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Convalescent Plasma Antibody Levels and the Risk of Death from COVID-19 (NEJM)

Bottom Line: Administration of convalescent plasma with high antibody titers (>18.45) results in decreased risk of death among patients diagnosed with COVID-19 not requiring mechanical ventilation when compared to effects of convalescent plasma with low antibody titers (<4.62).

Details: Eligible participants included adults aged 18 years or older hospitalized with a lab-confirmed COVID-19 diagnosis who have evidence of severe infection or risk of progression to severe disease. The primary outcome was mortality at 30 days after receiving a transfusion of convalescent plasma. A subgroup analysis assessed effects based on mechanical ventilation status of participants. 3,082 patients were included in the analysis. 26.9% of patients experienced death within 30 days overall, with 29.6% in low-titer group, 27.4% in medium-titer group, and 22.3% in the high-titer group. Patients who received convalescent plasma with high antibody titers group had a lower relative risk of death (RR: 0.75; 95% CI: 0.61 – 0.93) at 30 days after transfusion than patients receiving convalescent plasma with lower antibody titers. After adjustment for covariates, it shows the same association but no longer significant (RR: 0.82; 95% CI: 0.67 – 1.00). In the subgroup analysis, individuals not requiring mechanical ventilation who received high-titer plasma demonstrated decreased relative risk of death at 30 days when compared to individuals who received low-titer plasma (RR: 0.22, 95% CI: 18.2 – 26.7). No significant difference in relative risk of death was noted amongst patients requiring mechanical ventilation after adjusting for covariates (RR: 1.02; 95% CI: 0.78 – 1.32).

Key Takeaways:

- Convalescent plasma may represent a therapy to improve outcomes among individuals diagnosed with COVID-19 not requiring mechanical intubation.
- Receiving convalescent plasma within 3 days of diagnosis of COVID-19 may result in lower risk of death than receiving transfusion 4 or more days after COVID-19 diagnosis.
- Age identified as important predictor of death amongst study participants.

Interim Results of a Phase 1–2a Trial of Ad26.COV2.S COVID-19 Vaccine (NEJM)

Bottom Line: Evaluation on the safety and immunogenicity of the Ad26.COV2.S vaccine for COVID-19 among younger (aged 18-55 years) and older (aged ≥65 years) adults supports further development of this vaccine candidate.

Details: This was a randomized controlled phase 1–2a trial of the Ad26.COV2.S vaccine for COVID-19. The Ad26.COV2.S vaccine uses the DNA of a modified adenovirus (the common-cold virus) to create an immune response. The study randomized 805 adults aged 18 - 55 years (cohort 1) and those ≥ 65 years (cohort 3) to receive either a low or high dose of the Ad26.COV2.S vaccine. The most common adverse events among cohort 1 and 3 after the first dose and cohort 1 after the second dose were: fatigue, headache, muscle pain, and injection-site pain. Systemic (circulatory system) adverse events were not as common in cohort 3 and in those who received the low dose vaccine. The most common systemic adverse event was fever. Adverse events were less common among participants after receiving the second dose. Neutralizing-antibody titers (amount of antibodies in the blood) were found in ≥ 90% of participants 29 days after the first dose (mean titers: 224 - 354) and in 100% of participants 57 days after the first dose (mean titers: 288 - 488). Mean titers were stable until about day 71. A second dose increased the amount of titers (mean titer: 827 - 1266). CD4+ T-cell response was

detected in 76% - 83% of those in cohort 1 and 60 - 67% of those in cohort 3. CD8+ T-cell (cells that kill the virus) responses were strong overall (51 - 64%) but lower in cohort 3 (24 - 36%). The safety, antibody response, and immune response of the Ad26.COV2.S vaccine, warrants further investigation and development.

Key Takeaways:
- An early phase trial of the Ad26.COV2.S vaccine demonstrated safety and effective antibody and immune response in younger adults (18-55 years) and older adults (≥65 years).
- These results provide a basis to move on to phase 3 trials to determine the effectiveness and safety of the lower-dose Ad26.COV2.S vaccine in either single- or two-doses.

Allergic reactions including anaphylaxis after receipt of the first dose of Pfizer-BioNTech COVID-19 Vaccine (MMWR)

Bottom Line: Anaphylaxis is rare but has been reported in approximately 1 out of every 100,000 Pfizer-BioNTech vaccine doses administered.

Details: In the first week of vaccine roll out in the United States from December 14th - December 23rd, 2020, there were 4,393 (0.2%) reported adverse events after receiving Pfizer BioNTech COVID-19 vaccine. Of those, 175 cases were further reviewed for potential severe allergic reaction. Of the 175 cases, there were 21 cases of anaphylaxis identified out of 1,893,360 first doses of the Pfizer-BioNTech COVID-19 vaccine. This results in 11.1 cases per million doses of vaccine (or approximately 1/100,000). 17 of the 21 cases of anaphylaxis occurred in individuals with a history of allergies or allergic reactions, and 7 had a personal history of anaphylaxis. The median time of developing symptoms was 13 minutes after receiving the vaccine. 20 of the 21 cases had follow up information available and all recovered. Of the additional cases reviewed 86 were determined to be non-anaphylaxis allergic reactions and 61 were non-allergic adverse events.

Key Takeaways:
- Anaphylaxis is rare but has been reported to occur at a rate of approximately 1 out of every 100,000 doses of Pfizer- BioNTech received. The risk is higher for individuals with a history of allergy or anaphylaxis.
- When anaphylaxis did occur, it was most commonly rapid, within 15 minutes of receiving the vaccine.
- Vaccine administration sites should be prepared to manage and treat anaphylaxis.

Continuation versus discontinuation of renin-angiotensin system inhibitors in patients admitted to hospital with COVID-19: a prospective, randomized, open-label trial (Lancet)
Bottom Line: Renin-angiotensin system inhibitors can be safely continued in patients admitted to hospitals with COVID-19.
Details: In this prospective, randomized, open-label trial, eligible participants who were aged 18 years or older, were admitted to a hospital with COVID-19, and were receiving a renin-angiotensin system (RAS) inhibitor prior to admission were randomly assigned either continuation or discontinuation of RAS inhibitor. Primary outcome was a global rank score incorporating time to death, duration of mechanical ventilation, time on renal replacement or vasopressor therapy, and multi-organ dysfunction during hospitalization. Patients were enrolled

between March 31 and August 20, 2020 at twenty large referral hospitals in seven countries worldwide. In total, 152 participants were enrolled, with 75 assigned to continuation group and 77 to discontinuation of RAS inhibitor. Compared with discontinuation of RAS inhibitors, continuation had no effect on global rank score (median rank 73 for continuation vs 81 for discontinuation; β-coefficient: 8; 95% CI: –13 to 29). There was no difference in blood pressure, serum potassium, or creatinine during follow-up for the two groups.

Key Takeaways:

- Previous biological theories suggested that RAS inhibitors might influence the severity of COVID-19.
- Consistent with international society recommendations, this study found that RAS inhibitors can be safely continued in patients admitted with COVID-19.

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Reopening Schools and the Dynamics of SARS-CoV-2 Infections in Israel: A Nationwide Study (CID)

Bottom Line: In this study, school re-openings were not found to be a major contributor of Israel's COVID-19 resurgence in the summer of 2020; large gatherings likely were major contributors.

Details: In Israel (as in much of the world), there have been waves of COVID-19 resurgences. This study looked at the time relationship between different policy decisions made by the Israeli government with regard to COVID-19 containment and changes in the rate of infections. It examined weekly COVID-19 infection rates (both incidence and prevalence), hospitalizations, and deaths before and after school reopening and before and after the easing of restrictions that limited the size of social gatherings to less than 250 people. They found that while COVID-19 infection rates increased for adults in the weeks following the reopening of schools in May 2020, this was not associated with increases in children's infections, hospitalizations, or mortality. In contrast, the weeks following the easing of restrictions that limited the size of social gatherings (beginning June 12th, 2020) had increases in infection rates across all ages, more hospitalizations, and greater mortality.

Key Takeaways:

- In the weeks following school re-opening, adults aged 20-59, not children, seemed to have the greatest increase in COVID-19 infections; overall hospitalizations and mortality did not increase following reopening of schools.
- In the weeks following the easing of restrictions on large gatherings, more overall and more serious COVID-19 infections were observed, with increases in hospitalizations and mortality.

Association of Home Quarantine and Mental Health Among Teenagers in Wuhan, China, During the COVID-19 Pandemic (JAMA Pediatrics)

Bottom Line: In this study, over 20% of adolescents in Wuhan in late May/early April had anxiety and depression.

Details: This study looked at the frequency of depression and anxiety among adolescents in Wuhan, China, and the relationship between lifestyle changes and these mental health outcomes. Over 10,000 adolescents between the ages of 12-18 who resided in Wuhan and had not been diagnosed with COVID-19 were recruited from junior and senior high schools to complete an online questionnaire from 3/30-4/7/20. Survey questions gathered information on daily life during lockdown and sociodemographic questions, and an anxiety and depression scale was used to assess symptoms. 7,890 participants completed the survey; 21.7% and 24.6% reported symptoms of anxiety and depression, respectively. After controlling for covariates, leaving one's home, perceived discrimination, food insufficiency, poor sleep quality, less in-person communication with family members, and less pleasure derived from interests were significantly associated with increased risks of anxiety and depression. Increased risk of anxiety was also associated with changes in behaviors with regard to study, screen time, and looking up information about COVID-19 resulting from stay-at-home restrictions.

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Key Takeaways:

- Lockdown restrictions may have negative effects on adolescent mental health, in part due to dramatic lifestyle changes and various stressors.

Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 Infection at Two Community-Based Testing Sites — Pima County, Arizona, November 3–17, 2020 (MMWR)

Bottom Line: When compared with polymerase chain reaction (PCR) testing, the BinaxNOW rapid antigen test had high specificity (proportion of people without SARS-CoV-2 that have a negative test result) but lower sensitivity (proportion of people with SARS-CoV-2 that have a positive test result) when used to test samples from asymptomatic versus symptomatic persons (35.8% vs 64.2%, respectively). Sensitivity was higher for samples with positive viral culture (92.6% and 78.6% for symptomatic and asymptomatic persons, respectively).

Details: Rapid antigen tests (RATs), such has the Abbott BinaxNOW test, return test results more quickly and at lower cost than much more sensitive nucleic acid amplification tests, such as polymerase chain reaction (PCR). RATs have received FDA Emergency Use Authorization for testing samples from individuals with symptomatic disease; more research is needed on test performance in asymptomatic persons. This study compared the performance of BinaxNOW against real-time PCR testing using 3,419 paired specimens collected at two Arizona testing sites in November from persons 10 and over. When compared with PCR testing, the BinaxNOW rapid antigen test had high specificity (proportion of people without SARS-CoV-2 that have a negative test result, near 100%) but lower sensitivity (proportion of people with SARS-CoV-2 that have a positive test result) when used to test samples from asymptomatic (35.8%) versus symptomatic (64.2%) persons. Sensitivity was higher for samples with positive viral culture (92.6% and 78.6% for symptomatic and asymptomatic persons, respectively), though there were samples that had negative antigen test results but viable virus (false negatives). Rapid antigen tests may help limit transmission through the more rapid identification of infectious persons for isolation, particularly when part of a serial (testing at different points, versus a single point, in time) testing strategy.

Key Takeaways:

- Despite their lower sensitivity to detect infection compared to real-time PCR tests, BinaxNOW sensitivity was higher among samples with positive viral culture, suggesting these tests may perform better in patients with infectious virus present.
- Rapid antigen tests such as BinaxNOW may be a useful screening tool in particular settings and for certain testing strategies (e.g., serial testing) due to their rapid turnaround time, lower cost, and high specificity, or in situations where PCR tests are not readily available or have long turnaround times, though confirmatory testing by nucleic acid amplification tests may be warranted. Consideration is needed with regard to logistical and staffing resources needed for strategies like serial testing.