

Good morning and TGIF

Under COVID-19 News, an update that more healthcare organizations are opting for mandatory vaccinations.

For Journal Review I start with an article on placenta pathology in women vaccinated during pregnancy. I hope this help dispel the fake science on mRNA vaccines affecting fertility etc. The second article is a systemic review on co-infection and superinfection in patients with Covid-19. The next report was a surprise to me on late uptick for RSV infections – boy what a year this has been! The last article is a meta-analysis on use of anakinra in the treatment of patients infected with Covid-19.

Have a wonderful weekend

Ed

COVID-19 News

Mandatory COVID-19 Vaccination

Two more organizations, U Penn Health System and RWJ Barnabas, have announced they are making COVID-19 vaccination mandatory. U Penn immunization rate was only ~70% which is similar to other organizations that have volunteered their immunization rates.

Comment: Clearly 70% is disappointing. Houston Methodist, the first healthcare organization to mandate COVID-19 vaccinations, is now close to 90%.

Journal Review

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination in Pregnancy: Measures of Immunity and Placental Histopathology

OB GYN published online May 12, 2021

DOI: [10.1097/AOG.0000000000004457](https://doi.org/10.1097/AOG.0000000000004457)

The objective of this study was to evaluate the frequency of key placental lesions in patients who received SARS-CoV-2 vaccination in pregnancy. They report results from patients who tested negative for SARS-CoV-2 infection on PCR who received a vaccine (delivering between January and April 2021) and unvaccinated women in a control group (negative for SARS-CoV-2 infection by polymerase chain reaction, immunoglobulin G- and immunoglobulin M-negative) who delivered between April 2020 and April 2021) from an ongoing coronavirus disease 2019 (COVID-19) cohort study.

They report findings in 84 women who received a SARS-CoV-2 vaccine during pregnancy and 116 women in a control group who did not receive a vaccine. Vaccinated women showed robust antibody responses, whereas women in the control group were negative as expected. Placental examination in women with vaccination showed no increased incidence of decidual arteriopathy, fetal vascular malperfusion, low-grade chronic villitis, or chronic histiocytic intervillitis compared with women in the control group. Incidence of high-grade chronic villitis was higher in the control group than in the vaccinated group.

Comment: In this cohort of vaccinated pregnant patients, there was no observed increase in the incidence of findings characteristic of SARS-CoV-2 infection in pregnancy and no evidence of vaccine-

triggered breakdown in maternal immunologic tolerance of the fetus. These findings add to the growing literature supporting the safety of SARS-CoV-2 vaccination in pregnancy.

Prevalence and Outcomes of Co-Infection and Superinfection with SARS-CoV-2 and Other Pathogens: A Systematic Review and Meta-Analysis

PLOS ONE published online May 6, 2021

[doi.org/ 10.1371/journal.pone.0251170](https://doi.org/10.1371/journal.pone.0251170)

A total of 118 studies were included in this meta-analysis. Approximately half of the studies were retrospective cohort studies, 35% were case series, and 9% were prospective cohort studies. Study data showed that the pooled prevalence of co-infection was 19% (95% confidence interval [CI] 14-25; $I^2 = 98\%$), whereby the highest prevalence was observed among non-ICU patients at 29% (95% CI 14-46). Meanwhile, the pooled prevalence of superinfection was 24% (95% CI 19-30), with the highest prevalence among ICU patients (41% [95% CI: 24%-58%]).

When stratified by pathogen type among the reported co-infections and superinfections, researchers found that bacterial superinfections had the highest prevalence at 20% (95% CI 13-28), followed by viral co-infections (10% [95% CI 6-14]), bacterial co-infections (8% [95% CI 5%-11%]) and fungal superinfections (8% [95% CI 4-13]). Meanwhile, the prevalence of viral superinfections and fungal co-infections was each at 4%.

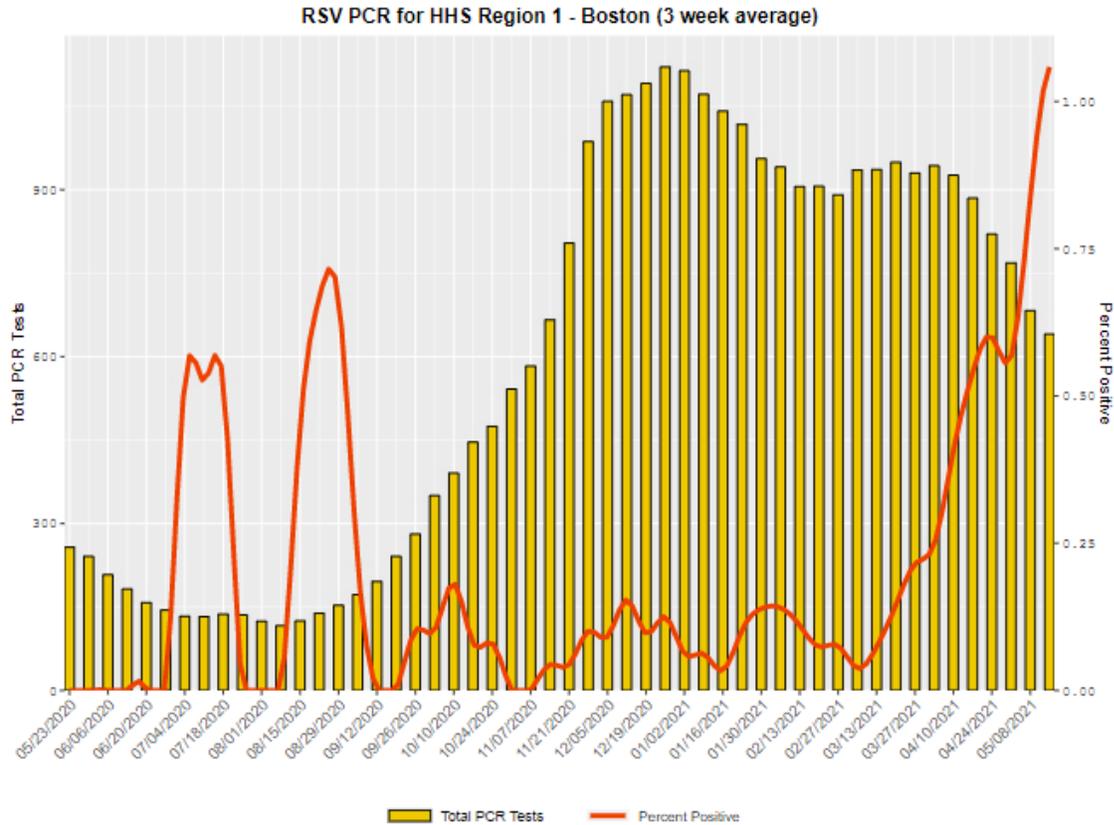
A total of 78 studies reported data on specific organisms associated with co-infection or superinfection in COVID-19 patients. Among patients with co-infections, the most frequently identified bacteria were *Klebsiella pneumoniae* (9.9%), *Streptococcus pneumoniae* (8.2%), and *Staphylococcus aureus* (7.7%), while the most frequently identified viruses among co-infected patients were influenza type A (22.3%), influenza type B (3.8%), and respiratory syncytial virus (3.8%). For fungi, *Aspergillus* was the most frequently reported among those co-infected. Meanwhile, among those with superinfections, the most frequently identified bacteria were *Acinetobacter spp.* (22.0%), *Pseudomonas* (10.8%), and *Escherichia coli* (6.9%). For viruses, *Rhinovirus* was the most frequently identified among those with superinfections, and for fungi, *Candida sp.* was the most prevalent (18.8%). In addition, the researchers found that patients with a co-infection or superinfection had a higher mortality risk than those who only had SARS-CoV-2 infection (odds ratio [OR] 3.31, 95% CI 1.82–5.99).

Comment: Two previous reviews found a prevalence of bacterial co-infection of 7-8% [some <5%] and viral co-infection of 3% in SARS-CoV-2 infected patients, which are lower than the estimates in this report. Respiratory virus diagnostic testing protocols should take into account that co-infection with SARS-CoV-2 is not infrequent, and therefore viral panel testing may be advisable in patients with compatible symptoms. With the next respiratory season, I expect we will see several respiratory viruses circulating perhaps in addition to SARS-CoV-2. The ability to provide real time results will be very helpful. See below.

RSV HHS Regional Trends

May 18, 2021, CDC report

According to CDC RSV has surged in recent weeks. This is months after the traditional seasonal peak. The epidemiology of RSV and other respiratory viruses including influenza has changed significantly in the last year.



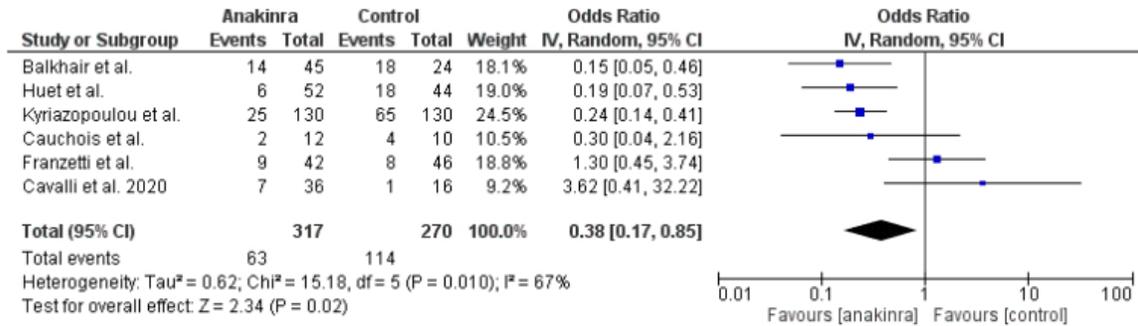
Comment: The explanation for this change is not clear. Perhaps the change may be due to masking, reduced contact with others, and improved compliance with hand hygiene. Another possibility may be the interaction between SARS-CoV-2, RSV, and influenza making infection less likely. (SARS-CoV-2 more fit).

Anakinra in Hospitalized Non-Intubated Patients with Coronavirus Disease 2019: A Systematic Review and Meta-Analysis

Rheumatology published online May 17, 2021.
[doi/10.1093/rheumatology/keab447/6276997](https://doi.org/10.1093/rheumatology/keab447/6276997)

The authors performed a meta-analysis to assess the efficacy of anakinra (IL-1 receptor antagonist) in adult safety of hospitalized non-intubated patients with COVID-19.

Nine studies (n=1,119) were eligible for inclusion in the present meta-analysis. In pooled analyses, anakinra reduced the need for invasive mechanical ventilation (odds ratio, OR: 0.38, 95% confidence interval, CI: 0.17- 0.85, p=0.02, I2=67%; 6 studies, n=587) and mortality risk (OR: 0.32, 95% CI: 0.23-0.45, p<0.00001, I2=0%; 9 studies, n=1,119) compared with standard of care therapy. There were no differences regarding the risk of adverse events, including liver dysfunction (OR: 0.75, 95% CI: 0.48-1.16, p>0.05, I2=28%; 5 studies, n=591) and bacteremia (OR: 1.07, 95% CI: 0.42-2.73, p>0.05, I2=71%; 6 studies, n=727).



Comment: The present meta-analysis shows that anakinra reduces the need for invasive mechanical ventilation and lowers mortality risk in hospitalized non-intubated patients with COVID-19, without increasing the risk of adverse events. Anakinra, which blocks the activity of the proinflammatory cytokines IL-1 α and IL-1 β and has been previously approved for the treatment of autoinflammatory disorders, such as adult-onset Still’s disease, systemic-onset juvenile, idiopathic arthritis, and familial Mediterranean fever. The authors conclude that although no placebo-controlled RCTs have been completed yet, accumulating evidence favors the use of anakinra for the treatment of COVID-19. Most studies in this meta-analysis enrolled patients with hyperinflammation. This report is in line with recent RCTs (RECOVERY and REMAP-CAP) using tocilizumab, an IL-6 inhibitor, demonstrated the efficacy of active treatment in hospitalized COVID-19 patients with increased inflammatory markers. They acknowledged limitations of this meta-analysis related with the design of the included studies, their sample size, and follow-up disparities, along with the different dosage and route of anakinra administration. This meta-analysis found high bias risk with reference to the assessed parameters, use of therapeutics etc. We need more robust RCTs to help define timing and patient selection. Until these trials are done, we have good evidence for dexamethasone with or without tocilizumab.