Recent epidemiological publications and summaries:

Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30566-3/fulltext
Journal: The Lancet *Published Online: March 9, 2020*
Authors from: China

Retrospective, multicentre cohort study included all 191 adult inpatients with confirmed COVID-19 from Jinyintan Hospital and Wuhan Pulmonary Hospital who had been discharged (n=137) or had died (n=54) by Jan 31, 2020. 48% of patients had comorbidity, with hypertension being the most common (30%), followed by diabetes (19%) and coronary heart disease (8%). Multivariable regression showed increased **odds of in-hospital death** associated with **older age** (odds ratio 1·10, 95% CI 1·03–1·17, per year increase; p=0·0043), higher **SOFA** score (5·65, 2·61–12·23; p<0·0001), and **d-dimer greater than 1 µg/L on admission** (18·42, 2·64–128·55; p=0·0033). **The median duration of viral shedding was 20·0 days** in survivors, but SARS-CoV-2 was detectable until death in non-survivors. **The longest observed duration of viral shedding in survivors was 37 days.**

Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2763184
Journal: JAMA Internal Medicine *Published Online: March 13, 2020*
Authors from: China

A retrospective cohort study of 201 patients (median age 51 yrs, 63.7% were men) with confirmed COVID-19 pneumonia admitted to Wuhan Jinyintan Hospital in China between December 25, 2019, and January 26, 2020. The final date of the follow-up was February 13, 2020. **ARDS developed in 41.8%** of patients and more than half **of those (52.4%) died**. In those who developed ARDS, compared with those who did not, more patients presented with **dyspnea** (59.5% vs. 25.6%) and had comorbidities such as **hypertension** (27.4% vs.13.7%) and **diabetes** (19.0% vs.5.1%). In bivariate Cox regression analysis, **risk factors associated with the development of ARDS** and **progression from ARDS to death** included **older age** (hazard ratio [HR], 3.26 and HR, 6.17 respectively), **neutrophilia** (HR, 1.14 and HR, 1.08), **organ and coagulation dysfunction** (eg, **higher lactate dehydrogenase** [HR, 1.61 and HR, 1.30] **and D-dimer** [HR, 1.03 and HR, 1.02]). **High fever (39 °C) was associated with a higher likelihood of ARDS development** (HR, 1.77) **and a lower likelihood of death** (HR, 0.41). Among patients with ARDS, treatment with **methylprednisolone decreased the risk of death** (HR, 0.38).

Novel coronavirus 2019-nCoV: prevalence, biological and clinical characteristics comparison with SARS-CoV and MERS-CoV
https://www.europeanreview.org/article/20379
Journal: European Review for Medical and Pharmacological Sciences

Published Online: February 2020
Authors from: Saudi Arabia

Worldwide, **SARS-CoV** involved 32 countries, with 8422 confirmed cases and 916 (10.87%) casualties from November 2002 to August 2003. **MERS-CoV** spread over 27 states, causing 2496 cases and 868 (34.77%) fatalities during the period April 2012 to December 2019. However, the novel coronavirus **2019-nCoV** spread swiftly the global borders of 27 countries. It infected 34799 people and resulted in 724 (2.08%) casualties during the period December 29, 2019, to February 7, 2020. **The fatality rate of coronavirus MERS-CoV was (34.77%) higher than SARS-CoV (10.87%) and 2019-nCoV (2.08%); however, the 2019-nCoV transmitted rapidly in comparison to SARS-CoV and MERS-CoV.**

Coronavirus Disease 2019 (COVID- 19): What we know?
https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25766
Journal: Journal of Medical Virology First Published: *14 March 2020*
Authors from: China

SARS-CoV-2 (the virus that causes COVID-19) is a novel member of coronaviruses, which are a large group of highly diverse, **enveloped, positive-sense, single-stranded RNA viruses**. Recent research reported that SARS-CoV-2 likely originated in bats, based on its genetic sequence. The intermediate animal host of SARS-CoV-2 between a probable bat reservoir and humans is unknown. The purpose of this article is primarily to review the pathogen, clinical features, diagnosis, and treatment of COVID-19, but also to comment briefly on the epidemiology and pathology.

The envelope **spike (S) protein** is functionally divided into the S1 domain, responsible for receptor binding, and S2 domain, responsible for cell membrane fusion. SARS-CoV-2 uses **angiotensin-converting enzyme II receptor** (ACE2) as an entry receptor in the ACE2-expressing cells. The biophysical and structural analysis indicated that S protein of SARS-CoV-2 binds ACE2 with approximately 10- to 20- fold higher affinity than S protein of SARS-CoV. The high affinity of S protein for human ACE2 may facilitate the spread of SARS-CoV-2 in human populations.

The major route of transmission of COVID-19 is droplet and close contact. Mean reproductive number (R0) was ranging from 2.20 to 3.58, meaning that each patient has been spreading the infection to 2 or 3 other people. The **mean incubation period is about 5 days**, ranging from 1-14 days and 95% of patients are likely to experience symptoms within 12.5 days of contact. However, an asymptomatic carrier was reported and the incubation period was 19 days, suggesting the complicated challenge to contain the outbreak
The main symptoms include self-reported **fever, fatigue, dry cough, myalgia, and dyspnea**. The uncommon symptoms include sputum production, headache, hemoptysis, and diarrhea. If the disease progressed, the median duration period from illness onset to dyspnea was 8.0 days, and to mechanical ventilation was 10.5 days. Common clinical laboratory findings include leukopenia and lymphopenia. **Lymphopenia is a cardinal feature** of COVID-19. One study

investigated the changes of several cytokines in serum in the COVID-19 patients and suggested that the initiation of the immune response results in the **production of chemokines and cytokines, which damage normal host lung.**

The radiologic manifestations of SARS-CoV-2 infected patients are diverse and progressing rapidly and nearly half of the patients had five affected pulmonary lobes. The most common manifestations are **patchy ground-glass opacities** (GGO) and **patchy consolidation** which were mainly distributed in the **middle and outer zone** of the lung.

RT-PCR is routinely used to detect causative viruses from respiratory secretions. **The positive rate of RT-PCR for throat swab samples was reported to be about 60%** in the early stage of COVID-19. Lower respiratory tract samples provide higher viral loads. During the COVID-19 epidemic in China, 10567 patients were diagnosed as clinically diagnosed cases. Authors strongly recommend that the criteria of clinically diagnosed cases based on the **symptoms, exposure history** and typical manifestations on **chest CT** imaging should be used in COVID-19 affected areas that are **in shortage of RT-PCR** testing kits to control the COVID-19 epidemic.

An effective antiviral treatment has yet not been identified. oseltamivir, ribavirin, ganciclovir, lopinavir, and ritonavir have been used in attempts to reduce viral load and to prevent the likelihood of respiratory complications in several studies. **Remdesivir** was reported in the treatment of a patient with COVID-19 in the United States and got an effective result. However, the efficacy of these antiviral drugs for COVID-19 need to be verified by randomized, controlled clinical trials. Current evidence in patients with SARS and MERS suggests that receiving corticosteroids did not have a survival benefit, but rather delayed viral clearance. Therefore, according to this review, routine corticosteroids should be avoided unless they are indicated for other reasons. Arbidol is used empirically in China because of its direct antiviral effect on SARS-CoV in cell culture

Diagnosis:

A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa247/5803302
Journal: Clinical Infectious Diseases *Published: 12 March 2020*
Authors from: China

Nineteen 2019-nCoV pneumonia (COVID-19) and fifteen other pneumonia patients (OTHER) in out of Hubei places were involved in this study. All patients were confirmed by real-time RT-PCR. All patients had a history of exposure to confirmed case of 2019-nCoV or travel to Hubei before the illness. The median duration, respectively, was 8 (IQR:6~11) and 5 (IQR:4~11) days from exposure to onset in COVID-19 and OTHER. The clinical symptoms were similar between COVID-19 and OTHER. **78.95% COVID-19 but only 26.67% of OTHER patients had bilateral involvement** while **89.47% COVID-19 but 6.67% OTHER had multiple mottling and ground-**

glass opacity of chest CT images. Compared to OTHER, COVID-19 presented remarkably more abnormal laboratory tests including AST, ALT, γ-GT, LDH and α-HBDH.

Can Lung US Help Critical Care Clinicians in the Early Diagnosis of Novel Coronavirus (COVID-19) Pneumonia?
https://pubs.rsna.org/doi/10.1148/radiol.2020200847
Journal: Radiology *Published Online: March 13, 2020*
Authors from: Italy

Twelve patients (9 male and 3 female, mean age 63 yrs) with flu-like symptoms in the last 4–10 days and COVID-19 infection underwent bedside lung US and CT. Two patients had emphysema but without the need for oxygen therapy at home. None of the patients had severe respiratory distress (PaO2/FiO2 257–376 mmHg).
In all the patients, the authors found a **diffuse B-pattern with spared areas**. Only **three patients had posterior subpleural consolidations**. A Chest CT scan was performed in all 12 patients and **showed a strong correlation with US**: bilateral lung involvement with ground-glass opacity; five of 12 patients had a crazy-paving pattern. Organizing pneumonia was confirmed in four patients as well as detected with lung US.

Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis
https://www.sciencedirect.com/science/article/pii/S0009898120301066?via%3Dihub
Journal: Clinica Chimica Acta *Published Online: 3 March 2020*
Authors from: Italy

Procalcitonin values are not substantially modified in patients with viral infections, but it may play a role in distinguishing patients **with or without severe COVID-19**. Substantial increase in procalcitonin would probably reflect **bacterial coinfection** in those developing severe form of the disease. Additional studies are compellingly needed to verify the putative bacterial origin of procalcitonin increase in patients with severe COVID-19.

CT Features of Coronavirus Disease 2019 (COVID-19) Pneumonia in 62 Patients in Wuhan, China
https://www.ajronline.org/doi/10.2214/AJR.20.22975
Journal: American Journal of Roentgenology *Published Online: February 19, 2020*
Authors from: China

A total of 62 consecutive patients (39 men and 23 women; mean age 52.8 years) with COVID-19 pneumonia were evaluated. 24 out of 30 patients who underwent routine blood tests (80.0%) had a **decreased lymphocyte count**. Of 27 patients who had their erythrocyte sedimentation rate and high-sensitivity C-reactive protein level assessed, **66.7% had an increased ESR** and **100.0% had an elevated hsCRP.** Multiple lesions were seen on the **initial CT scan** of 83.9% patients, 77.4% had predominantly peripheral distribution of lesions, more in lower zones.

40.3% had ground-glass opacities (GGO), 33.9% consolidation; 62.9% GGO plus a reticular pattern; 54.8% vacuolar sign, 45.2% microvascular dilation sign; 56.5% fibrotic streaks; 33.9% a subpleural line; and 53.2% a subpleural transparent line. 72.6% had air bronchogram, and 17.7% had bronchus distortion. In terms of pleural changes, CT showed that 48.4% had pleural thickening, 56.5% had pleural retraction sign, and 9.7% had pleural effusion. **Advanced-phase disease** (8–14 days after the onset of symptoms) was characterized by significantly increased frequencies of GGO plus a reticular pattern, vacuolar sign, fibrotic streaks, a subpleural line, a subpleural transparent line, air bronchogram, bronchus distortion, and pleural effusion; however, GGO significantly decreased in advanced-phase disease.

Pathophysiology:

Dysregulation of immune response in patients with COVID-19 in Wuhan, China

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa248/5803306
Journal: Clinical Infectious Diseases *Published: 12 March 2020*
Authors from: China

Of the 452 patients with COVID-19 recruited, 286 were diagnosed with severe infection. Severe cases tend to have lower lymphocytes counts, higher leukocytes counts, and neutrophil-lymphocyte-ratio (NLR), as well as lower percentages of monocytes, eosinophils, and basophils. Most of the severe cases demonstrated **elevated levels of infection-related biomarkers and inflammatory cytokines**. The number of **T cells significantly decreased**. Both helper T cells and suppressor T cells in patients with COVID-19 were below normal levels. The percentage of naïve helper T cells increased and memory helper T cells decreased in severe cases. Patients with COVID-19 also have a lower level of regulatory T cells. **The novel coronavirus might mainly act on lymphocytes, especially T lymphocytes.** Surveillance of NLR and lymphocyte subsets is helpful in the early screening of critical illness, diagnosis, and treatment of COVID-19.

Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection

https://link.springer.com/article/10.1007%2Fs11684-020-0754-0
Journal: Frontiers in Medicine *Published Online: February 8, 2020*
Authors from: China

The virus 2019-nCoV invades human cells via the receptor angiotensin-converting enzyme II (ACE2). Moreover, lung cells that have ACE2 expression may be the main target cells during the 2019-nCoV infection. To construct a risk map of different human organs at risk, authors analyzed the **single-cell RNA sequencing** (scRNA-seq) datasets derived from major human physiological systems and identified as potentially vulnerable the following: l**ung, heart, esophagus, kidney, bladder, and ileum,** and located specific cell types (i.e., **type II alveolar cells (AT2), myocardial cells, proximal tubule cells of the kidney, ileum, and esophagus epithelial cells, and bladder urothelial cells**.

Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein.
https://linkinghub.elsevier.com/retrieve/pii/S0092867420302622
Journal: Cell *Published Online: March 19, 2020*
Authors from: USA, France

Coronavirus spike (S) glycoproteins promote entry into cells and are the main target of antibodies. Authors show that SARS-CoV-2 S uses ACE2 to enter cells and that the receptor-binding domains of SARS-CoV-2 S and SARS-CoV S bind with similar affinities to human ACE2, correlating with the efficient spread of SARSCoV-2 among humans. The authors found that the **SARSCoV-2 S glycoprotein harbors a furin cleavage site** at the boundary between the S1/S2 subunits, which is processed during biogenesis and **sets this virus apart from SARS-CoV and SARS-related CoVs.** The authors determined cryo-EM structures of the SARSCoV-2 S ectodomain trimer, providing a **blueprint for the design of vaccines and inhibitors of viral entry.** Finally, authors demonstrate that **SARS-CoV S murine polyclonal antibodies potently inhibited SARSCoV-2 S mediated entry** into cells, indicating that cross-neutralizing antibodies targeting conserved S epitopes **can be elicited upon vaccination**.

Prevention:

Protecting Health Care Workers during the COVID-19 Coronavirus Outbreak – Lessons from Taiwan's SARS response
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa255/5804239
Journal: Clinical Infectious Diseases Published Online: *12 March 2020*
Authors from: USA, Taiwan

The article provides basic information on the protection of health-care workers (HCW). To counteract the potential decline in HCW availability due to fear and anxiety, and to decrease the risk of nosocomial infection, it is critical to strengthen HCW safety and trust in the system. Authors recommend implementing Traffic Control Bundling (TCB) – a tool that proved effective in **dramatically reducing infection rates among HCWs in Taiwan during the SARS outbreak**. The essence of TCB involves: **Triage outside of hospitals** (in tents or other shelters) and; Zones of Risk – clearly delineating separate zones, including contamination, transition, and clean zone each separated by checkpoints.
TCB adjusted for COVID-19 begins with **outdoor Triage.** Patients testing positive for COVID-19 are directed to an isolation ward **(hot zone)** where they are placed in individual isolation rooms for further care. Patients exhibiting atypical symptoms or whose tests remain inconclusive are directed to a quarantine ward **(intermediate zone**) where they remain for the extent of the incubation period. Patients directed to the isolation or quarantine wards travel via a designated route that avoids contact with the **clean zone**. Thus, patients move along routes other than those taken by HCWs (here we include nurses, physicians, janitorial staff and other hospital staff).

Pediatrics:

Detection of Covid-19 in Children in Early January 2020 in Wuhan, China
https://www.nejm.org/doi/full/10.1056/NEJMc2003717?query=featured_home
Journal: NEJM *Published: March 12, 2020*
Authors from: China

From January 7 to January 15, 2020, a total of 366 hospitalized children (≤16 years of age) were enrolled in a retrospective study of respiratory infections at three branches of Tongji Hospital, Wuhan. The most frequently detected pathogens were influenza A virus (in 6.3%) and influenza B virus (in 5.5%). **SARS-CoV-2, the virus that causes Covid-19, was detected in 6 patients (1.6%).** Patients were 1 to 7 years old and all of them have been previously completely healthy. Common clinical characteristics included high fever (>39°C) (in all six patients), cough (in all six), and vomiting (in four). Laboratory investigations showed that the levels of lymphocytes, white cells, and neutrophils were below the normal range in six, four, and three patients, respectively. **Four of the six patients had pneumonia,** as assessed radiographically, with computed tomographic scans of the chest showing typical viral pneumonia patterns. One child was admitted to the pediatric intensive care unit (ICU) and received pooled immune globulin from healthy donors. All the patients were treated empirically with antiviral agents, antibiotic agents, and supportive therapies. All the patients recovered after hospitalization for a median of 7.5 days (range, 5 to 13).

Pregnancy

Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy
https://www.journalofinfection.com/article/S0163-4453(20)30109-2/fulltext
Journal: Journal of Infection *Published Online: 27 February 2020*
Authors from: China

The authors identified all 13 hospitalized pregnant patients with laboratory-confirmed SARS-CoV-2 infection between December 8, 2019, and February 25, 2020, officially reported by the central government, in areas outside Wuhan, China. Patients were 22 to 36 years old, two women were less than 28 weeks of gestation and the other 11 patients were in their third trimesters at presentation. None of the patients had an underlying medical disease. 77% of patients presented with fever, mostly accompanied by fatigue. Only 23% of pregnant patients complained of dyspnea. One had no symptoms but got a positive RNA test result of oropharyngeal swabs after close contact to a diagnosed family member. Three of the patients (23%) improved after hospitalization and got discharged with an uncomplicated ongoing pregnancy. The other 10 patients **(77%) underwent a cesarean section**. Five of the 10 patients were delivered by emergency cesarean section because of pregnancy complications including **fetal distress** (in three of ten patients), **premature rupture of the membrane** (in one of ten) and **stillbirth** (in one of ten). Six patients **(46%) had preterm labor between 32- 36 weeks of gestation.** One patient's condition deteriorated during hospitalization, prompting **intensive care unit (ICU) admission** with multiple organ dysfunction syndrome (MODS)

including acute respiratory distress syndrome (ARDS) requiring intubation and mechanical ventilation, acute hepatic failure, acute renal failure, and septic shock. As of February 25th, she was still in the support of **Extracorporeal Membrane Oxygenation** (ECMO). The other 12 pregnant patients were all discharged with no obvious complication. Except for 1 stillbirth, nine newborn infants got a 1-min Apgar score of 10. **There was no clinical or serologic evidence suggestive of vertical transmission of SARS-CoV-2**.

ECMO in COVID-19

Data for ECMO in COVID-19 are so far extremely limited. Some information may be possibly extrapolated from SARS, MERS and Influenza A H1N1 epidemics.

Extracorporeal membrane oxygenation support in 2019 novel coronavirus disease: indications, timing, and implementation

https://journals.lww.com/cmj/Citation/publishahead/Extracorporeal_membrane_oxygenation_support_in.99366.aspx

Journal: Chinese Medical Journal *Published Ahead-of-Print: February 28, 2020*
Authors from: China

ECMO has been proven valuable in treating viral pneumonia complicated by refractory hypoxemia, ARDS and multi-organ failure during the pandemic influenza A H1N1 in 2009 and MERS in 2012. The article contains suggested **indications for ECMO** in this clinical setting as well as **bullet-point simplified clinical algorithm** for its initiation and maintenance. Early "awake ECMO" should be considered in the group of younger and otherwise healthier patients.

Preparing for the Most Critically Ill Patients With COVID-19: The Potential Role of Extracorporeal Membrane Oxygenation

https://jamanetwork.com/journals/jama/fullarticle/2761778

Journal: JAMA *Published Online: February 19, 2020*
Authors from: Singapore, USA

A brief summary of a possible role of ECMO in the COVID-19 setting intended for general medical staff. Because ECMO does not provide direct support for organs other than the lungs or heart beyond increasing systemic oxygen delivery, its role in multiorgan failure cases in the overwhelmed medical system is more limited. Nevertheless, it is likely that non-ECMO centers will refer early to ECMO centers in anticipation of impending clinical deterioration. This will disproportionately affect hospitals with ECMO programs, even when ECMO is not required. ECMO is not a therapy to be rushed to the frontline when all resources are stretched in a pandemic. In less well-resourced countries, many more lives will be saved by ensuring oxygen and pulse oximetry are widely available. It is crucial to slow the epidemic, so all patients are provided correct management.

Coronavirus epidemic: preparing for extracorporeal organ support in intensive care

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30060-6/fulltext

Journal: Lancet Respir Med 2020 *Published Online: February 6, 2020*

Authors from: Italy, Belgium

A general article about the role of ECMO for COVID-19 patients, the epidemiological introduction is not up-to-date with the current situation. In some regions, more than in others, shortness of ECMO devices could occur and might impose choices that come with important ethical questions. Clinical presentation, comorbidities, age, number of days of mechanical ventilation before indication for ECMO, and risk for complications are all factors influencing a potentially favorable outcome. 2019-nCoV might also cause severe myocarditis resulting in acute heart failure, which might indicate, in the most severe forms, the need for venous-arterial ECMO support.

Treatment strategies:

Remdesivir: A Promising Antiviral Against Coronaviruses
https://www.jwatch.org/na50889/2020/03/03/remdesivir-promising-antiviral-against-coronaviruses
Journal: NEJM Journal Watch *Published Online:*
Author from: USA

Although no CoV treatments have been approved, pharmacotherapies studied previously for MERS-CoV may lay the foundation for the treatment of difficult cases of COVID-19 (caused by SARS-CoV-2), given the relatedness of these viruses. Three new reports support this approach. Using a recombinant MERS-CoV engineered to express a reporter nanoluciferase, Sheahan and colleagues now show that **remdesivir and interferon beta (IFN-β)** have **superior antiviral activity to lopinavir/ritonavir** (LPV/RTV) in **cultured human lung cells.** In a **murine model, remdesivir at both prophylactic and therapeutic doses improved lung function, reduced lung injury, and reduced virologic loads**, whereas LPV/RTV–IFN-β results were significantly less pronounced. The efficacy of prophylactic and therapeutic remdesivir was also examined by de Wit and colleagues **in a rhesus macaque model** of MERS-CoV. **Remdesivir prophylaxis** initiated 24 hours before inoculation with MERS-CoV caused **significantly lower viral loads** than control treatment in the lungs and prevented clinical infection in this model. Remdesivir therapy initiated 12 hours after inoculation significantly reduced MERS-CoV loads in other respiratory tissues, decreased lung disease, and strongly attenuated clinical signs of infection compared with control treatment. Wang and colleagues show that **remdesivir and chloroquine can each inhibit SARS-CoV-2 in vitro**. Chloroquine, an old antimalarial drug, exerts its antiviral activity in part by interfering with cell fusion by increasing endosomal pH.

Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30317-2/fulltext
Journal: The Lancet *Published Online: February 6, 2020*
Authors from: UK

Corticosteroids were widely used during the outbreaks of severe acute respiratory syndrome (SARS)-CoV and Middle East respiratory syndrome (MERS)-CoV, and are being used in patients with 2019-nCoV in addition to other therapeutics. However, **current interim guidance from WHO** on clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected (released Jan 28, 2020) **advises against the use of corticosteroids unless indicated for another reason.** Acute lung injury and ARDS are partly caused by host immune responses. Corticosteroids suppress lung inflammation but also inhibit immune responses and pathogen clearance. **No clinical data exist to indicate that net benefit is derived from corticosteroids in the treatment of respiratory infection due to RSV, influenza, SARS-CoV, or MERS-CoV.** The available observational data suggest increased mortality and secondary infection rates in influenza, impaired clearance of SARS-CoV and MERS-CoV, and complications of corticosteroid therapy in survivors. If it is present, the effect of steroids on mortality in those with septic shock is small and is unlikely to be generalizable to shock in the context of severe respiratory failure due to 2019-nCoV. Overall, no unique reason exists to expect that patients with 2019-nCoV infection will benefit from corticosteroids, and they might be more likely to be harmed with such treatment. We conclude that **corticosteroid treatment should not be used for the treatment of 2019-nCoV-induced lung injury or shock outside of a clinical trial**.

Discovering drugs to treat coronavirus disease 2019 (COVID-19)
https://www.jstage.jst.go.jp/article/ddt/14/1/14_2020.01012/_article
Journal: Drug Discoveries & Therapeutics *Published: 2020*
Authors from: China

According to the 6th edition of the Chinese Guidelines for the Prevention, Diagnosis, and Treatment of Novel Coronavirus-induced Pneumonia, antivirals may be used in COVID-19. **IFN-α** is a broad-spectrum antiviral that is usually used to treat hepatitis, though it is reported to inhibit SARS-CoV reproduction in vitro. The specific method for administration is a vapor inhalation. **Lopinavir/ritonavir** is a medication for the human immunodeficiency virus (HIV). Lopinavir/ ritonavir has anti-SARS-CoV activity in vitro and in clinical studies. **Ribavirin** is a nucleoside analog with a broad-spectrum of antiviral effects. A study compared 111 patients with the severe acute respiratory syndrome (SARS) treated with ribavirin monotherapy and 41 patients with SARS treated with **lopinavir/ ritonavir and ribavirin**; patients treated with the **combined therapy had a lower risk of ARDS and death**. **Chloroquine** is a widely used antimalarial that was found to be a potential broad-spectrum antiviral in 2006. Chloroquine was found to block SARS-CoV-2 infection. **Arbidol** is an antiviral that can be used to treat the influenza virus. A study has revealed that arbidol can effectively inhibit SARS-CoV-2 infection.

Besides the drugs above that have been included in the Guidelines, **favipiravir** is a new type of RNA-dependent RNA polymerase (RdRp) inhibitor. In addition to its anti-influenza virus activity, favipiravir is capable of blocking the replication of some RNA viruses. Favipiravir is converted into an active phosphoribosylated form (favipiravir-RTP) in cells and is recognized as a substrate by viral RNA polymerase, thus inhibiting RNA polymerase activity. Therefore, favipiravir may have potential antiviral action on SARS-CoV-2. The preliminary results from a

total of 80 patients (including the experimental group and the control group) indicated that **favipiravir had more potent antiviral action than that of lopinavir/ritonavir.** No significant adverse reactions were noted in the favipiravir treatment group, and it had significantly fewer adverse effects than the lopinavir/ritonavir group.

A nucleoside analog and a broad-spectrum antiviral **remdesivir** is another potential drug for the treatment of COVID-19. Animal experiments indicated that remdesivir can effectively reduce the viral load in lung tissue of mice infected with MERSCoV, improve lung function, and alleviate pathological damage to lung tissue. **Wang et al. found that remdesivir potently blocks SARS-CoV-2 infection**. **Holshue et al. reported that remdesivir yielded promising results in the treatment of a patient with COVID-19 in the United States**. In order to evaluate the efficacy and safety of the drug in patients with COVID-19, a **randomized, placebo-controlled, double-blind, multicenter, phase III clinical trial was launched** on February 5, 2020, in China and is expected to conclude by the **end of April 2020**.

Some other drugs have been tested: **darunavir** inhibited SARS-CoV-2 infection in vitro. Other potential drugs include **type II transmembrane serine protease (TMSPSS2) inhibitors**. SARS-CoV-2 uses the SARS-CoV receptor, ACE2, and the cellular protease TMPRSS2 to enter target cells. A TMPRSS2 inhibitor would block entry and thus constitute a treatment option. **BCR-ABL kinase inhibitor imatinib** has anticoronal activity primarily because it inhibits the fusion of virions with the endosomal membrane.

A joint research team from Shanghai performed drug screening in silicon and an enzyme activity test, and they reported 30 agents with potential antiviral activity against SARS-CoV-2. These agents are **indinavir, saquinavir, lopinavir, carfilzomib, ritonavir, remdesivir, atazanavir, darunavir, tipranavir, fosamprenavir, enzaplatovir, presatovir, abacavir, bortezomib, elvitegravir, maribavir, raltegravir, montelukast, deoxyrhapontin, polydatin, chalcone, disulfiram, carmofur, shikonin, ebselen, tideglusib, PX12, TDZD-8, cyclosporin A, and cinanserin.**

Soluble angiotensin-converting enzyme 2: a potential approach for coronavirus infection therapy?
https://portlandpress.com/clinsci/article/134/5/543/222345/Soluble-angiotensinconverting-enzyme-2-a-potential
Journal: Clinical Science Published Online: *March 13 2020*
Authors from: USA

It has been known since the 2003 SARS epidemic that the receptor critical for SARS-CoV entry into host cells is the angiotensin-converting enzyme 2 (ACE2). The S1 domain of the spike protein of SARS-CoV attaches the virus to its cellular receptor ACE2 on the host cells. Functionally, there are **two forms of ACE2**. The full-length ACE2 contains a structural transmembrane domain, which anchors its extracellular domain to the plasma membrane. The extracellular domain has been demonstrated as a receptor for the spike (S) protein of SARS-

CoV, and recently, for the SARS-CoV-2. The **soluble form of ACE2** lacks the membrane anchor and circulates in small amounts in the blood. Authors propose that this soluble form may act as a **competitive interceptor of SARS-CoV and other coronaviruses by preventing binding of the viral particle to the surface-bound, full-length ACE2**. In vitro studies showed that SARS-CoV replication was blocked by a soluble form of ACE2 in the cell culture. Moreover, **ACE2 fused to the Fc portion of immunoglobulin** has just been reported to neutralize SARS-CoV-2 in vitro and the SARS-CoV-2 binds ACE2 with higher affinity than SARS-CoV. Soluble recombinant ACE2 protein has therapeutic potential for a vast array of therapeutic indications and novel shorter ACE2 variants are being tested in mouse studies for treatment of kidney diseases.

In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa237/5801998
Journal: Clinical Infectious Diseases Published Online: *March 9, 2020*
Authors from: China

Chloroquine has been sporadically used in treating SARS-CoV-2 infection. **Hydroxychloroquine** shares the same mechanism of action as chloroquine, but its **more tolerable safety profile** makes it the preferred drug to treat malaria and autoimmune conditions. The immunomodulatory effect of hydroxychloroquine also may be useful in **controlling the cytokine storm** that occurs late-phase in critically ill SARS-CoV-2 infected patients. Currently, there is no evidence to support the use of hydroxychloroquine in SARS-CoV-2 infection. The pharmacological activity of chloroquine and hydroxychloroquine was tested using **SARS-CoV-2 infected Vero cells**. Hydroxychloroquine concentrations in lung fluid were simulated under 5 different dosing regimens to explore the most effective regimen whilst considering the drug's safety profile. **Hydroxychloroquine (EC50=0.72 μM) was found to be more potent than chloroquine (EC50=5.47 μM) in vitro**. Based on physiologically-based pharmacokinetic models, a **loading dose of 400 mg twice daily of hydroxychloroquine** sulfate given orally, **followed by a maintenance dose of 200 mg given twice daily for 4 days** is recommended for SARS-CoV-2 infection, as **it reached three times the potency of chloroquine phosphate when given 500 mg twice daily 5 days in advance**

SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor
https://www.cell.com/cell/fulltext/S0092-8674(20)30229-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420302294%3Fshowall%3Dtrue#%20
Journal: Cell Published online: *March 05, 2020*
Authors from: Germany, Austria, Russia

Cell entry of coronaviruses depends on the binding of the viral spike (S) proteins to cellular receptors and on S **protein priming by host cell proteases**. Unraveling which cellular factors

are used by SARS-CoV-2 for entry might provide insights into the viral transmission and reveal therapeutic targets. Here, authors demonstrate that SARS-CoV-2 **uses the SARS-CoV receptor ACE2 for entry** and the **serine protease TMPRSS2 for S protein priming**. A **TMPRSS2 inhibitor approved for clinical use blocked entry** and might constitute a treatment option. Finally, authors show that the **sera from convalescent SARS patients cross-neutralized SARS-2-S-driven entry**.

Angiotensin receptor blockers as tentative SARS- CoV- 2 therapeutics

https://onlinelibrary.wiley.com/doi/full/10.1002/ddr.21656

Journal: Drug Development Research *Published Online: 04 March 2020*
Author from: Israel

Developing vaccines against the SARS- CoV- 2 virus may take many months. Moreover, **vaccines based on viral- encoded peptides may not be effective against future coronavirus** epidemics, as virus **mutations could make them futile**. A tentative suggestion based on existing therapeutics, which would likely be resistant to new coronavirus mutations, is to use **available angiotensin receptor 1 (AT1R) blockers**, such as **losartan**, as therapeutics for reducing the aggressiveness and mortality from SARS- CoV- 2 virus infections. This idea is based on observations that the angiotensin- converting enzyme 2 (ACE2) very likely serves as the binding site for SARS- CoV- 2. This commentary elaborates on the idea of considering AT1R blockers as a tentative treatment for SARS- CoV- 2 infections. Moreover, the **percentage of people chronically medicated with AT1R blockers in the general population should be compared with the percentage among hospital admissions of SARS- CoV- 2** infected patients presenting serious symptoms. If the latter percentage would be found to be significantly smaller, this would support the notion that AT1R antagonists confer protection from severe symptoms among SARS- CoV- 2 infected individuals.

Perspectives on monoclonal antibody therapy as potential therapeutic intervention for Coronavirus disease-19 (COVID-19)

http://apjai-journal.org/wp-content/uploads/2020/03/5_AP-200220-0773.pdf

Journal: Asian Pacific Journal of Allergy and Immunology *Published Online:*
Authors from: Thailand

The continuing **emergence of coronaviruses at regular intervals** poses a significant threat to human health and the economy. Ironically, even after a decade of research on coronavirus, still, there are no licensed vaccines or therapeutic agents. Monoclonal antibodies represent the **major class of biotherapeutics for passive immunotherapy** to fight against viral infection. The therapeutic potential of monoclonal antibodies has been well recognized in the treatment of many diseases. Here, authors summarize the potential monoclonal antibody-based therapeutic intervention for COVID-19.

Anti-HCV, nucleotide inhibitors, repurposing against COVID-1

https://www.sciencedirect.com/science/article/pii/S0024320520302253?via%3Dihub

Journal: Life Sciences *Published Online: 28 February 2020*

Authors from: Egypt, Saudi Arabia

This study aims to test anti-HCV drugs against COVID-19 RNA dependent RNA polymerase (RdRp) and sequence analysis, modeling, and docking are used to build a model for Wuhan COVID-19 RdRp. Additionally, the newly emerged Wuhan HCoV RdRp model is targeted by anti-polymerase drugs, including the approved drugs Sofosbuvir and Ribavirin. The results suggest **the effectiveness of Sofosbuvir, IDX-184, Ribavirin, and Remidisvir as potent drugs against the newly emerged HCoV disease**. The present study presents a perfect model for COVID-19 RdRp enabling its testing in silico against anti-polymerase drugs. Besides, the study presents some drugs that previously proved its efficiency against the newly emerged viral infection.

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