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Laboratory Diagnosis of Coronavirus Disease-2019 (COVID-19)

Background

SARS-CoV-2 coronavirus disease-2019 (COVID-19) was first identified in late December 2019 (Zhu, 2019). Chinese health authorities investigated a cluster of atypical pneumonia cases occurring primarily in individuals who had visited a seafood and wet market in Wuhan, Hubei Province, China. Patients reported fever and cough, and most developed chest discomfort and/or respiratory distress, with a diagnosis of pneumonia being made by chest radiographs and/or computed tomographic scan (Zhu, 2019). Pneumonia appears to be the most frequent serious manifestation of infection, characterized primarily by fever, cough, dyspnea, and bilateral infiltrates on chest imaging (Guan, 2020, Huang 2020, Chen 2020, Wang 2020). There are no specific clinical features that can reliably distinguish COVID-19 from other viral respiratory infections. Hence there is a need for scalable, effective, and accurate screening tests for COVID-19.

Laboratory Testing Methods and Applications

Current tests for SARS-CoV-2, the virus that causes COVID-19, assess the presence of the virus (viral nucleic acid or antigens) through specimens obtained from saliva or nasal or oral swabs, using Polymerase Chain Reaction (PCR) methodology. However, these tests cannot identify people who were infected, recovered, and have cleared the virus from their bodies. Serology testing, on the other hand, can identify previous infection by detecting antibodies to SARS-CoV-2 (Wang, 2020). Serology testing for antibodies, especially for neutralizing antibodies (NAbs), is important because it measures the active immune response of an individual against any virus (Coughlan, 2012). NAbs prevent reinfections by blocking entry of a virus to the cell or killing the virus by opsonization (Coughlan, 2012). In particular, serum IgG NAbs, play a major role in neutralization of COVID-19 (Deng, 2020). A combination of antigen, cytokine and antibody testing are important in diagnosis, treatment and management of patients and antibody testing is essential in confirming the diagnosis and determining the immune status of the patient (Zhang, 2020).

Studies of COVID-19 antibodies are sparse and vary somewhat in documenting antibody responses. In a study from Beijing, China (Guo, 2020), the median time to IgM and IgA antibody detection after onset of symptoms was 5 days, while IgG was detected at 14 days, with a positive rate of 85.4%, 92.7% and 77.9% respectively. In another study by Zheng et al, IgM antibodies start increasing at day 9 and peak at day 18. SARS-CoV-2 specific IgG begins increasing from day 9 to day 15 and persists at elevated level from day 15 to 39. The positive rate for IgG reached 100% around 20 days after onset of symptoms (Zheng, 2020). Long et al, reported that the median day of seroconversion for both IgG and IgM was 13 days after onset of symptoms. IgG was positive in 100% patients (19/19) and antibody levels plateaued within 6 days of seroconversion (Long, 2020).

Table 1. Seroconversion Timing in COVID-19
(Median Seroconversion Time, Post-Symptom Onset)

Antibody Type	Days
Total Anti-SARS-CoV-2 antibodies	11 Days
Total Anti-SARS-CoV-2 IgM antibodies	12 Days
Total Anti-SARS-CoV-2 IgG antibodies	15 Days

Zhao et al, noted the presence of antibodies was <40% among patients in the first 7 days of illness, then rapidly increased to 100% 15 days after onset (Table 1). In contrast, the positive rate of viral RNA decreased from 66.7% (58/87) in samples collected before day 7 to 45.5% (25/55) from days 15 to 39. Combining RNA and antibody detections significantly improved the sensitivity of pathogenic diagnosis for COVID-19 patients even in early phase one week from onset. Moreover, a higher titer of Ab was independently associated with worse clinical classification. In addition to antibodies, the measurement of cytokines and other biomarkers of lung injury can be helpful in management of COVID-19 patients. An extreme response from a patient's immune system, termed "cytokine storm" is associated with disease severity and poor prognosis in COVID-19 patients. Continuous high levels of the cytokines are associated with disease deterioration and fatal outcome (Mehta, 2020).

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These studies illustrate the value of antibody and cytokine detection in COVID-19 patients over the course of SARS-CoV-2 infection. Antibodies offers additional information that is vital for contact tracing, management of infected populations and identification of individuals in whom the COVID-19 infection has been resolved and have some protection from the virus. A compilation of studies and internal data is presented graphically in Figure 1.

KSL Diagnostics offers the viral, antibody and cytokine testing.

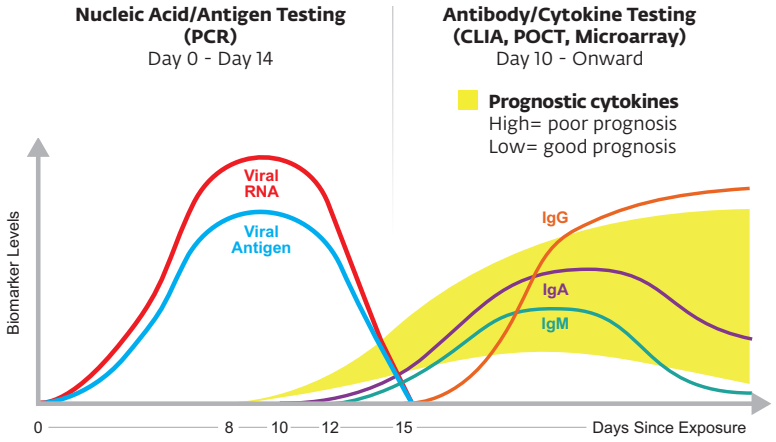

Figure 1. KSL Biomarker Profile: Antigen, antibody and cytokines.[3]

Test Menu and Specimen Requirements

Test Code	Description	CPT	Test Method	Specimen Type
230	**Coronavirus Disease (COVID-19) virus testing by RT-PCR**	87365	RT-PCR	Viral: OP or NP swab in viral transport medium, Eswab™ or saline; OP or NP wash/aspirate in sterile cup; BAL in sterile cup
234	**Coronavirus Disease (COVID-19) IgG Antibody Testing by chemiluminescence immunoassay (CLIA)**	86769	CLIA	Serum or Plasma
237	**COVID-19 panel Includes tests 230, 234**	87365, 86769	RT-PCR, CLIA	Swab, Serum and Plasma

Specimen collection kits can be ordered at www.ksldx.com or by calling 1.800.960.1080.

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