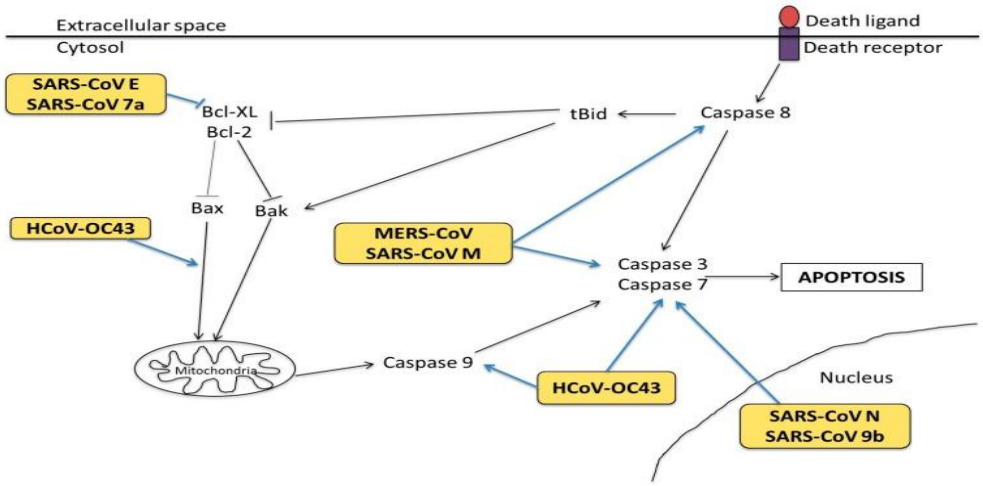
ABSTRACT

Coronaviruses are a large family of respiratory viruses that can cause diseases ranging from the common cold to the Middle-East Respiratory Syndrome (MERS) and the Severe Acute Respiratory Syndrome (SARS), as per WHO. So far, the main clinical signs and symptoms reported in the Wuhan outbreak include fever, difficulty in breathing, and chest radiographs showing bilateral lung infiltrates. However, not enough is known about the epidemiology of 2019-nCoV to draw definitive conclusions and the intensity of the human-to-human transmission, and the original source of the outbreak. Coronavirus is causing an outbreak first identified in Wuhan City, Hubei Province, China. Cases have been exported to Thailand, Japan, and South Korea external icon. According to the World Health Organization, common signs of infection include fever, cough, and respiratory difficulties like shortness of breath. Serious cases can lead to pneumonia, kidney failure and even death. A human coronavirus, called the Middle East respiratory syndrome coronavirus (MERS-CoV), Meanwhile, global concern rests on the ability of MERS-CoV to cause major illness in close contacts of patients.

KEYWORDS: Respiratory Syndrome, cold, illness.

INTRODUCTION

The severe acute respiratory syndrome (SARS) has recently been identified as a new clinical entity. SARS is thought to be caused by an unknown infectious agent. A novel coronavirus was identified in patients with SARS. The virus was isolated in cell culture, and a sequence 300 nucleotides in length was obtained by a polymerase-chain-reaction (PCR)–based random-amplification procedure. Genetic characterization indicated that the virus is only distantly related to known coronaviruses (identical in 50 to 60 percent of the nucleotide sequence). On the basis of the obtained sequence, conventional and real-time PCR assays for specific and sensitive detection of the novel virus were established. Virus was detected in a variety of clinical specimens from patients with SARS but not in controls. High concentrations of viral RNA of up to 100 million molecules per milliliter were found in sputum.[1] Viral RNA was also detected at extremely low concentrations in plasma during the acute phase and in feces during the late convalescent phase. Infected patients showed seroconversion on the Vero cells in which the virus was isolated. Human coronaviruses (HCoVs) are known respiratory pathogens associated with a range of respiratory outcomes. In the past 14 years, the onset of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have thrust HCoVs into spotlight of the research community due to their high pathogenicity in humans.[2] The study of HCoV-host interactions has contributed extensively to our understanding of HCoV pathogenesis. In this review, we discuss some of the recent findings of host cell factors that might be exploited by HCoVs to facilitate their own replication cycle. We also discuss various cellular processes, such as apoptosis, innate immunity, ER stress response, mitogen-activated protein kinase (MAPK) pathway and nuclear factor kappa B (NF-κB) pathway that may be modulated by HCoVs. SARS-CoV first emerged in 2002–2003 in Guangdong, China as an atypical pneumonia marked by fever, headache and subsequent onset of respiratory symptoms such as cough and pneumonia, which may later develop into life-threatening respiratory failure and acute respiratory distress syndrome A coronavirus was first isolated in 1937 from an infectious bronchitis virus in birds that has the ability to seriously devastate poultry stocks. These viruses are responsible for between 15 and 30 percent of common colds.[3] Over the last 70 years, scientists have found that coronaviruses can infect mice, rats, dogs, cats, turkeys, horses, pigs, and cattle.



CORONAVIRUSES

How it spreads

Novel Coronavirus (nCoV) first spread to humans from an animal the South china Seafood Wholesale market. The virus is transmitted between humans touching up to 3 feet or shaking hands with already infected person or object and his or her mouth, nose or eye.[1]

How it can kill

Most victims of the virus die from complications including pneumonia and swelling in the lungs. The virus also causes swelling in the respiratory system, which can make it hard for the lungs to pass oxygen into the blood stream. Severe pneumonia can kill people by causing them to 'drown' in the fluid flooding the cause illnesses ranging from a common cold to severe diseases.[2]

Where and how did the infection start

The first known and reported case emerged from the Chinese city of Wuhan in December Coronaviruses are zoonotic, meaning they are transmitted between animals and people.[3]

What to do to keep the disease at bay

- Observe for
- Practice to cover your mouth and nose while sneezing and coughing
- In case you feel symptoms pertaining to severe respiratory issues, don't delay in seeking medical help

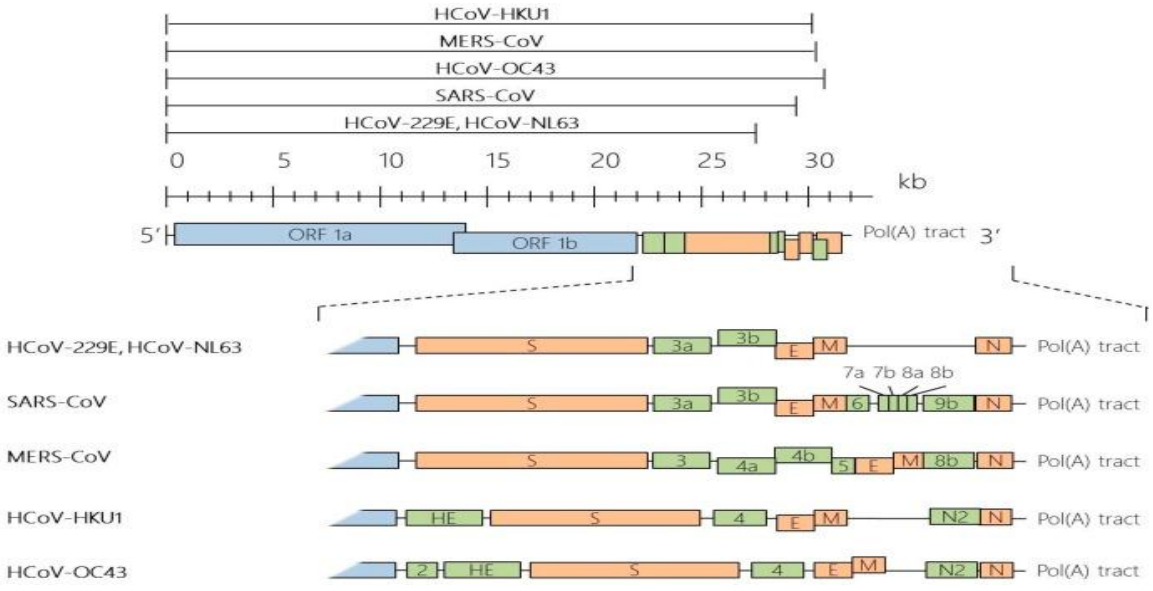
The source

The outbreak has not been identified but initially bats and snakes. Detailed investigations found that SARS transmitted from civet cats to humans and MERS from dromedary camels to humans.

Good personal hygiene

- Make a frequent habit to wash hands with soap or alcohol based hand rub
- In case of respiratory symptoms such as cough or running nose, make a practice to wear a mask
- Avoid being in close contact, public gathering and close proximity when you are experiencing cough and fever.[4]

Human Coronavirus



SPECIAL FEATURES

1. Early supportive therapy and monitoring

There is no current evidence from RCTs to recommend any specific anti-nCoV treatment for patients with suspected or confirmed 2019-nCoV infection.

- Give supplemental oxygen therapy immediately to patients with SARI and respiratory distress, hypoxaemia, or shock.[5]

➢ Remarks: Initiate oxygen therapy at 5 L/min and titrate flow rates to reach target SpO2 ≥90% in non-pregnant adults and SpO2 ≥92-95 % in pregnant patients. Children with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive oxygen therapy during resuscitation to target SpO2 ≥94%; otherwise, the target SpO2 is ≥90%. All areas where patients with SARI are cared for should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, simple face mask, and mask with reservoir bag). Use contact precautions when handling contaminated oxygen interfaces of patients with nCoV infection.

- Use conservative fluid management in patients with SARI when there is no evidence of shock.

➢ Remarks: Patients with SARI should be treated cautiously with intravenous fluids, because aggressive fluid resuscitation may worsen oxygenation, especially in settings where there is limited availability of mechanical ventilation.[6]

- Give empiric antimicrobials to treat all likely pathogens causing SARI. Give antimicrobials within one hour of initial patient assessment for patients with sepsis.

➢ Remarks: Although the patient may be suspected to have nCoV, administer appropriate empiric antimicrobials based on the clinical diagnosis (community-acquired pneumonia, health careassociated pneumonia [if infection was acquired in healthcare setting], or sepsis), local epidemiology and susceptibility data, and treatment guidelines within ONE hour of identification of sepsis. Empiric therapy includes a neuraminidase inhibitor for treatment of influenza when there is local circulation or other risk factors, including travel history or exposure to animal influenza viruses. Empiric therapy should be de-escalated on the basis of microbiology results and clinical judgment.

- Do not routinely give systemic corticosteroids for treatment of viral pneumonia or ARDS outside of clinical trials unless they are indicated for another reason.[7]

➢ Remarks: A systematic review of observational studies of corticosteroids administered to patients with SARS reported no survival benefit and possible harms (avascular necrosis, psychosis, diabetes, and delayed viral clearance, whereas in influenza it shows higher risk of mortality and secondary infections with corticosteroids. Finally, a recent study of patients receiving corticosteroids for MERS used a similar statistical approach and found no effect of corticosteroids on mortality but delayed lower respiratory tract (LRT) clearance of MERS-CoV.

- Closely monitor patients with SARI for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately.

- Understand the patient's co-morbid condition(s) to tailor the management of critical illness and appreciate the prognosis. Communicate early with patient and family.

➢ Remarks: During intensive care management of SARI, determine which chronic therapies should be continued and which therapies should be stopped temporarily. Communicate proactively with patients and families and provide support and prognostic information.[8]

2: Management of hypoxemic respiratory failure and ARDS

- Recognize severe hypoxemic respiratory failure when a patient with respiratory distress is failing standard oxygen therapy.

➢ Remarks: symptoms: increased work of breathing or hypoxemia even when oxygen is delivered via a face mask with reservoir bag. Hypoxemic respiratory failure in ARDS commonly results from intrapulmonary ventilation-perfusion mismatch or shunt and usually requires mechanical ventilation.

- High-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) should only be used in selected patients with hypoxemic respiratory failure. The risk of treatment failure is high in patients with MERS treated with NIV, and patients treated with either HFNO or NIV should be closely monitored for clinical deterioration.[9]
- Endotracheal intubation should be performed by a trained and experienced provider using airborne precautions.
- Implement mechanical ventilation using lower tidal volumes (4–8 ml/kg predicted body weight, PBW) and lower inspiratory pressures (plateau pressure <30 cmH2O).
- In patients with severe ARDS, prone ventilation for >12 hours per day is recommended.
- Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion.
- In patients with moderate or severe ARDS, higher PEEP instead of lower PEEP is suggested.
- In patients with moderate-severe ARDS (PaO2/FiO2 <150), neuromuscular blockade by continuous infusion should not be routinely used.

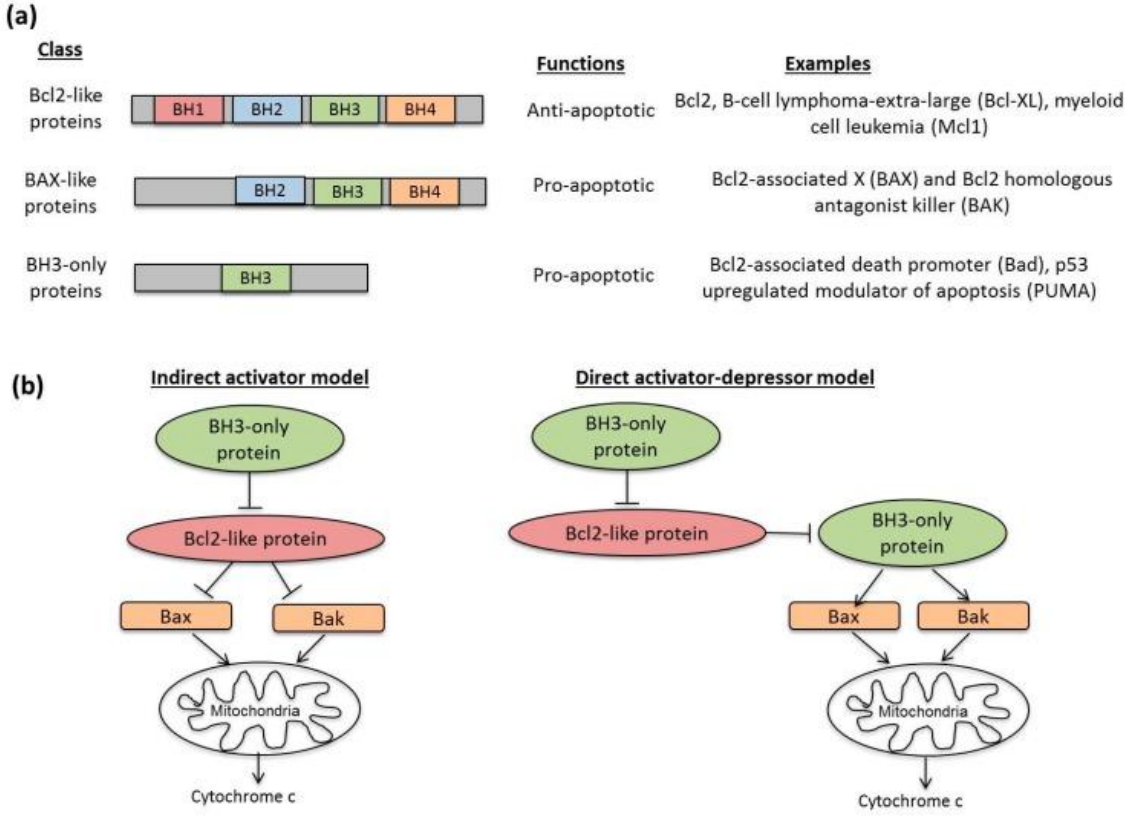
- In settings with access to expertise in extracorporeal life support (ECLS), consider referral of patients with refractory hypoxemia despite lung protective ventilation.
- Avoid disconnecting the patient from the ventilator, which results in loss of PEEP and atelectasis. Use in-line catheters for airway suctioning and clamp endotracheal tube when disconnection is required (for example, transfer to a transport ventilator).

3: Management of septic shock

- Recognize septic shock in adults when infection is suspected or confirmed AND vasopressors are needed to maintain mean arterial pressure (MAP) ≥65 mmHg AND lactate is ≥2 mmol/L, in absence of hypovolemia. Recognize septic shock in children with any hypotension (systolic blood pressure [SBP] <5th centile or >2 SD below normal for age) or 2- 3 of the following: altered mental state; tachycardia or bradycardia (HR <90 bpm or >160 bpm in infants and HR <70 bpm or >150 bpm in children); prolonged capillary refill (>2 sec) or warm vasodilation with bounding pulses; tachypnea; mottled skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia. Remarks: In the absence of a lactate measurement, use MAP and clinical signs of perfusion to define shock. Standard care includes early recognition and the following treatments within 1 hour of recognition: antimicrobial therapy and fluid loading and vasopressors for hypotension.
- In resuscitation from septic shock in adults, give at least 30 ml/kg of isotonic crystalloid in adults in the first 3 hours. In resuscitation from septic shock in children in well-resourced settings, give 20 ml/kg as a rapid bolus and up to 40-60 ml/kg in the first 1 hr.
- Do not use hypotonic crystalloids, starches, or gelatines for resuscitation. Fluid resuscitation may lead to volume overload, including respiratory failure. If there is no response to fluid loading and signs distension, crackles on lung auscultation, pulmonary oedema on in children), then reduce or discontinue fluid administration. This step is particularly important where mechanical ventila suggested when caring for children in resource Remarks: Crystalloids include normal saline and Ringer's lactate. Determine need for additional fluid boluses (250-1000 ml in adults or 10 improvement of perfusion targets. Perfusion targets include targets in children), urine output (>0.5 ml/kg/hr in adults, 1 ml/kg/hr in children), and improvement of skin mottling, capillary refill, level of consciousness, and lactate.
- Administer vasopressors when shock persists during or after fluid resuscitation. The initial blood pressure target is MAP
- If central venous catheters are not available, vasopressors can be given through a peripheral IV, but use a large vein and closely necrosis. If extravasationthrough intraosseous needles.
- If signs of poor perfusion and cardiac dysfunction persist despite achieving MAP target with fluids and vasopressors, consider.[10]

Remarks: Vasopressors (i.e. norepinephrine, epinephrine safely given through a central venous catheter at a strictly controlled rate, but it is also possible to safely administer them via peripheral vein frequently and titrate the vasopressor to the minimum dose necessary to maintain perfusion and prevent side effects. Norepinephrine is considered first vasopressin can be added to achieve reserve dopamine for selected patients with low risk of tachyarrhythmia In children with cold shock (more common), epinephrine is considered first norepinephrine is used in patients with warm shock (less common). dobutamine to placebo for clinical outcomes of volume overload appear (for example, jugular venous imaging, or hepatomegaly ventilation is not available. Alternate fluid regimens are resource-limited settings. 10-20 ml/kg in children) based on clinical response and MAP (>65 mmHg or age ≥65 mmHg in adults and age-appropriate targets in children. monitor for signs of extravasation and local tissue occurs, stop infusion. Vasopressors can also be an inotrope such as dobutamine. epinephrine, vasopressin, and dopamine) are most nister and intraosseous needle. Monitor blood pressure first-line in adult patients; epinephrine or the MAP target. Because of the risk of tachyarrhyth or those with bradycardia. No RCTs have compared outcomes. age-appropriate administered, tachyarrhythmia, first-line.[11]

Human Coronavirus Infection and Apoptosis.



CORONAVIRUS TREATMENT

Scientists, researchers and doctors are working on studying the virus also known as 2019-CoV; however, there is no vaccine that can treat Coronavirus, since this is a new strain that had previously not been identified in humans. The standard recommendations to prevent infection spread include regular hand-washing, covering mouth and nose when coughing and sneezing, thoroughly cooking meat and eggs and avoiding any close contact with persons showing symptoms of respiratory illness such as coughing and sneezing, says WHO.[12]

If you have travelled to any of the affected countries in the last 14 days and show any of the above-mentioned symptoms, notify your physician and share complete history.

- Ensure that you maintain standard precautions which include adequate hand and respiratory hygiene.
- Keep your environment clean at all times.
- Wear a medical mask if any of the symptoms are prevalent.
- Cover your nose and mouth while coughing and sneezing.
- Wash your hands after contact with respiratory secretions.
- Avoid close contact with anyone with cold and flu symptoms

BASIC PROTECTIVE MEASURES AGAINST THE NEW CORONAVIRUS

Stay aware of the latest information on the COVID-19 outbreak, available on the WHO website and through your national and local public health authority. Most people who become infected experience mild illness and recover, but it can be more severe for others. Take care of your health and protect others by doing the following.[13]

1. Wash your hands frequently Regularly and thoroughly clean your hands with an alcohol-based hand rub or wash them with soap and water. Washing your hands with soap and water or using alcohol-based hand rub kills viruses that may be on your hands. Maintain social distancing Maintain at least 1 metre (3 feet) distance between yourself and anyone who is coughing or sneezing.
2. When someone coughs or sneezes they spray small liquid droplets from their nose or mouth which may contain virus. If you are too close, you can breathe in the droplets, including the COVID-19 virus if the person coughing has the disease. Avoid touching eyes, nose and mouth.
3. Hands touch many surfaces and can pick up viruses. Once contaminated, hands can transfer the virus to your eyes, nose or mouth. From there, the virus can enter your body and can make you sick.
4. Practice respiratory hygiene Make sure you, and the people around you, follow good respiratory hygiene. This means covering your mouth and nose with your

bent elbow or tissue when you cough or sneeze. Then dispose of the used tissue immediately.

5. Droplets spread virus. By following good respiratory hygiene you protect the people around you from viruses such as cold, flu and COVID-19. If you have fever, cough and difficulty breathing, seek medical care early.
6. Stay home if you feel unwell. If you have a fever, cough and difficulty breathing, seek medical attention and call in advance. Follow the directions of your local health authority.
7. National and local authorities will have the most up to date information on the situation in your area. Calling in advance will allow your health care provider to quickly direct you to the right health facility. This will also protect you and help prevent spread of viruses and other infections. Stay informed and follow advice given by your healthcare provider.
8. Stay informed on the latest developments about COVID-19. Follow advice given by your healthcare provider, your national and local public health authority or your employer on how to protect yourself and others from COVID-19.
9. National and local authorities will have the most up to date information on whether COVID-19 is spreading in your area. They are best placed to advise on what people in your area should be doing to protect themselves.

PROBABLE CASE

A suspect case for whom testing for the COVID-19 virus is inconclusive or B. Inconclusive being the result of the test reported by the laboratory. A suspect case for whom testing could not be performed for any reason. Confirmed case A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms. Technical guidance for laboratory testing can be found here. Definition of 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.[14]

1. Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes;
2. Direct physical contact with a probable or confirmed case.
3. Direct care for a patient with probable or confirmed COVID-19 disease without using proper personal protective equipment1 ; OR
4. Other situations as indicated by local risk assessments. 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.[15]

PROTECTION MEASURES FOR AREAS WHERE COVID-19 IS SPREADING:

Persons who are in or have recently visited (past 14 days) areas where COVID-19 is spreading

- Follow the guidance outlined above.[16]
- Stay at home if you begin to feel unwell, even with mild symptoms such as headache and slight runny nose, until you recover. Why? Avoiding contact with others and visits to medical facilities will allow these facilities to operate more effectively and help protect you and others from possible COVID-19 and other viruses.[17]
- If you develop fever, cough and difficulty breathing, seek medical advice promptly as this may be due to a respiratory infection or other serious condition. Call in advance and tell your provider of any recent travel or contact with travelers. Why? Calling in advance will allow your health care provider to quickly direct you to the right health facility. This will also help to prevent possible spread of COVID-19 and other viruses.
- Genome organisation of human coronaviruses

Involvement of Host Factors in Viral Replication and Pathogenesis:

CURRENT SITUATION IN 2020

- WHO has developed a dashboard for Novel confirmed cases globally, which includes cases in China by provinces, regions and cities, as well as confirmed cases outside China by country. WHO Clinical Management Guidelines for hospitalised adult and paediatric patients with severe acute respiratory infection (SARI) of suspected nCoV.[18]
- China has exonerated a doctor who was officially reprimanded for warning about the coronavirus outbreak and later died of the disease. The party's top disciplinary body said the police force in Wuhan had revoked its admonishment of Dr. Li Wenliang that had included a threat of arrest. It also said a "solemn apology" had been issued to Li's family and that two police officers, identified only by their surnames, had been issued "disciplinary punishments" for the original handling of the matter. In death, Li became the face of simmering anger at the ruling Communist Party's controls over information and complaints that officials lie about or hide disease outbreaks, industrial accidents, natural disasters and financial frauds, while punishing whistleblowers and independent journalists.
- After seeing thousands of new cases daily at the peak of the city's outbreak a month ago, Wuhan on Friday had its second consecutive day with no new confirmed or suspected cases. The National Health Commission said all of the 39 new cases recorded Friday in China were brought from overseas, showing that rigid travel restrictions and social distancing requirements appear to have had their desired effect.
- China has loosened some travel restrictions in Hubei, the province surrounding Wuhan, although its provincial border remains closed and Wuhan itself remains under lockdown. Officials say they

will only lift the quarantine after Wuhan goes 14 consecutive days with no new cases.[19]

- Police in December had reprimanded eight doctors including Li for warning friends on social media about the emerging threat. China's supreme court later criticized the police, but the ruling party continued to tighten its grip on information about the outbreak.
- The party has faced similar accusations of bungling or thuggish behavior following previous disasters. They include the 2003 outbreak of Severe Acute Respiratory Syndrome, a 2005 chemical spill that disrupted water supplies to millions of people in China's northeast, sales of tainted milk that sickened thousands of children and the failure of private finance companies after the global economic crisis.

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