

Title of Paper	Journal	Pub. Date	Category	Article highlights	Problem/Background	Design	Groups, for clinical studies	Results
<u>Histopathology and Ultrastructural Findings of Fatal COVID-19 Infections</u>	medRxiv	4/21/20	Biology	Besides significant pathology in the lungs, diffuse organ damage is associated with fatal COVID-19 with pathology identified in the kidney, trachea, heart, GI tract, and brain.	What is the whole body pathology associated with COVID-19?	Basic science	Post-mortem analysis of 12 fatal COVID-19 cases from Washington State	Virus was identified in type I and II pneumocytes by EM in the kidney, trachea, large intestines and heart. Histologic pathology was noted in the lungs, liver, heart, trachea, spleen, brain, stomach, and kidneys. Gross pathology noted in the lungs, liver, heart, spleen, kidney, and brain.
<u>Presence of SARS-CoV-2 reactive T cells in COVID-19 patients and healthy donors</u>	medRxiv	4/22/20	Diagnosis & Prevention	Some healthy adults who have not been exposed to SARS-CoV-2 may have CD4+ T cells reactive to SARS-CoV-2 Spike protein antigens; this protein has homology to Spike proteins of circulating human coronaviruses.	Currently available antibody tests have high false positive and negative rates, which must be resolved before antibody testing can be reliably used on a large scale.	Basic science		SARS-CoV-2 patients make CD4+ T cells that react against both N- and C-terminal SARS-CoV-2 Spike protein peptides; some healthy donors in adult population have reactivity to C-terminal Spike protein peptides (likely due to exposure to known human coronaviruses due to local homology)
<u>Effectiveness and Safety of Glucocorticoids to Treat COVID-19: A Rapid Review and Meta-Analysis</u>	medRxiv	4/22/20	Treatment	In the available low and very-low quality evidence, systemic glucocorticoids do not reduce mortality or the duration of lung inflammation for patients with COVID-19. They may reduce the duration of fever, but as they increase the risk of adverse reactions, they are not currently recommended as a treatment option.	Glucocorticoids are used to treat inflammation of the respiratory tract caused by different illnesses, however, it is unclear if the benefits outweigh the risks in the treatment of COVID-19 patients. As such, this is currently a point of controversy.	Meta-analysis		The review's inclusion criteria yielded 23 papers (one RCT and 22 cohort studies) about MERS (1), SARS (17), and COVID-19 (5). The risk of death was not significantly decreased for SARS and COVID-19 and was increased in MERS, duration of fever in COVID-19 decreased by an average of 3.2 days, and COVID-19 patients treated with glucocorticoids stayed an average of 2.4 more days in the hospital than those who did not receive the treatment.
<u>Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area</u>	JAMA	4/22/20	Epidemiology	Large case series including 5700 COVID-19 patients in the NYC area. Common comorbidities were hypertension, obesity, and diabetes. For those whose outcome data were available, 14.2% required ICU care, 12.2% required ventilators, 3.2% required dialysis, and 21% died. Mortality was 88.1% for those on ventilators.	Limited information on the presenting characteristics and outcomes of COVID-19 patients in the US	Case reports/series	5700 patients hospitalized with COVID-19 in the Northwell Health system in New York City, Long Island, and Westchester County between 3/1/20 and 4/4/20	Median age was 63 and 39.7% were female. Common comorbidities include hypertension (56.6%), obesity (41.7%), and diabetes (33.8%). At baseline, 30.7% were febrile, 17.3% had tachypnea, 27.8% received supplemental oxygen, and 2.1% had co-infection with other respiratory virus. Outcomes were available for 2634 patients, of whom 14.2% required ICU care, 12.2% received invasive ventilation, 3.2% received dialysis, and 21% died. Mortality for those on ventilators was 88.1%.
<u>Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review</u>	JAMA Pediatr	4/22/20	Prognosis	In general, pediatric patients with COVID-19 have mild or no symptoms, and most have a good prognosis.	Limited reports on pediatric patients infected with SARS-CoV-2	Systematic review	18 studies with 1065 participants with confirmed SARS-CoV-2 infection: 444 were children younger than 10 years, and 553 were children from age 10 to 19	Most children had mild respiratory symptoms (fever, dry cough, fatigue) or were asymptomatic. Common imaging findings were bronchial thickening and ground-glass opacities, which were also seen in asymptomatic cases. Only 1 case of severe infection was reported. No deaths were reported in children 0-9 years; 1 death was reported in the age range of 10-19 years.
<u>Rapid development of an inactivated vaccine for SARS-CoV-2</u>	bioRxiv	4/19/20	Diagnosis & Prevention	A purified inactivated SARS-CoV-2 vaccine candidate PiCoVacc induces specific neutralizing antibody response in mice, rats, and non-human primates. Immunization confers complete protection in macaques against SARS-CoV-2 challenge.	Urgent need for SARS-CoV-2 vaccines	Basic science		A representative array of SARS-CoV-2 strains were isolated from 11 patients from around the world. One strain was chosen to produce purified inactivated virus vaccine, which produced strong antibody response in mice and rats with potent neutralization activity against multiple strains. Vaccination in rhesus macaques conferred protection against viral challenge, without evidence of excessive immunopathology.
<u>Human monoclonal antibodies block the binding of SARS-CoV-2 spike protein to angiotensin converting enzyme 2 receptor</u>	Cellular & Molecular Immunology	4/20/20	Treatment	Two human monoclonal antibodies cloned from memory B cells isolated from recovered COVID-19 patients exhibit blocking activity against the SARS-CoV-2 RBD and ACE2 receptor interaction.	Monoclonal antibodies can be potentially used as prophylactic or therapeutic drugs against COVID-19	Basic science		Three out of 26 recovered patients produced antibodies with effective inhibition of SARS-CoV-2 RBD binding to ACE2. Antibody sequences were cloned from single memory B cells sorted from these patient samples. Two out of the three cloned antibodies successfully blocked RBD-ACE2 interaction and pseudovirus entry into ACE2-expressing host cells.
<u>SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues</u>	Cell	journal pre-proof	Biology	ACE2 and TMPRSS2 co-expression was detected in type II pneumocytes, ileal absorptive enterocytes, and nasal goblet secretory cells. ACE2 was found to be a human interferon-stimulated gene.		Basic science		Using various scRNA-seq datasets, ACE2 and TMPRSS2 co-expressing cells were identified within type II pneumocytes, ileal enterocytes, and nasal goblet cells. ACE2 expression was associated with components of the INF signaling pathway. Type I INF, and to a lesser extent type II INF, induced ACE2 expression in a primary human upper airway basal cell culture, suggesting that ACE2 may be an interferon-stimulated gene.

<u>A multibasic cleavage site in the spike protein of SARS-CoV-2 is essential for infection of human lung cells</u>	Molecular Cell	journal pre-proof	Biology	<p>The authors report in this study that the cellular protease furin cleaves the SARS-CoV-2 spike protein and the S1/S2 site and is essential for S protein-mediated cell-cell fusion and entry into human lung cells.</p>	<p>It is known that the SARS-CoV-2 S-protein has a S1/S2 cleavage site with multiple arginine residues (multibasic) unlike other closely related animal coronaviruses, but the role of this multibasic site in SARS-CoV-2 infection is not completely understood.</p>	Basic science		<p>Using various combinations of viral pseudotypes of coronavirus spike (S) protein with different variations of the S1/S2 cleavage site, the multibasic SARS-CoV-2 S1/S2 cleavage site is suggested to be needed for efficient cleavage by furin before it can be further cleaved by TMPRSS2 and further suggested to be required for cell-cell fusion as well as viral entry into human TMPRSS2+ Calu3 cells. Authors note that work will need to be extended into primary human respiratory epithelial cells, use real virus instead of the pseudotype they were using, and also that furin inhibition for prolonged periods could have unwanted toxic effects.</p>
<u>Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease</u>	Science	4/22/20	Treatment	<p>In this paper, the authors design and test two lead compounds to target the main protease of SARS-CoV-2.</p>	<p>While various drugs are under investigation to be possible forms of treatment for COVID-19, there is still an urgent need for both efficient and safe anti-SARS-CoV-2 drugs.</p>	Basic science		<p>Two lead compounds (referred to as 11a and 11b) display an IC50 of $0.053\pm0.005 \mu\text{M}$ (11a) and $0.040\pm0.002 \mu\text{M}$ (11b) and inhibit enzyme activity of the SARS-CoV-2 Mpro by occupying the substrate-binding pocket. In vitro studies in Vero E6 cells display an EC50 of $0.53\pm0.01 \mu\text{M}$ (11a) and $0.72\pm0.09 \mu\text{M}$ (11b), both with a CC50 of $>100 \mu\text{M}$. Both compounds displayed good pharmacokinetic properties in vivo with 11a performing well when administered through IV drip and also displaying low toxicity.</p>
<u>Rural areas are at risk during COVID-19 pandemic</u>	Lancet Infectious Disease	4/17/20	Epidemiology	<p>Interventions addressing the COVID-19 pandemic should systematically focus on both rural and urban areas, rather than solely large cities.</p>	<p>While COVID-19 cases were initially concentrated in large urban areas, infectious disease spreads along transportation routes, as people move from these cities to less densely populated areas.</p>	Ideas, editorials, reviews or opinions		<p>Models that aim to spread information into rural communities, such as recruiting community leaders to spread public health campaign messages, will be helpful. Additionally, international institutions must aid national governments to provide resources necessary for mobilization of resources.</p>
<u>Chloroquine or hydrochloroquine for prophylaxis of COVID-19</u>	Lancet Infectious Disease	4/17/20	Diagnosis & Prevention	<p>While chloroquine has been tentatively used as treatment for COVID-19, given that no specific treatment is available, prior studies have not evaluated its use in prophylaxis.</p>	<p>In vitro studies have demonstrated chloroquine's effectiveness against SARS-CoV by disrupting early replication of the virus and mediating an anti-inflammatory response.</p>	Ideas, editorials, reviews or opinions		<p>Inhibition of replication of SARS-CoV-2 may be essential to prevent the spread of this highly contagious virus. Future studies should explore this possible avenue of prophylaxis and evaluate dosing, schedule of administration, and potential side effects.</p>
<u>COVID-19 Critical Illness Pathophysiology Driven by Diffuse Pulmonary Thrombi and Pulmonary Endothelial Dysfunction Responsive to Thrombolysis</u>	medRxiv	4/22/20	Biology	<p>Abnormal coagulation in COVID-19 may lead to pulmonary thrombi which disrupt oxygenation and respiratory function.</p>	<p>Abnormal coagulation and gas exchange with preserved lung mechanics has been noted in COVID-19. Do thrombi in the pulmonary vasculature contribute to COVID-19 pathogenesis?</p>	Basic science	4 patients with severe COVID-19 pneumonia, respiratory failure, and shock.	<p>Tissue plasminogen activator was administered to pre-terminal patients. Three of four patients survived with one patients demonstrating a clear temporal link to their improved status. Three patients had a decreased need for vasopressors.</p>
<u>Multicenter initial guidance on use of antivirals for children with COVID-19/SARS-CoV-2</u>	Journal of the Pediatric Infectious Diseases Society	4/22/20	Treatment	<p>Panel of pediatric ID physicians set guidance statements for using antivirals to treat children with COVID-19</p>	<p>Although COVID-19 is mild in nearly all children, a small number develop critical illness. There are few guidelines on if they should be treated with antivirals.</p>	Ideas, editorials, reviews or opinions		<p>Antiviral therapy for COVID-19 is not necessary for the great majority of pediatric patients. For those rare children who develop critical disease, use remdesivir and be part of a clinical trial.</p>
<u>COVID-19 Antibody Seroprevalence in Santa Clara County, California</u>	medRxiv	4/17/20	Epidemiology	<p>Seroprevalence in Santa Clara County is estimated to range from 2.49% to 4.16%, corresponding to 48000 to 81000 cases, which is 50- to 85- fold more than the number of confirmed cases</p>	<p>Many current analyses and policies were designed without seroprevalence data</p>	Cross-sectional study	3330 participants in Santa Clara County recruited using Facebook ads targeting a representative sample by zip codes	<p>The unadjusted crude prevalence of positive antibodies to SARS-CoV-2 was 1.5%. After weighting to match county population by zip, race, and sex, the prevalence was 2.81%. Estimated prevalence accounting for test performance characteristics ranged from 2.49% to 4.16%, representing between 48000 and 81000 infection, which is 50- to 85- fold more than the number of confirmed cases.</p>

These summaries were prepared by medical and graduate students at Washington University in St. Louis

Please note that medRxiv and bioRxiv articles have not yet been peer-reviewed.

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