

*Veterinary medicine has a significant need for in-clinic point-of-care (POC) tests that can deliver rapid, reference lab-quality sensitivity and specificity data.*

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# RAPID POINT-OF-CARE DIAGNOSTICS IN ANIMAL HOSPITALS

In the veterinary clinic setting, rapid point-of-care tests allow for accurate insights to be derived from the results, so clinicians have more confidence in their prescribed treatment plans. Furthermore, the rapid nature of this type of testing lends itself to producing results in real time, possibly while the patient is still in the hospital, removing the impact of time delays experienced with traditional reference laboratory testing methods. These innovations are on the cutting edge of both veterinary and human diagnostics.

## THE NEED FOR FASTER RESULTS

In veterinary medicine, clinicians rely on available diagnostic technologies to confirm diagnoses and provide clinical insight into patient care. In the case of suspected bacterial infections, culture and susceptibility (C&S) tests are routinely ordered to provide definitive insight into the causative pathogens, and to determine whether

antimicrobial resistance is present. Commonly, however, the need to make treatment decisions often precedes obtainment of the C&S results, requiring antibiotics to be prescribed empirically in order to address the suspected infection, improve the patient's symptoms, and to give the client peace of mind that their pet has been offered solutions-focused patient care. Once the C&S results are received, the empiric antibiotic selection is either confirmed as effective, or if resistance is demonstrated, the antibiotic is changed.

When culture testing is ordered, the collected samples are typically shipped to centralized reference laboratories for C&S testing. The downside of these current testing methods is the time delay involved in shipping samples offsite, in addition to laboratory processing times. The standard turnaround time for C&S testing is three to five days, with some cases taking up

to one week or longer for certain infection types, or in the case of practices located in rural areas that may be some distance away from testing facilities.

Urinary symptoms, such as straining to urinate and blood in the urine, are common reasons for dogs and cats to be taken to the emergency room, with urinary tract infections (UTIs) often being one of the top differentials. A previous study evaluating the prevalence of UTIs diagnosed via C&S demonstrated that 17.5% of cases were positive for at least one bacterial isolate.<sup>1</sup> Some of these results could be false negatives; however, the negative samples could also indicate an underlying non-infectious pathology, such as bladder stones or cancer. For some of these disease conditions, the long turnaround time for C&S testing could potentially delay the pursuit of further diagnostics, and achieving a definitive diagnosis, thereby delaying the start of effective treatment for the patient.

### PROMISING RESULTS FROM EARLY CLINICAL TRIALS

Ethos Veterinary Health is a network of 25 emergency and specialty hospitals located across the US, with significant experience in conducting veterinary clinical trials. Ethos has been working with the molecular diagnostics provider LexaGene to help quickly advance this emerging technology through the development of an in-house PCR analyzer capable of providing accurate infectious disease testing with a rapid turnaround time. In June 2019, Ethos launched the first beta trial of LexaGene's automated PCR analyzer for the detection of urinary tract infections. This trial demonstrated 98.2% concordance between the analyzer results and standard C&S testing. LexaGene and Ethos now seek to conduct further clinical trials for other disease indications, including infectious disease, inflammatory disease, and cancer.

### ANTIMICROBIAL STEWARDSHIP

The use of POC molecular testing allows for the improved implementation of antimicrobial stewardship programs that encourage the judicious use of antimicrobials to reduce antimicrobial resistance rates. The focus on antimicrobial resistance to date has been predominantly to measure its impact on human health; however, there is now an increasing focus on veterinarians to adopt a One Health<sup>2</sup> approach in veterinary medicine in an effort to curb the development of antimicrobial resistant bacteria. Studies in human healthcare have shown that antimicrobial resistance, especially multidrug resistant infections, significantly impact the ability of practitioners to properly treat infections — a risk that has been described as one of the greatest threats to human health worldwide.<sup>3</sup> Antimicrobial resistance in veterinary patients presents similar treatment challenges for veterinarians and has the potential to transfer this bacterial resistance to humans, which is of particular concern to government, industry, academia, and veterinary organizations who play an active role in the stewardship of antimicrobials used in animals.<sup>4</sup> By providing insight into causative pathogens and antibiotic resistance factors, PCR testing can facilitate the use of first-line antibiotics that will reasonably treat the infection and mitigate the temptation for veterinary practitioners to prescribe higher tier antibiotics in treatment, which would represent a divergence from good antibiotic stewardship practices.

*Continued on page 34.*

## FINANCIAL BENEFITS FOR CLIENTS AND CLINICS

Rapid POC testing has the potential benefit of reducing the overall cost of care for the pet owner. If a definitive diagnosis is reached earlier, the need for further diagnostics may be reduced and a more focused treatment plan can be made. The course of an empirically prescribed antibiotic can represent an initially reasonable cost to owners; however, for patients that are found to have complicated infections or antibiotic resistance, there can be further costs associated with multiple hospital visits, diagnostic tests, and adjustments to the treatment plan.

The potential cost to the client for rapid POC testing is in line with the cost of prolonged antibiotic treatment, and if used as a first line diagnostic could reduce the overall cost of care to owners whose pets have complicated or resistant infections. The revenue potential represented by POC testing for veterinary practices can complement prescribing revenue, and shift the expense of laboratory services to an incremental revenue stream opportunity for in-clinic testing.



## DRAWBACKS OF POC ANTIBODY TESTS

When in-clinic point-of-care (POC) testing for infectious diseases is available, it can provide clinicians with a greater level of confidence in the therapies they are prescribing. However, in-house POC antibody tests have been shown to lack the sensitivity and specificity that is achieved with laboratory testing utilizing polymerase chain reaction (PCR), which is deemed a gold-standard chemistry used in diagnostics. Also, most antibody tests screen for just one to three pathogens. The one-pathogen tests (singleplex test) are the hardest to support as they often generate false negative results, since many infections can be caused by numerous organisms. This drawback supports the use of more highly multiplexed syndromic testing panels. For example, many POC tick-borne disease tests typically consist of only two or three disease targets, and therefore don't represent the full spectrum of possible tick-borne infections that can be seen in veterinary patients. This can create the potential for misdiagnosis, and possibly the prescribing of ineffective treatments.

Another disadvantage of antibody tests is that they do not provide information on the presence of antibiotic resistance. In contrast, genetic-based tests such as PCR can not only identify the pathogen that causes the symptoms, but can also be used to identify gene sequences that confer resistance to antibiotics. The advantage of highly multiplexed syndromic testing panels is that they allow for the screening of multiple pathogen targets at the same time, in addition to antibiotic resistance markers. This method is highly desirable for syndromic testing, reducing the need for numerous diagnostic tests to obtain a diagnosis, and increasing the chances of a positive, informative result the first time.

*Continued from page 33.*

## IMPROVED CARE FOR COMPLEX INFECTIONS

In addition to antimicrobial stewardship, POC molecular diagnostics could also improve the diagnostic and treatment process in patients with chronic, recurrent, or complicated infections. These patients can often have more complex infections with multiple pathogens, each potentially with a different antimicrobial susceptibility profile. Furthermore, traditional culturing techniques might not always be representative of the full spectrum of pathogens that are present at the site of infection. With these patients being at a higher risk for multidrug resistant infections, there is a higher possibility that they could be started on an ineffective antibiotic pending their C&S testing results. These patients, even more so than those with simple infections, would likely benefit the most from a rapid POC test, especially in the setting of severe infections where a delay in effective treatment could result in progression to sepsis and a significantly higher mortality risk.

## TRANSITIONING TO MOLECULAR-BASED POC TESTING

The use of molecular-based POC tests is a novel diagnostic approach in veterinary medicine and is not a typical component of the standard diagnostic workflow. Since the empirical prescription of antibiotic treatment is so prevalent in the face of long turnaround times for test results, there may be a reluctance among practitioners to depart from a known treatment practice and financial model. However, as the development of molecular diagnostics progresses in veterinary medicine, and they are demonstrated to have acceptable accuracy, it is expected that their use will eventually become more commonplace. Furthermore, there is significant ongoing research in molecular diagnostics in both human and veterinary medicine, opening the door for a wide range of disease applications that this technology can be used for.

Ethos Veterinary Health plans to incorporate molecular-based POC testing at its locations to rapidly triage infections as an innovative approach to patient care and adoption of cutting-edge veterinary medicine technology. LexaGene plans to launch its MiQLab™ system — an automated, easy-to-use PCR analyzer for point-of-care testing — this fall. For further information, visit <https://www.ethosvet.com> and <https://lexagene.com>.

### *Author disclosure statement:*

The work expressed in this article is from Dr. Stewart's research experience with LexaGene and the MiQLab through his role at Ethos Veterinary Health.

<sup>1</sup>Hall JL, Holmes MA, Baines SJ. "Prevalence and antimicrobial resistance of canine urinary tract pathogens". *Vet Rec*. 2013;173(22):549.

<sup>2</sup>One Health-AVMA. Available at: <https://www.avma.org/resources-tools/one-health>.

<sup>3</sup>Llor C, Bjerrum L. "Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem". *Ther Adv Drug Saf*. 2014;5(6):229-241.

<sup>4</sup>"Supporting antimicrobial stewardship in veterinary settings: goals for fiscal years 2019-2023 — FDA Center for Veterinary Medicine". Available at: <https://www.fda.gov/media/115776/download>.