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a literature review

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Studies on viral pneumonia related to novel coronavirus SARS-CoV-2, SARS-CoV, and MERS-CoV: a literature review

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Summary

Coronaviruses are a class of RNA viruses that can cause respiratory and intestinal infections in animals and humans. SARS-CoV, MERS-CoV and a novel coronavirus (SARS-CoV-2 [2019-nCoV]) belong to the family Coronaviridae and the genus Betacoronavirus. At present, the understanding of SARS-CoV-2 is getting deeper and deeper. In order to better prevent and treat SARS-CoV-2, this article compares the infectivity, pathogenicity, and related clinical characteristics of the three human pathogenic coronaviruses, SARS-CoV-2, SARS-CoV and MERS-CoV to help us further understand the pathogenic characteristics of novel coronaviruses.

Key words: SARS-CoV-2, SARS-CoV；MERS-CoV；pneumonia；clinical features

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Epidemiology

1) Coronavirus and epidemiology

Coronaviruses (CoVs) are positive-sense, single-stranded RNA viruses with an envelope that can infect a variety of animals, including humans, and cause respiratory, intestinal, liver, and nervous system diseases (1). The viral genome encodes four or five structural proteins, namely spike protein, membrane protein, nucleocapsid protein, hemagglutinin esterase protein, and envelope protein. Spike protein is the most important surface membrane protein of coronavirus, which determines the host range and specificity of the virus. As the largest known RNA virus, the CoV subfamily is further divided into four genera: alpha, beta, gamma, and delta coronavirus. Including SARS-CoV-2, we have now identified seven human pathogenic coronavirus. Like SARS-CoV and MERS, SARS-CoV-2 belongs to beta-coronavirus (SARS-CoV and SARS-CoV-2: B lineage;

MERS-CoV: C lineage). Each SARS-CoV-2 virion is approximately 50–200 nm in diameter. Like other coronaviruses, SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins. Based on genome sequencing, 2019-nCoV is about 82% identical to human SARS-CoV and about 50% to MERS-CoV (2).

The origin of the coronavirus remains unclear. In the early days of the SARS and MERS outbreaks, palm civet cats and camels were considered natural hosts for these two human coronaviruses (HcoVs). However, further virological and genetic studies have shown that bats are natural hosts for SARS-CoV and MERS-CoV (3, 4), and the palm civet and camel are intermediate hosts, before final transmission to humans. Studies have shown that bat coronavirus is the gene source of most alpha- and beta-coronaviruses, that thus far, all identified CoVs that can infect humans belong to these two genera. Special attention has been paid to beta-coronaviruses, which have caused two unexpected coronaviral epidemics, SARS and MERS, in the past decade. SARS-CoV-2 (2019-nCoV) is 96.2% identical to the coronavirus on bats at the genome-wide level, suggesting that bats are also natural hosts for the virus (5). At present, it is unclear whether there are one or more hosts in the process of transmitting bat-to-human SARS-CoV-2.

How SARS-CoV, MERS-CoV, and SARS-CoV-2 infect humans through animals is unknown. It may be related to direct contact with intermediate host animals or eating raw meat or infected milk. The SARS-CoV person-to-person transmission route is mainly by droplets, and the population is generally susceptible. MERS-CoV possible transmission routes between humans are droplet transmission and close contact transmission (6). MERS-CoV has been epidemic in hospitals and caused medical personnel to suffer from MERS (7, 8); SARS-CoV-2 spreads among the population by droplets and contact. In high-concentration environments, SARS-CoV-2 may be transmitted through aerosols (9). The population is generally susceptible to SARS-CoV-2. No SARS cases have

been reported globally since 2004. MERS was first diagnosed in Saudi Arabia in 2012. MERS spread to 27 countries and regions in the Middle East, Asia, and Europe, and 80% of cases came from Saudi Arabia (10, 11). SARS-CoV-2 is currently causing widespread epidemics worldwide.

2) Pathogenic mechanism

At present, the understanding of the pathogenic mechanism of HCoVs is limited. The key to HCoV infection is through binding to specific receptors into susceptible host cells.

Angiotensin-converting enzyme 2 (ACE2) is a receptor for SARS-CoV (12). The receptor is a surface molecule located on arteriovenous endothelial cells, arterial smooth muscle cells, small intestinal epithelium and the respiratory tract. Hamming et al (13) have explored the expression of ACE2 protein in human organs (oral, nasal mucosa, nasopharynx, lung, stomach, small intestine, colon, skin, lymph nodes, thymus, bone marrow, spleen, liver, kidney, and brain). The results show that ACE2 is most abundantly expressed on the surface of alveolar epithelial cells and small intestinal epithelial cells, and ACE2 is also abundantly expressed on endothelial cells and smooth muscle cells in almost all organs. The amino acid sequence and predicted protein structure between the SARS-CoV-2 and the SARS-CoV receptor-binding domain (RBD) in the spike protein are highly similar. It is speculated that SARS-CoV-2 can use alveolar type II epithelial cells ACE2 as a receptor for cell invasion, thereby entering the bronchial epithelial cells. It is expected that there will be similarities in the clinical characteristics associated with the two viruses, especially in severe cases (14). Studies have shown that the affinity of SARS-CoV-2 for binding to ACE2 is higher than SARS-CoV (15).

Pipeptidyl peptidase 4 (DPP4, also known as CD26) is a receptor for MERS-CoV (16), a versatile cell surface protein that is widely expressed on kidney, small intestine, liver, prostate epithelial cells and activated leukocytes. DPP4 is expressed in the upper respiratory epithelium of camels. In the

human respiratory tract, DPP4 is mainly expressed in the alveoli rather than the nasal or upper airways (17).

3) Diagnostic criteria

Chinese COVID-19 diagnosis criteria (9):

Suspected cases:

a. Where there are any of the epidemiologic history items, and any 2 of the clinical presentations are met.
b. Where there is no clear epidemiological history, and at least 3 of the clinical presentations are met.

1). Epidemiological history: a. Within 14 days prior to onset, had history of travel or residence in Wuhan or surrounding regions, or other communities reporting cases; b. Within 14 days prior to symptom onset, having had contact with patients infected with SARS-CoV-2 (positive nucleic acid test); c. Within 14 days prior to onset, had contact with patients who had a fever or respiratory tract symptoms that had come from Wuhan, its surrounding regions, or other communities reporting cases. d. Clustered onset (Within a span of 2 weeks, 2 or more cases with fever and/or respiratory symptoms appear in a small area, such as a family, an office, or a school class)

2). Clinical presentations: a. Fever and/or respiratory tract symptoms; b. Having the imaging features of novel coronavirus pneumonia, such as ground-glass opacity, paving stone sign and consolidation; c. During the early stages of the disease, white blood cell and lymphocyte count are normal or reduced and progressively decreased in severe stages.

Confirmed cases:

A COVID-19 diagnosis is confirmed if the suspected cases also have one of the following etiological or serological evidence.

1). Positive result in real-time fluorescence RT-PCR detection of novel coronavirus nucleic acid;

2). The sequence of the virus is highly homologues to that of SARS-CoV-2.

3). Specific IgM and IgG antibodies against SARS-CoV-2 test positive in the serum; IgG antibodies specific to SARS-CoV-2 test positive after previous negative results, or increased by more than 4 times in the recovery phase compared to the acute phase.

Criteria for the diagnosis of SARS (10):

Suspected cases:

A person presenting with fever > 38 ºC; and cough or difficulty breathing; and either close contact with a person who is a suspect or probable case of SARS and/or history of travel or residence in an area with recent local transmission of SARS within 10 days of symptom onset.

Clinical diagnosis of SARS:

A suspected case with radiographic findings of pneumonia or acute respiratory distress syndrome (ARDS); or a suspected case positive for SARS-CoV in one or more laboratory assays;

Confirmed cases:

A clinical diagnosis case with SARS-CoV RNA detected, or a positive SARS-CoV antibody, or a 4-fold or higher antibody titer.

MERS laboratory confirmation criteria (6):

Suspected cases:

The patient meets the epidemiological history and clinical manifestations, but there is no laboratory confirmation basis. a. Epidemiological history. Within 14 days prior to onset, had history of travel or residence in the Middle East and outbreak areas; or a history of close contact with suspected / clinical diagnosis / confirmed cases. b. Clinical manifestations. Fever that is difficult to explain with other pathogenic infections, with respiratory symptoms.

Clinically diagnosed cases:

a. Patients who meet the criteria for suspected cases and only have laboratory-positive screening results (such as PCR or serum antibody positive). b. Patients who meet the criteria for suspected cases, and who have negative laboratory test results or cannot judge the results because there is only a single specimen collected or processed improperly.

Confirmed cases:

Have one of the following 4 items: a. at least dual target PCR test positive; b. single target PCR positive products, confirmed by gene sequencing; c. isolated MERS-CoV from the respiratory specimen; d. The serum level of MERS-CoV antibody in the early phase was more than 4 times higher than that in the acute phase.

The overall diagnostic criteria for SARS, MERS, and COVID-19 coronavirus pneumonia are similar. They all need to be based on epidemiological history, clinical manifestations, and etiological results. The difference is that the diagnostic criteria for SARS does not emphasize laboratory tests. The confirmed cases of MERS did not mention the epidemiological history and clinical manifestations, only the etiology basis, and the diagnosis basis did not include imaging evidence. The diagnosis of COVID-19 emphasizes peripheral white blood cell and lymphocyte counts, and epidemiological history highlights clustered onsets. See Table 1 for details.

Clinical features

1) Differences in latency, incidence and high-risk population, clinical symptomology and prognosis:

SARS, MERS, and COVID-19 are similar in their incubation period. Older ages and underlying diseases (chronic lung disease, cardiovascular disease, diabetes, malignant tumor, kidney disease, cerebrovascular disease, and immunosuppression) are high risk factor for development to severe disease or death in the three diseases (6, 9, 20-22). All three can cause complications such as acute lung injury (ALI), acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), shock, and multiple organ failure, which are life-threatening (6, 9, 23, 24).

Differences:

A. Progression of disease: MERS can progress into severe disease within one week (6). SARS and COVID-19 mostly progress after one week; COVID-19 is mostly mild, but critical illness progresses quickly (9, 25);

B. The affected population: The majority of SARS patients are young adults. According a study (26) about 5327 cases in China, the main age of onset is between 20-60 years old (85% of the total

number of cases), of which 20-29 years old have the highest proportion (30%). Half of MERS cases occur in people over 50 years old (27). Analysis of 4021 confirmed COVID-19 patients in China (the diagnosis date is January 26) shows that people of all ages are generally susceptible, of which 71.45% are 30-65 years old (28).

C. Clinical symptoms: COVID-19 has fewer gastrointestinal symptoms than SARS and MERS (29), lack of fever is more common in the early stages. Studies have shown that 43.8% of patients with COVID-19 initially develop fever symptoms, and no fever is more common than SARS-CoV (1%) and MERS-CoV infection (2%) (29). SARS patients do not often have upper respiratory tract catarrhal symptoms (18). Clinically asymptomatic cases have been seen in MERS and COVID-19 (6, 9). It has been reported (30) that compared with SARS, patients with MERS have a higher proportion of chronic diseases, developing respiratory failure, and receiving invasive mechanical ventilation. The incidence of AKI, the use of vasopressin, and the mortality rate are also higher in MERS. See Table 2 for details.

Laboratory features are generally similarIn principle all 7 can give pneumonia…

2)

The laboratory tests of the three types of coronavirus pneumonia are roughly the same. They all emphasize that the total number of white blood cells in the peripheral blood is normal, the number of lymphocytes is reduced, and the progressive reduction is severe (9). SARS proposes that the absolute value of lymphocytes is less than 0.9×10^9/L as the basis for auxiliary diagnosis, and> 1.2×10^9/L does not support diagnosis (18, 34). SARS highlights a reduction in CD4 + in peripheral blood T lymphocyte subsets (18). Blood routine, liver enzymes, myocardial enzymes, renal function, albumin levels, coagulation function, and electrolyte conditions suggest disease prognosis (6, 9, 23, 24, 29, 31, 32). See Table 3 for details.

3) Phased and characteristic evolution of coronavirus-induced pneumonia

Thoracic imaging is of great value in the diagnosis of COVID-19, monitoring of therapeutic efficacy and patient discharge assessment. A high-resolution CT is highly preferable in diagnosis.

The imaging features of SARS, MERS and COVID-19 are the same:

A. Staging evolution: Early lesions are limited, lesions are small, ground glass is dominant, the scope of the advanced stage is enlarged, the lesions become solid, and even show "white lung", the scope of the recovery period is reduced, and the density is reduced, fibrosis may appear in later stage (18, 21, 36).

B. Main manifestations: Ground glass, consolidation, and "paving stone sign". The ground glass was mainly in the initial stage, and the onset was mainly distributed in the lower lung and extra pulmonary zone (6, 18, 36, 38, 39).

Differences:

A. Image classification: SARS can be divided into four types: Type 1, the initial image performance deteriorates to a peak level, and then gradually improves; Type 2, static imaging performance; Type 3, fluctuating imaging changes; Type 4, progressively worsening imaging findings (45).

B. Main manifestations: Pleural effusion is relatively rare in cases of viral infection in the lungs, and is only found in SARS and COVID-19 heavy and critically severe phases (40, 41). However, MERS can be associated with pleural effusion (42), and is associated with prognosis adverse correlations (38), and studies (38, 39) showed that patients who died of MERS could see pleural effusion at week one. In addition, bilateral lung involvement is one of the risk factors for patients with MERS staying in the ICU (31). Organizing pneumonia can occur in patients with MERS and

SARS (39, 43). In some cases of COVID-19, "halo sign" and "anti-halo sign" can be seen (37). See Table 4 for details

Treatment

At present, the main treatment methods for three types of coronavirus pneumonia are: symptomatic supportive treatment, close monitoring of patients' condition, active prevention and treatment of complications, and maintenance of intestinal function (6, 9, 18). With the continuous advancement of medical technology, symptomatic supportive therapies mainly based on oxygen therapy have gradually increased, such as nasal high-flow oxygen, external membrane oxygenation support technology (ECMO).

1) Antiviral therapy: There is currently no effective specific antiviral therapy. The currently available antiviral drugs include lopinavir, ritonavir, ribavirin, and remdesivir may be effective drugs in the future. (18, 30, 48). The combined use of ribavirin and lopinavir/ritonavir gives a better clinical outcome in treatment of SARS (48). The main problem with ribavirin is the significant incidence of adverse events (49). Lopinavir/ritonavir can improve MERS-CoV infection in animal models. *In vitro* experiments, interferon can effectively inhibit SARS-CoV and MERS-CoV (50, 51). Alpha-interferon nebulization, lopinavir/ritonavir, or ribavirin (9) may be used to treat COVID-19, but clinical efficacy needs to be further verified (52). Chinese national guideline on diagnosis and treatment of novel coronavirus pneumonia (9) recommends lopinavir/ritonavir for adult: 200mg/50mg/tablet, 2 tablets twice daily; the length of treatment should not exceed 10 days; ribavirin (in combination with interferon or lopinavir/ritonavir) for adult: 500mg twice or three times daily via IV, the length of treatment should not exceed 10 days. Remdesivir has demonstrated good inhibitory effects on SARS-CoV and MERS-CoV *in vitro* and in animal models, and the drug may be an effective therapeutic drug for COVID-19 (52). Chloroquine phosphate has anti-coronal virus activity, and has been recommended to treat COVID-19, but the side effects and the

interaction of other drugs must be paid attention to (53). Chloroquine has been shown to be effective *in vitro* against a broad range of viruses, and the preventive and therapeutic effects of this drug on patients with COVID-19 are also being further evaluated (54). Clinical studies have shown that the superiority of chloroquine compared with treatment of the control group in terms of reduction of exacerbation of pneumonia, duration of symptoms and delay of viral clearance. This drug could also reduce the length of hospital stay and improve the evolution of COVID-19 (55)

2) Glucocorticoids: Glucocorticoid therapy should strictly follow the indications, usage and dosage, and be alert to complications. The main indications are the deterioration of lung lesions and the appearance of ALI or ARDS. Glucocorticoid were widely used during the SARS outbreak, often in combination with ribavirin (30), but glucocorticoid therapy was associated with a subsequent higher plasma viral load (56) and increased complications. The use of glucocorticoid may be helpful in treating suspected MERS-induced pneumonia (43). Retrospective studies of SARS and MERS have shown that improper use of glucocorticoid can increase mortality (52). Studies have shown that 18.6% of 1099 patients with COVID-19 were treated with systemic glucocorticoids, and the proportion of patients in the severe group was higher than that in the non-severe group (44.5% vs 13.7%, $P < 0.001$) (29).

3) Antibacterial drugs: It is often used in secondary bacterial or fungal infections. Irrational use of antibacterial drugs should avoid (47).

4) Other treatments: Serum therapy, psychological therapy, and traditional Chinese medicine treatment during recovery period (6, 18). Patients' convalescent plasma may contain antibodies that can neutralize the virus, which can be used as a potential therapy for sudden infectious diseases such as SARS-CoV and MERS-CoV (57-59). The seventh edition of China's New Coronary Virus Pneumonia Diagnosis and Treatment Program includes recovery period serum therapy into the

treatment method, and proposes its indications as patients with rapid disease progression, severe and critically ill. Its safety and effectivity need further exploration (52). See Table 5 for details.

Summary

SARS-CoV-2 is the seventh coronavirus that can infect human beings discovered so far. It belongs to the coronavirus β genus with MERS-CoV and SARS-CoV. The main transmission routes are droplet transmission and contact transmission. The clinical features of pneumonia caused by SARS-CoV, MERS-CoV, and SARS-CoV-2 are similar, but there are also differences. In terms of diagnosis, SARS diagnostic criteria does not emphasize relevant laboratory tests, MERS diagnosis does not include imaging evidence, and COVID-19 diagnosis emphasizes peripheral blood leukocyte and lymphocyte counts and aggregated onset. In terms of clinical characteristics, SARS is more common in young people, Mild cases COVID-19 is more common, and the proportion of patients with initial fever and gastrointestinal symptoms is less than MERS and SARS; MERS and COVID-19 are more common in middle-aged people; Asymptomatic cases can be seen in MERS and COVID-19. In terms of imaging, pleural effusion in MERS is more common than the other two coronavirus pneumonia and is associated with prognosis of disease. About 20% of patients whose can suddenly become worse and develop into severe and critical cases, during the progression stage of SARS and COVID-19. In terms of treatment: symptomatic supportive therapy is currently dominating, and there is no effective specific antiviral therapy. Antiviral therapy or other related therapies still need further research to find more precisely clinical evidence. Irrational use of antibacterial drugs and glucocorticoids should be avoided, and indications require strict control.

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Table 1. Comparing diagnostic criteria for SARS-CoV, MERS-CoV, SARS-CoV-2 related pneumonia [6, 9, 18, 19]

	SARS	MERS	COVID-19
Suspected cases	Lack of epidemiological history (EH), but with other support for SARS	EH + symptoms (fever which is difficult to explain with other pathogenic infections, with respiratory symptoms)	EH + clinical presentations (CP) (a. fever and/or respiratory tract symptoms; b. chest imaging features; c. white blood cell and lymphocyte count are normal or reduced.)
Clinical diagnosis	EH + symptoms + imaging + exclusion of other diseases	Suspected cases + pathogen (laboratory screening results)	EH + 2 of CP or 3 of CP without EH
Confirmation of diagnosis	Clinical diagnosis + pathogen identified	Pathogen identified	Suspected cases + pathogen identified
Difference	Clinical diagnosis emphasizes exclusion;	Clinical symptoms emphasize differentiation;	Epidemiological history including clustered onset
	Suspected cases may lack a clear epidemiological evidence	Confirmed cases depend only on etiology; No mention of imaging	Emphasis on peripheral blood test results

Table 2. Comparing clinical features of SARS-CoV, MERS-CoV, SARS-CoV-2 related pneumonia (6, 9, 18, 20-23, 25, 29-34)

	SARS	MERS	COVID-19
Incubation period	2-14 days	2-14 days	1-14 days, most cases are 3-7 days
Onset and course evolution	Urgent onset, mostly in 8-14 days, dyspnea and hypoxemia often appear 6-12 days after onset	Severe cases usually progress to severe pneumonia within one week	Severe cases often have dyspnea and / or hypoxemia one week after onset
Age	20-60 years old, mainly young adults	Median age: 56 years old, 50% >50 years old	40-60 years old
Clinical features	Fever > 38°C, persistent fever; chills, myalgias, fatigue; dry cough, sore throat; respiratory distress; diarrhea, vomiting; often without catarrhal symptoms	Fever; chills, fatigue, myalgia; cough, chest pain, dyspnea; vomiting, diarrhea; some patients may be asymptomatic	Fever (low or medium grad fever in severe and critical cases or even no fever); fatigue; dry cough; stuffy nose, runny nose, sore throat; diarrhea; mild cases may not have pneumonia symptoms
High risk factors	> 50 years; suffering from other diseases; recent major surgical history; progressive decrease in peripheral blood lymphocyte count	> 65 years; obesity; suffering from other diseases; co-infection	≥65 years; T <37.5 ℃; suffering from other diseases; In peripheral blood: WBC < 4×10^9/L or > 10×10^9/L, lymphocyte count and platelet reduction
Severe features	R>30 times/min, multilobular lesions > 1/3 of total lung area, lesion enlargement >50% and 1/4 of total lung area in 48h, oxygenation index <300mmHg, shock or MODS	Double lung involvement with ARDS, acute renal failure, MODS	R>30 times/min, oxygen saturation <93%, oxygenation index <300mmHg; respiratory failure, mechanical ventilation requires, shock, combined with other organ failure, requires ICU monitoring
Complications	Acute lung injury, ARDS, AKI, shock, AMI, arrhythmia, MODS, difficult to correct metabolic acidosis, coagulation dysfunction, etc.		
Difference	More common in young people; Urgent onset, No catarrh symptoms;	Short time to development of severe illness; Visible asymptomatic cases;	Most cases are mild cases, rapid progress in severe cases; No fever in early stage is common; Less gastrointestinal symptoms; there are asymptomatic cases;

ARDS: Acute respiratory distress syndrome

AKI: Acute kidney injury

AMI: Acute myocardial injury

MODS: Multiple organ dysfunction syndrome.

Table 3. Comparing laboratory examination characteristics of SARS-CoV, MERS-CoV, SARS-CoV-2 related pneumonia [6, 9, 18, 23, 24, 29, 31-33]

	SARS	**MERS**	**COVID-19**
WBC	WBC normal or decrease	Reduction of absolute lymphocyte count	lymphocyte progressive decrease in Severe cases
Biochemistry	Creatine kinase (CK), liver enzymes, lactate dehydrogenase (LDH), creatinine, myoglobin, and troponin increase.		
	$CD3^+$, $CD4^+$, $CD8^+$ are all decreased, $CD4^+$ significantly decreased		C-reactive protein (CRP), erythrocyte sedimentation, and D-dimer are increased, procalcitonin normal
Risk factors for poor or severe prognosis	High neutrophil count, blood urea nitrogen, serum creatinine and CK, longer partial thromboplastin time, low blood sodium concentration and platelets	Peripheral blood lymphocytes and neutrophils decrease ($<0.5 \times 10^9$/L), thrombocytopenia, albumin decrease (<35g/L)	LDH, liver enzymes, total bilirubin, blood urea nitrogen, blood creatinine, troponin, D-dimer and CRP increase; WBC and neutrophil, hemoglobin concentration, and blood potassium concentration decrease

Table 4. Comparing imaging features of SARS-CoV, MERS-CoV, SARS-CoV-2 related pneumonia [6, 9, 18, 19, 21, 23, 24, 31, 36-47]

	SARS	MERS	COVID-19
Image staging (type)	Early, progressive and recovery stages. Type I (70.3%), II (17.4%) III (7.3%), IV (5.1%)*	Type I-IV**	Early, progressive, sever and critical stages
Common features	Ground glass (common, early stage), consolidation, "paving stone sign" (early stage)	Ground glass (wider), consolidation	Ground glass (common), consolidation, “white lung”, "paving stone sign",
Other features	Mediastinal emphysema, pneumothorax	Pleural effusion, pneumothorax	"Halo Sign", "Anti-Halo Sign"
Rare features	Pleural effusion, lymphadenopathy, cavitation, calcification, mesh, nodule	Cavitation	Lymph node enlargement, pleural effusion only seen in severe and critical stages
Distributed	All are extrapulmonary and more common in the lower lung		
Process evolution	Severe progress is rapid and can be significantly worsened in 2 days; Ground glass → mixed density → consolidation; focal → multifocal → diffusion; lower lobe → diffusion; single lung → double lung; outer band → inner and outer band → diffusion (SARS); outer band → mid-outer band → diffusion (COVID-19); can eventually be "white lung"; In recovery stage, range of lesions becomes smaller and the density becomes lighter; a few cases develop pulmonary fibrosis		

***** Four imaging modes of SARS:

Type I: Initial image deteriorates to a peak level and then gradually improves; Type II: Fluctuating imaging changes; Type III: Static imaging presentation; Type IV: Progressive deteriorating imaging (45).

**Four imaging modes of MERS:

Type I: Initial image deteriorates to a peak level and then gradually improves; Type II: Static imaging presentation; Type III: Fluctuating imaging changes; Type IV: Progressive deteriorating imaging (38).

Table 5. Comparing treatment of SARS-CoV, MERS-CoV, SARS-CoV-2 related pneumonia [6, 9, 18, 25, 29, 30, 43, 48-52, 54-57]

	SARS	MERS	COVID-19
General treatment	Supportive treatment: bed rest, maintaining caloric intake, water and electrolyte balance		
Monitor	All vital signs, arterial blood gas analysis, hematology panel, routine urinalysis, CRP, biochemistry, coagulation, chest radiography, etc.		
Respiratory support	Nasal catheter, oxygen mask, mechanical ventilation	The left three + ECMO	The left four + high flow nasal cannula
Antiviral drugs	No specific drugs have been found;	No clear effective drugs;	No confirmed effective antiviral treatment; can try Interferon-alpha, lopinavir/ritonavir, ribavirin and chloroquine
Glucocorticoid	Indication: One of the followings, Severe poisoning symptoms, persistent high fever; rapid progress on chest radiographs; ALI or ARDS. Improper using can increase mortality	Indication: Presence of organizing pneumonia; Improper using can increases mortality	Indication: Confirmed diagnosis with rapidly progression; sever and critical stage; persistent high fever > 39°C, CT imaging or > 30% lung; CT rapid progression > 50% lung in 48 hrs; IL-6 ≥ 5 ULN
Recovery serum	Potential therapies for high-risk patients	Latent therapy	Rapidly progression; severe, and critically ill patients
Other treatment	Antibacterial treatment, psychological treatment, Chinese medicine treatment, maintaining gastrointestinal function		