REGIONAL MEDICAL LABORATORY

MEMORANDUM

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

From: Regional Medical Laboratory, Inc.
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Date: September 13, 2021

Subject: COVID 19 Vaccination and IgG Serology

RML has two available 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.

Interpretation of the assay results:

- **SARS-CoV-2 IgG, Nucleocapsid** test evaluates for the presence of IgG Nucleocapsid antibody produced by the patient following a SARS-CoV-2 infection only. Nucleocapsid antibody production will NOT occur following vaccination alone. However, some patients may produce very little anti-nucleocapsid antibodies and thus may be negative, particularly if testing is performed more than 60 days after onset of symptoms.
- **SARS-CoV-2 IgG, Spike** antibody test evaluates for the presence of IgG Spike antibody produced by the patient following a SARS-CoV2 infection or spike initiating vaccination, thus it is an excellent metric for determining the level of spike neutralizing antibody activity generated following vaccination or infection. Younger patients (<50 yo) may benefit from antibody testing to determine if they have had prior COVID 19 infection, particularly if they had asymptomatic or mild or undocumented disease.

These assays perform semi-quantitative detection of IgG antibodies, and they can aid in discerning as to whether the patient has had a COVID 19 infection or a vaccination. Results are reported both as qualitative (positive or negative) and semi-quantitative values. The semi-quantitative values may be useful to determine the level of antibody activity following seroconversion as well as to follow the status of the levels of antibody activity over time since recent studies demonstrate decline of antibodies over time and booster vaccinations may be of interest depending on clinical scenario.

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Additional information to aid in interpretation of the assay results:
The FDA has given Early Use Authorization (EUA) to Abbott for the SARS-CoV-2 IgG II assay which provides an anti-SARS-CoV-2 spike protein IgG 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 that the anti-spike is considered to be a neutralizing antibody[3]. Intuitively, if the antibody level is decreasing over time, this implies that the level of neutralizing antibodies is waning, and this occurs naturally in most individuals.

The results must be interpreted with consideration that the IgG anti-spike protein has an estimated half life of 197 days; however, some recent unpublished data suggests the half-life of anti-spike protein to range from 2-6 months, depending on the specific patient. The half life of IgG anti-nucleocapsid has a reported half life of 76 days [4].

The literature suggests that patients who have recovered from COVID 19 infection, regardless of severity of disease, may only need one vaccination injection. The literature suggests antibody testing 15 days following the initial vaccine may be prudent to determine if a booster injection is needed [5, 6, 7] . Further, for patients with documented prior COVID 19 infection, the literature indicates that they should initiate SARS-CoV-2 vaccination no sooner than 90 days post onset of symptoms.

Additionally, these patients might want to have the level of IgG anti-Spike determined 15 days after the first vaccination, and if the patient has generated a high level of anti-spike antibody, then the literature discourages further vaccination for the time being. 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 of the T cell immune response[8]. Pfizer has clearly stated that the protective immune response following vaccination is present for at least 6 months; however, it may be advantageous to follow the level of anti-spike protein IgG 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].

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Disclaimer: As of March 5, 2021, CDC had stated that antibody testing for assessing 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. The IgG anti-SARS-CoV-2 spike protein is the preferred antibody assay for the management of infected and/or vaccinated patients. Previously vaccinated or infected individuals require careful clinical correlation and judgement when deciding vaccination course of action as this is a rapidly increasing and changing body of knowledge.

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

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

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