CMO SPECIAL REPORT: COVID-19 UPDATE

FROM THE DESK OF
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UPSTATE UNIVERSITY HOSPITAL

May 4, 2020

Serologic Testing Education from Jana Shaw, MD, MPH

Provider Education About Abbott SARS-CoV-2 IgG serology

Executive summary
IgG antibodies are a marker of a prior exposure to SARS-CoV-2 virus.
We do not know if the presence of IgG antibodies will protect a person from infection or disease.
IgG antibodies should not be used for diagnosis of acutely ill patients suspected of COVID-19.
Patients should continue to follow strict physical distancing, hand hygiene, cough etiquette and universal masking rules regardless of their SARS-CoV-2 IgG antibody status.

General Considerations
There is little known about the test performance in the clinical setting. However, antibody testing is a marker of the immune response and indicates exposure to the virus. Seroprevalence data will be important in understanding the scale of the pandemic. The test can identify people who were infected and were not tested in early phases of their disease or people who did not know that they were infected as they had very mild or asymptomatic disease.

- Test is performed using the Abbott Architect SARS-CoV-2 IgG assay for use under the FDA's Emergency Use Authorization (EUA) to allow for rapid response during a declared public health emergency. This assay was validated by the Department of Pathology SUNY Upstate Medical University. Additional information is available on the following FDA website for health care providers and recipients. https://www.fda.gov/media/137381/download https://www.fda.gov/media/137382/download
- When you use the serological (antibody) test be aware of its limitations.
- This is not a point-of-care test (POC).
- We currently do not know if infection leads to protection but this is being actively explored.
- Do not use serological (antibody) testing as the sole basis to diagnose acute coronavirus disease 2019 (COVID-19), but instead to provide information about whether a person may have been exposed to the virus.
- Among 73 patients with confirmed COVID-19, all mounted detectable IgG antibodies 14 days or longer after the symptom onset.
- Based on a recent random sampling performed by the NYSDOH, just 3.6 percent of those tested outside NYC and Long Island, had been infected and recovered from the disease. (https://abc7ny.com/coronavirus-nyc-update-corona-virus-cases/6124749/)
- Symptomatic patients suspected to have COVID-19 should be tested using a molecular assay to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA.

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- Immunocompromised patients who have COVID-19 may have a delayed antibody response and produce levels of antibody which may not be detected as positive by the assay.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as SARS-CoV-2 IgG that employ mouse monoclonal antibodies.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed.
- Rheumatoid factor (RF) in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.

Assay performance (information based on Abbott package insert: https://www.corelaboratory.abbott/us/en/offerings/segments/infectious-disease/sars-cov-2#isi)

Analytical Specificity

The SARS-CoV-2 IgG assay was evaluated for potential cross reactivity from individuals with other medical conditions. A total of 182 specimens from 36 different disease categories were tested. One hundred eighty-one (181) specimens were negative and one specimen (patient with CMV infection) was positive by the SARS-CoV-2 IgG assay.

Clinical Performance

A study was performed to determine the clinical performance of the SARS-CoV-2 IgG assay. To estimate the positive percent agreement (PPA), between the SARS-CoV-2 IgG assay and the PCR comparator, 122 serum and plasma specimens were collected at different times from 31 subjects who tested positive for SARS-CoV-2 by a polymerase chain reaction (PCR) method and who also presented with COVID-19 symptoms. Each specimen was tested using the SARS-CoV-2 IgG assay. The PPA and the 95% confidence interval (CI) were calculated. To estimate the negative percent agreement (NPA), 1070 serum and plasma specimens from subjects assumed to be negative for SARS-CoV-2 were tested. Of the 1070 specimens, 997 specimens were collected prior to September 2019 (pre-COVID-19 outbreak). An additional 73 specimens were collected in 2020 from subjects who were exhibiting signs of respiratory illness but tested negative for SARS-CoV-2 by a PCR method. All 1070 specimens were tested using the SARS-CoV-2 IgG assay. The NPA and the 95% CI were calculated. The results of both groups are presented in the following 2 tables.

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Positive Agreement by Days Post-Symptom Onset

Days Post-Symptom Onset	n	Positive	Negative	PPA (95% CI)
< 3	4	0	4	0.00% (0.00, 60.24)
3 - 7	8	2	6	25.00% (3.19, 65.09)
8 - 13	22	19	3	86.36% (65.09, 97.09)
≥ 14	88[a]	88	0	100.00% (95.89, 100.00)

[a] Five specimens from 1 immunocompromised patient were excluded from the study. Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert for further information. When the results from these specimens were included, the PPA at ≥ 14 days post-symptom onset was 96.77% (95% CI: 90.86, 99.33).

Negative Agreement by Category

Category	n	Positive	Negative	NPA (95% CI)
Pre-COVID-19 Outbreak	997	4	993	99.60% (98.98, 99.89)
Other Respiratory Illness	73	0	73	100.00% (95.07, 100.00)
Total	1070	4	1066	99.63% (99.05, 99.90)

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Interpretations

SARS-CoV-2 IgG antibodies were detected. Results suggest recent or prior infection with SARS-CoV-2. Correlation with epidemiologic risk factors and other clinical and laboratory findings is recommended. Based on *preliminary* results from the NYSDOH, seroprevalence in our region appears to be low (3.6%). More robust local estimates are needed to guide interpretation of results in our patient population. Infrequently, false-positive results may be due to prior infection with other human coronaviruses. Be aware that COVID-19 antibody tests with high specificity (96-98%), may mean that a positive test result is more likely a false-positive result than a true positive result if the prevalence or pretest probability is 5% or less. (https://www.idsociety.org/globalassets/idsa/public-health/covid-19/idsa-covid-19-antibody-testing-primer.pdf)

SARS-CoV-2 IgG antibodies were not detected. Patient was not exposed to the virus or serum was collected too soon following infection, or in immunosuppressed patients.

Specimen collection

Minimum of 0.5mL of serum (at least 1 mL of whole blood) is required.
Use GOLD tube or Red microcontainer is also acceptable if finger stick is performed.
Anticipated turn-around-time is 24 h from the receipt of the specimen. This test will be batch tested Monday-Friday till 1:30pm.

Recovery Plan from Amy Tucker MD and Jeremy Joslin MD

It is with a posture of guarded optimism that we begin work towards our recovery as a hospital and health care enterprise. To this end, we have begun to assemble a comprehensive team to plan and execute a phased and measured reopening and recovery.

The team will be both strategic and tactical. It will need to consider challenges related to patient access, the patient experience and staff safety. The recovery of both our community's health and our institution's fiscal health must be addressed. Operationally, the team will need to closely monitor hospital capacity and COVID activity, taking swift action to react to any surges in hospitalizations or infections.

We expect the road to recovery will have some ups and downs, but the determination and exceptional talent we've seen demonstrated across all aspects of our institution will see us through together.

Remdesivir Receives FDA Emergency Use Authorization from Luke Probst, Pharm.D., BCPS

Background: Remdesivir is an investigational nucleotide analog with broad-spectrum antiviral therapy which has been and continues to be studied for the treatment of COVID-19. On May 1, 2020, the FDA granted an emergency use authorization (EUA) for Remdesivir in the treatment of COVID-19. This will allow the

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distribution and broader use of Remdesivir to treat hospitalized patients with severe COVID-19 disease in the United States. This therapy remains an investigational drug and has not been fully approved by the FDA. More information about the Remdesivir EUA can be found on the following link: https://www.gilead.com/news-and-press/press-room/press-releases/2020/5/gileads-investigational-antiviral-remdesivir-receives-us-food-and-drug-administration-emergency-use-authorization-for-the-treatment-of-covid19

Clinical trial data are ongoing. Efficacy and safety results remain incomplete. Recently released data from one ongoing clinical study among hospitalized patients with advanced COVID-19 and lung involvement demonstrated a statistically significant reduction in median time to recovery when Remdesivir was compared to placebo (11 days versus 15 days, p<0.001). A statistically significant reduction in mortality has not been demonstrated to date with Remdesivir therapy. A full understanding of Remdesivir's efficacy and safety remains incomplete.

Expected availability for patient care: Per the drug's manufacturer: "Allocation of the currently limited available supply of Remdesivir will be made based on guiding principles that aim to maximize access for appropriate patients in urgent need of treatment, with direction from and in collaboration with the government." The U.S. government will coordinate the donation and distribution of Remdesivir to hospitals in cities most heavily impacted by COVID-19. Hospitals with intensive care units and other hospitals that the government deems most in need will receive priority in the distribution of Remdesivir. The drug's manufacturer is working with the U.S. government on the logistics of Remdesivir distribution and will provide more information when the company begins shipping the drug under the EUA. Upstate will continue to closely monitor for the availability of Remdesivir for our patients who meet eligibility criteria. **Further updates will be provided to the Upstate Community as more definitive information is discovered about therapy availability.**

Eligible patients: Remdesivir is authorized for use under the EUA only for treatment of patients with suspected or laboratory-confirmed SARS-CoV-2 infection and severe COVID-19 disease. Severe disease is defined as hospitalized patients with an oxygen saturation (SpO2) ≤ 94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO). It is authorized for use in both pediatric and adult patients.

Dosing and monitoring:
Duration of Remdesivir therapy is based upon severity of patient illness.

- For adult and pediatric patients weighing ≥40 kg requiring invasive mechanical ventilation and/or ECMO, a 10-day duration of therapy is recommended.
    - 200mg IV on day 1, followed by 100mg IV daily for days 2 through 10.
- For adult and pediatric patients weighing ≥40 kg who are NOT requiring invasive mechanical ventilation and/or ECMO, a 5-day duration of therapy is recommended. *The duration of therapy may be extended based upon patient response.*

  - 200mg IV on day 1, followed by 100mg IV daily for days 2 through 5.
- Complete dosing and monitoring recommendations can be found on the following link, including dosing for pediatric patients weighing < 40kg. https://www.gilead.com/-/media/files/pdfs/remdesivir/eua-fact-sheet-for-hcps_01may2020.pdf?la=en&hash=B56F8C441364B7EDA15543F75E8EC88F
- All patients must have a baseline eGFR determined before dosing. Remdesivir is not recommended in adult and pediatric patients with eGRF < 30 mL/min unless the potential benefit outweighs the potential risk. Hepatic function should also be monitored prior to therapy initiation.
- Healthcare providers and/or their designee will be responsible for mandatory FDA MedWatch reporting of all medication errors and serious adverse events or deaths that occur during Remdesivir treatment and are considered to be potentially attributable to Remdesivir. Such events must be reported within 7 calendar days from the onset of the event. Pharmacy staff will help with this process at Upstate.

Clinical Documentation Improvement (CDI) from Dr. Emily Albert and Dr. Ali Khan, Co-Directors, CDI

Why does your documentation matter?

Not only are you using it to communicate your patients' conditions, your plan for their care and their response to it, but it represents corresponding codes in the ICD system which are used for Quality / Risk adjustment. Thankfully, you don't need to know these know these codes, that's why you have CDI specialists.

We work closely with all of you and our hospital coding department to ensure accurate and complete code assignment. Be sure to answer queries and continue complete documentation throughout the hospital record into the discharge summary – it's one of the most important documents in the medical record.

Please refer to the attached tip sheet for more information and contact the CDI Hotline with questions at 315-464-5455.

Keep fighting the good fight. And stay safe.

Amy

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Clinical Documentation Improvement
Tip of the Month – Why Documentation Matters
Applies to all providers

Many organizations provide quality rankings for physicians and hospital systems—determined after risk adjustment is applied. Risk adjustment is based on clinician documentation. Only coded diagnoses are included in the risk adjustment.

Did You Know?

There are no ICD-10 codes for the organ-system approach to medical record documentation. You must document specific diagnoses for which there are corresponding codes in the ICD system, and validate each diagnosis, if you hope to receive the credit you deserve for the work you do.

You don't need to know the codes – that's why you have CDI Specialists!

ICD-10 specific documentation is paramount to demonstrating quality!

Quality Measures impacted by risk adjustment based on clinical documentation include:

Mortality Rate/Scoring	Hospital Rankings
Readmission Rates	Length of Stay

Unintentionally downgrading the severity of a patient's clinical condition in the medical record can lead to insurance company denial opportunities.

Physician Queries serve many purposes and can come from Coders and CDI professionals.
During the patient's hospitalization - queries come from CDI
After discharge - queries come from Coding:

To support documentation of conditions that are evident clinically but without complete documentation of corresponding diagnoses or condition.	To clarify diagnoses documented without documentation of clinical validation.
To clarify procedure objectives and details	To support appropriate Present on Admission (POA) code indicator assignment.
To establish acuity and specificity of documented diagnoses, whenever possible	To establish relevance and diagnostic status, "history of" vs. chronic conditions, active or ruled out diagnoses
To resolve conflicting documentation	To establish clear cause-and-effect relationship between medical conditions

Be sure to continue complete documentation & carry all diagnoses through the Discharge Summary! It's one of the most important documents in the medical record and is:

The first document hospital coders review when they start coding any given hospitalization
Considered the final diagnostic statement for the entire hospitalization
The first document Recovery Auditors review in their efforts to deny any given hospitalization and remove important diagnoses