Will Antigen Testing Remain Relevant in the Point-of-Care Testing Environment?

Lindsey E. Nielsen, PhD, D(ABMM)[a,*], Steven Mahlen, PhD, D(ABMM)[b], Deena E. Sutter, MD[c]

KEYWORDS

• Antigen assay • Point-of-care • Waived testing • Molecular assay
• Pathogen detection • Diagnostic infectious diease assay

KEY POINTS

- Molecular testing platforms typically provide optimal sensitivity and specificity for detection of infectious pathogens.
- Historical barriers to implementing molecular assays include cost-per-test, reimbursement rate, need for a higher level of staff training, and specific requirements for infrastructure.
- Multianalyte molecular testing reduces the total number of assays performed and reduces the time to diagnosis with a significant advantage over older molecular assays.
- Many antigen platforms require negative results to be reflexed to a molecular assay for confirmation, with resultant increased costs and delays in diagnosis.
- Overcoming barriers to implementation and costs associated with molecular platforms may enable point-of-care laboratories to eliminate most antigenic assays in favor of more sensitive and accurate nucleic acid testing platforms.

INTRODUCTION AND BACKGROUND

Before the molecular age, cell culture was the gold standard for confirmatory diagnosis of viral and atypical infectious diseases. Typical cell culture methodologies are costly, require days (or weeks) for results, and require significant technical expertise. As a result, cell culture is impractical for timely diagnostic testing in most of the health care environments, especially in point-of-care (POC) testing environments. Traditional bacterial culture methods, although typically less complex than cell culture, also have disadvantages due to the need for incubation, subsequent identification of pathogens, and significant technical expertise.

[a] LN Laboratory Consulting, NE, USA; [b] Sanford Health, Bismark, ND, USA; [c] Tenet Physician Resources/Baptist Health System, San Antonio, TX, USA
* Corresponding author. LN Laboratory Consulting, LLC, Wood River, NE, USA.
E-mail address: lindseynielsenpc@gmail.com

Clin Lab Med 43 (2023) 167–179
https://doi.org/10.1016/j.cll.2023.02.003 **labmed.theclinics.com**

The introduction of antigen diagnostic tests that detect protein of a pathogen revolutionized the POC setting. The ease of sample collection, specimen manipulation, and test performance in the POC environment has made antigen testing a common practice in multiple settings, from provider offices to hospital laboratories. In context of ideal diagnostic tests, antigen assays fulfilled many of the World Health Organization ASSURED criteria relative to culture or preexisting diagnostic methods, that is, they are affordable, sensitive, specific, user-friendly, rapid/robust, equipment-free, and deliverable.[1–3]

Another option for diagnostic testing is molecular assays, often referred to as nucleic acid amplification tests (NAATs). These options provide several advantages over antigen testing based on reliability but were not routinely available in the POC setting based on meeting the ASSURED criteria. Molecular assays increasingly meet ASSURED criteria and are being used as replacements for antigen-based assays due to technology advances and elimination of cumbersome, multistep processing protocols. Other health care system advances, such as use of computerized electronic health records (EHR) and laboratory information system (LIS), have allowed for interfacing of NAAT results and alleviated the requirement for manual transcription of antigen results. The use of computerized systems and considerations for specimen collections have prompted WHO to update the ASSURED criteria to RE-ASSURED, which includes real-time connectivity and ease of specimen collection.[2,4]

One advantage that more sensitive molecular systems have over antigen assays is a reduced requirement for confirmatory testing of negative results, leading to increased confidence in accuracy of results. Still, multiple obstacles remain for NAATs to be widely accepted and used in the POC setting. Barriers such as cost of processing, POC infrastructure and design, and increased need for staff training and expertise may delay implementation of NAAT tests. This article discusses the general considerations of antigen and molecular assays and the merits and factors to consider when implementing diagnostic assays for several common pathogens.

General Considerations

When selecting a platform for diagnostic assays universal considerations include the test performance, need for confirmation, time-to-diagnosis, risk of false results and impact on public health, limit of detection, laboratory infrastructure, and cost and reimbursement rates.5

Assay Performance

Molecular assays will often have higher sensitivities than antigen assays[6–9]; this is directly related to the limit of detection of the NAAT method that can accurately detect very low quantities of the pathogen's nucleic acid. NAAT assays detect as few as 10 to 100 copies of the targeted nucleic acid sequence. The amplification of a targeted gene or genetic marker, coupled with sensitive detection methods such as fluorescence, allows detection of the pathogen's signature (analyte) at earlier stages of infection or disease and well before the concentration of any antigen allows detection via antigen assays. Hence, the limit of detection of a molecular assay is always much lower than with any antigenic method.[10]

A diagnostic assay's performance is generally measured by its sensitivity and specificity as compared with an established "gold standard." The gold standard was traditionally culture-based, but in the modern era, the baseline comparator is more often a molecular assay. Relatively high-sensitivity and -specificity assays may have widely variable positive and negative predictive values depending on disease incidence and prevalence; this concept is critically important to relay to clinicians for appropriate

interpretation of results. In general, antigen-based tests will have a better predictive value during periods of higher disease prevalence than low prevalence despite their lower sensitivity than NAAT assays. There is typically less variation in negative and positive predictive values using molecular methods because the sensitivity and specificity of NAATs are superior to antigen assays. Thus, antigen assays generally perform less optimally when a pathogen is associated with dynamic seasonal variations.

Specificity between molecular and antigen-based testing methods are generally comparable for overall diagnostic purposes. The specificity for influenza A and B, for example, is greater than 98% for both molecular and most antigen methods and provides an accurate diagnosis for a positive test result. Group A *Streptococcus* (GAS), *Trichomonas*, and SARS-CoV-2 are additional examples of similar specificity between antigen and NAAT performance, whereas other antigen tests are lower (**Table 1**).

Assay Confirmation

Most antigen assays suggest confirmatory testing by molecular methods due to relatively low limit-of-detection, sensitivity, and, occasionally, specificity. It is important to understand the need for confirmatory testing, as, in the case of a negative antigen result, there are 2 possibilities: the patient does not have the disease or infection or the pathogen is present but not in a high enough concentration for detection; this further explains discordant results between NAAT and antigen methods and the rationale for why negative antigen results should be reflexed for confirmation. Commercially available POC antigen tests should provide guidance on indications for confirmatory testing of possible false-negatives or, in some scenarios, suspected false-positive results. POC laboratories may have limited capacity to run such confirmatory assays, which are often referred out to larger commercial laboratories. Confirmatory testing also allows for evaluation of discordant results, changes to patient care plans, and insight into general test performance in your patient population.

Staff Training/Competency

Simple POC assays such as urine-based pregnancy tests, urinalysis by dipstick method, rapid SARS-CoV-2, rapid influenza, respiratory syncytial virus (RSV), GAS, and simple blood glucose tests are easy to use and familiar to many POC laboratory and clinical staff. Although the analytes and specimens may be different, the same principle of application of a clinical sample to a lateral flow chamber and waiting for development of a positive and control line are easily understood by most personnel at POC laboratories, such as urgent care clinics, physician office laboratories, or hospital wards. Despite some subjectivity on “positive” versus “negative” lines, these simplified kits decrease the perception of user-error concerns and minimize troubleshooting steps.

Costs

Antigen tests are historically much cheaper than molecular tests and require simplistic integration instruments, if one is required at all. Many antigen tests are less than $10 USD, and many purchasing contracts will include necessary equipment, such as an optical analyzer, without additional charge. In contrast, the cost of a single molecular run has decreased significantly, yet the cost per analyte still remains higher than an antigen test. The CMS 2022 Q4 Clinical Laboratory Fee Schedule reimbursement rates are between 2.1 and 6.8 times higher for NAAT than antigen methods (**Table 2**). These increased reimbursement rates are intended to defray additional costs associated with performance of molecular assays, including analyzer instrument

Table 1
Assay parameters of select commercially available point-of-care antigen diagnostic assays

Assay	Manufacturer	Specimen Source	Sensitivity (%)	Specificity (%)
QuickVue Dipstick Strep A Test	Quidel	Throat swab	92[a]	98[a]
QuickVue Influenza A + B Test	Quidel	Nasal/Nasopharyngeal (NP) swab	81.5/80.9[b]	97.8/99.1[b]
QuickVue SARS Antigen Test	Quidel	Nares swab	96.8[c]	99.1[c]
Determine HIV-1/2 Ag/Ab Combo Test	Abbott	Fingerstick whole blood	99.9[d]	99.8[d]
QuickVue RSV Test	Quidel	NP aspirate/NP/Nasal wash/NP wash	99/92/83[e]	92/92/90[e]
BinaxNOW *Streptococcus pneumoniae*				
Antigen Card	Abbott	Urine, CSF	86/97[f]	94/99[f]
BinaxNOW Legionella Urinary				
Antigen Card	Abbott	Urine	95[g]	95[g]
OSOM Trichomonas Rapid Test	SEKISUI Diagnostics	Vaginal swab	83[h]	99[h]
Immunocard Stat! Giardia	Meridian	Stool	100[i]	100[i]

[a] Compared with bacterial culture.
[b] Compared with molecular assay. Sensitivity and specificity for influenza A and influenza B, respectively.
[c] Compared with molecular EUA assay. Sensitivity and specificity for fresh specimens.
[d] Compared with patients who had tested positive/negative with enzyme immunoassay (EIA)/western blot.
[e] Compared with RSV culture. Sensitivity and specificity for nasopharyngeal (NP) aspirate/NP/nasal wash and NP wash, respectively, for pediatric patients.
[f] Compared with blood culture positive and negative patients and cerebrospinal fluid (CSF)-positive and -negative patients. Sensitivity and specificity for urine and CSF sources, respectively.
[g] Compared with archived positive and negative patient urine specimens.
[h] Compared with composite reference standard (wet mount and culture).
[i] Compared with microscopic reference standard. Product insert provides disclaimer that the relative comparison assay and no judgment can be made on the comparison assay's accuracy to predict disease.

Table 2
Comparison of Centers for Medicare and Medicaid Services clinical laboratory fee schedule for antigen and molecular diagnostic assay[a]

	Antigen		Molecular		
Assay	CPT Code[b]	Reimbursement Amount	CPT Code[c]	Reimbursement Amount	Fold Increase
RSV	87420	$13.91	87634	$70.20	5.1
Influenza A/B	87400	$14.13	87502	$95.80	6.8
Group A Strep	87430	$16.84	87651	$35.09	2.1
Trichomonas	87808	$15.29	87661	$35.09	2.3

[a] Based on publicly available 2022 quarter 4 laboratory fee schedule for clinical laboratories (www.cms.gov). This table is for illustrative purposes only and each laboratory must independently verify proper CPT code for their technology and assay employment.
[b] Current procedural terminology (CPT) codes are based on the waived (QW) designation using an instrument for detection and result interpretation.
[c] Molecular CPT code based on amplified probe technique.

maintenance, warranties, and ancillary consumables, along with potential cold storage requirements.

Time-to-Result and Time-to-Diagnosis

Time-to-result influences the decision to choose an antigen or a molecular-based assay. Most antigen detection assays result at 15 to 25 minutes where modern commercial NAAT assays typically require a minimum of 20 to 45 minutes to complete. Commercial manufacturers continue to optimize the timing of molecular assays for POC testing, and some molecular assays include early termination of testing cycles with results as soon as the molecular target is detected. Although this may equalize the time to positivity between methods for a positive result, a negative NAAT will not be reported until all amplification cycles have completed; this is to ensure there is no late amplification in cases of low copy numbers. Although this delay may be beneficial during high disease prevalence and decreases the requirement for reflex to confirmatory testing, delayed results may affect patient care flow in busy patient care settings.

Additional concerns of molecular platform implementation include the potential of backlog in patient testing because, to justify cost, only a single polymerase chain reaction (PCR) analyzer capable of performing testing on one to a few specimens at a time is likely. this limits how many specimens a laboratory can process at one time, increasing the time-to-result while decreasing the patient and provider satisfaction.

Laboratory Infrastructure

Molecular POC assays require meticulous handling and processing to reduce contamination and subsequent risk of inaccurate (primarily false-positive) results.

Potential sources of contamination include the reuse of disposable laboratory coats, failure to change gloves between samples, and opening more than one sample at a time. Environmental barriers such as biosafety cabinets to limit air currents are paramount to prevent cross-contamination. Personnel must be properly and routinely trained to ensure adherence with these procedures. Good laboratory practices dictate the same care should be present during antigen testing; however, the higher limit of detection and lack of amplified product will often mask low-level contamination not afforded to molecular methodology. Other infrastructure concerns include too few

or poorly located electrical outlets, inadequate benchtop space, and lack of LIS/EHR integration.

Detecting Multiple Etiologic Agents

Another significant advantage of molecular-based assays is the ability to perform one test and return multiple results of 2 or more pathogenic agents. The presentation of the patient and medical history may help the provider elucidate the most likely pathogen but this is more difficult when symptoms and exposure to multiple circulating infectious agents is possible; this is especially true during respiratory viral season when influenza, SARS-CoV-2, respiratory syncytial virus, parainfluenza, adenovirus, and rhinovirus/enterovirus can all present with similar symptoms. Although treatment may not be altered by testing outcome, the impact on public health, isolation of the patient, and insight into secondary complications is medically necessary to the health care and local community alike.

The POC assays selected for these cases becomes important and leaves the provider with difficult decisions for additional testing if negative assay results only correlate to a single pathogen. Guidance from current epidemiology of circulating infectious agents and patient history may help but, when the differential diagnosis includes multiple pathogens, a POC multianalyte panel may be the best choice and no other testing methodology is robust as multitargeted PCR panels. Current POC PCR panels include a 19-target respiratory pathogen panel that detects common viral and bacterial agents and combinatory influenza and RSV panels.

SPECIFIC ASSAY CONSIDERATIONS

Group A Streptococcus

GAS (*Streptococcus pyogenes)* is a common pathogen, and POC testing for this organism is frequently an antigen-based throat swab. A meta-analysis from 2014 identified GAS antigen testing had a pooled sensitivity of 86% (95% confidence interval [CI] of 83%–88%) and specificity of 96% (95 CI of 94%–97%). Increased sensitivity is gained by molecular methods without a change in collection methods or specimen source. A major benefit of NAAT detection of GAS is that secondary culture-based testing to confirm false-negative antigen testing is not required.[11] Because of the analytical target for *S pyogenes* remains relatively stable compared with other etiologic agents, such as viral targets, the choice of antigen versus molecular is condensed to best patient care and reimbursement rate.

Influenza

Influenza virus types A and B are considered cyclic, seasonal infections. Although antigen assays and most molecular waived POC option detect presence and absence of each influenza virus type A and B, Biofire Diagnostics (Salt Lake City, UT, USA) currently offers a waived multianalyte NAAT that will report subtypes. If a POC laboratory is licensed to perform assays registered by the Food and Drug Administration as moderate-complexity, additional commercial assays that will report subtype are available. Viral subtype detection is important to assist providers and public health professionals in determination of infection risk and early detection of novel strains that may have crossed zoonotic lines. Each year, as people are vaccinated against the predicted dominant strains of influenza, a knowledge of the circulating subtypes in the local community and the impact to the assay's performance is beneficial.

Viral detection by molecular and antigen method performance can be influenced by the viral subtype and, if a variant arises, may limit the ability of the assays, with the

antigen assay being most negatively affected. This case was demonstrated in 2009 with the novel influenza H1N1 outbreak. The accuracy of the antigen assay was reduced to 37.8% due to a high false-positive rate, sensitivity was estimated as low as 17.8% compared with the molecular assay with a sensitivity of 97.8%, and the specificity was estimated between 48.1% and 50.7%. [12–15]

SARS-CoV-2

Molecular testing for SARS-CoV-2 is best for both patient care and public health prevention; however, the inability of some clinics to implement molecular testing or inability of a patient to be seen by a health care provider lends initial screening to antigen testing as a matter of convivence. Although POC and home-test COVID antigen assays are abundant, the assay's performance in terms of sensitivity and high limit-of-detection favors the molecular test method for early detection. Antigen testing for SARS-CoV-2 peaks 4 to 5 days after symptom onset, and a direct comparison of antigen to NAAT favored molecular methods for earlier detection of SARS-CoV-2 compared with antigenic methods if both are performed in tandem.[6,16]

Although molecular assays have higher sensitivity and can identify early infection and drive initial isolation decisions and public health response, the overall selection of antigen or molecular tests is dependent on the medical indication and progress of disease. The COVID19 pandemic illustrated this concept well, as early detection was best done using molecular methods but could not determine the risk of shedding long-term infectious virus due to assay detection of remnant, noninfectious viral RNA.[17] The antigen test, however, has a delay in positivity rate. Reports are varied on conducting antigen testing after a positive result as a predictor of active of infectious viral shedding. A few studies suggest a positive antigen result during or after symptom resolution is a marker of infectious viral shedding but evidence is limited and current guidance by the Infectious Disease Society of America has not endorsed this viewpoint because there is too few clinical trials and studies to make a strong claim.[18–21] Together, guidance from public health officials has evolved from early testing algorithms to suggest molecular testing should not be used to guide long-term isolation decisions and symptom resolution after isolation is sufficient for predicting contagiousness. Current Centers for Disease Control and Prevention (CDC) guidance only suggests an individual who has resolved symptoms can discontinue masking before 10 days if their symptoms are resolved and 2 antigen tests, conducted at least 48 hours apart, are negative.[22] Overall, the best strategy for early COVID19 detection is using a molecular-based method for recent onset of symptoms, but, to confirm resolution, a negative result based on antigen methods or waiting the minimum of 10 days after symptom onset is recommended.

Human Immunodeficiency Virus

Fourth-generation human immunodeficiency virus (HIV) testing that incorporates detection of the p24 antigen is one of the most common antigen tests on the market. Sensitivity of an HIV antigen test is sufficiently high at time of a symptomatic patient presentation that current practices only use molecular methods for confirmation and treatment response. Rarely is a false-negative a concern of HIV p24 rapid antigen POC tests with symptomatic patients due to the assay's high sensitivity; however, the assay has many false-positives due to its lowered specificity, and, like other sexually acquired infections, the time-to-diagnosis is essential in reducing public health impact through community spread. Because false-positives are far more common with the p24 antigen test, confirmatory testing by NAAT is a necessity. Currently, no point-of-care molecular test for HIV is available but the risk of false-negatives and

effects is significant that false-positive antigen testing followed by confirmation using molecular is best suited for the POC setting.

Respiratory Syncytial Virus

In the recent decade, molecular testing for RSV has increased in outpatient setting but remain stable in emergency departments and in-patient settings.[23] Although data presented from national databases on RSV positivity seem that antigen testing is more accurate than PCR, this is not the case because most PCR tests are done as a confirmatory test of a negative antigen and most RSV positive patients have been screened out before PCR testing. The national database data also suggest the reason why molecular testing has not increased in the in-patient and emergency departments is that those healthcare POC settings are less likely to reflex a negative test than outpatient settings.

Sensitivity comparisons between antigen and molecular methods clearly support molecular methods for all demographics but especially in adult populations. A meta-analysis found sensitivity of antigen testing in pediatric populations was 81% (95% CI, 78%–84%) compared with adults at 29% (95% CI 11%–48%).[24] Another study published in 2022 found that specimens collected on the same patient during presentation to an emergency room found that use of PCR methods more than doubled diagnosis of RSV.[25] Considering the assay performance, molecular testing is still best for patient diagnosis but the associated costs and management of patients in these 3 distinct health care environments may sway testing protocols.

Current POC RSV molecular assays are combined with other respiratory illnesses, most notably influenza. In children younger than 6 years, RSV was detected with influenza or human metapneumovirus more often than other age groups, suggesting the risk of coinfection was greatest in pediatric patients.[26] For this age group, a strong consideration for multianalyte molecular testing is warranted compared with a nonpediatric demographic where the single-analyte antigen assays carry less likelihood of excluding an additional diagnosis due to coinfection.

Streptococcus pneumoniae

Streptococcus pneumoniae is a common pathogen responsible for community-acquired pneumonia. A 27-study meta-analysis of the *S pneumoniae* urine antigen assay found a sensitivity of 74% and specificity of 97.2% relative to culture methods.[27] Current antigen assays on the market result at 15 minutes compared with NAATs, which are greater than 1 hour. Initial, single gene targeted NAAT assays were lackluster with detection rates as low as 62%.[28] As other gene targets were challenged, sensitivities improved but the question of positive prediction value was questioned, as *S pneumoniae* can be a commensal organism at low concentrations but pathogenic at elevated amounts. Currently, there is only one commercial, moderate-complexity NAAT option on market that distinguishes between the intensity of gene amplification product to determine commensal versus pathogenic states.[29]

This multianalyte molecular panel uses sputum or bronchoalveolar lavage, leaving many POC settings to choose the antigen test by necessity of cost, easier specimen collection, and processing advantages. Although the convenience of antigen testing for POC environment outweighs NAAT options, false-negatives compared with positive blood or sputum cultures are still prevalent.[30] Other *Streptococcus* species also cross-react with the urine antigen test causing false-positives, especially if used to diagnosis *S pneumoniae* in children.[31] Together, although the urine antigen test may be an attractive option, the limitations of result accuracy warrants consideration of removal of the POC test in favor for molecular methods, even at the cost of time for reference laboratory testing.

Legionella pneumophila

Legionellosis can be diagnosed by NAAT using sputum as the source; however, urine antigen testing is the only available option in a Clinical Laboratory Improvement Amendments of 1988 (CLIA)-waived registered POC setting where both multipanel analyte NAAT methods and urine antigen methods can be used in a POC setting registered to perform moderate-complexity assays.[32] Antigen testing provides easier specimen collection and lower cost in a POC setting compared with NAAT; however, considering the rarity of *Legionella* and patient presentation between Legionellosis and other bacterial causes of pneumonia, a provider suspecting *Legionella* should strongly consider a multianalyte molecular panel over the antigen test. One multicenter study found a false-negative rate of greater than 44% of the urine antigen test, leading to a missed diagnosis in 39% of the patient population.[33] Fortunately, few providers develop a differential diagnosis that includes Legionellosis as a primary concern, and, therefore, few POC locations stock the urine antigen tests and prefer to send out to reference for multianalyte testing.

Trichomonas vaginalis

Trichomonas vaginalis is a parasite implicated in the sexually transmitted infection trichomoniasis. Commercial POC antigen assays are widely available, and some providers choose to diagnosis *T vaginalis* by wet mount microscopy despite the low sensitivity.[34] To fill this gap, Trichomonas antigen testing was introduced in the mid-1980s and became the preference of many waived POC laboratories with increased sensitivities compared with microscopy of greater than 90%; however, this increase is misleading considering the insensitivity of microscopy.[35] When the antigen assay is compared with a composite comparator of microscopic method and culture, the sensitivity increases to 83% to 86% largely due to culture methods, which are not routinely performed in reference clinical settings. Molecular assays compared with antigen methods demonstrate sensitivities between 98% and 100% but these are only available to laboratories registered to perform nonwaived testing.[36] Recently, in addition to the commonly tested genital or rectal specimens, requests to diagnosis *T vaginalis* from pharyngeal specimens are increasing, largely due to the low limits of detection and high sensitivity of the molecular assays. Although inclusion of pharyngeal specimens for molecular sexually transmitted infection (STI) testing opens capabilities for increased diagnostic capabilities over antigen testing, this area must be studied more, as cross-reactivity with other organisms present in the upper respiratory tract may lead to false-positives.[37] Although the barrier to implement a molecular testing platform may seem daunting for a small POC clinic and require nonwaived testing registration, the impact on STI diagnosis would benefit patients, providers, and public health.

Giardia

Giardia detection was traditionally performed by microscopic means but was labor- and time-intensive with potential low sensitivity due to the expertise required for parasitic identification. Specificity was high for the genus but speciation for public health needs was not possible. Antigen testing improved sensitivity for the general testing personnel compared with microscopic methods and greatly reduced time-to-result, helping to diminish outbreak potential. Although specificity remained suboptimal, some early reports show sensitivity as high as 94% compared with microscopic methods but other studies suggest much lower sensitivity such as 60.7% during a waterborne outbreak case.[38,39] Although antigen detection enabled POC settings to

perform testing, the CDC still recommends testing 3 stool samples over the course of several days to increase antigen result accuracy. Because most POC settings do not lend to multiple patient visits, the utility of the *Giardia* antigen test and proper use is questionable when molecular options demonstrate improved sensitivity and specificity and one sample is considered diagnostic.

PERSONAL PERSPECTIVES AND FUTURE PROSPECTS

Antigen testing revolutionized the ability to diagnosis, accurately prescribe, and track local epidemiology within the POC setting. Antigen testing is relatively low cost, does not require sophisticated instrumentation, is portable, and can easily be implemented in both first- and third-world POC scenarios. As convenient as antigen testing is, there are drawbacks in the time-to-initial-diagnosis postsymptom onset due to lower limit of detection, sensitivity, and, occasionally, specificity that molecular options overcome. Alas, only a few POC-waived molecular options are currently in the US market, with some laboratories opting to elevate their CLIA registration to moderate complexity to perform molecular tests in the POC setting. As NAAT testing becomes more familiar to health care clinics and the public, and impeding operational costs and implementation are overcome, there will be an increased demand for these molecular assays and a shift away from their antigen counterpart in POC settings. Although molecular testing offers a greater prospect for definitive diagnosis and patient care, they will not fully replace antigen tests in the POC setting in the near future unless overhead and testing costs are reduced and more commercial options for waived molecular options are developed.

A longer-term future prospect of antigen assays is a shift from the POC setting to at-home testing. The release of at-home COVID-19 antigen assays during the pandemic raises the question if antigen assays could be primarily used in the home testing environment while molecular assays remain exclusive to the health care setting. The implications are still early and highly debatable. At-home antigen testing and interpterion would require significant public education by public health experts and providers. Nonetheless, antigen tests will always have a role in the health care system but only the future will determine the degree that molecular tests will dominant the POC setting and drive an at-home testing if antigen tests become more available.

CLINICS CARE POINTS

- Antigen-based diagnostic assays are often similar in specificity to molecular assays but have a lower sensitivity which increases the risk of false-negative results.
- Negative antigen test results should be confirmed by a molecular assay, especially if the patient is presenting early with symptoms, the prevalence of the infectious agent is high, or the infection is high on the differential diagnosis.
- Positive HIV antigen test results, should always be confirmed by a secondary testing method, commonly a molecular assay, due to potential false-positives and to delineate between types of HIV strains that can impact treatment decisions.
- Antigen and molecular assay vary between the time-to-detection and how long the infectious agent can be detected. Ensure to select the correct assay type based on symptom onset and the objective of testing.
- Some molecular assays may remain positive after the patient symptoms have resolved. Consultation with an infectious disease provider, board-certified medical microbiologist, or epidemiologist may help determine clinical significance.

DISCLOSURES

The authors declare no relevant or material financial interests related to this publication.

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