

President's Message

Mariane Setyabudi

Greetings ASCLS-Michigan Members!

I am honored and excited for this opportunity to serve as your 2021-2022 ASCLS-Michigan President!

As we navigate challenges and opportunities this year, I would like to take a moment to thank all of you who continues to work and step up to the challenges to be a part of the laboratory profession contributing to patient care.

This past June I submitted a strategic plan that focuses on strong board and conference to achieve the goal of strong organization. To develop the strong board of directors for ASCLS Michigan, I would like to extend the invitation for our board meetings to our members. I remembered my first time going to a board meeting and while it was overwhelming, it was also exciting. I learn about the organization, develop professional skills and built friendships along the way. As the worlds is still navigating the pandemic, this year we plan on having both in person and virtual meetings. We will post the dates and the format of the meetings through our social media presence on Facebook and the ASCLS Member Connect Community.

As the past President John Ko noted in the last newsletter, ASCLS Michigan is centered around strong community. I am excited to see our community grows even in the midst of a pandemic!

Here's some dates that you might want to note on your calendar:

- October 25-25: ASCLS Legislative Symposium, Alexandria VA. See next page for details.
- January 10-17: Pride-Respect-Inclusion-Support-Momentum (PRISM)
- January 14-15: Emerging Lab Managers Collaborative Conference (ELMC2)
- April 10-13: ASCLS-MI Spring Conference

Inside This Edition:

President's Message

Page 1

Legislative Sympposium

Page 2

Blood Bank SA article: Pathogen Reduction

Pages 3-5

Serology SA Article: Covid-19

Pages 5-9

Save the Date! Attend the ASCLS Legislative Symposium and Labvocate!

Meighan Sharp, MLS(ASCP)^{CM}. - Government Affairs Committee Chair, ASCLS-Michigan

The ASCLS Legislative Symposium will take place this fall! Mark your calendars for October 25 and 26, 2021 at the Hilton Alexandria Old Town in Alexandria, Virginia. Some of legislative issues that will be discussed will include:

- Laboratory workforce shortages
- Laboratory developed tests (LDTs)
- The effects of the Protecting Access to Medicare Act (PAMA) relating to the laboratory
- Laboratory's role in the COVID-19 pandemic.

It is never too late to become a Labvocate! There are several ways to raise awareness to our Congressional leaders. Don't hesitate to reach out to your member of Congress. To discover who your Representative and Senators are, visit www.house.gov/representatives/find-your-representative and www.senate.gov. Call their offices and ask for the contact information for their congressional aide who handles health care issues. Someone in the office will be more than happy to give out an e-mail address. From there, start a conversation. Introduce yourself as a laboratory professional and let them know the issues you face daily and how decisions in Congress effect this profession.

To keep up on the issues, sign up for alerts on the Labvocate Action Center at www.ascls.org



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chigan**

ASCLS-Michigan *Newslinks*

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for a complete listing and contact information for all ASCLS-MI board members and a wealth of other information on the Society.

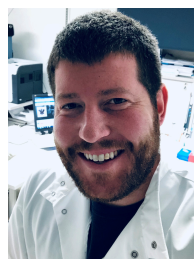
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Clinical Laboratory Science

A focus on what is happening in our profession

Featuring articles from Scientific Assembly Chairs.

Materials from all members are also welcomed. Submit to editor. See page 2 for details.



Pathogen-reduction technology and the INTERCEPT blood system

Shawn Videan, MS, MLS (ASCP)^{CM}, Scientific Assembly, Immunohematology

Like every discipline in the clinical laboratory, immunohematology/blood banking is an ever-changing field in response to constant new developments in the human body, newly emerging infectious diseases, and advances in technology. One technological advance which has played a vital role in laboratory blood banks and blood product management programs across the world, to some organizations much more recently than others, has been pathogen-reduction.

Pathogen-reduction techniques, or pathogen-inactivation, received its name because this technology has the ability to inactivate a wide array of potential pathogens and other organisms, including enveloped and non-enveloped viruses, gram-positive and gram-negative bacteria, white blood cells (leukocytes), parasites, and spirochetes, all of which can harm the human body following a blood product transfusion. Perhaps the most important of the aforementioned inactivation's is the ability to inactivate white blood cells, primarily because residual white blood cells in a donor unit can trigger an immune response in a recipient, leading to significant morbidity and mortality from events such as transfusion-associated graft-versus-host disease (TA-GVHD) and cytomegalovirus (CMV).

Traditionally, and still presently, prevention of TA-GVHD in bone marrow and organ transplant patients, patients with cell-mediated immunodeficiencies, and HLA-matched transfusions are accomplished via gamma irradiation of blood products between 25-50 Gray, which neutralizes the DNA in donor white blood cells, particularly lymphocytes, preventing a post-transfusion immune response in the recipient. Pre-

vention of CMV has traditionally been accomplished through leukoreduction of blood products, where the products are passed through filters and/or apheresis devices, commonly at the time of blood collection. These filters operate by removing negatively-charged leukocytes from the blood via electrostatic and Vander Waals forces. Although units are considered "CMV-safe" after these processes, there is still a 1-6.5% chance of post-transfusion CMV transmission due to the possibility of CMV being free in the plasma rather than being cell-bound.

Much to the aid of blood product recipients and blood banks alike, in an effort to prevent the previously mentioned, potentially fatal transfusion reactions, pathogen-reduction can be performed on all blood products, including fresh frozen plasma, red blood cells, and platelet concentrates, and is considered a safe, acceptable alternative to both gamma irradiation and "CMV-safe" blood products. There are a number of current methods available to achieve pathogen-reduction across the world, with some of the most prevalent being the INTERCEPT Blood System, MIRASOL PRT System, THERAFLEX UV-platelet system, S-303 PRT system, and TMB Plasma system.

The INTERCEPT Blood System is a treatment system for blood products, primarily platelets, that utilizes a psoralen-derived chemical known as amotosalen, and ultraviolet light. For this reason, pathogen-reduced platelet apheresis units prepared using INTERCEPT technology are commonly referred to as psoralen-treated platelets. To achieve pathogen-reduction using this system, a platelet apheresis unit

is passed through a sterile amotosalen container into an illumination container, where the platelets are illuminated using ultraviolet light between a wavelength of 320-400 nm. The illumination of the amotosalen-treated platelets creates a covalent cross-linkage of the amotosalen to any nucleic acids found in white blood cells, bacteria, viruses, parasites, and spirochetes that may be present in the platelet unit. This intercalation leaves the platelets unharmed while preventing the replication of any DNA or RNA from unwanted organisms.

Once the photochemical treatment process is completed, the platelets are transferred to a compound adsorption device and passed through a mesh pouch to minimize the level of remaining amotosalen, along with any potential unbound photoproducts from the ultraviolet light. The final step in the INTERCEPT pathogen-reduction process is the transfer of the treated platelets to a sterile storage bag/container, where they are then stable for 5 days at room temperature (20-24°C).

Munson Healthcare Cadillac Hospital (MHCH), my employer, recently began receiving pathogen-reduced platelet concentrates from Versiti Michigan in 2021 via the INTERCEPT Blood System. The standard apheresis platelet units the Munson Healthcare system received prior to this were stable for 3 days at room temperature and had to be monitored for bacterial contamination if used beyond the proposed 3-day shelf life. With psoralen-treated platelet concentrates, the shelf life of the stock unit of platelets at MHCH has now increased to 5 days and there is no need to perform bacterial testing on platelets used after day 3.

The cost of a psoralen-treated platelet apheresis unit is approximately \$100 higher than a regular platelet apheresis unit, but the increased cost should be compared to the additional costs associated with keeping regular apheresis platelets in stock, including the potential for bacterial testing of platelet units >3 days old, obtaining irradiated platelets, and obtaining CMV-negative platelets. The increased cost also needs to be compared to the potential for cost savings, realized from lower platelet expiration rates as a result of the longer shelf-life of pathogen-reduced units.

In conclusion, pathogen-reduction technology, especially the INTERCEPT Blood System, is one of the more recent developments in immunohematology with an aim not only to improve blood product management in our healthcare systems, but to increase the number and quality of positive patient outcomes we experience. As the future progresses and new technologies continue to become available, it is critical that we, as laboratorians, continue to re-evaluate the costs, benefits, and risks of these new technologies, and move forward accordingly with the laboratory and, more importantly, the patients we serve, in our hearts.

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Continued on next page

The INTERCEPT Blood System for Plasma



Step1
Amotosalen

Step2
Illumination

Step3
CAD

Process Complete
Storage

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One Lab's Experience with SARS-CoV-2 (Covid-19) Antibody Testing

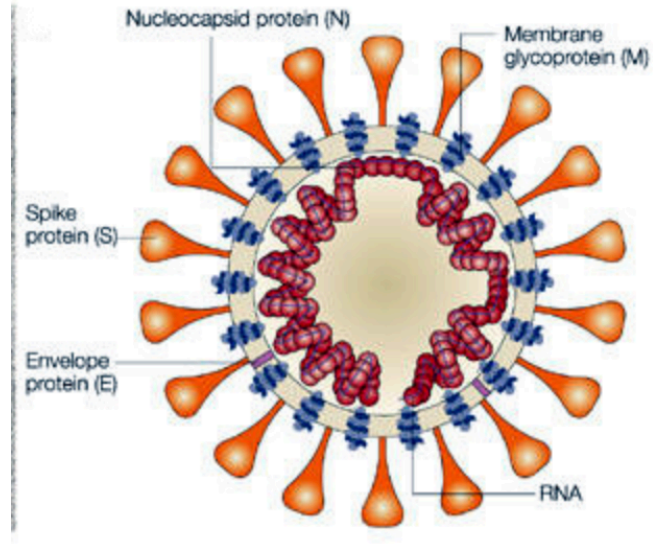
Paul Guthrie, Publications Chair



According to the CDC, 14 U.S. Covid-19 cases were noted by public health agencies between January 21 and February 23, 2020; all patients had traveled to China. The first non-travel case was confirmed in California on February 26, and the first U.S. death was reported on February 29th. Two years later tens of millions have been infected and hundreds of thousands have died in the US. Throughout this time frame, clinical laboratories have performed hundreds of millions of tests related to Covid-19, none of which existed less than two years ago.

The laboratory where I work in Kalamazoo, Michigan began sending out PCR tests to detect Covid-19 infection in March of 2020, and brought that testing in house in April of that year. That testing, with a nasopharyngeal swab sample, is what the general populations thinks of when they hear "Covid Test". This article is about our experience with the serology (blood) testing, which is performed less frequently. We began offering a test for total antibodies (IgM, IgG and IgA) to the nucleocapsid (capsid) protein of

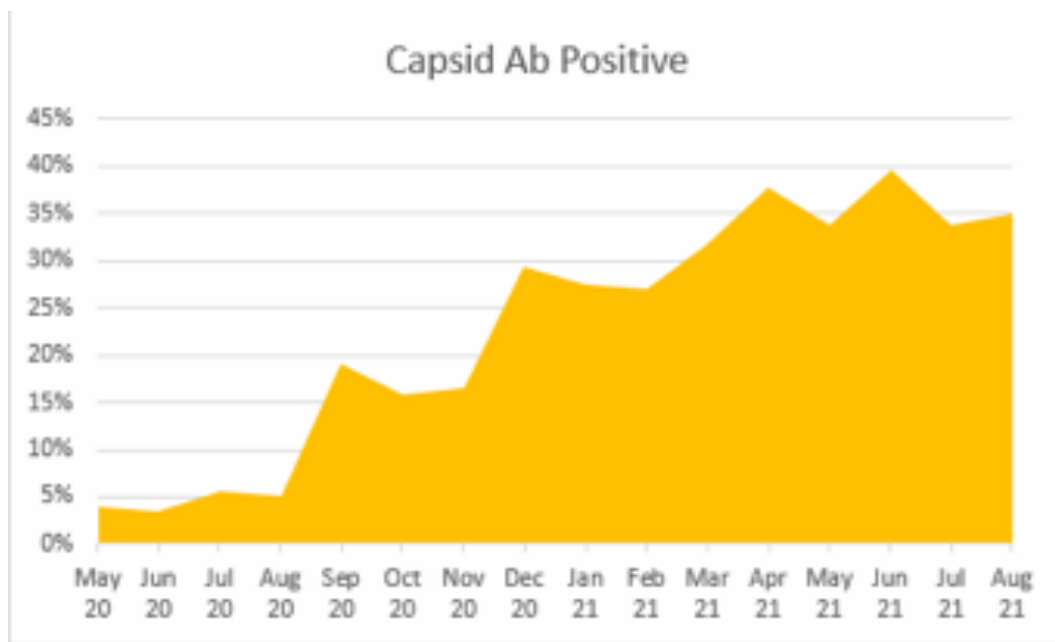
the SARS-CoV-2 virus in May of 2020. All SARS-CoV-2 viruses contain the capsid antigen and immunocompetent people form an immune response and have antibodies to this antigen. These capsid antibodies are not present in people who have never been infected. Capsid antibodies are also not formed in the uninfected who have received a Covid-19 vaccine. That's because current Covid-19 vaccines are all based upon the spike protein, and do not cause formation of antibodies to the capsid protein. In late February of 2021 we began offering a Covid Antibody Panel that consists of two tests: 1) Capsid Antibody and 2) Spike Antibody. Below are some key points about each of the tests.



SARS-CoV-2 Capsid Antibody

- This is a total antibody test to the Capsid protein and may detect IgG, IgM or IgA antibodies.
- The result is reported as Positive or Negative. Titers are not an option.
- A positive result indicates previous infection with COVID-19. Patients need to be counseled that the test does not confer immunity. Studies to determine immunity are ongoing.
- This tests does not become positive following vaccination for Covid-19.
- The test was validated by the vendor Roche on over 5,000 specimens and the specificity was 99.81%.
- The sensitivity at 14 days post PCR diagnosis was reported as 100%. Internal validation showed 21/21 patients positive at 14+ days, 11/11 at 7-13 days and 10/12 at 0-6 days. 32 PCR negative patients were all negative by serology.
- False positives are possible. With a hypothetical disease incidence of 5%, the positive predictive value would be 96%.

A review of our results from this test since implementation shows a steady increase in the % positive.



SARS-CoV-2 Spike Antibody

- The test detects total antibodies (IgG, IgM and IgA) to the SARS-CoV-2 spike protein
- This test is positive in individuals who have either been infected by or vaccinated for Covid-19
- Nearly 100% of individuals have detectable spike antibody within 14 days of infection or immunization
- Samples collected sooner than 14 days may give false negative results
- The analytical specificity when tested against 1,100 pre-pandemic samples positive for other coronavirus antibodies was 100%¹ (the test did not cross-react with other Coronaviruses)
- This test gives a numeric result in U/mL. Because there is no international standard for quantifying coronavirus antibodies, the FDA has classified the test as semi-quantitative but a higher number denotes a higher level of antibody
- Validation studies determined that a value greater or equal to 0.80 U/mL is a positive result (spike protein antibodies were detected)
- Internal dilution studies have shown that many individuals have values in excess of 2,500 U/mL after their 2nd dose of mRNA vaccine

Combining the two tests into a panel allows for better determination of a patient's serological picture:

Capsid Antibody	Spike Antibody	Status
Negative	Negative	Indicates neither vaccination nor infection
Negative	Positive	Indicates vaccination; no evidence of infection
Positive	Negative	Indeterminate. Could be early post infection or possible non-specific false positive
Positive	Positive	Indicates infection with or without vaccination

A review of the test results since implementation of the panel is shown below. Given the variety of patient populations tested, few conclusions can be made. One may observe a general trend for fewer patients to be both Capsid and Spike antibody negative, with an increasing number of Capsid Negative & Spike Positive patients.

	Capsid & Spike Negative	Capsid Negative, Spike Positive	Capsid Positive, Spike Negative	Capsid & Spike Positive	Total # Panels
Month 'YR	(No antibody response)	(No infection, Vaccine response)	Less typical response due to timing, etc.	(Infection with or w/o Vaccination)	
Mar '21	51%	17%	2%	30%	324
Apr '21	44%	19%	1%	36%	448
May '21	39%	27%	1%	33%	400
Jun '21	36%	25%	0%	39%	303
Jul '21	38%	28%	1%	33%	237
Aug '21	42%	23%	0%	35%	398

The current applications and clinical utility for COVID-19 serology testing include:

- The test is intended to detect antibodies to the virus, not to diagnose active infection.
- Seroprevalence and epidemiological studies
- Diagnosis of individuals who may have been infected more than 14 days before testing, after the virus may no longer be detectable by PCR or antigen tests
- Distinguishing whether a patient's positive SARS-CoV-2 PCR test represents current infection (serology test should be negative) or past infection (serology test should be positive)
- Identification of individuals who may serve as potential convalescent plasma donors.

Limitations of the test continue to be our lack of knowledge of how long detectable antibodies persist in the patient following either infection or immunization. We do not know what levels of antibodies indicate immunity or protection from infection, but preliminary studies suggest that the presence of anti-spike or anti-nucleocapsid IgG antibodies is associated with a substantially reduced risk of SARS-CoV-2 reinfection in the ensuing 6 months.²

The future applications of Covid-19 Antibody testing are not known, in large because this is a new evolving disease and we have much to learn. The CDC offers the following discussion of what is known:³

"How long anti-SARS-CoV-2 antibodies persist after infection remains unknown, although IgG antibodies, including IgG against the S and N proteins, persist for at least several months in most persons. Seroreversion has been reported among persons with mild disease. Persons with more severe disease appear to develop a more robust antibody response with IgM, IgG, and IgA all achieving higher titers and exhibiting longer persistence. The observed persistence of antibodies can vary by assay, and some studies have found that approximately 5-10% do not develop detectable IgG antibodies following infection. Although neutralizing antibodies may not be detected among patients with mild or asymptomatic disease, the humoral immune response appears to remain intact even with loss of specific antibodies over time. SARS-CoV-2 neutralizing antibodies that inhibit viral replication in vitro mainly target the RBD. A need exists for standardized assays that can correlate antibody titers with neutralization.

SARS-CoV-2 reinfection has been documented; however, studies indicate that persons with anti-SARS-CoV-2 antibodies are less likely to develop subsequent infection than persons without such antibodies. Outbreak investigations from a fishing vessel and a summer camp in the United States found that persons with pre-existing SARS-CoV-2 antibody were protected from subsequent infection. In sequential outbreaks among staff and residents of two British nursing homes, persons who tested antibody-positive following the first outbreak were approximately 96% less likely to become infected during the second outbreak four months later. In a British prospective cohort study of persons with and without SARS-CoV-2 antibody, the adjusted incident rate ratio for subsequent infection was 0.11 among persons followed for a median of 200 days after a positive antibody test, compared to those who tested negative for anti-SARS-CoV-2 antibody (21). Another British cohort study found an 83% reduction in SARS-CoV-2 infection incidence over a five-month period among persons who had tested antibody positive for SARS-CoV-2 or had prior infection documented by reverse transcription polymerase chain reaction (RT-PCR). A large study in the United States of commercial laboratory results linked to medical claims data and electronic medical records found a 90% reduction in infection among persons with antibody compared to persons without, and another study of military recruits found that seropositive individuals had an 82% reduction in incidence of SARS-CoV-2 infection over a 6-week period. Additionally, antibody development following SARS-CoV-2 in humans infection correlates with a marked decrease in viral load in the respiratory tract, although a clinical correlation with viral load in the respiratory tract has not been definitively established. Experiments on non-human primates support the above observations in humans. Experimentally infected rhesus macaques that developed humoral and cellular immune responses were protected against reinfection when re-challenged 35 days later. Another study found that transfer of purified IgG from rhesus macaques infected with SARS-CoV-2 was effective in protecting naïve rhesus macaques from infection and the threshold titers for protection, based upon binding and neutralizing antibodies, were determined.

Taken together, the above findings in humans and non-human primates suggest SARS-CoV-2 infection and development of antibody can result in some level of protection against SARS-CoV-2 reinfection. The durability of this immunity has yet to be determined. While life-long immunity has not been observed with endemic seasonal coronaviruses (27), studies of persons infected with the novel SARS-CoV-1 and Middle East Respiratory Syndrome (MERS-CoV) coronaviruses demonstrated measurable antibody for 18 – 24 months following infection (28, 29), and neutralizing antibody was present for 34 months in a small study of MERS-infected patients (30). It is not known to what extent persons re-infected with SARS-CoV-2 might transmit infection to others or whether the clinical spectrum differs from that of primary infection."

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