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Patricia R. Slev

In 2019, an emerging coronavirus, SARS-COV-2, was first identified. In the months since, SARS-CoV-2 has become a global pandemic of unimaginable scale. In 2021, SARS-CoV-2 continues to be a huge public health burden and a dominating issue in health care. In addition, SARS-CoV-2 has placed a spotlight on laboratory medicine and its key role in infectious disease management. The SARS-CoV-2 antibody testing landscape is vast and consists of dozens of antibody tests that have received EUA. The laboratory is faced with choosing the right test, staying current with the rapidly evolving recommendations, and updating test information for clients and clinicians. This review addresses what we know about the humoral response in SARS-CoV-2 infection and how this knowledge translates into appropriate serology test choice, utility, and interpretation.

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Elitza S. Theel

This review provides a broad summary of the performance characteristics of high-throughput severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serologic assays with Food and Drug Administration Emergency Use Authorization, which are commonly found in central clinical laboratories. In addition, this review discusses the current roles of serologic testing for SARS-CoV-2 and provides a perspective for the future.

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Lucy Ochola, Paul Ogongo, Samuel Mungai, Jesse Gitaka, and Sara Suliman

The coronavirus disease of 2019 (COVID-19) pandemic, caused by infection with the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has undoubtedly resulted in significant morbidities, mortalities, and economic disruptions across the globe. Affordable and scalable tools to monitor the transmission dynamics of the SARS-CoV-2 virus and the longevity of induced antibodies will be paramount to monitor and control the pandemic as multiple waves continue to rage in many countries. Serologic assays detect humoral responses to the virus, to determine seroprevalence in target populations, or induction of antibodies at the individual level following either natural infection or vaccination. With multiple

vaccines rolling out globally, serologic assays to detect anti-SARS-CoV-2 antibodies will be important tools to monitor the development of herd immunity. To address this need, serologic lateral flow assays (LFAs), which can be easily implemented for both population surveillance and home use, will be vital to monitor the evolution of the pandemic and inform containment measures. Such assays are particularly important for monitoring the transmission dynamics and durability of immunity generated by natural infections and vaccination, particularly in resource-limited settings. In this review, we discuss considerations for evaluating the accuracy of these LFAs, their suitability for different use cases, and implementation opportunities.

Alternative Methods to Detect Severe Acute Respiratory Syndrome Coronavirus 2 Antibodies

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Rashmi Patel, Siddharth Khare, and Vinay S. Mahajan

The COVID-19 pandemic has resulted in the development, validation, and rapid adoption of multiple novel diagnostic approaches. Hundreds of SARS-CoV-2 serologic assays have been developed and deployed to contain the spread of the virus, and to supply timely and important health information. Most of these serologic assays were based on a conventional enzyme-linked immunosorbent assay or the lateral flow assay format. The immunoassays that were developed were based on alternative technologies and are highlighted in this article with a brief discussion of the assay principle and the pros and cons for each assay. Measurement of neutralizing antibodies is also discussed.

Suboptimal Humoral Immunity in Severe Acute Respiratory Syndrome Coronavirus 2 Infection and Viral Variant Generation

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Shiv Pillai

This review describes the underlying basis for the sub-optimal humoral immune response in coronavirus disease (COVID)-19 including the absence of evidence for affinity maturation in the vast majority of patients and the absence of germinal centers even in severe disease. Suboptimal humoral and cellular immunity may provide the optimal conditions for the generation and selection of viral variants.

Antibody Dynamics and Durability in Coronavirus Disease-19

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Adam Zuiani and Duane R. Wesemann

Severe acute respiratory syndrome coronavirus 2 (COVID)-19 has emerged as the greatest global health threat in generations. An unprecedented mobilization of researchers has generated a wealth of data on humoral responses to SARS-CoV-2 within a year of the pandemic's beginning. The rapidly developed understanding of acute-phase antibody induction and medium-term antibody durability in COVID-19 is important at an individual level to inform patient care and a population level to help predict transmission dynamics. In this brief review, we will describe the development and maintenance of antibody responses to immunization and infections generally and the specific antibody dynamics observed for COVID-19. These crucial features of the humoral response have

implications for the use of antibody therapeutics against the virus and can inform the likelihood of reinfection of individuals by the virus.

Severe Acute Respiratory Syndrome Coronavirus 2 Antigens as Targets of Antibody Responses 97

Alana F. Ogata, Roey Lazarovits, Augusta Uwamanzu-Nna, Tal Gilboa, Chi-An Cheng, and David R. Walt

Humoral immunity to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during acute infection and convalescence has been widely studied since March 2020. In this review, the authors summarize literature on humoral responses to SARS-CoV-2 antigens with a focus on spike, nucleocapsid, and the receptor-binding domain as targets of antibody responses. They highlight serologic studies during acute SARS-CoV-2 infection and discuss the clinical relevance of antibody levels in COVID-19 progression. Antibody responses in pediatric COVID-19 patients are also reviewed. Finally, the authors discuss antibody responses during convalescence and their role in protection from SARS-CoV-2 reinfection.

Vaccine-Induced Severe Acute Respiratory Syndrome Coronavirus 2 Antibody Response and the Path to Accelerating Development (Determining a Correlate of Protection) 111

Amy C. Sherman, Michaël Desjardins, and Lindsey R. Baden

As new public health challenges relating to COVID-19 emerge, such as variant strains, waning vaccine efficacy over time, and decreased vaccine efficacy for special populations (immunocompromised hosts), it is important to determine a correlate of protection (CoP) to allow accurate bridging studies for special populations and against variants of concern. Large-scale phase 3 clinical trials are inefficient to rapidly assess novel vaccine candidates for variant strains or special populations, because these trials are slow and costly. Defining a practical CoP will aid in efficiently conducting future assessments to further describe protection for individuals and on a population level for surveillance.