An Overview of the BD MAX™ Vaginal Panel Assay on the BD COR™ System for Molecular Detection of Causes of Vaginitis

Barbara Van Der Pol

Heersink School of Medicine, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA

The BD COR™ System is an automated instrument utilizing polymerase chain reaction (PCR) technologies to detect a broad menu of infectious organisms. The system has only recently been utilized with the BD MAX™ Vaginal Panel, which detects multiple organisms related to bacterial vaginosis, candidiasis and trichomoniasis. Utilization of this assay on the BD COR™ may improve the quality of care for women presenting with vaginal health concerns including discharge syndromes. This overview provides a description of the system and the vaginitis assay.

Keywords

Vaginitis, molecular diagnostics, bacterial vaginosis, candidiasis, trichomonas

Disclosures: Barbara Van Der Pol reports receiving grants to her institution and/or honorarium and/or consulting fees directly from the following: Abbott, Becton Dickinson, BioFire, Cepheid, Cue Health, Detect, Hologic, MaGIC, Rheonix, Roche and Visby.

Review Process: Double-blind peer review

Compliance with ethics: This article is an opinion piece and does not report on new clinical data or any studies with human or animal subjects performed by any of the authors.

Data availability: Data sharing is not applicable to this article as no datasets were generated or analysed during the current study/during the writing of this article.

Authorship: The named author meets the criteria of the International Committee of Medical Journal Editors for authorship for this manuscript, takes responsibility for the integrity of the work as a whole and has given final approval for the version to be published.

Received: 30 August 2023

Accepted: 24 October 2023

Published online: 30 January 2024

Citation: *touchREVIEWS in Infectious Diseases.* 2024;3(1):Online ahead of journal publication

Corresponding author: Barbara Van Der Pol, UAB Heersink School of Medicine, Department of Medicine, 703 19th St South, ZRB 242, Birmingham, AL 35294, USA. E: bvanderp@uab.edu

Support: No funding was received in the publication of this article.

Vaginal symptoms are one of the most common reasons for women accessing acute healthcare in the USA.[1] Vaginitis is most commonly evaluated based on clinical observations, including assessment of discharge characteristics, vaginal pH and, in some settings, microscopic examination of vaginal fluids. However, many women are suboptimally treated and often seek additional healthcare within the next 90 days.[2] A substantial reason for this includes the common occurrence of multiple pathogens but treatment of only a single organism.[3,4] Clinical assessment of signs and symptoms of vaginitis have been demonstrated to be inaccurate when a single organism is present and even more so when multiple organisms are contributing to the syndrome.[5] As a result of our improved understanding of the multifactorial causes of vaginal symptoms and the poor accuracy of clinical assessment for disentangling the presentation of disease, laboratory diagnostic tools are needed to improve care for women with vaginitis.

Newer diagnostic assays offer solutions to improve the detection of causative agents of vaginitis and thus provide the opportunity to more accurately treat women and potentially reduce the need for follow-up healthcare visits. While several point-of-care (POC) options exist, they are associated with low accuracy or high cost. Molecular lab-based testing can reduce the cost, compared with POC tests, and improve diagnostic accuracy with a turn-around time that supports rapid adjustment (within a day or two) of clinical management decisions when appropriate. One such assay is the BD Vaginal Panel (BDVP) (Becton, Dickinson and Company, BD Life Sciences – Integrated Diagnostic Solutions, Sparks, MD, USA). This molecular assay detects several organisms associated with bacterial vaginosis (BV), several species of *Candida* (including *C. albicans, C. glabrata, C. krusei* and other species) and the sexually transmitted pathogen *Trichomonas vaginalis*.

BD MAX™ Vaginal Panel Assay and the BD COR™ system

The BDVP was developed for use on the BD MAX™ System (MAX; Becton, Dickinson and Company, BD Life Sciences – Integrated Diagnostic Solutions, Sparks, MD, USA), which uses unitized (one strip per sample) reagent and consumable strips for specimen processing with subsequent real-time polymerase chain reaction (PCR) performed on microfluidic cards for the detection of targets with fluorescence output to indicate the presence of those targets. The MAX system is a bench-top analyzer that can perform 24 tests per run, in approximately 3.5 hours, making it ideal for laboratories with low volume testing needs. The MAX system can also be used to perform a broad number of tests including a sexually transmitted infection (STI) panel, a respiratory panel and two enteric panels as well as other pathogen detection assays.[6–13]

In response to the need for higher throughput in some settings the BD COR™ System (COR; Becton, Dickinson and Company, BD Life Sciences – Integrated Diagnostic Solutions, Sparks, MD, USA) was developed. This unique platform can perform 96 tests in a single run using MAX technology, but can simultaneously detect and genotype human papilloma virus (HPV) using the Onclarity™ HPV assay (Becton, Dickinson and Company, BD Life Sciences – Integrated Diagnostic Solutions, Sparks, MD, USA), a PCR assay that was first approved for use with the BD Viper™ LT System (Becton, Dickinson and Company, BD Life Sciences – Integrated Diagnostic Solutions, Sparks, MD, USA).[14]

The Onclarity assay on the COR instrument uses the same chemistry and sample processing methodology as the Onclarity assay on the Viper LT instrument.[15] Thus, with the dual capacity to run two different PCR processes simultaneously, the COR system creates a laboratory solution that supports testing for multiple conditions on a single platform with the use of reagents and consumables in a variety of settings.

The COR is fully automated, combining all steps of specimen processing, amplification and detection on board the instrument. The system utilizes random access, allowing the user to load samples as they arrive in the lab and order any of the approved assays with batching managed internally. The use of unitized strips, common reagents and amplification parameters are unique features of the system that support random access to a broad menu with minimal reagent waste. Furthermore, the assay accepts multiple specimen types stored in diverse transport media, including vaginal swabs in sample buffer tubes (SBT) (Becton, Dickinson and Company, BD Life Sciences – Integrated Diagnostic Solutions, Sparks, MD, USA) that can be used for both BDVP testing and the BD CTGCTV2 (BD STI) panel. For HPV testing, the assays on board have claims for cervical brush diluent tubes (Becton, Dickinson and Company, BD Life Sciences – Integrated Diagnostic Solutions, Burlington, NC, USA), primary liquid based cytology (LBC) vials, BD SurePath™ (Becton, Dickinson and Company, BD Life Sciences – Integrated Diagnostic Solutions, Burlington, NC, USA) and Hologic PreservCyt® (Hologic, Inc. Marlborough, MA, USA), as well as manually aliquoted LBC specimens.[16]

The COR system comprises three modules: the pre-analytical processing PX module, the GX module that performs the Onclarity assay for HPV detection and genotyping, and the MX module that utilizes MAX technology for detection of other infectious diseases, including the BDVP and STI panel that detects *Chlamydia trachomatis, Neisseria gonorrhoeae* and *T. vaginalis*. The automation of the PX module includes uncapping and recapping of specimens, which is a source of repetitive motion injury for many laboratorians, control preparation and specimen batching. For the BDVP assay, the PX instrument scans the barcode on the sample buffer tubes, creates a batch and vortexes them. Next, the sample buffer tubes are placed by the instrument into racks which are moved to the MX instrument. The MX transfers a rack to the processing deck and takes a sample aliquot from each tube. The MX extracts nucleic acid, loads extracted nucleic acid into a cartridge, and moves the cartridge into the MX reader. The MX reader performs amplification and detection for the assay. The COR software processes the results, creates reports and sends to the laborarory interface system (LIS) software. With the capacity to perform 96 tests in ~3 hours, over 300 results can be generated per 8-hour shift.

For the BDVP, results are reported as BV positive/negative, *Candida spp*. positive/negative, *C. glabrata* positive/negative, *C. krusei* positive/negative and *T. vaginalis* positive/negative. For BV, the system software performs bioinformatic analysis to assess the relative abundance of amplified DNA from *Lactobacillus spp*., including *L. crispatus* and *L. jensenii* (expected to be in low abundance) and bacteria associated with BV, including *Gardnerella vaginalis, Atopobium vaginae, Megasphaera-1*, and bacterial vaginosis associated bacterium type 2 (BVAB-2) (expected to be in high abundance) in order to call a positive reaction.[17] For Candida, if any of *C. albicans*, *C. tropicalis*, *C. parapsilosis* or *C. dubliniensis* are detected above a clinically relevant cutoff point, the *Candida spp*., result is positive. These species are grouped together based on the relatively infrequent identification of non-albicans species in the general population. *C. glabrata* and *C. krusei* results are shown separately due to different treatment and management requirements if either of these pathogens is detected.[17] *T. vaginalis* is labelled positive or negative based on the presence or absence of a single *T. vaginalis* gene target. The target is the same as the one used in the BD STI assay. The BDVP has excellent performance characteristics when compared to standard of care diagnostics, culture and Nugent criteria for BV. For BV, Candida and trichomonas, the sensitivity estimates of the assay were 90.5%, 90.9% and 93.1%, respectively.[17] Given the lack of a strong standard for comparison, these estimates are likely to be conservative.

Use of the BD COR System enables clinicians to offer symptomatic women comprehensive care while requiring only a single vaginal sample by performing the BDVP and BD STI tests at the same time. The BDVP and STI assays are performed as described above with an additional round of identical steps for the STI panel. After the PX scans the barcode on the sample buffer tubes, it creates both a BDVP batch and an STI batch order for all samples requiring dual testing. The sample aliquoting steps are performed twice and the aliquots for each assay are moved through the system. The MX extracts nucleic acid in separate sections of the deck for each of the assays, loads extracted nucleic acid into separate cartridges and moves the cartridges into separate MX readers. The respective MX readers perform amplification and detection for each assay and the system software processes the data, creates reports and sends them on to the LIS. Thus from a single vaginal sample, BDVP and BD STI results are generated in parallel with no additional hands-on time of user interface requirements.

Discussion

From a laboratory perspective, the COR system can be used to support women's health by supporting HPV screening of women seeking routine healthcare, as well as a diagnostic test for women with vaginal complaints using a single, fully automated platform. Including the BD STI panel with the BDVP assay will ensure comprehensive care of women. Given the high prevalence of *T. vaginalis*, and the shared mode of transmission of this pathogen, simultaneous testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* is reasonable since women exposed to one STI may be exposed to all STIs. Studies have shown that up to 15% of women seeking care for vaginal complaints have a detectable STI when molecular diagnostics are utilized.[18] This proportion increases to nearly 25% when considering only women with BV.

Future studies should focus on the health economics of utilizing such a platform, as well as the impact of utilizing molecular tools for both cervical cancer screening and for the highly accurate identification of the multiple causes of vaginal complaints that cause a high number of healthcare visits, including a potentially avoidable number of return visits for unresolved symptoms. A highly automated system can provide many laboratory efficiencies and data are needed to support adoption of such platforms. ❑

1. Kong AM, Jenkins D, Troeger KA, et al. Diagnostic testing of vaginitis: Improving the value of care. *Popul Health Manag*. 2021;24:515–24. DOI: 10.1089/pop.2021.0143.
2. Hillier SL, Austin M, Macio I, et al. Diagnosis and treatment of vaginal discharge syndromes in community practice settings. *Clin Infect Dis*. 2021;72:1538–43. DOI: 10.1093/cid/ciaa260.
3. Goje OT, Brown H, Nyirjesy P, et al. Diagnosis of vaginitis: New thinking for a new era. *Popul Health Manag*. 2021;24:616–21. DOI: 10.1089/pop.2021.29006.rtd.
4. Lillis RA, Parker RL, Ackerman R, et al. Clinical evaluation of a new molecular test for the detection of organisms causing vaginitis and vaginosis. *J Clin Microbiol*. 2023;61:e0174822. DOI: 10.1128/jcm.01748-22.
5. Schwebke JR, Gaydos CA, Nyirjesy P, et al. Diagnostic performance of a molecular test versus clinician assessment of vaginitis. *J Clin Microbiol*. 2018;56:00252–00218. DOI: 10.1128/JCM.00252-18.

6. Van Der Pol B, Torres-Chavolla E, Kodsi S, et al. Clinical performance of the BD CTGCTV2 assay for the BD MAX™ system for detection of Chlamydia Trachomatis, *Neisseria Gonorrhoeae* and trichomonas vaginalis infections. *Sex Transm Dis*. 2021;48:134–40. DOI: 10.1097/OLQ.0000000000001280.
7. Van Der Pol B, Williams JA, Fuller D, et al. Combined testing for *Chlamydia*, *Gonorrhea*, and trichomonas by use of the BD MAXCT/GC/TV assay with genitourinary specimen types. *J Clin Microbiol*. 2017;55:155–64. DOI: 10.1128/JCM.01766-16.
8. Faron M, Ledeboer N, Van Der Pol B, et al. A-252 differentiation of SARS-Cov-2, influenza A and B, and respiratory syncytial virus using a single SWAB: A clinical performance evaluation of the BD MAX system Multiplex PCR assay. *Clin Chem*. 2023;69:Supplement_1. DOI: 10.1093/clinchem/hvad097.223.
9. Dalpke AH, Hofko M, Zorn M, Zimmermann S. Evaluation of the fully automated BD MAX Cdiff and Xpert *C. difficile* assays for direct detection of *Clostridium difficile* in stool specimens. *J Clin Microbiol*. 2013;51:1906–8. DOI: 10.1128/JCM.00344-13.
10. Stokes W, Simner PJ, Mortensen J, et al. Multicenter clinical validation of the molecular BD MAX enteric viral panel for detection of enteric pathogens. *J Clin Microbiol*. 2019;57:00306–19. DOI: 10.1128/JCM.00306-19.
11. Antonelli A, Arena F, Giani T, et al. Performance of the BD MAX™ instrument with check-direct CPE real-time PCR for the detection of carbapenemase genes from rectal swabs, in a setting with endemic dissemination of carbapenemase-producing Enterobacteriaceae. *Diagn Microbiol Infect Dis*. 2016;86:30–4. DOI: 10.1016/j.diagmicrobio.2016.06.002.
12. Cárdenas AM, Edelstein PH, Alby K. Development and optimization of a real-time PCR assay for detection of herpes simplex and varicella-zoster viruses in skin and mucosal lesions by use of the BD max open system. *J Clin Microbiol*. 2014;52:4375–6. DOI: 10.1128/JCM.02237-14.
13. Ellem JA, Olma T, O'Sullivan MVN. Rapid detection of MRSA and MSSA directly from positive blood cultures using the BD MAX™ Staph SR. *J Clin Microbiol*. 2015.
14. Young S, Vaughan L, Yanson K, et al. Analytical and clinical sample performance characteristics of the onclarity assay for the detection of human papillomavirus. *J Clin Microbiol*. 2020;59:02048–02020. DOI: 10.1128/JCM.02048-20.
15. Ejegod DM, Pedersen H, Pedersen BT, et al. Clinical validation of the onclarity assay after assay migration to the high-throughput COR instrument using surepath screening samples from the Danish cervical cancer screening program. *Am J Clin Pathol*. 2022;157:390–8. DOI: 10.1093/ajcp/aqab138.
16. Taylor SN, Eckert K, Rucki AA, et al. Evaluation of the onclarity HPV assay on the high-throughput COR system. *Expert Rev Mol Diagn*. 2021;21:333–42. DOI: 10.1080/14737159.2021.1894132.
17. Gaydos CA, Beqaj S, Schwebke JR, et al. Clinical validation of a test for the diagnosis of vaginitis. *Obstet Gynecol*. 2017;130:181–9. DOI: 10.1097/AOG.0000000000002090.
18. Van Der Pol B, Daniel G, Kodsi S, et al. Molecular-based testing for sexually transmitted infections using samples previously collected for vaginitis diagnosis. *Clin Infect Dis*. 2019;68:375–81. DOI: 10.1093/cid/ciy504.