Clinical pathology selected abstracts

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Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination

June 2021—Adverse events reported following administration of the ChAdOx1 nCoV-19 AstraZeneca vaccine were similar to those reported for the Johnson & Johnson/Janssen COVID-19 vaccine. The latter was paused in the United States in April due to concerns about thrombocytopenia, cerebral venous thrombosis, and a heparin-induced thrombocytopenia (HIT)-like syndrome that was a rare occurrence post-vaccination in women under the age of 60. In Norway, the AstraZeneca vaccine was approved for use in health care professionals younger than 65 years of age who did not have close contact with patients with COVID-19. By the time administration of the AstraZeneca vaccine was stopped due to concerns about adverse risk, 132,686 people in Norway had received the first dose, and none had received the second dose. The authors reported on the findings for five patients who presented with venous thrombosis and thrombocytopenia seven to 10 days after receiving their first dose of the AstraZeneca vaccine. Within 10 days of receiving their first dose, the health care workers, who were between the ages of 32 and 54 years, presented with thrombosis in unusual sites and severe thrombocytopenia. Four of the patients had major cerebral hemorrhage, and the outcome was fatal in three. A common denominator described in all patients was a high level of antibodies to PF4-polyanion complexes. The authors proposed that these cases represent a vaccine-related variant of spontaneous HIT that they named vaccine-induced immune thrombotic thrombocytopenia (VITT). In these patients, the characteristic antibodies were identified after initiating anticoagulation treatment with low-molecular–weight heparin for life-threatening thrombosis and thrombocytopenia. Clinicians had to balance continued use of heparin against other anticoagulation options in these patients. Platelet counts continued to rise in all five patients, despite continuing heparin. The authors note that this finding indicates that early use of intravenous immune globulin and prednisolone is highly effective against spontaneous HIT-like syndrome. They concluded that the most important implication of their findings is that physicians should have a low threshold for requesting ELISA testing for PF4-polyanion antibodies. This testing should include confirmatory functional testing in patients who have unexpected symptoms after vaccination.

Schultz NH, Sorvoll IH, Michelsen AE, et al. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. *N Engl J Med*. 2021. doi:10.1056/NEJMoa2104882

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Effects of storage temperature and media/buffer on SARS-CoV-2 nucleic acid detection

The diagnostic workup of active SARS-CoV-2 infection is based on molecular tests and real-time reverse transcription-quantitative polymerase chain reaction (RT-qPCR). RT-qPCR can not only help diagnose patients but also determine the extent of infection and predict disease progression. More specifically, the cycle threshold of RT-qPCR can be used to infer infectivity and disease severity. General laboratory practices recommend immediately storing samples for testing in a refrigerator at 2°C to 8°C for up to 72 hours after collection. When a delay in testing or shipping is expected, specimens should be stored at –70°C or below. Due to the high number of SARS-CoV-2 infections and concerns about insufficient levels of refrigeration and freezing facilities, media, collection kits, and medical staff in some countries, the authors conducted a study in Korea to assess how such factors as storage period, temperature, media or buffer, and sample type influence the results of SARS-CoV-2 RT-qPCR. They selected 132 SARS-CoV-2–positive respiratory specimens in which 76 were a combination of nasopharyngeal swabs (NPS) and oropharyngeal swabs (OPS) and 56 were saliva. The authors then selected 80 of those samples and divided them into two groups of 40—half were NPS or OPS contained in Universal Transport Medium and half were sputum in phosphate-buffered saline. RT-qPCR testing was performed on samples on the date of collection, and the

remaining tests were conducted one day, two days, and one week later to confirm serial cycle threshold values according to temperature and storage length. The results showed no significant difference in qualitative positivity between the two media or buffer conditions when they were stored at three different temperatures and compared for seven days. However, RT-qPCR cycle threshold values did differ based on temperature. When stored at 2°C to 8°C, all 80 samples showed no significant change for seven days. However, when stored at 20°C to 22°C or above 35°C, the results were negatively affected, even after one day. This resulted in a lower probability of detecting viral nucleic acids in samples stored at higher temperatures because of degradation. Of note, samples stored in pH-controlled media or buffer were more stable than those stored in non-buffer Universal Transport Medium or phosphate-buffered saline. The authors concluded that these results show the importance of maintaining adequate storage temperature, using proper media or buffer, and performing RT-qPCR for SARS-CoV-2 testing as soon as possible after sample collection. They recommend storing samples in pH-controlled media or buffer and at a low temperature in the event that a molecular test is delayed. They also note the need for proper sample transportation, especially in hot weather. This study may serve as a suitable reference for determining effective shipping and storage conditions to ensure that SARS-CoV-2 virus can be detected from patient samples.

Kim N, Kwon A, Roh EY, et al. Effects of storage temperature and media/buffer for SARS-CoV-2 nucleic acid detection. *Am J Clin Pathol*. 2021;155:280–285.

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