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Assessment of Maternal and Neonatal SARS-CoV-2 Viral Load, Transplacental Antibody Transfer, and Placental Pathology in Pregnancies during the COVID-19 Pandemic (JAMA)

Bottom Line: In a cohort study of 64 pregnancies where the mother had SARS-CoV-2 there was no evidence of placental infection or vertical transmission.

Details: Prospective cohort study of 64 pregnancies presenting for care and had positive RT-PCR result for SARS-CoV-2. These women were compared to a convenient sample of 63 pregnant women presenting for care to the same centers in the same time period (4/2-6/13) but without SARS-CoV-2 infection. Among the women with SARS-CoV-2, 36% were asymptomatic, 34% had mild disease, 11% had moderate disease, 16% had severe disease, and 3% had critical disease. 14% of women were diagnosed in the second trimester and 86% in the third trimester. There were 2 fetal/neonatal deaths in the SARS-CoV-2 positive group: 1 intrauterine fetal demise at 35-weeks in an asymptomatic woman and 1 neonatal death at 22-weeks related to prematurity in the setting of preterm labor and placental abruption in a symptomatic woman. There was no detectable virus in the blood of any woman with SARS-CoV-2 and no detectable virus in any umbilical cord blood tested. Among 77 neonates tested for SARS-CoV-2 antibodies in the umbilical cord blood, only 1 had IGM to the SAR- CoV-2 nucleocapsid protein. Among 88 placentas that were tested, no SARS COV 2 viral RNA was detected. Of the women with SARS-CoV-2 infection, anti-RBD (receptor binding domain) IGG was detected in 65% of them and anti nucleocapsid was detected in 70% of them. Mother to child transfer of anti-SARS-CoV-2 antibodies was lower than transfer of anti-influenza antibodies and did not differ by maternal disease severity. Compared to non-pregnant hospitalized women of reproductive age with SARS-CoV-2, there were no differences in antibody titers by pregnancy status.

Key Takeaways:

- No evidence of vertical transmission was found in a prospective cohort study of 64 pregnancies where the mother had SARS-CoV-2.
- Low levels of SARS-CoV-2 placental antibody transfer were noted indicating neonates may not have any protection against infection even if the mother had SARS-CoV-2 during pregnancy.

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine (NEJM)

Bottom Line: The two-dose regimen of the mRNA-1273 vaccine resulted in 94.1% efficacy in preventing symptomatic COVID-19 infection. No individuals who received the mRNA-1273 vaccine developed severe COVID-19 infection.

Details: This phase 3, randomized, placebo-controlled trial involved individuals ages 18 or older with no history of SARS-CoV-2 infection. Individuals were stratified into the following groups: age greater than 65, age 18-65 without risk of severe COVID-19 infection, and age 18-65 at risk of severe COVID-19 infection. Participants were randomly assigned to receive the mRNA 1273 vaccine or placebo. Recipients received two doses that were administered 28 days apart. The primary endpoint measured vaccine efficacy at preventing symptomatic SARS-CoV-2 infection at least 14 days after the second dose. Secondary endpoints included vaccine efficacy at preventing severe COVID-19 infection, vaccine efficacy 14 days after a single dose. Participants were monitored for local and systemic adverse reactions for 7 days after each

injection and unsolicited adverse reactions for 28 days after each injection, in addition to adverse events requiring medical attention and serious adverse events from day 1 to day 759. 30,420 individuals were randomized, with 15,210 persons in each group receiving the vaccine of placebo. The study population's median age was 51 with 79.2% identifying as White, 20.5% as Hispanic and 10.2% as Black. Median follow-up for study participants included in analysis was 64 days after the second dose. Both solicited injection-site and systemic adverse events were more common among vaccinated individuals when compared to placebo. Younger participants and individuals with negative test results for SARS-CoV2 infection at baseline were more likely to experience adverse events. Frequency of unsolicited adverse events and serious adverse events did not vary amongst participants. The mRNA-1273 vaccine demonstrated 94.1% efficacy at preventing symptomatic COVID-19 infection with similar findings across age groups and demographic characteristics. Similar vaccine efficacy was noted after individuals received a single dose. All individuals who developed severe COVID-19 were in the placebo group.

Key Takeaways:

- The mRNA-1273 vaccine efficacy is similar across age groups and demographics.
- While the trial was not designed to evaluate efficacy of a single dose of mRNA-1273, study results are encouraging.
- Younger individuals and individuals who were negative for SARS-CoV-2 infection were more likely to experience injection-site and systemic adverse reactions.

A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19 (NEJM)

Bottom Line: LY-CoV555 antibody treatment may not be effective in improving COVID-19 outcomes among hospitalized patients.

Details: Among outpatients, LY-CoV555 monoclonal antibody has been demonstrated to decrease viral load and reduce hospitalization and emergency department visits. This randomized trial included hospitalized COVID-19 patients who did not have end-organ failure. Patients were randomized 1:1 to receive either LY-CoV555 or a placebo. All patients received supportive care as background therapy and 95% received remdesivir. The primary outcome was time to recovery during a 90-period. The study included 314 patients (163 receiving LY-CoV555 and 151 receiving a placebo). The median time from the onset of symptoms to randomization was 7 days. At day 5, 50% (n=81) of patients receiving LY-CoV555 and 54% (n=81) of patients receiving the placebo had improved pulmonary outcomes and did not need supplemental oxygen. This difference was not significant. There was also no significant difference in the primary safety outcome (a composite score of death and adverse events) between patients receiving LY-CoV555 and placebo (19% and 14%, respectively). The LY-CoV555 monoclonal antibody was not effective in improving clinical outcomes among hospitalized COVID-19 patients.

Key Takeaways:

- LY-CoV555 did not improve clinical outcomes in patients hospitalized for Covid-19 compared to a placebo.
- Rigorous assessment of other potential antiviral therapies for Covid-19 still need to be prioritized.

Initial Guidance on Use of Monoclonal Antibody Therapy for Treatment of COVID-19 in Children and Adolescents (J Pediatric Infect Dis Soc)

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Bottom Line: Based on available evidence, this expert panel suggests against routine administration of monoclonal antibody therapy for treatment of COVID-19 in children or adolescents, including those designated at high risk.

Details: In November 2020, the FDA provided Emergency Use Authorization for two monoclonal antibody therapies, bamlanivimab and REGN-COV2, for treatment of mild to moderate COVID-19 in adolescents and adults in specified high-risk groups. To develop guidance on the potential use of these agents for treatment of mild to moderate COVID-19 in high risk adolescents and young adults, as authorized by the current EUAs, the authors assembled a panel of experts in pediatric infectious diseases, pharmacy, pediatric intensive care medicine, and pediatric hematology from 29 geographically diverse North American institutions to evaluate the evidence for safety and efficacy of these agents in pediatric patients. Based primarily on the current lack of efficacy or safety data in pediatric patients, the generally lower risk of progression to severe disease in children and adolescents, and the apparently modest efficacy of these treatments in adults, the panel suggested against routine administration of monoclonal antibody therapy. In this context, along with documented adverse events in adult studies, and plausibility for differential efficacy or safety in younger patients, the potential costs and risks of administration of these products was felt to outweigh the benefits even in children or adolescents designated as being at higher risk. Clinicians choosing to use these agents on an individualized basis should consider risk factors supported by pediatric-specific evidence, and ensure implementation of a system for safe and timely administration that does not exacerbate existing healthcare disparities.

Key Takeaways:

- Based on the lack of efficacy or safety data in pediatric patients, the generally lower risk of progression to severe disease in children and adolescents, and the apparently modest efficacy of these treatments in adults, the panel suggested against routine administration of monoclonal antibody therapy in pediatric and adolescent patients.
- Clinicians choosing to use these agents on an individualized basis should consider risk factors supported by pediatric-specific evidence, and ensure implementation of a system for safe and timely administration that does not exacerbate existing healthcare disparities.

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Allergic Reactions Including Anaphylaxis after Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine: United States, December 14-23, 2020 (MMWR)

Bottom Line: From 12/14-12/23, 21 cases of anaphylaxis following administration of over 1.89 million first doses of the Pfizer-BioNTech COVID-19 vaccine were identified through the U.S. Vaccine Adverse Event Reporting System (VAERS).

Details: This report reviewed adverse events following administration of the Pfizer-BioNTech COVID-19 vaccine during December 14 through 23rd submitted to the CDC's Vaccine Adverse Event Reporting System (VAERS). By 12/23, 1,893,360 initial doses of the Pfizer-BioNTech COVID-19 vaccine had been administered in the US, with 4,393 (0.2%) adverse event reports submitted to VAERS. Of those adverse event reports, 175 underwent further review as possible cases of severe allergic reaction (including anaphylaxis, which occurs rarely but is life threatening). 21/175 cases were determined to be anaphylaxis, for a case rate of 11.1 per million doses of vaccine administered, and 17 of 21 cases were in individuals with a documented history of allergies/allergic reactions. Of the 20 persons with follow up information available, all had recovered or been discharged home. Most anaphylaxis cases occurred in women, although 64% of initial doses were administered in women. Median time from vaccine receipt to symptom onset was 13 minutes (range was 2-150 minutes), with 86% of anaphylaxis cases experiencing symptom onset within 30 minutes. Of the 154 reports not determined to be anaphylaxis, 86 were non-anaphylaxis allergic reactions, 61 were nonallergic adverse events, and 7 were still under investigation. CDC offers guidance on management of anaphylaxis following administration of COVID-19 vaccines, including: ensuring that vaccine locations have adequate anaphylaxis management supplies, such as epinephrine and syringes; screening vaccine recipients for contraindications and precautions; putting postvaccination observation periods in place (e.g., 15-30 minutes depending on history of allergic reactions); ensure vaccinators recognize early signs and symptoms of anaphylaxis; and immediately treat suspected anaphylaxis with an intramuscular epinephrine injection.

Key Takeaways:

- Early safety monitoring of the Pfizer-BioNTech COVID-19 vaccine thus far suggests that anaphylaxis following vaccination occurs but appears to be uncommon, though comparisons of anaphylaxis risk with non-COVID-19 vaccines require more data and enhanced monitoring.
- Recommendations for administering COVID-19 vaccines include: ensuring adequate supplies to manage anaphylaxis, screening recipients for contraindications and precautions, putting into practice post-vaccination observation periods as recommended, ensuring vaccinators recognize early signs and symptoms of anaphylaxis, and immediately treating suspected anaphylaxis cases with an intramuscular epinephrine injection.

Prevalence and 6-month Recovery of Olfactory Dysfunction: A Multicentre Study of 1,363 COVID-19 Patients (Journal of Internal Medicine)

Bottom Line: In this study of loss of smell and changes in the way odors are perceived

(olfactory dysfunction, or OD) in patients with COVID-19, OD was much more common in mild COVID-19 cases than in more moderate/severe cases.

Details: This study analyzed epidemiological and clinical data at baseline and 2 months post-infection from 2581 patients with COVID-19 from 18 European hospitals to explore the prevalence and recovery of olfactory dysfunction (OD), or loss of smell and changes in the way odors are perceived. OD prevalence was highest in patients with mild COVID-19 cases (86%); moderate and critical cases had significantly lower OD prevalence (4.5% and 6.9%, respectively). Of 1916 patients with OD, 71.1% (n=1363) completed evaluations. 328/1363 (24.1%) self-reported that they did not recover from OD 60 days after symptoms began. The average length of time patients self-reported OD was 21.6 days. Objective olfactory evaluations identified loss of smell/reduced sense of smell in 54.7% and 36.6% of mild and moderate/critical COVID-19 cases, respectively. 15.3% and 4.7% of patients with loss/reduced sense of smell did not objectively recover their sense of smell at 60 days and 6 months post-symptom onset, respectively.

Key Takeaways:

- Based on objective evaluations of sense of smell in patients with COVID-19, olfactory dysfunction went away in about 95% of cases at 6 months.

Immunological Memory to SARS-CoV-2 Assessed for up to 8 Months After Infection (Science)

Bottom Line: In this study of immunological memory to SARS-CoV-2 among previously infected individuals, responses from antibodies, memory B cells, and T cells can last for at least eight months post symptom onset.

Details: This study examined various components of immune memory to SARS-CoV-2 (CD4+ T cells, CD8+ T cells, and antibody-mediated immunity) in order to better characterize their dynamics relative to each other and understand the likelihood of durable protective immunity. 188 individuals were recruited into the study, reflecting a range of COVID-19 case severity, though most (93%) had cases not requiring hospitalization. Most (97%) individuals had symptomatic COVID-19 disease. Study participants provided a blood sample between 6 and 240 days post-symptom onset; 51 participants provided blood samples 2-4 times over the course of several months. SARS-CoV-2-specific circulating antibodies, memory B cells, CD4+ T cells, and CD8+ T cells were measured. Immunoglobulin G (IgG) antibodies against the virus' spike protein were durable, as were receptor binding domain (RBD) IgG. Spike IgG levels declined slightly at 6-8 months post symptom onset. Five to 8 months post-symptom onset, almost all individuals in the study were positive for SARS-CoV-2 spike and RBD IgG. Spike protein-specific memory B cells were found in almost all participants, which increased 6 months post symptom onset. T cells declined with a half-life of 3-5 months post symptom onset. These findings suggest that durable immunity against subsequent COVID-19 disease is possible in most individuals, though protective immunity varies considerably from person to person.

Key Takeaways:

- Long-lasting immunity against subsequent COVID-19 disease is possible in most individuals, though protective immunity varies considerably from person to person.