REGIONAL MEDICAL LABORATORY

MEMORANDUM

To: All Regional Medical Laboratory, Inc. (RML) Clients

From: Regional Medical Laboratory, Inc.
Gerald C. Miller, Ph.D, Chief of Immunology and Microbiology
Cindi Starkey, M.D., Ph.D, Medical Director of Regional Medical Laboratory
C. Terrance Dolan, M.D., President of Regional Medical Laboratory

Date: April 14, 2021

Subject: COVID 19 Vaccination and IgG Serology

RML has implemented two COVID 19 IgG serologic assays:

- These assays perform semi-quantitative detection of IgG antibodies, one to the COVID 19 nucleocapsid **(SARS-CoV-2 IgG, nucleocapsid**) and the other to the COVID 19 spike protein **(SARS-CoV-2 IgG, spike).** The IgG antibodies to the nucleocapsid only arise following a SARS-CoV-2 infection. IgG antibodies to the spike protein will follow infection and/or vaccination with a *spike initiating vaccine*. The assays can aid in discerning as to whether the patient has or has not had a COVID 19 infection or a vaccination. The semi-quantitative values (reported as AU/ml) are important to determine the level of antibody activity in seroconversion as well as to follow the status of the levels of antibody activity over time. Results are reported both as qualitative (positive or negative) and semi-quantitative values.

TEST NAME	SARS-CoV-2, IgG Nucleocapsid	SARS-CoV-2, IgG Spike
TEST CODE	6901550	6907251
CPT CODE	86769	86769
SPECIMEN TYPE	Serum - Serum Separator Tube (Red or Gold) Alternate - Plasma Separator Tube (Lithium Heparin, Light Green)	Serum - Serum Separator Tube (Red or Gold) Alternate - Plasma Separator Tube (Lithium Heparin, Light Green)
SPECIMEN STABILITY	Room Temp: 2 Days Refrigerated: 7 Days	Room Temp: 2 Days Refrigerated: 7 Days
LOINC CODES	94507-1	94505-5
TAT	1-2 days, Mon-Fri	1-2 days, Mon-Fri

Interpretation of the assay results:

- **SARS-CoV-2 IgG, Nucleocapsid** antibody is produced by the patient following a SARS-CoV-2 infection. It provides valuable information for patients who have had the infection. However, some patients may produce very little anti-NP antibodies and thus may be negative, particularly if testing is performed more than 30 days after onset of symptoms.
- **SARS-CoV-2 IgG, Spike** antibody is produced by the patient following an infection and/or vaccination with a spike initiating vaccine, thus it is an excellent metric for determining the level of spike neutralizing antibody activity generated following vaccination or infection.

Recent published data for consideration in the management of vaccinated patients. The FDA has given Early Use Authorization (EUA) to Abbott for the SARS-CoV-2 IgG II assay which provides an IgG anti-SARS-CoV-2 spike protein antibody level, recognized to be a neutralizing antibody to the SARS-CoV-2 virus[1].

Effectiveness of full immunization with an mRNA vaccine ≥ 14 days after second dose was 90% against the SARS-CoV-2 infections; effectiveness of partial immunization defined as ≥ 14 days after first dose but before second dose was 80%**[2].**

Patients with **comorbidities** and those **>60 years** of age **may benefit** from determination of the level of antibody activity to the spike protein 15 days following the booster vaccination. Plaque Reduction Neutralization Test (PRNT) assays have reported that the anti-spike and PRNT levels correlate and the anti-spike is considered to be a neutralizing antibody[3]. The FDA has provided Abbott the value of >840 AU/ml as the value to consider their anti-spike protein antibody completely and fully immune; however, unpublished data suggests >4,000 AU/ml as the level of full protective immunity. Further, if a low level was detected (<840 AU/ml), it may be of value to repeat testing periodically. Intuitively, if the level is decreasing over time, this implies that the level of neutralizing antibodies is waning. However, the results must be interpreted in consideration of the IgG anti-spike protein after infection has an estimated half life of 197 days while the IgG anti-nucleocapsid has a half life of 76 days **[4].**

Younger patients (<50 yo) may benefit from antibody testing to determine if they have had COVID 19 infection, particularly if they had asymptomatic or mild disease. The literature suggests that recovering COVID 19 patients, regardless of severity of disease, may only need one vaccination. The literature suggests to test 15 days following the initial vaccine to determine if a booster is needed **[5, 6, 7].**

Patients with PCR documented infection with COVID 19: The literature indicates that for previously infected patients who are initiating the SARS-CoV-2 vaccination, it is recommend to receive first vaccine no sooner than 90 days post onset of symptoms, and that they might want to have the level of IgG anti-Spike determined 15 days after the first vaccination. If the level is >4,000 AU/ml then the patient has ample immunity and does not need further vaccination. Giving the booster to a patient who is already fully immune to the virus has been reported to have a dampening of the immune response to the vaccine, particularly with the T cell immune response**[8].**

Persistence of antibody level: Pfizer has clearly stated that the protective immune response is present for at least 6 months; however, it may be advantageous to follow the level of IgG anti-spike protein in COVID 19 recovering and/or vaccinated patients every 6-12 months to determine the persistence of the anti-spike neutralizing antibody[4]

Convalescent plasma donors: The literature recommends that patients with a prior COVID 19 infection and who desire to be a volunteer for convalescent plasma should have their level of IgG anti-spike protein determined and the results made available for determining their suitability as a donor[9].

Acute Allergic Reactions to mRNA COVID 19 Vaccines: Rates of acute allergic reactions with Pfizer is 11.1/1 million and Moderna is 2.5/1 million doses given. The CDC has requested that health-care providers monitor patients for 15 minutes after vaccination and 30 minutes for those who have a history of allergic reactions. CDC has also recommended that anyone having a severe allergic reaction after getting the first dose of a COVID-19 vaccine, should NOT get the second dose, even if the allergic reaction was not severe enough to require emergency care[10].

If you have questions regarding the material in this document, please contact Gerald C. Miller, Ph.D., Cindi Starkey, M.D., Ph.D. or Terrence Dolan, M.D. at 918-744-2553

Disclaimer: As of March 5, 2021, CDC had stated that antibody testing for assessing for immunity to SARS-CoV-2 following COVID 19 vaccination has no clinical utility. However, this summary provides up-to-date information from many preprints providing the current status in the scientific community of IgG anti-SARS-CoV-2 antibody testing. Whether the IgG anti-SARS-CoV-2 spike protein and the IgG anti-SARS-CoV-2 nucleocapsid assays are of value in the management of your vaccinated patients requires careful clinical correlation and judgement as this is a rapidly increasing and changing body of knowledge.

REFERENCES

1. K.A. Earle et al. medRxiv preprint doi: https://doi.org/10.1101/2021.03.17.20200246
2. Morbidity and Mortality Weekly Report (MMWR) early release on March 29, 2021.
3. E. Salazar et al. https://doi.org/10/1172/jci141206
4. J. Van Elsande, accepted manuscript by Oxford University Press for the Infectious
    a. Diseases of Society of America
5. J.E. Ebinger et al. medRxiv preprint doi: https://doi.org/10.1101/2021.02.23.21252230
6. A. Mazzoni et al. medRxiv preprint doi: https://doi.org/10.1101/2021.03.05.21252590
7. M. Velasco et al, medRxiv preprint doi: https://doi.org/10.1101/2021.03.08.21253065
8. C. Camara et al. bioRxiv preprint doi: https://doi.org/10.1101/2021.03.22.436441
9. M. Joyner et al. DOI:10.1056/NEJMoa2031893
10. Blumenthal, K. et al. JAMA published online. DOI:10.1001/jama.2021.3976