Articles about COVID-19 for May 25th to May 29th

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Name of Article + Link	Journal, Date	Category of Study	Question it asks	Results in Brief	Implications + Limitations	Initials
Clinical and Chest Radiography Features Determine Patient Outcomes In Young and Middle Age Adults With COVID-19	Radiology, May 14,2020	Clinical	Does Chest X Ray give prognostic value for young to middle age adults with COVID-19?	In this retrospective multicenter study, 338 pts aged 21-50 were evaluated for the relationship between clinical parameters, CXR scores, and pt outcomes. Chest X-ray was divided into 3 zones per lung and scored based on opacity (max score 6). Score of 2 or higher associated with hospital admission (OR 6.2, 95% CI 3.5-11, p<0.001). Score of 3 or higher predictor of intubation (OR 4.7, 95% CI 1.8-13, p=0.002). Obesity was also found to be associated with hospital admission for COVID19 (OR 2.4, 95% CI 1.1-5.4, no p value given)	CXR has low sensitivity for COVID19 (69%) [means higher chance of false negatives] but there is an unmet need for predicting clinical outcomes. This study shows CXR can be used to predict hospitalization and intubation (in pts with already confirmed COVID19). Limitations: Only 2 radiologists scored all the CXRs (they did have concordance score of 0.88 however). Left lower lung zone was found not to be correlated with hospitalization/intubation but this zone is often obscured so data may have been missed. Study was retrospective so high chance of observer bias. CXR reports were available to physicians so	PT

					may have overestimated relationship due to being more likely to admit. No follow up was done beyond 20 days so no long-term data can be inferred from this study. Also, they excluded pts over age 50, which limits our ability to generalize this data to geriatrics.	
Remdesivir for the Treatment of COVID-19 Preliminary Report	New England Journal of Medicine May 22, 2020	Therapeutic	Is remdesivir an efficacious treatment for COVID 19? (proven in vitro but not in vivo yet)	In this phase III, multicenter, double blind, randomized, placebo-controlled trial: 1059 pts were monitored for time to recovery of 200 mg LD then 100 mg daily for 9d IV remdesivir v placebo (0.9% NS) for 10 days. Ratio of recovery of remdesivir to placebo was 1.32; 95% CI 1.12-1.55; P<0.001 (11d compared to 15d). Secondary outcome of improvement of ordinal scale showed odds of improvement of remdesivir to placebo was 1.5 (95% CI 1.18-1.91, P=0.001). Safety: 21.1% (n=114) of pts in remdesivir had	Limitations: Halfway through trial the primary outcome became their secondary outcome while the secondary outcome became the primary. (Old primary was based on clinical status using the 8 pt ordinal scale of 1=not hospitalized to 8=dead). Paper claims this was proposed by statisticians who were blinded to Tx assignments and outcome data. Seventy-two pts was already enrolled before the switch, so no interim data is available on them. During the trial, the safety and data monitoring board decided to report closed data if physicians requested even if they	PT

				severe ADE compared to 27% (n=141) in placebo 10d remdesivir IV is superior to placebo (especially in pts with baseline ordinal score of 5 [receiving oxygen])	had not completed day 29d of the study. This means that some originally in the placebo control could have been given remdesivir***. No statistically significant effect was found on mortality (this means that monotherapy is not enough to stop the current problem of high mortality). Many hospitals are in low contact/work from home mode so some training/visits/monitoring was done remotely which may have skewed assessments/data. The trial is still waiting on data for some of the patients so final results and a full statistical analysis are not yet available. Gilead (make of remdesivir) provided free drug to the study but no financial support.	
Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19	*NEJM,* 21 May 2020	Clinical	How do the lung specimens of Covid-19 compare to H1N1 specimens?	Researchers took autopsy specimens from 7 patients that had laboratory confirmed Covid-19 and 7 patients that had confirmed H1N1 influenza that were matched for	Implications: There was a vascular angiogenesis distinction in the pulmonary pathobiology of Covid-19 compared to a severe influenza virus infection. This provides	MCG

				disease severity, age, and sex. The Covid-19 and influenza lungs showed similar numbers of CD3+ T cells, but the neutrophil and CD4+ T cell counts were grater in the Covid-19 lung samples. Both sets of lungs showed thrombi in the pulmonary arteries and fibrin thrombi of the alveolar capillaries. However, the lungs from Covid-19 patients showed unique vascular features which included severe endothelial injury associated with intracellular virus and disrupted cell membranes, widespread microangiopathy and occlusion of alveolar capillaries and significant new vessel growth through intussusceptive (non-sprouting) angiogenesis. The pulmonary angiogenic feature count was plotted against the length of hospital stay, the degree of intussusceptive angiogenesis increased significantly for the	some insight into the pathophysiological differences between the two disease courses and draws attention further research in what these results mean for clinical outcomes/courses. Limitations: This was a small study with only 7 Covid-19 samples and 7 influenza ones. Additionally, none of the patients who had Covid-19 received mechanical ventilation as a treatment, whereas 5/7 of the influenza patients did receive high pressured mechanical ventilation. Lastly, these findings do not provide insights into the clinical course of this disease, so additional research is required to determine such connection.	

				duration of hospitalization for patients with Covid-19. In patients with influenza there was less intussusceptive angiogenesis and no increase over hospitalization time.		
Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomized, first-in-human trial	*The Lancet,* 22 May 2020	Therapeutic/Vaccine	Dose dependent investigation into Ad5 SARS-CoV-2 vaccination in healthy controls looking at adverse reactions and immunogenicity.	In this phase 1 trial, 108 participants were identified in Wuhan, China that were negative for a current and previous Covid-19 infection. The participants were aged 18 – 60 years and were divided into 3 dosing groups (low, medium, and high) with the average age being matched in each group. The participants were monitored daily for the first 14 days, with labs being drawn on 7 days post vaccination. The participants were also followed up with on the 28th day postvaccination. In the first 7 days post vaccination there was no significant difference in overall number of adverse reactions across the dosing groups, with fever, fatigue, headache, and muscle	Implications: This study indicated that the Ad5 has mild/common adverse reactions and produces an immunogenetic effect. Therefore, more studies are warranted to determine long term efficacy in a larger trial. Limitations: The study only followed patients for 28 days, they are hoping to follow up in 6 months to determine long term effects. There are concerns that the adenoviral delivery system will increase the risk of HIV-1 acquisition because of the Ad5 activated CD4+ cells. The mechanisms of this phenomenon is unclear, but the risk is being considered when determining a delivery	MCG

				aches being the most common (suspected side effect from the adenovirus vector). The vaccine was found to be immunogenic. At 14 days post vaccination, there was rapid binding antibody response to RBD observed in all three dosing groups. There was peak antibody response at 28 days, with the higher dosing tending to have a higher titer of binding. The neutralizing antibodies peaked at day 28 post vaccination. IFN-gamma was detected from CD4+ and CD8+ T cells after vaccination day 14 and 28 from all doses. TNFalpha levels from CD4+ cells were lower in the low dose group compared to the middle and high dose on day 14. These results suggest that the vaccine produced a humoral and T cell response rapidly in most participants. However, regardless of dosing, participants aged 45 – 60 had lower	system. This group plans to follow participants in phase 2 and 3 trials to determine the risk for such acquisition.	

				seroconversion on neutralizing antibody compared to the younger patients.		
Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis	*The Lancet,* 22 May 2020	Clinical	What are clinical outcomes of hydroxychloroquine or chloroquine use in the treatment of COVID-19?	Multinational registry analysis of 671 hospitals in 6 continents examined hospitalized COVID-19 patients who received chloroquine (CQ) or hydroxychloroquine (HCQ) with or without a macrolide within 48 hours of diagnosis and not on ventilation and not on remdesivir. 96,032 patients were included, mean age 53.8 years, 46.3% women. 14,888 were in treatment groups, 81,144 in control. **Control mortality was 9.3%**, **HCQ 18.0%** (hazard ratio 1.335 95% CI 1.223-1.457), **HCQ with macrolide 23.8%** (1.447, 1.368-1.531), **CQ 16.4%** (1.365, 1.218-1.531) **CQ with macrolide 22.2%** (1.368, 1.273-1.469). Each were independently associated with increased in-hospital mortality.	Each of the drug regimens was associated with decreased in-hospital survival and increased frequency of ventricular arrhythmias. These increased risk of death more than underlying health conditions: diabetes, hypertension, COPD, hyperlipidemia, smoking, and immunosupression. Don't use them. Controlled for confounding factors: age, sex, race or ethnicity, body-mass index, underlying cardiovascular disease and its risk factors, diabetes, underlying lung disease, smoking, immunosuppressed condition, and baseline disease severity) NOT a multicenter randomized control trial.	TP

				Control risk for de-novo ventricular arrythmia was 0.3%, **HCQ 6.1%** (2.369, 1.935-2.900), **HCQ with macrolide 8.1%** (5.106, 4.106-5.983), **CQ 4.3%** (3.561, 2.760-4.596), **CQ with macrolide 6.5%** (4.011, 3.344-4.812). Each were independently associated with increased risk of de-novo ventricular arrhythmia.		
Epidemiology and Transmission of COVID-19 in 391 Cases and 1286 of Their Close Contacts in Shenzen, China: A Retrospective Cohort Study	*Lancet Infectious Disease*, 27 Apr 2020	Public Health/Epi	What are the key metrics of disease course, transmission and impact of control measures?	Cases (mean age 45 years) were tracked and analyzed in Shenzen, China with the support of the CDC. Cases were balanced according to gender (male n=187 and female n=204). 91% of cases had mild or moderate clinical severity at initial assessment. Moderate clinical severity was defined as: fever, respiratory symptoms, radiographic evidence of pneumonia. Cases were followed from January 14, 2020 to February 12, 2020. 1286 close contacts were found	Implications: Datasets like these are important considerations for reopening parts of the US. It is possible that we could take some of the measures taken in this paper to contact trace if further outbreaks of COVID-19 arise. The authors stated that the analysis shows that isolation and contact tracing reduce the R number; however, it is highly dependent on the number of asymptomatic cases, since these are nearly impossible to track. They also touch on	LP

				to be related to the 391 cases analyzed. On February 22, 2020, it was found that three cases had died and 225 had recovered (median time to recovery 21 days; 95% CI 20-21). Cases were isolated on average 4·6 days (95% CI 4.1–5.0) after developing symptoms. Contact tracing was found to reduce isolation by 1.9 days (95% CI 1.1–2.7). Household secondary attack rate was 11.2% (95% CI 9.1–13.8). Household contacts were defined as those who share sleeping arrangements with the infected case. Household contacts and those who travelled were at a higher risk of infection. This study found that children were as likely as adults to be infected (infection rate 7.4% in children <10 years vs population average of 6.6%). The observed reproductive number (R) was 0·4 (95% CI 0·3–0·5),	children being monitored as well, although they mention that children face less severe disease symptoms (pre-Kawasaki findings). Limitations: The authors cite numerous limitations in this study: collection protocols that multiple teams were using changed throughout the study as the need arose; the definition of a confirmed case changed during the study (but the authors state that this does not qualitatively change the results); impossible to identify every contact an individual had during their time infected (so R number is probably lower than it is actually is); issues with symptom-based surveillance and asymptomatic surveillance (sensitivity of RT-PCR test); recovery time inflated due to mass isolation even of asymptomatic cases	

				and the mean serial interval of 6.3 days (95% CI 5.2–7.6).		
Scope, quality, and inclusivity of clinical guidelines produced early in covid-19 pandemic: rapid review	*BMJ,* 26 May 2020	Clinical	What is the quality/accuracy of the clinical guidelines created at the beginning of the covid-19 pandemic?	This was a rapid review of clinical guidelines for the management of covid-19 produced early in the pandemic. Guidelines from international and national scientific organizations and government and non-governmental organizations. No exclusions for language, but they excluded regional/hospital guidelines. The searched from the beginning of the pandemic up until 14 February 2020, and then extended the search up until 14 March 2020. Two reviewers independently appraised eligible guidelines by using the AGREE II instrument: 6 domains: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence.	Implications: This study highlights some of the shortcomings in producing guidelines in a crisis and what should and should not be compromised in an emergent setting. Regardless of the severity, conflict of interests should be clearly stated, so clinicians can utilize editorial independence to make clinical decisions. Future guidelines should be audited and monitored as they are produced, regardless of the severity of the crisis. Vulnerable populations and communities with limited access to certain technologies and treatments should be included in guideline preparation. This data can be used to evaluate the changes in quality of clinical guidelines as the Covid-19 pandemic has progressed. A new framework needs to be	MCG

				Eventually 42 studies were eligible with 18 being Covid-19 and 24 being SARS/MERS. Clinical guidelines were embedded within a document that mostly focused on infection control and most guidelines were non-specific and covered a narrow range. Most countries relied on WHO guidelines to generate their own. Few made specific recommendations on the use of treatments such as NSAIDs and recommendations on non-invasive ventilation varied widely. Based on the AGREE II tool the quality was poor across the board with WHO guidelines receiving 265.42/600, which was the highest score. Guidelines from China and South Korea received 145/600 and 156/600, respectively. There was no evidence that guidelines received external review before release. Additionally, the	created to help with guideline creation and validation during a time of crisis. Limitations: AGREE II tool may have some elements that are ill suited for guideline production during a crisis. The authors admit that they may have missed some guidelines based on the publication of guidelines and the tools they used to search. They tried to use native speakers when possible, but sometimes they did use translating software which may have lost some of the nuances.	

				guidelines did not take special consideration of vulnerable populations (pregnant women and children, older adults, and immunocompromised). Comparing WHO guidelines for MERS to their Covid-19 guidelines showed that MERS scored significantly higher in all AGREE II domains except for rigor. However, the WHO MERS guidelines still score low in applicability, editorial independence and stakeholder involvement.		