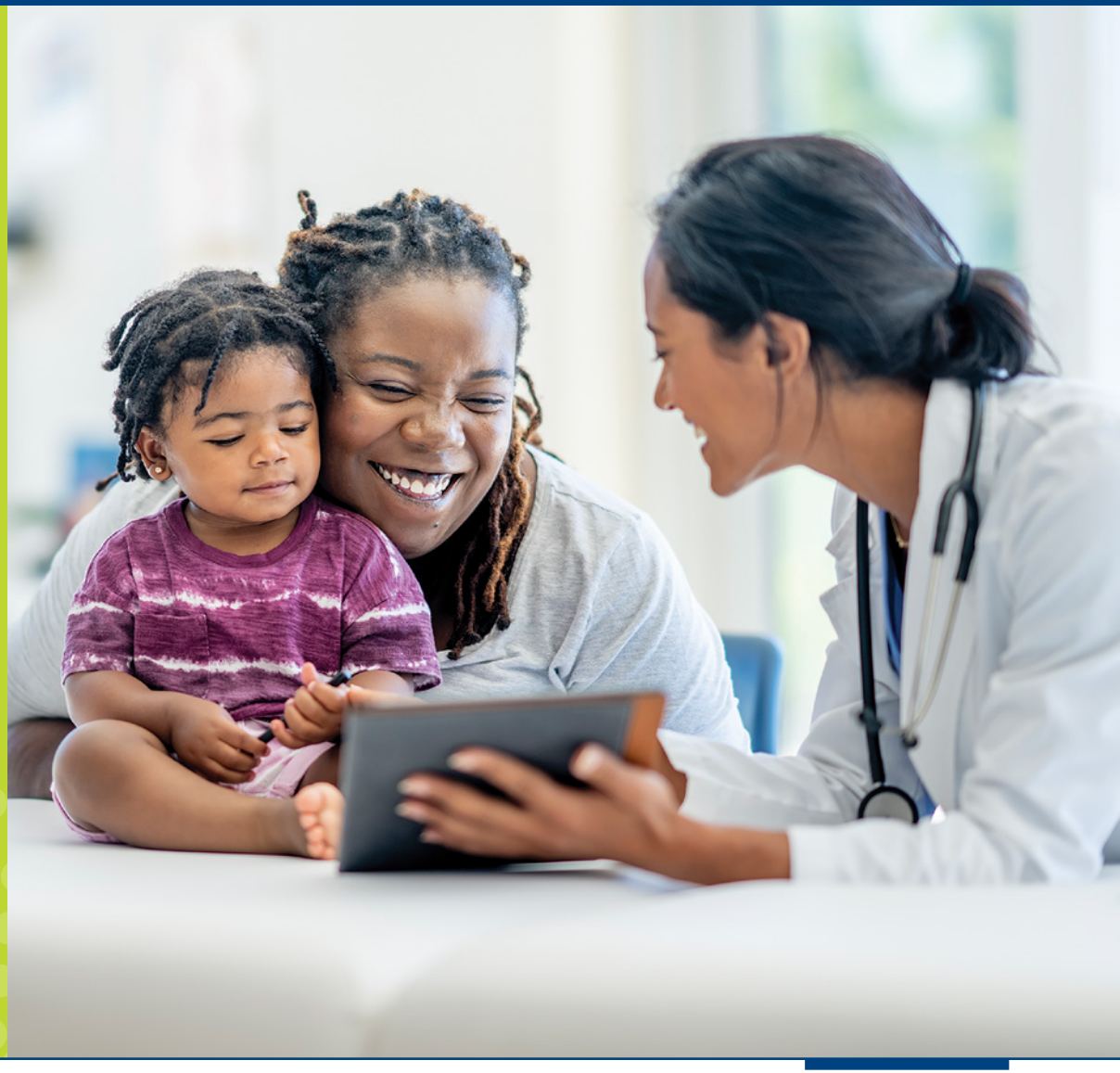
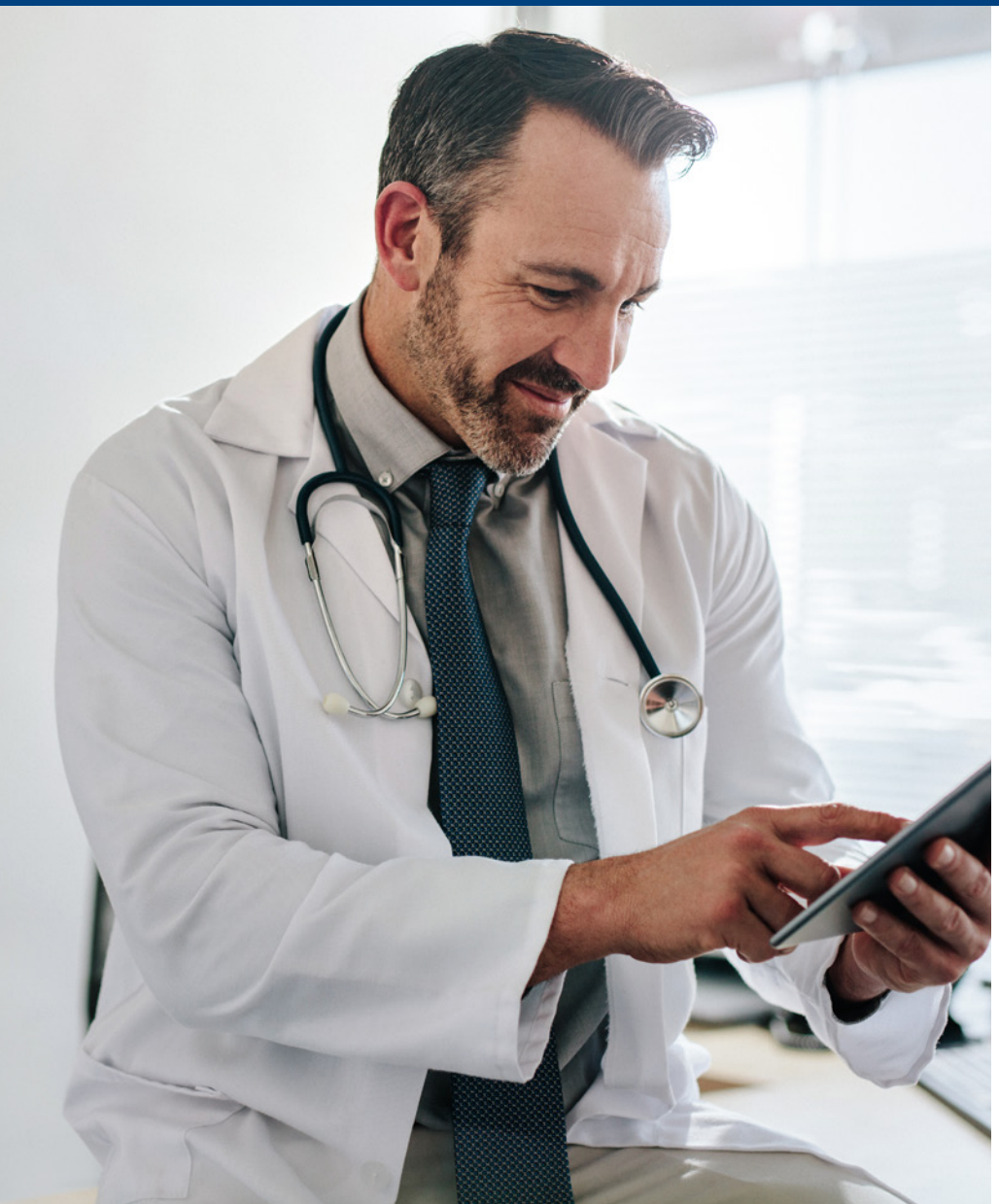
BIOMÉRIEUX

AN **INTRODUCTORY GUIDE**

THE SYNDROMIC APPROACH

Unveiling the Cost-Efficiency and Transformational Role of Multiplex PCR Infectious Disease Testing





Contents

Key Takeaways

What you need to know about syndromic testing:

1 What it is

Syndromic testing uses multiplex polymerase chain reaction (PCR) to test for multiple pathogens linked to infectious diseases at the molecular level. This process significantly cuts turnaround times, helping clinicians quickly identify specific infections, especially when signs and symptoms are unclear.

2 The clinical value

Syndromic testing provides numerous benefits, such as notably shorter testing times, increased sensitivity and specificity, simplified workflows, and improved antimicrobial management.[1] Syndromic testing can enhance patient outcomes by guiding more precise and timely therapies, lowering hospital admissions, and reducing the misuse of antibiotics.[2]

3 Potential cost savings

Despite initial costs, syndromic testing can be cost-effective in the long run by reducing hospital readmissions and shortening stays.[3] The quick diagnostic capabilities of syndromic testing have been shown to generate significant savings by reducing the need for other diagnostic tests, like chest X-rays and endoscopies.[4]

An innovative approach to diagnostic testing

Speed to diagnosis is imperative for treating infectious diseases today. It is not only important for addressing the patient's condition, but also for preventing antimicrobial resistance stemming from the misuse or overuse of antimicrobials. Clinical labs now have a better option for rapid diagnostic testing that provides clinicians with key information at considerably faster turnaround times than in the past. It's called syndromic testing, a method that enables highly sensitive and specific detection of multiple pathogens related to an infectious disease—all conducted simultaneously. With the syndromic approach, clinicians can jumpstart testing to help identify specific infectious pathogens when a patient's signs, symptoms, or syndromes are unclear. It can be used to identify bacteria, viruses, fungi, parasites, and even antimicrobial resistance genes.

Syndromic testing has been revolutionizing diagnostic testing, yet many healthcare professionals do not have an understanding of how this approach can be used effectively to identify infectious diseases.

In this introductory guide, we'll review the fundamentals of syndromic testing, highlight how syndromic testing can lead to signifi ant cost savings compared to traditional diagnostic approaches, consider factors that impact the successful use of syndromic testing, and clarify which pathogen targets can be identified

What is syndromic testing?

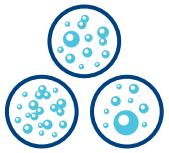
Syndromic testing enables microbiology teams in acute settings, reference labs, and outpatient clinics to test for multiple pathogens at one time. Traditionally, clinicians suspecting an infectious disease would order a single test or a series of tests targeting only a few pathogens to validate an initial assessment based on a patient's signs and symptoms. Many of these tests, like growing bacterial cultures, take days, slowing time to treatment and potentially leading to antimicrobial misuse or overuse. Additionally, for many infectious diseases, like upper respiratory infections, the signs and symptoms aren't distinguishable (e.g., a cough) and could relate to a wide variety of potential health conditions. Syndromic testing alleviates these burdens by allowing labs to test on a molecular level for multiple pathogens and antimicrobial resistance genes at one time.

Syndromic testing is conducted using a chemical process known as PCR. PCR amplifies DNA so that a large number of copies can be created and tested from the smallest of samples. Multiplex PCR panels target a comprehensive grouping of pathogens that could be causing a specific syndrome and test them all at once, enabling timely answers.

Traditional and Syndromic Testing: A Comparison

Traditional Testing

Traditional methods of pathogen identification can be time-consuming and lack sensitivity.[4]

				
One or multiple samples	Multiple testing methods	Results take hours to days	Individual results in multiple separate reports	May have longer patient length of stay

Syndromic Testing

Syndromic testing provides a streamlined workflow and fast, comprehensive results.

				
One sample	One comprehensive test	Results in about 15 minutes to one hour	Comprehensive results in a single report	May shorten patient length of stay

What are the top 5 advantages of syndromic testing?

1 Reduced Turnaround Time

- Respiratory infection testing reduced from more than one day to roughly one hour
- Blood culture identification decreased by more than a day[5]
- Gastrointestinal panels reduced from up to five days to a couple of hours[5]
- Meningitis panels have shortened testing time by more than three days[5]

2 Better Quality Testing

- Higher sensitivity and specificity than traditional testing[6]
- Can be used in bacterial testing even in cases where the organism will not grow a culture
- More accurate epidemiological analysis both within the healthcare setting and in the community[7]
- Increased organism detection for GI panels compared to traditional testing[5]
- Ability to test for uncommon pathogens, which potentially leads to diagnoses that might otherwise have been missed

3 Improved Workflow

- Streamlined and faster sample-to-answer workflows[3]
- Fewer send-out tests[2]
- Minimal hands-on time and sample preparation[2]

4 More Effective Antimicrobial Management

- Reduced time to antimicrobial treatment[3]
- Shorter duration for use of antibiotics[7]
- Lower misuse or overuse of antibiotics, helping to prevent antibiotic resistance[8,9]

5 Better Outcomes

- Fewer hospital admissions and shorter lengths of stay[3]
- Less use of other diagnostic tests, such as chest X-rays or endoscopies[1]
- Reduced hospital-acquired infections (HAI)[10] and community-acquired infections (CAI)[11]

Syndromic testing improves diagnostics

CASE STUDY

An elderly woman was admitted to an intensive care unit (ICU) after a chest X-ray showed pneumonia in the right upper and lower lobes. And she was running a fever. The ICU conducted their routine tests. A sputum gram stain showed Gram-positive cocci and normal flora. The MRSA nasal swab results were disregarded as inaccurate. The patient was given piperacillin-tazobactam therapy. But after three days, her symptoms were not relieved, and she was still running a fever. A multiplex PCR test for pneumonia was conducted after collecting a Bronchoalveolar Lavage specimen. The tests detected parainfluenza virus, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and the AMR genes of MRSA, which indicated that the current treatment was not optimal. On the fourth day, teicoplanin was added and the patient's health improved.

Conclusion: Had the syndromic testing been conducted upon admission to the ICU, effective treatment could have reduced time to effective treatment and shortened the patient's ICU stay.

Patient Satisfaction

Onsite testing is directly tied to patient satisfaction. In fact, 77% of patients prefer onsite laboratory services.

67% of patients will drive up to 20 minutes to visit a clinic with onsite lab services.[12]

Did You Know?

Onsite PCR testing allows clinicians to give patients answers fast—possibly before the end of their visit. Rapid and comprehensive results may also reduce the need for follow-up visits, and they may facilitate valuable patient/provider conversations about the appropriate use of antimicrobials.

What are the cost savings of syndromic testing?

While syndromic testing requires a higher initial investment than traditional tests, its advanced technology leads to more accurate diagnoses, improved patient outcomes, and potentially reduced long-term costs.[6]

By enabling rapid and more accurate diagnoses, reducing the need for additional tests, and minimizing hospital stays and readmissions, syndromic testing may represent a valuable investment in more efficient, effective, and patient-centered healthcare.[1,3,7]

Studies researching the impact of syndromic testing consistently demonstrate direct and indirect cost savings, among other benefits.

Some examples follow.

Cost savings of syndromic testing

Respiratory Testing

One study estimates the total costs of influenza could be as high as $167 billion per year.[13] While targeted influenza A/B and respiratory syncytial virus (RSV) testing is the standard of care, this approach runs the risk of missing several pathogen detections and co-detections. Syndromic testing may save costs and offer additional benefits by:

- Significantly reducing hospital lengths of stay[14]
- Shortening the time to treatment[15]
- Reducing antibiotic durations[15]
- Avoiding unnecessary antibiotic use[15]
- Promoting antimicrobial stewardship goals[16]

Bloodstream Infection Testing

Septicemia is the most expensive condition treated in US hospitals, accounting for over $23 million in healthcare costs each year.[17] Depending on the severity, a single case of sepsis costs an average of $7,970 but can cost as much as $44,027.[18]

Other cost-saving benefits may include:

- Fewer days spent in the ICU[19,20]
- Decreased length of hospital stay[19,20]
- Decreased pharmacy costs[19,20]
- Reduced treatment for patients with coagulase-negative staphylococci-contaminated blood cultures[21]

Gastrointestinal Testing

Traditional stool testing methods are slow, labor-intensive and often fail to reveal the etiology of a patient's gastrointestinal symptoms. This not only adds costs but also results in physicians making patient management decisions without reliable test results.

Syndromic testing for gastro-intestinal infections speeds time to treatment, improves diagnostic accuracy and may lead to significant cost savings, such as:

- Reducing downstream stool tests and procedures, such as endoscopies, CT scans, X-rays and ultrasounds[22]
- Lowering the average length of stay by 12 hours per patient[23]
- Prescribing fewer antibiotics[22]

The data represents potential economic outcomes and is subject to variability based on care setting and patient population.

Cost savings of syndromic testing

Pneumonia Testing

A hospital spends an average of $36,000 to diagnose and treat a single patient with pneumonia.[24] In the US, this translates into an economic burden of about $10.6 billion annually.[25]

Rapidly determining the etiology of pneumonia and helping distinguish colonizing bacteria from true infectious agents with semiquantitative PCR results may facilitate cost-savings benefit, such as:

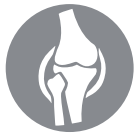
- De-escalation of antibiotics in up to half of cases, for an average reduction of 6.2 days of antibiotic therapy per patient[26]
- Adjustments to antibiotic courses in up to 71% of cases[27]
- Identification of a pathogen not covered by empiric therapy in patients who failed empiric therapy[28]

Meningitis/ Encephalitis Testing

Syndromic testing for meningitis and encephalitis not only enhances diagnostic accuracy but also yields substantial cost savings, which could reach as high as $3,481 per case.[29]

Testing for multiple pathogens at one time, and delivering pathogen-specific results quickly, also helps clinicians distinguish between bacterial and viral etiologies for meningitis/ encephalitis—a significant challenge in an accurate diagnosis. These benefits can lead to further cost savings, including:

- ~2.5x increased pathogen detection compared to standard of care methods[30,31]
- Reducing hospital lengths of stay by an average of two days for both pediatric and adult patients[30,31]
- Shortening antibiotic and antiviral therapy by two days for both pediatric and adult patients[30,32]



Joint Infection Testing

Joint infections cause a tremendous economic burden on hospitals and patients. The combined annual hospital costs related to prosthetic joint infections (PJI) of the hip and knee were estimated to be $1.85 billion by 2030.[33]

An illustration of the potential savings lies in offsetting the cost of a single, two-stage revision surgery, which can save between $50,000 and $100,000.[34] The adoption of syndromic testing for joint infections may also save costs by:

- Decreasing the length of antibiotic therapy[35,36]
- Reducing the length of stay[35,36]
- Increasing the likelihood of antibiotic de-escalation[35]

The data represents potential economic outcomes and is subject to variability based on care setting and patient population.

What key factors impact the success of syndromic testing?

Communication, collaboration, and interpretation are critical factors for the successful integration of syndromic testing. Many of the limitations of syndromic testing can be countered via diagnostic stewardship—expert consultation for the selection of the right tests as well as analysis, interpretation, and communication of results by microbiology professionals and infectious disease specialists. This improves clinical relevance related to syndromic testing results.[7] For example, diagnostic stewardship in the emergency department (ED) has been shown to have an immediate effect on hospital admissions, patient isolation, and antimicrobial therapy; has increased bed availability and speed to treatment; and has led to better patient outcomes and lower treatment costs.[37]

Standards and guidelines have also driven improvements in syndromic testing outcomes, including:

Standards

- Utilization management strategies to define internal standards for who to test, how often the same patient gets tested, and what targets should be reported for the patient population[7]
- Requiring an infectious disease consult to preauthorize certain syndromic test orders to ensure clinical relevance[38]
- Refraining from testing asymptomatic patients[7]

Guidelines

- Implementing automatic testing restrictions to prevent overuse (e.g., preventing respiratory panel repetition in less than 20 days or testing for viruses that have no treatment options)[37]
- Using syndromic testing for critically ill and immunosuppressed patients, including HIV, transplant, and cancer patients, who may benefit more by detecting all pathogens, including those indicative of less common infections[39]

Which infectious pathogens can be identified using Syndromic testing?

Currently, there are multiplex PCR panels for infectious causes related to respiratory, bloodstream, gastrointestinal, pneumonia, meningitis, and joint infections. Below is a preview of the panel menus—which include pathogen targets and antimicrobial resistance genes—offered by bioMérieux's multiplex tests.

Respiratory

BACTERIA
- *Bordetella parapertussis*
- *Bordetella pertussis*
- *Chlamydia pneumoniae*
- *Mycoplasma pneumoniae*

VIRUSES
- Adenovirus
- Coronavirus 229E
- Coronavirus HKU1
- Coronavirus NL63
- Coronavirus OC43
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- Human metapneumovirus
- Human rhinovirus/enterovirus
- Influenza A virus
- Influenza A virus A/H1
- Influenza A virus A/H3
- Influenza A virus A/H1-2009
- Influenza B virus
- Parainfluenza virus 1
- Parainfluenza virus 2
- Parainfluenza virus 3
- Parainfluenza virus 4
- Respiratory syncytial virus

Bloodstream

GRAM-NEGATIVE BACTERIA
- *Acinetobacter calcoaceticus-baumannii* complex
- *Bacteroides fragilis*
- *Enterobacterales*
  - *Enterobacter cloacae* complex
  - *Escherichia coli*
  - *Klebsiella aerogenes*
  - *Klebsiella oxytoca*
  - *Klebsiella pneumoniae* group
  - *Proteus* spp.
  - *Salmonella* spp.
  - *Serratia marcescens*
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Pseudomonas aeruginosa*
- *Stenotrophomonas maltophilia*

GRAM-POSITIVE BACTERIA
- *Enterococcus faecalis*
- *Enterococcus faecium*
- *Listeria monocytogenes*
- *Staphylococcus* spp.
  - *Staphylococcus aureus*
  - *Staphylococcus epidermidis*
  - *Staphylococcus lugdunensis*
- *Streptococcus* spp.
  - *Streptococcus agalactiae*
  - *Streptococcus pneumoniae*
  - *Streptococcus pyogenes*

YEAST
- *Candida albicans*
- *Candida auris*
- *Candida glabrata*
- *Candida krusei*
- *Candida parapsilosis*
- *Candida tropicalis*
- *Cryptococcus (C. neoformans/C. gattii)*

ANTIMICROBIAL RESISTANCE GENES
- **Carbapenemases**
  - IMP
  - KPC
  - OXA-48-like
  - NDM
  - VIM
- **Colistin Resistance**
  - *mcr-1*
- **ESBL**
  - CTX-M
- **Methicillin Resistance**
  - *mecA/C*
  - *mecA/C* and MREJ (MRSA)
- **Vancomycin Resistance**
  - *vanA/B*

Gastrointestinal

BACTERIA
- *Campylobacter (C. jejuni/C. coli/C. upsaliensis)*
- *Clostridioides (Clostridium) difficile* (toxin A/B)
- *Plesiomonas shigelloides*
- *Salmonella*
- *Vibrio (V. parahaemolyticus/V. vulnificus/V. cholerae)*
  - *Vibrio cholerae*
- *Yersinia enterocolitica*
- Diarrheagenic *Escherichia coli/Shigella*
  - Enteroaggregative *E. coli* (EAEC)
  - Enteropathogenic *E. coli* (EPEC)
  - Enterotoxigenic *E. coli* (ETEC) *lt/st*
  - Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*
    E. coli 0157
  - Shigella/Enteroinvasive *E. coli* (EIEC)

VIRUSES
- Adenovirus F40/41
- Astrovirus
- Norovirus GI/GII
- Rotavirus A
- Sapovirus (I, II, IV, and V)

PARASITES
- *Cryptosporidium*
- *Cyclospora cayetanensis*
- *Entamoeba histolytica*
- *Giardia lamblia*

Pneumonia

BACTERIA (SEMI-QUANTITATIVE)
- *Acinetobacter calcoaceticus-baumannii* complex
- *Enterobacter cloacae* complex
- *Escherichia coli*
- *Haemophilus influenzae*
- *Klebsiella aerogenes*
- *Klebsiella oxytoca*
- *Klebsiella pneumoniae* group
- *Moraxella catarrhalis*
- *Proteus* spp.
- *Pseudomonas aeruginosa*
- *Serratia marcescens*
- *Staphylococcus aureus*
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

ATYPICAL BACTERIA (QUALITATIVE)
- *Chlamydia pneumoniae*
- *Legionella pneumophila*
- *Mycoplasma pneumoniae*

VIRUSES
- Adenovirus
- Coronavirus
- Human metapneumovirus
- Human rhinovirus/enterovirus
- Influenza A virus
- Influenza B virus
- Parainfluenza virus
- Respiratory syncytial virus

ANTIMICROBIAL RESISTANCE GENES
- **Carbapenemases**
  - IMP
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  - OXA-48-like
  - VIM
- **ESBL**
  - CTX-M
- **Methicillin Resistance**
  - *mecA/C* and MREJ (MRSA)

Meningitis/Encephalitis

BACTERIA
- *Escherichia coli K1*
- *Haemophilus influenzae*
- *Listeria monocytogenes*
- *Neisseria meningitidis*
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*

VIRUSES
- Cytomegalovirus (CMV)
- Enterovirus (EV)
- Herpes simplex virus 1 (HSV-1)
- Herpes simplex virus 2 (HSV-2)
- Human herpesvirus 6 (HHV-6)
- Human parechovirus (HPeV)
- Varicella zoster virus (VZV)

YEAST
- *Cryptococcus (C. neoformans/C. gattii)*

Joint Infection

GRAM-POSITIVE BACTERIA
- *Anaerococcus prevotii/vaginalis*
- *Clostridium perfringens*
- *Cutibacterium avidum/granulosum*
- *Enterococcus faecalis*
- *Enterococcus faecium*
- *Finegoldia magna*
- *Parvimonas micra*
- *Peptoniphilus*
- *Peptostreptococcus anaerobius*
- *Staphylococcus aureus*
- *Staphylococcus lugdunensis*
- *Streptococcus* spp.
  - *Streptococcus agalactiae*
  - *Streptococcus pneumoniae*
  - *Streptococcus pyogenes*

GRAM-NEGATIVE BACTERIA
- *Bacteroides fragilis*
- *Citrobacter*
- *Enterobacter cloacae* complex
- *Escherichia coli*
- *Haemophilus influenzae*
- *Kingella kingae*
- *Klebsiella aerogenes*
- *Klebsiella pneumoniae* group
- *Morganella morganii*
- *Neisseria gonorrhoeae*
- *Proteus* spp.
- *Pseudomonas aeruginosa*
- *Salmonella* spp.
- *Serratia marcescens*

YEAST
- *Candida* spp.
  - *Candida albicans*

ANTIMICROBIAL RESISTANCE GENES
- **Carbapenemases**
  - IMP
  - KPC
  - NDM
  - OXA-48-like
  - VIM
- **ESBL**
  - CTX-M
- **Methicillin Resistance**
  - *mecA/C* and MREJ (MRSA)
- **Vancomycin Resistance**
  - *vanA/B*

Amplify your diagnostic efforts with syndromic testing

The syndromic approach takes molecular testing to a new level by testing multiple pathogens at one time to identify infectious causes. These tests have higher sensitivity and specificity rates than traditional testing and can produce results in record time.[7] As a result, clinicians can quickly determine the best strategy for antibiotic therapy that does not contribute to antimicrobial resistance.[5] Syndromic testing increases speed from sample to answer as well as possibly reducing hospital admissions, isolation, lengths of stay, and use of other diagnostic tests.[7] Ultimately, this may lead to better patient care and lower costs for treatment. That makes syndromic testing a valuable rapid diagnostic tool in the arsenal of diagnostic testing.

Resources

To learn more about syndromic testing, go to the bioMérieux web page.

Visit Page

You can also learn more about the parameters and outcomes of specific bioMérieux syndromic testing for different infections by clicking on the icons below:

Respiratory

Pneumonia

Gastrointestinal

Meningitis/ Encephalitis

Blood Culture ID

Joint Infection

A major player in *in vitro* diagnostics for more than 60 years, bioMérieux has always been driven by a pioneering spirit and unrelenting commitment to improve public health worldwide.

Our diagnostic solutions bring high medical value testing to healthcare professionals, providing them with the most relevant and reliable information, as quickly as possible, to support treatment decisions and better patient care.

bioMérieux's mission entails a commitment to support medical education, by promoting access to diagnostic knowledge for as many people as possible. Focusing on the medical value of diagnostics, our collection of educational booklets aims to raise awareness of the essential role that diagnostics test results play in healthcare decisions.

Other educational booklets are available. Consult your local bioMérieux representative or visit biomerieux.com/en/education/educational-booklets

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