**COVID-19 Evidence Digest 04/09/21**

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## Potential benefit of convalescent plasma transfusions in immunocompromised patients with COVID-19 (Lancet)

**Bottom line:** Findings from a small pilot study (n=14) with no comparison group, suggests that immunosuppressed patients with early COVID-19 infection and no detectable anti-SARS-CoV-2 IgG may be potential candidates for convalescent plasma treatment.

**Details:** This is a small pilot study of 14 immunosuppressed patients with COVID-19 and no detectable IgG antibodies that were administered with convalescent plasma. About 50% of patients were female (n=7) with a median age of 65 years [IQR: 58-70], and 8 patients were immunosuppressed due to solid organ transplant, 4 due to allogenic stem cell transplant, and 2 due to hematological malignancy. The mean time from diagnosis to plasma transfusion was 5.14 days (SD: 5.14), with 11 patients receiving 3 transfusions, 2 patients receiving 2 transfusions, and 1 receiving just 1 transfusion. A total of 13 out of 14 developed antibodies within 24-48 hours after the last transfusion. The median initial disease severity was 5 out of 10 on the WHO Clinical Progression Scale (range: 4-6), and 8 (57%) of patients showed clinical improvement (e.g. 1 point or more improvement on WHO Clinical Progression Scale) 5 days after the last infusion. A total of 12 patients were ultimately discharged (86%) and 2 patients died, due to secondary infection. Overall this study suggests that immunosuppressed patients with early COVID-19 infection and no detectable anti-SARS-CoV-2 IgG may be potential candidates for convalescent plasma treatment. This study is limited by the fact that it is a small (n=14) pilot study with no comparison group.

**Key Takeaways:**

- Immunosuppressed patients with early COVID-19 and no detectable anti-SARS-CoV-2 IgG may be potential candidates for convalescent plasma treatment.
- An IgG titer following transfusion, may be a predictive parameter for treatment success.
- This study is limited by the fact it is a small (n=14) pilot study with no comparison group.

## Thromboembolism and the Oxford–AstraZeneca COVID-19 vaccine: side-effect or coincidence? (Lancet)

**Bottom Line:** The number of cases of venous thromboembolic events (VTE) amongst ChAdOx1 nCoV-19 (AZD1222) vaccine from Oxford-AstraZeneca recipients in the European Economic Area is not higher than expected estimates based on nationwide incidence rates of VTE in adults in Denmark.

**Details:** The European Medicines Agency (EMA) has reported 30 cases of predominantly VTEs amongst the 5 million individuals who have received the AZD1222 vaccine from Oxford-AstraZeneca in the European Economic Area. Researchers analyzed nationwide population health data from Denmark in order to estimate natural incidence of VTE.

Researchers identified Danes aged 18 years old and above between January 1, 2010 and November 30, 2018. The outcome of interest was first primary or secondary inpatient hospital diagnosis or outpatient clinical diagnosis of VTE in the general adult population, including deep vein thrombosis (DVT), pulmonary embolism (PE), and other venous thrombi affecting various locations, including the intracranial venous system. A second analysis limited outcomes to only

DVT and PE cases given the frequency of these diagnoses. Data was further stratified by age and sex. Calculated incidence rates of these outcomes were used to estimate the number of expected cases of VTE over one week and one month in a population the same size as that receiving AstraZeneca vaccine in Europe.

Individuals (n = 4,915,426) aged 18-100 were included in this analysis, contributing over 38 million person-years. Among these, 3,963,153 of the individuals were aged 18-64 with over 29 million person-years. The incident rate per 1000 person-years for DVT/PE for Danish adults aged 18-100 was 1.70 (95% confidence interval [CI]: 1.68-1.71). The incident rate per 1000 person-years for DVT/PE for Danish adults aged 18-64 was 0.91 (95% CI: 0.89-0.92). Both incident rates were similar between sexes. Using these incidence rates, the expected cases of DVT/PE would be 91 cases per week and 398 cases per month in 18-64 year olds. Expected cases of DVT/PE would be 169 cases per week and 736 cases per month in 18-99 year olds.

**Key Takeaways:**

- The rates of VTE after receipt of ChAdOx1 nCoV-19 (AZD1222) vaccine from Oxford-AstraZeneca does not appear to be higher than incidence in the general population.
- Of note, analysis of thrombocytopenia, bleeding and rare multiple thrombosis events is not included in this analysis and are still being evaluated.

**Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for COVID-19 (NEJM)**

**Bottom Line**: Findings from this corresponding letter regarding antibody duration elicited by the Moderna mRNA-1273 SARS-CoV-2 vaccine, shows that antibody persists through 6 months after the second dose in three different serologic assays among 33 healthy adult participants.

**Details**: In this corresponding letter regarding the durability of protection of the Moderna mRNA-1273 SARS-CoV-2 vaccine, the authors described the vaccine-elicited binding and neutralizing antibodies at 180 days after the second dose (day 209) in 33 healthy adult participants among the ongoing phase 1 trial, stratified by age. On day 209, antibody activity were still high in all age groups: the geometric mean end-point titers (GMTs) of the receptor-binding antibodies using enzyme-linked immunosorbent assay (ELISA) were 92,451 among 15 participants aged 18-55 years old (95% confidence interval [CI]: 57,148-149,562), 62,424 among 9 participants aged 56-70 years old (95% CI: 36,765-105,990), and 49,373 among 9 participants aged 71 years old and above (95% CI: 25,171-96,849). In a pseudovirus neutralization assay, almost all participants had detectable activity: the 50% inhibitory dilution ($ID_{50}$) GMTs were 80 for participants aged 18-55 (95% CI: 40-135), 57 for participants aged 56-70 (95% CI: 30-106), and 59 for participants aged 71 and above (95% CI: 29-121). In a more sensitive live-virus focus-reduction neutralization mNeonGreen test, all participants had detectable activity, with significantly lower GMTs in participants aged 56-70 (P = 0.02) and in those aged 71 and above (P = 0.004), compared to those aged 18-55 years.

Model estimations on half-life of antibodies were consistent with literature looking at 8 months post-symptom onset among convalescent patients with COVID-19: using an exponential decay model (assumes a steady decay rate over time), the estimated half-life after day 43 was 52 days (95% CI: 46-58) for binding antibodies, 69 days (95% CI: 61-76) for pseudovirus neutralization, and 68 days (95% CI: 61-75) for live-virus neutralization. Using a power-law model (assumes

decay rates decrease over time), the estimated half-life was 109 days (95% CI: 92-136), 173 days (95% CI: 144-225), and 202 days (95% CI: 159-272), respectively.

**Key Takeaways**:

- Data from 33 healthy adult participants in an ongoing phase 1 trial of the Moderna mRNA-1273 SARS-CoV-2 supports that the vaccine-elicited antibodies will persist through 6 months after the second dose using three different serologic assays, which supports the use of the Moderna mRNA vaccine.

- Antibody titers and assays that best assess vaccine efficacy are still not known. Ongoing studies are evaluating immune responses beyond 6 months and the effect of booster dose in lengthening the duration and breadth of activity against variants.