



SARS-CoV-2 was previously provisionally named 2019 novel coronavirus or 2019-nCoV disease (COVID-19).

SARS-CoVs, MERS-CoVs and SARS-CoV-2 are classified in beta-coronavirus family members¹.

Recent published research suggests that SARS-CoV-2 shares 79.0% nucleotide identity to SARS-CoV and 51.8% identity to MERS-CoV².

We found, while studying the new coronavirus, RNA sequences from HIV that could not have naturally become part of SARS-CoV-2. Molecular tools are required to insert an HIV sequence into the genome, and this can only be done in a laboratory. Luc Montagnier³.

Montagnier was not the first to discover this curiosity. An Indian team of researchers would also have found HIV-RNA sequences in the virus, but then came under pressure to withdraw its paper⁴.

PATHOGENESIS

- Inflammation
- Cytokine storm
- Apoptosis of epithelial and endothelial cells
- Increased VEGF - edema

In SARS-CoV and MERS-CoV infected animal model, marked inflammatory and immune responses may activate a “cytokine storm”, and apoptosis of epithelial cells and endothelial cells; subsequently, vascular leakage, abnormal T cell and macrophages responses ensue and induce acute lung injury or acute respiratory distress syndrome or even death⁵.

In the blood of patients with COVID-19, there was a marked increase in interleukin 1 β (IL-1 β), interferon γ (IFN- γ), interferon-inducible protein 10 (IP-10), and monocyte chemoattractant protein 1 (MCP-1), as well as IL-4 and IL-10 when compared to that of SARS patients. This suggests some potential difference from SARS and MERS in the pathogenesis of coronavirus⁶.

There is also a potential repressed immune function in COVID-19 patients with the hypo-albuminemia, lymphopenia, neutropenia, and decreased percentage of CD8 T cell⁷.

PATHOGENIC EXAMINATION

The pathogenic examination of lung specimens from mild COVID-19 patients (who were retrospectively found to have COVID-19 at the time of lung cancer surgery) showed edema, proteinaceous exudate with globules, patchy inflammatory cellular infiltration and moderate formation of hyaline membranes⁸. In a postmortem assessment of a COVID-19 patient with severe ARDS, specimens of infected lungs demonstrated bilateral diffuse alveolar damage with edema, pneumocyte desquamation and hyaline membrane formation⁹.

Though these pathological reports were reported in only a small number of cases, the findings do resemble the pathological features found in SARS- and MERS-induced pneumonia¹⁰.

TRANSMISSION¹¹

It is spread by human-to-human transmission via droplets or direct contact, and infection has been estimated to have mean incubation period of 6.4 days and a basic reproduction number of 2.24-3.58.

WEARING FACE MASKS

The size of the SARS-CoV particle from the 2002–2004 outbreak was estimated as 0.08 to 0.14 μm^{12} ; assuming that SARS-CoV-2 has a similar size, surgical masks are unlikely to effectively filter this virus. Neither surgical nor cotton masks effectively filtered SARS-CoV-2 during coughs by infected patients¹³.

In a review of 10 RCTs they found no significant reduction in influenza transmission with the use of face masks¹⁴.

HAND HYGIENE

In a systematic review they did not find evidence of a major effect of hand hygiene on laboratory-confirmed influenza virus transmission¹⁵.

SURFACE CLEANING

They found no evidence that surface and object cleaning could reduce influenza transmission¹⁶.

AIR TEMPERATURE AND AIR HUMIDITY¹⁷

Air temperature and air humidity showed significantly negative associations with COVID-19.

Every 1°C increase in the air temperature led to a decrease in the daily confirmed cases by 36% to 57% when air humidity was in the range from 67% to 85.5%.

Every 1% increase in air humidity led to a decrease in the daily confirmed cases by 11% to 22% when air temperature was in the range from 5.04°C to 8.2°C.

SYMPTOMS^{18,19,20}

Fever	85.6 %
Cough	65.7 %

Fatigue 42.4 %

Dyspnea 21.4 %

Bilateral lung involvement with ground-glass opacity was the most common finding from computed tomography images of the chest.

So far, only 15 to 20% of cases have become severe. Those with weakened immune systems may develop more serious symptoms, like pneumonia or bronchitis. So far, only people 40 years old and older have developed the Wuhan coronavirus infection.

COMORBIDITIES²¹

Diabetes 7.7 %

Hypertension 15.6 %

Cardiovascular disease 4.7 %

Malignancy 1.2 %

RISK OF SEVERITY

12.6 to 23.5%²².

COMPLICATIONS

- Sepsis²³
- Cardiac arrest²⁴
- Acute Lung Injury²⁵
- Acute Respiratory Distress Syndrome²⁶

RISK OF MORTALITY²⁷

2.0 to 4.4 %.

THERAPY

Chinese Medicine²⁸. There were 3 studies using CM for prevention of SARS and 4 studies for H1N1 influenza. None of the participants who took CM contracted SARS in the 3 studies. The infection rate of H1N1 influenza in the CM group was significantly lower than the non-CM group (relative risk 0.36, 95% confidence interval 0.24-0.52; n=4). For prevention of COVID-19, 23 provinces in China issued CM programs.

Lysine - HCoV229E²⁹. Cells were infected with human coronavirus 229E (HCoV-229E) and MERS-CoV. D, L-lysine acetylsalicylate + glycine (LASAG, C15H22N2O6, 326.3 g/mol) was obtained as "Asprin i.v. 500mg[®]" and dissolved in dH2O to provide a stock concentration of 1 M. BAY11-7082 was solved in DMSO at a stock concentration of 50 mM and stored at -20°C until further usage. The results indicate that the reduction in the viral titre observed under LASAG (Lysine-Acetylsalicylic acid-Glycine) treatment could be related to the negative effect of LASAG on the viral protein and RNA production.

Lysine - Herpes Simplex. Lysine reduced recovery time, clinical manifestations and recurrence³⁰.

Lower outbreak frequency with 1248mg lysine daily compared with placebo³¹.

Less frequent recurrences, decreased severity, shorter duration with lysine therapy. Increased lesion formation after high arginine intake in previous 12–36 hr³².

Fewer outbreaks, reduced healing time, and milder

symptoms with lysine compared with placebo³³.

Lysine - Influenza Virus. The addition of large amount of lysine to incubated influenza virus cells stops the protein synthesis of the virus³⁴.

Lysine - Reovirus. Lysine is essential for the replication of infectious reovirus. Omission of lysine from the extracellular medium not only permitted the continued synthesis of structural viral proteins and viral double-stranded ribonucleic acid (RNA), but also caused an enhanced formation of viral structures which were separable by isopycnic sedimentation of CsCl into a top band consisting of empty particles with a buoyant density of 1.29 g/cm³ and essentially free of viral RNA, and two lower bands which were difficult to resolve and had an average buoyant density of 1.37 g/cm³. The lower bands contained most of the viral nucleic acid. The above effects were reversed when lysine was restored early after infection³⁵.

Lysine - Varicella Zoster Virus. Lysine substitutions against alanine in the viral proteins induced a 440% increase in cell-to-cell fusion, while lysine substitution against arginine induced a 2-fold fusion³⁶.

Melatonin

1. Ameliorating septic shock³⁷
2. Suppressing VEGF³⁸
3. Reducing sepsis-induced renal injury³⁹
4. Reducing septic cardiomyopathy⁴⁰
5. Reducing liver injury⁴¹
6. Enhancing the immune response by improving proliferation and maturation of: natural killing cells
 - T and B lymphocytes
 - granulocytes and monocytes in both bone marrow and other tissues

Melatonin is not viricidal but it has indirect anti-viral actions⁴² due to its antiinflammation, antioxidation and immune enhancing features^{43,44,45,46}.

There are situations in which melatonin suppresses the features of viral infections. In mice whose central nervous system is infected by virus (e.g., encephalitis), the use of melatonin caused less viremia, reduced paralysis and death, and decreased virus load⁴⁷.

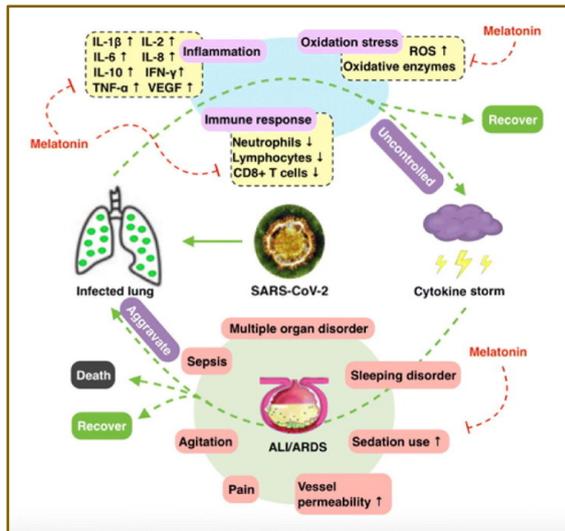
Viral infections and their replication constantly generate oxidized products.

Melatonin exerts regulatory actions on the immune system and directly enhances the immune response by improving proliferation and maturation of natural killing cells, T and B lymphocytes, granulocytes and monocytes in both bone marrow and other tissues⁴⁸.

In macrophages, antigen presentation is also augmented after the application of melatonin, where the up-regulation of complement receptor 3, MHC class I and class II, and CD4 antigens were detected⁴⁹.

In a randomized controlled trial, 8-week oral intake of 6 mg/d melatonin caused a significant decrease in serum levels of IL-6, TNF- α and hs-C-reactive protein (hs-CRP) in

patients with diabetes mellitus and periodontitis⁵⁰. In another trial of patients suffering with severe multiple sclerosis, orally 25 mg/d of melatonin for 6 months also promoted a significant reduction in serum concentrations of TNF- α , IL-6, IL-1 β and lipoperoxides⁵¹. In the acute phase of inflammation, including during surgical stress⁵², brain reperfusion⁵³, and coronary artery reperfusion⁵⁴, melatonin intake of 10 mg/d, 6 mg/d and 5 mg/d of melatonin for less than 5 days induced a reduced level of pro-inflammatory cytokines.



Putative pathogenesis of COVID-19 and potential adjuvant use of melatonin.

Melissa - Herpes simplex. The Melissa extract and rosmarinic acid inhibited HSV-1 attachment to host cells in a dose-dependent manner for acyclovir-sensitive and acyclovir-resistant strains. These results indicate that mainly rosmarinic acid contributed to the antiviral activity of Melissa extract. Penetration of herpes viruses into cells was inhibited by Melissa extract at 80% and 96% for drug-sensitive and drug-resistant viruses, respectively. Melissa extracts exhibits low toxicity and affects attachment and penetration of acyclovir-sensitive and acyclovir-resistant HSVs in vitro⁵⁵.

Melissa - Influenza virus. The study showed that lemon balm essential oil could inhibit influenza virus replication through different replication cycle steps especially throughout the direct interaction with the virus particles⁵⁶.

Selenium - H1N1. Whereas the mortality of the virus-infected Se-deficient mice was 75%, along with a marked

reduction in body weight, lower levels of TNF- α and IFN- γ and lower serum selenium concentrations, the mortality of mice maintained on feed containing 0.5 mg Se/kg in the form of sodium selenite was 25%. There were no significant differences, however, in viral titer between the Se-adequate and the selenium-supplemented groups⁵⁷.

Selenium - H9N2. In this study, we have evaluated the effects of supplementation of chicken diets with organic (Selenium Enriched Yeast; SEY) and inorganic selenium (Sodium Selenite; SS) on low pathogenicity avian influenza virus (H9N2) shedding in the cloacal and oropharyngeal swab samples as well as examined the expression of immune related genes. Chickens were fed two doses (High- 0.30mg/kg of feed; Low- 0.15mg/kg of feed) of selenium supplementation for 2 weeks followed by low pathogenicity avian influenza virus challenge. Our results showed that the cloacal shedding of virus in all the selenium supplemented groups was significantly lower when compared to the non-supplemented control groups. In addition, the oropharyngeal shedding of virus in chickens fed with organic selenium supplementation was significantly lower than that in the chickens that received either inorganic selenium supplemented feed or controls.

Spermidin⁵⁸. SARS-CoV-2 infection limits autophagy. Exogenous administration of spermidine, AKT inhibitor MK-2206, and the Beclin-1 stabilizing, antihelminthic drug niclosamide inhibited SARS-CoV-2 propagation by 85, 88, and >99%, respectively.

Vitamin C - Influenza Virus. Control (463) vs Test (252). 1g hourly for 6 hours, than 3x1g a day. Reported flu and cold symptoms in the test group decreased 85% compared with the control group after the administration of megadose Vitamin C⁵⁹.

Vitamin D - HIV. This review suggests that VitD deficiency may contribute to the pathogenesis of HIV infection. VitD supplementation and restoration to normal values in HIV-infected patients may improve immunologic recovery during combination antiretroviral therapy, reduce levels of inflammation and immune activation, and increase immunity against pathogens⁶⁰.

Zinc Pythirione - Influenza Virus/Poliovirus. Increasing the intracellular Zn(2+) concentration with zinc-ionophores like pythirione (PT) can efficiently impair the replication of a variety of RNA viruses, including poliovirus and influenza virus⁶¹.

		Prophylaxis
Chinese Herbs	Radix astragali (Huangqi)	n.s.
	Radix glycyrrhizae (Gancao)	
	Radix saphoshnikoviae (Fangfeng)	
	Rhizoma Atractylodis Macrocephalae (Baizhu)	
	Loniceræ Japonicæ Flos (Jinyinhua)	
	Fructus forsythia (Lianqiao)	
DHEA		n.s.
Growth Hormone		n.s.
Lysine		at least 3 g a day
Melissa		at least 143 mg extract
Melatonin		3-10 mg a day
Selenium		at least 200 mcg a day
Spermidine		n.s.
Triiodthyronine (T3)		n.s.
Vitamin C		at least 1 g a day
Vitamin D		at least 3.000 IE a day
Zinc		at least 50 mg a day

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